History of Immunology

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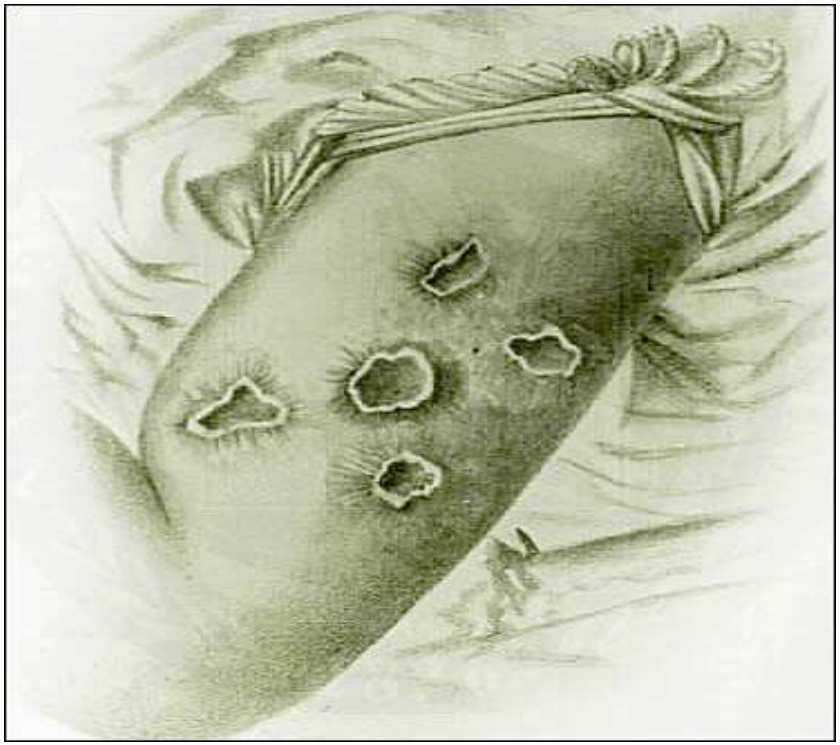
Small pox: A dreaded disease of mankind



- An acute contagious disease - caused by variola virus - member of the orthopoxvirus family
- One of the most devastating diseases known to humanity
- For centuries, repeated epidemics swept across continents
- Decimated populations and changed the course of history

Small pox: first disease eradicated from earth

- **As late as the 18th century, smallpox killed every 10th child born in Sweden and France- every 7th child born in Russia**
- **Edward Jenner's demonstration, in 1798, that inoculation with cowpox could protect against smallpox brought the first hope that the disease could be controlled.**
- **In the early 1950s, an estimated 50 million cases of smallpox occurred in the world each year.**
- **In 1967, when WHO launched eradicate smallpox program**
- **Single last natural case, reported from Somalia in 1977. The global eradication of smallpox was certified.**
- **The only other disease "officially" declared eradicated is "Rinderpest" in the year 2011.**

Lady Mary Montague-1718

- The wife of the British ambassador to Constantinople,
- Observed the positive effects of variolation on the native population
- Allowed variolation performed on her own children.

