

# Immunity

→ Immunity : immunity is resistance exhibited by host against microbes, and its products.

Study of immunity and aspects, mainly called Immunology.

\* Different diversity of pathogens are attacking humans from viruses (small) to giant parasitic worm (kidney worm) named *Dioctophyme renale* (L=100cm, W=10mm).

\* Evolution of immune system is important steps in multicellular organisms lifecycle.

## Historic perspective :

① Immunology grew out of observation that individuals who had recovered from certain diseases, were thereafter protected from the diseases.

② Latin term "immunis" meaning "exempt" is source of English word "immunity".

③ Thucydides, Greek historian in 250 BC, described plague in Athens. He observed those who recovered from plague could nurse the sick person.

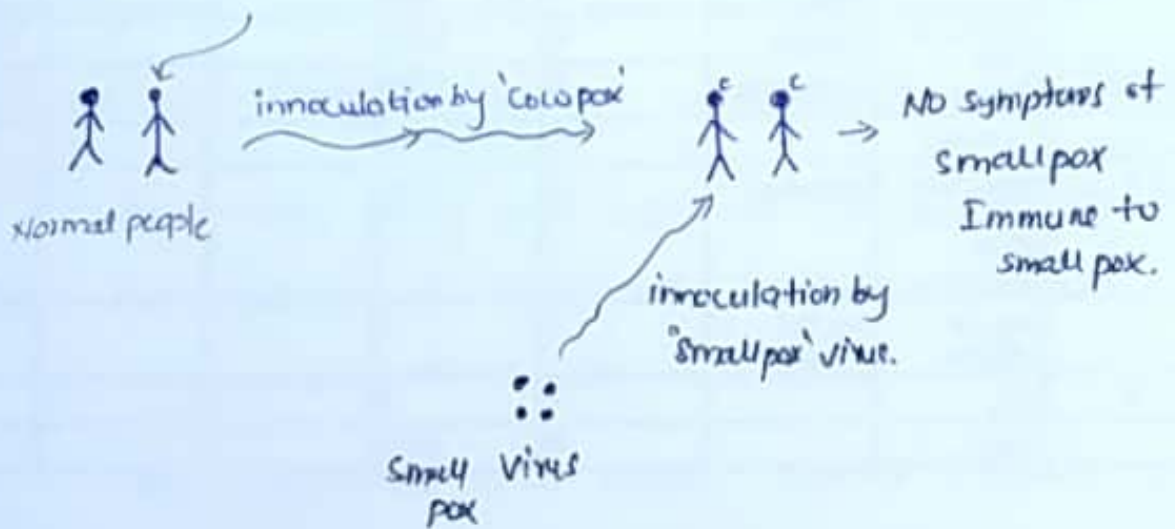
## Early vaccination studies :

① In 15th century, Chinese and Turkes had performed a technique called variolation on people having smallpox.

Dried crust from smallpox pustules → inhaled or inserted into skin cuts of people.

② Edward Jenner, English physician. had inoculated, people with cowpox virus. Then, when they are re-inoculated, with "smallpox", they found to be immune to smallpox.

Edward Jenner's → milk maid, who are contract with cowpox found to be immune to smallpox.



### Edward Jenner's vaccination for smallpox

These techniques spread throughout Europe. To test his idea he inoculated an 8 year old boy. with cowpox, and later intentionally infected the child with smallpox.

These sort of studies cannot be conducted under current medical standards of medical ethics.

### ③ Induction of immunity to cholera (fowl cholera).

(i) Louis Pasteur, had succeeded in growing the bacterium that cause fowl cholera in culture, and confirmed this by injecting in to chickens, then they develop "fowl cholera".