Edward Jenner

• 1798 – First demonstration of vaccination against small pox

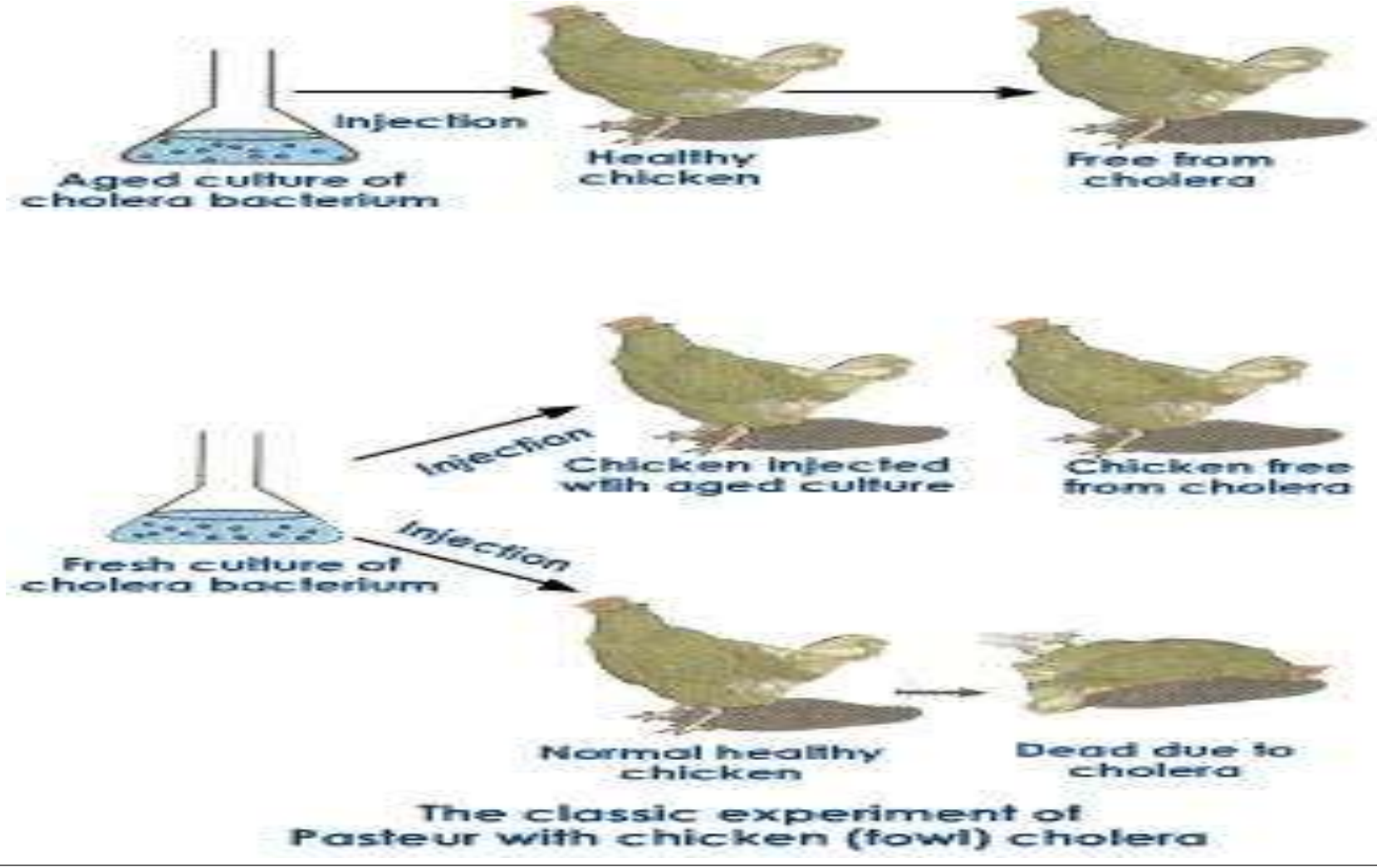
• Vaccinated “ James Phipps” (8 year old) using material collected from cow pox scab lesions

•Challenged with virulent small pox virus

•Edward Jenner is regarded as Father of Immunology.

Louis Pasteur

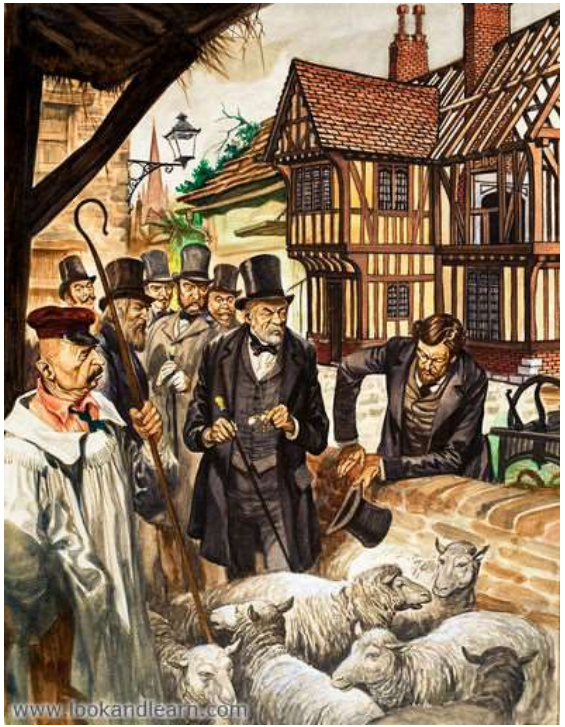
- 1880 – 1881 -Proposed principles of attenuation
- Developed vaccines against Fowl cholera and Anthrax
- Coined word “vaccine” in the honour of “Edward Jenner”
- 1885 – Introduced concept of a "therapeutic vaccination“, first report of a live "attenuated" vaccine for rabies.
- Regarded as “Founder of Immunology”



The classic experiment of Pasteur with chicken (fowl) cholera

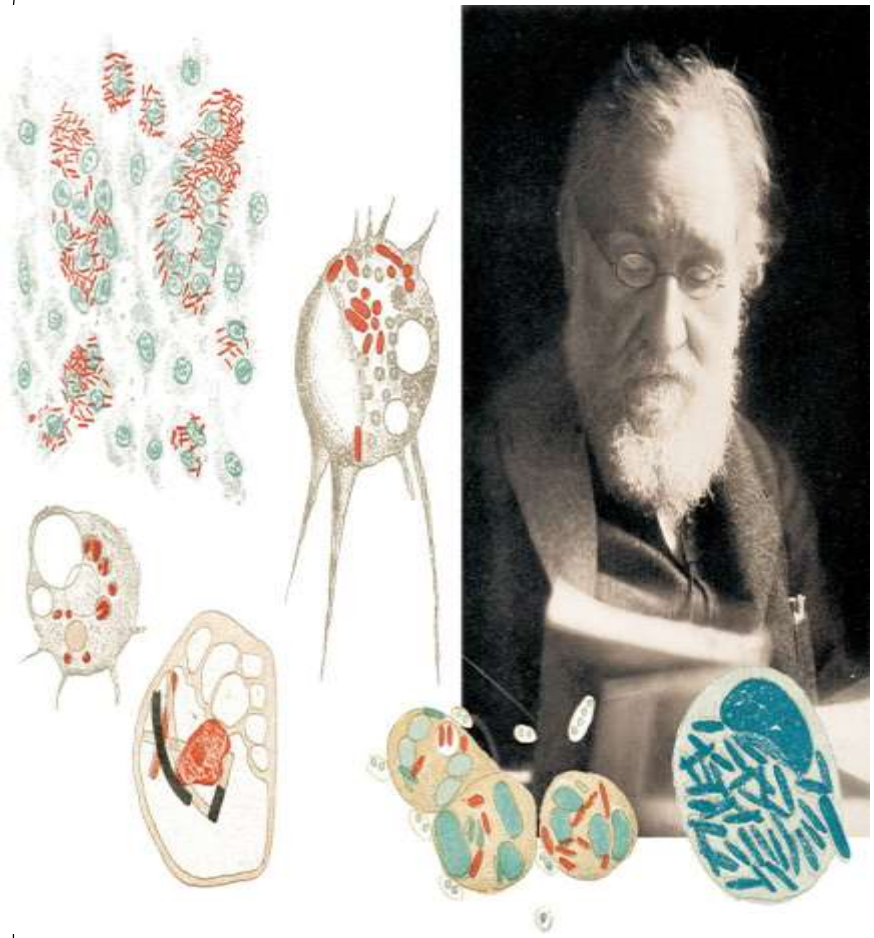
Anthrax vaccine:

- Pasteur prepared vaccine against "Anthrax" by culturing *Bacillus anthracis* at 42 ^{0}C.
- Vaccine was tested in Sheep
- Upon challenge with virulent *Bacillus anthracis* all vaccinated sheep survived while non vaccinated sheep died



Louis Pasteur: First Anti-Rabies vaccine

- Joseph Meister received the first anti-rabies vaccine
- First person to survive after rabid dog bite