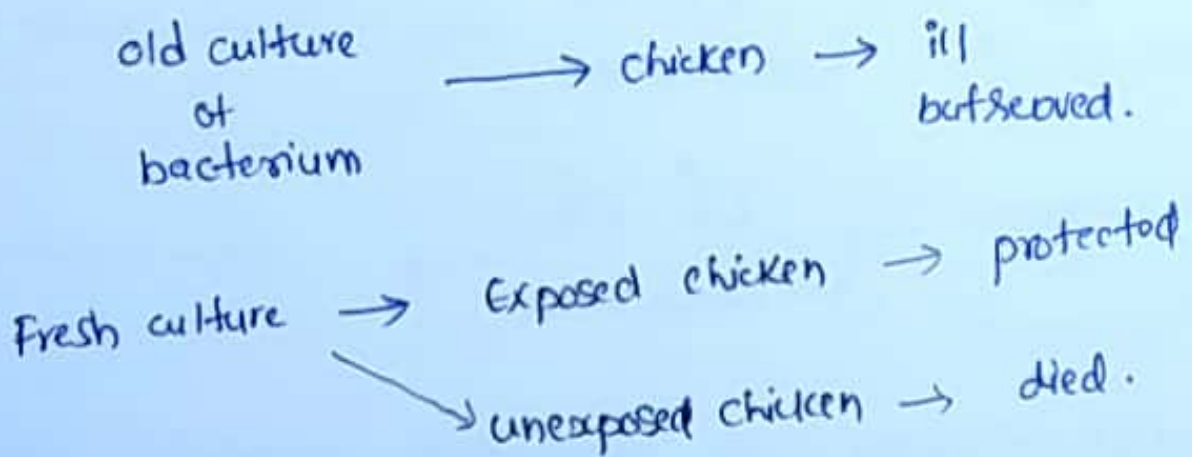
fowl  
cholera  
culture → chickens → fowl cholera  
disease.

(ii) He injected old culture of fowl cholera into chickens, they found to be ill, but recovered.

He then grew, fresh culture of bacterium, into a mixture of previously exposed chickens and unexposed birds. Freshly injected chickens died but chickens which are exposed to old bacterial culture were protected from disease.

He showed aging had weakened the, virulence of pathogen, such weakened strain called "attenuated strain", could be administered to provide immunity.

This weakened strain called "vaccine" (Latin "vacca" means "cow").