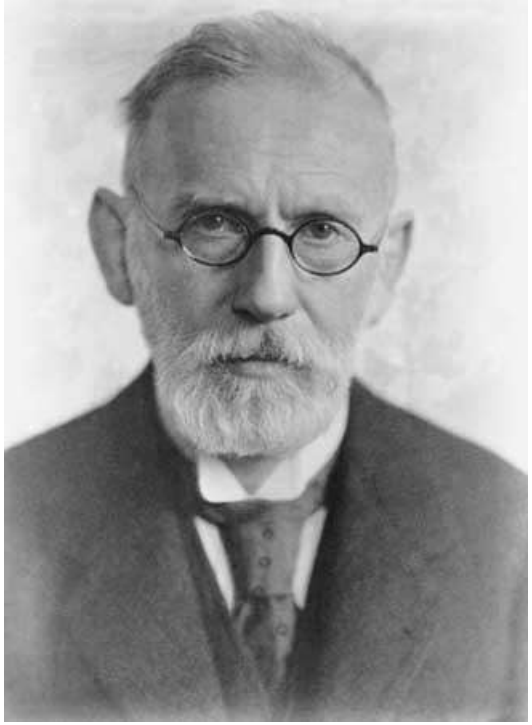


Elie Metchnikoff (1845-1916)

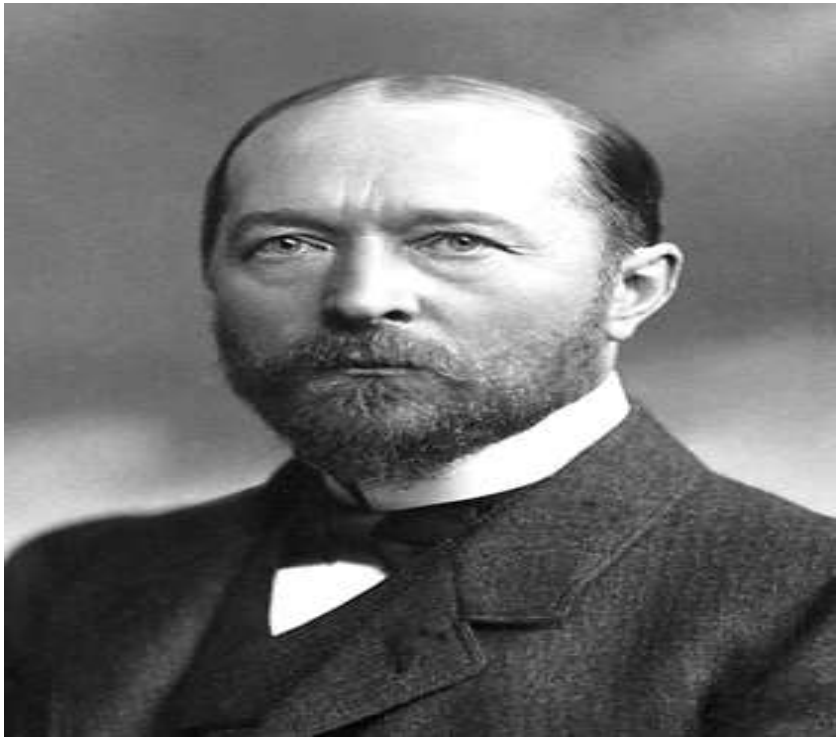
- Discovered “Macrophages”
- Proposed ***“Cellular theory of Immunity”***
- Got Nobel prize in the Year 1908.

Paul Ehrlich:

- 1900 – Proposed side Chain theory of antibody formation.
- 1909 –proposed *"immune surveillance"* hypothesis of tumor recognition and eradication
- Shared Nobel prize in the year 1908 with Elie Metchnikoff

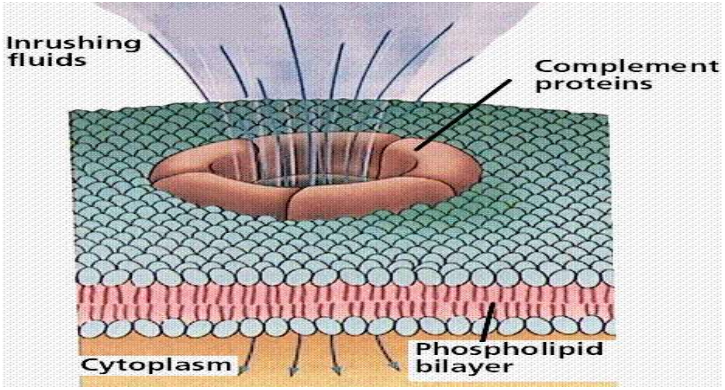


Emil von Behring



- 1890 – along with Kitasato Shibasaburo demonstrated antibody activity against diphtheria and tetanus toxins
- Proposed ***"Humoral theory of immunity".***
- Won first Nobel prize in Medicine (1901) for production and use of serum anti-toxins

Jules Bordet



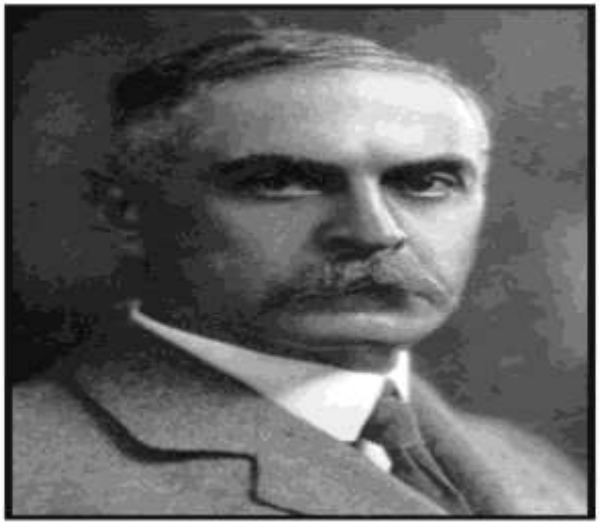
- Received Nobel prize in 1919 for discovery of role of complement in bacteriolysis
- Bordet found that the bacteria-killing phenomenon was due to the combined action of two distinct substances:

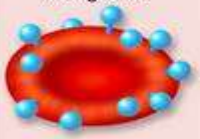
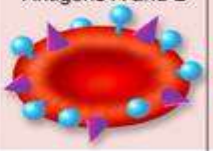
  a) an antibody in the antiserum, act specifically against a particular kind of bacterium;

  b) and a non-specific substance, sensitive to heat, found in all animal serums, which

Bordet called "alexine" (later named "complement")

Karl Landsteiner



	Antigen A	Antigen B	Antigens A and B	Neither antigen A nor B
RBC				
Plasma	Anti-B antibodies 	Anti-A antibodies 	Neither anti-A nor anti-B antibodies	Both anti-A and anti-B antibodies 
Blood Type	**Type A** Erythrocytes with type A surface antigens and plasma with anti-B antibodies	**Type B** Erythrocytes with type B surface antigens and plasma with anti-A antibodies	**Type AB** Erythrocytes with both type A and type B surface antigens, and plasma with neither anti-A nor anti-B antibodies	**Type O** Erythrocytes with neither type A nor type B surface antigens, but plasma with both anti-A and anti-B antibodies

- Awarded Nobel Prize in 1930
- Discovered ABO blood group in Human
- Worked on Hapten; explained specificity of immune response
- 1940 – Identification of the Rh factor along with Alexender Weiner

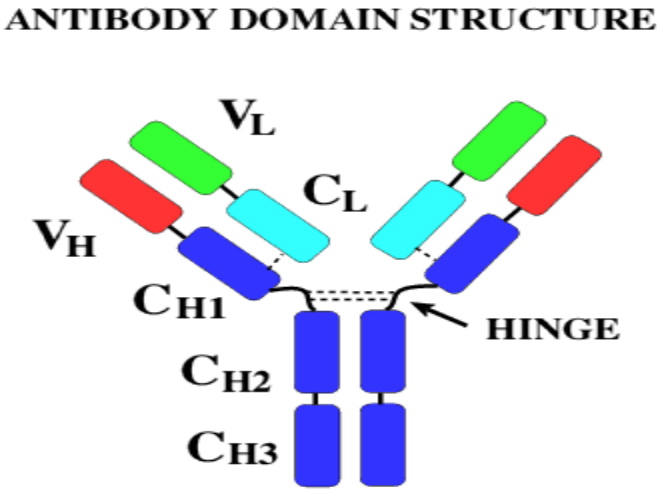
Max Theiler

- Proved that the cause of yellow fever is not a bacterium but a filterable virus.
- Theiler developed a safe, 17D vaccine
- Got Nobel prize in 1951

Edelman & Porter

Gerald M. Edelman
(1929 -)

Rodney R. Porter
(1917 - 1985)



- **1959–1962 – Discovery of antibody structure**

- **Got Nobel prize in the year 1971**

Rosalyn Yalow: Radio Immuno Assay (RIA)

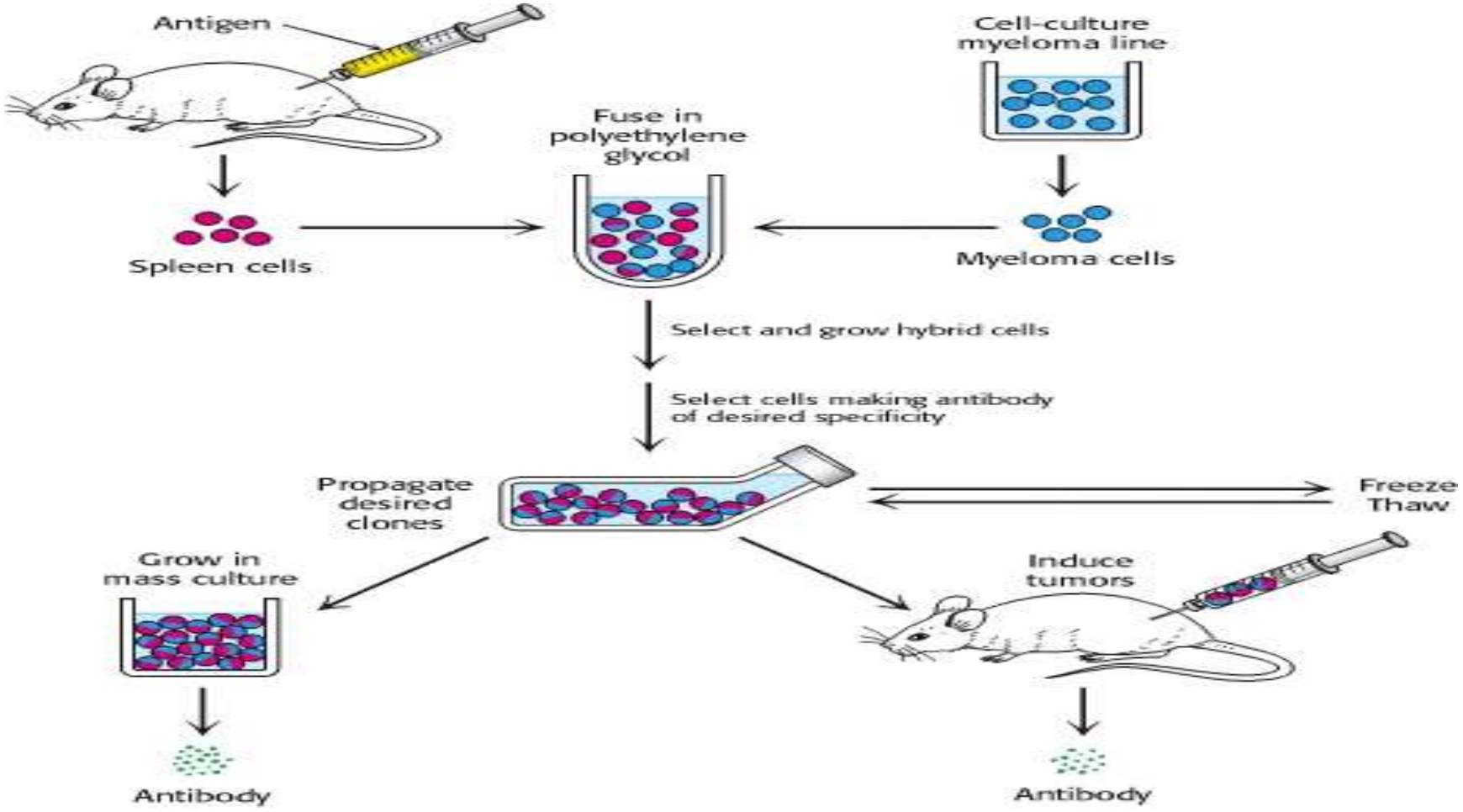
•Awarded the Nobel Prize in physiology or medicine in 1977

•Developed radioimmunoassay (RIA).

• RIA used for measuring concentrations of insulin in blood

George Kohler and Cesar Milstein

- 1975 – Generation of the first monoclonal antibodies
- Hybridoma Technique


Antigen
Cell-culture myeloma line
Fuse in polyethylene glycol
Spleen cells
Myeloma cells
Select and grow hybrid cells
Select cells making antibody of desired specificity
Propagate desired clones
Freeze Thaw
Grow in mass culture
Induce tumors
Antibody
Antibody

Other Important developments

Year	Scientist	Contribution
1888	Roux and Yersin	– Identification of bacterial toxins (diphtheria bacillus)
1891	Robert Koch	Demonstration of cutaneous (delayed type) hypersensitivity
1902	Paul Portier and Charles Richet	Immediate hypersensitivity anaphylaxis
1921	Prausnitz and Kustner	Cutaneous allergic reaction
1946	George Snell & Peter Gorer	identification of mouse MHC (H2)
1957	Macfarlane Burnet, Niels Jerne & David Talmage	Clonal selection theory of antibody production

Other Important developments

Year	Scientist	Contribution
1957	Alick Isaacs and Jean Lindenmann	Discovery of Interferon
1967	Kimishige Ishizaka	Identification of IgE as reaginic antibody
1971	Peter Perlmann and Eva Engvall	Invented ELISA
1974	Rolf Zinkernagel and Peter Doherty	T-cell restriction to major histocompatibility complex
1976	Susumu Tonegawa	Identification of somatic recombination of immunoglobulin genes
1994	Polly Matzinger	Danger Model of Immunological tolerance
2011	**Bruce A Beutler& Jules Hoffman** **M. Steinmann**	**Activation of Innate Immunity** **Dendritic cells & their role in Adaptive Immunity**
2018	**James P. Allison and Tasuku Honjo**	**Cancer therapy by inhibition of negative immune regulation of T cells**

TABLE 1-1 Nobel Prizes for immunologic research

Year	Recipient	Country	Research
1901	Emil von Behring	Germany	Serum antitoxins
1905	Robert Koch	Germany	Cellular immunity to tuberculosis
1908	Elie Metchnikoff Paul Ehrlich	Russia Germany	Role of phagocytosis (Metchnikoff) and antitoxins (Ehrlich) in immunity
1913	Charles Richet	France	Anaphylaxis
1919	Jules Border	Belgium	Complement-mediated bacteriolysis
1930	Karl Landsteiner	United States	Discovery of human blood groups
1951	Max Theiler	South Africa	Development of yellow fever vaccine
1957	Daniel Bovet	Switzerland	Antihistamines
1960	F. Macfarlane Burnet Peter Medawar	Australia Great Britain	Discovery of acquired immunological tolerance
1972	Rodney R. Porter Gerald M. Edelman	Great Britain United States	Chemical structure of antibodies
1977	Rosalyn R. Yalow	United States	Development of radioimmunoassay
1980	George Snell Jean Daussct Baruj Benacerraf	United States France United States	Major histocompatibility complex
1984	Cesar Milstein Georges E. Köhler	Great Britain Germany	Monoclonal antibody
	Niels K. Jerne	Denmark	Immune regulatory theories
1987	Susumu Tonegawa	Japan	Gene rearrangement in antibody production
1991	E. Donnall Thomas Joseph Murray	United States United States	Transplantation immunology
1996	Peter C. Doherty Rolf M. Zinkernagel	Australia Switzerland	Role of major histocompatibility complex in antigen recognition by by T cells

THE END

The images for slides are taken from resources available on internet and used for the purpose of teaching students

Small Pox vaccine response