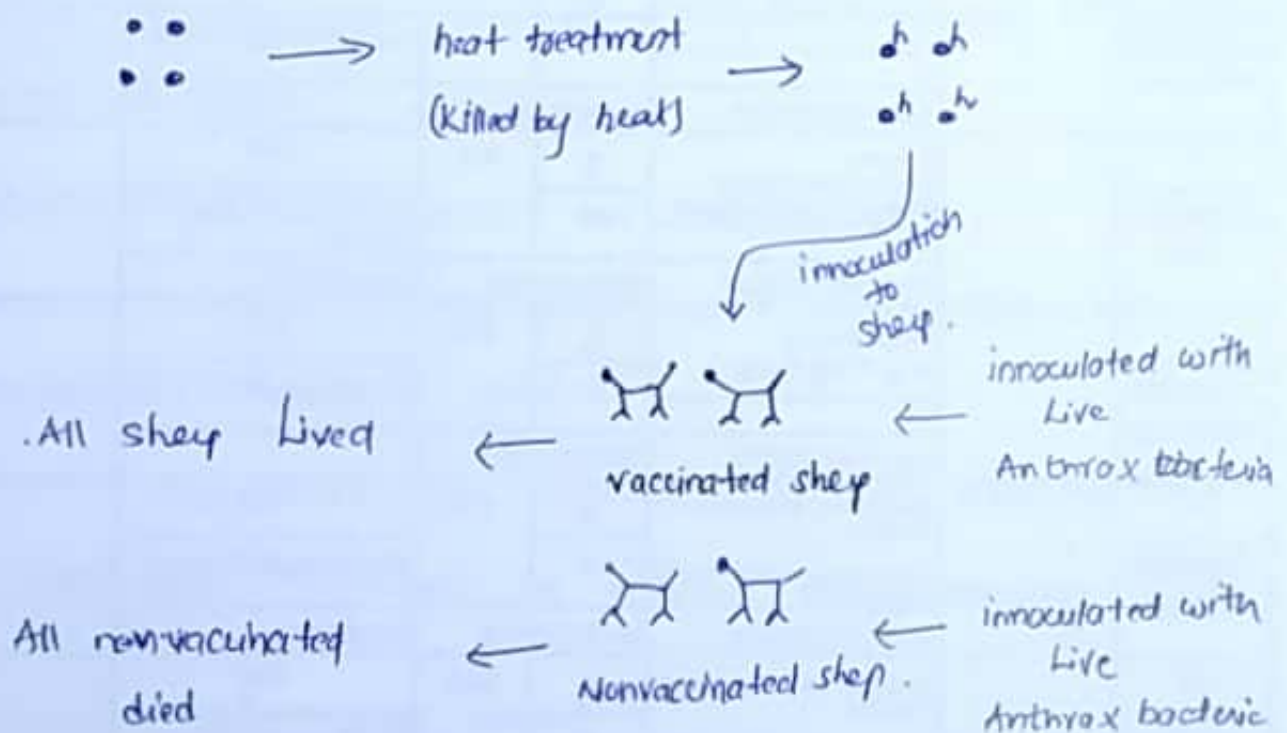


Effect of Aging on strain.

Attenuated strain / vaccine

(iii) Pasteur, showed a pathogen can be "attenuated" or weakened, this attenuated strain can be administered as vaccine.

He vaccinated a group of sheep with anthrax bacteria that were weakened by heat treatment. He inoculated anthrax bacteria in vaccinated sheep and unvaccinated sheep. These are beginning of immunology. All vaccinated sheep lived and unvaccinated sheep died.



④ In 1885, Pasteur administered first vaccine to human a young boy who had bitten by a dog with rabies. The boy Joseph Meister, was inoculated with a series of attenuated rabies virus, administered successfully, shortly after exposure, as long as virus not yet reached central nervous system.

⑤ Many countries had eradicated smallpox, basically through vaccination. As people acquired protective immunity, either through vaccination / or by infection. They acts as buffer for rest. There is herd immunity. overtime, no of people with no immunity, to disease will begin to rise.

vaccination for smallpox, largely ended in mid 1970. leaving half of population susceptible.

Measles, smallpox, pertussis, Mumps → vaccines.

⑥ Vaccination strategies should be changed to avoid infectious diseases in future.

⑦ main challenges for vaccination are malaria, AIDS.

infectious diseases spread. preventing infection, and transmission should be done.

Antibiotics are introduced in 1920's. worrying trend is Antibiotic resistance in microbes are increasing.

⑧ Immoral and cellular components!

(i) In 1890, Emil von Behring and Shibasaburo. insights into mechanism of immunity, earning Behring Nobel prize for physiology & medicine in 1901.

Von Behring, Kitasto showed that serum (from animals, previously immunised with diphtheria could transfer immune state to unimmunised animals.

Serum → component recovered from coagulated blood,

These serum, previously immunized with diphtheria, could transfer immunity to unimmunised animal.

immunised animal → Transfer to unimmunised animal  
Serum

[immunity is transferred to unimmunised animal]

→ Elie Metchnikoff (Nobel prize winner, demonstrated that cells also play role in immunity. He found WBC, called phagocytes ingested microbes, and killed it.

humoral immunity: active immune component in blood, could neutralize or precipitates toxins and could agglutinate bacteria.

Elvin Kabat, conducted studies and found that, gamma globulin, responsible for immunity. Soluble component in immunoglobulins called Antibody.

→ Antiserum, (antibody containing serum, fraction from a pathogen exposed individual, derived from horses, had given to patient suffering from diphtheria, tetanus.

Antibody against snake bites, (serum containing) is used.

→ The form of immunity transferred b/w individuals are called passive immunity.

Newborn individual are protected from maternal antibodies.

passive immunity: - shortlived, limited

↓  
[cell producing antibodies are not transferred].

Administration of vaccines, (or) natural infection, is said to be called active immunity. (production of one's own immunity)

long live protection from specific diseases

Cell mediated immunity:

→ Merrill Chase → transferred WBC, from guinea pigs, suffered from TB. immunity had transferred.

Lymphocyte → identified  
↓  
(cell played role).

→ Bruce Glick at MSU, performed experiments on chicken, indicated existence of two lymphocytes, (T-cell, B-cell).

T-cell, B-cell.  
↓ ↓  
Thymus Bone Marrow.

How are foreign substances recognised by immune system?

The specificity of immune response, for a foreign body called antigens.

Jules Bordet, demonstrated even, that nonpathogenic substances, RBC, from other species, serves as antigen.

Injecting nonself substances, produces antibodies. Even difference in single amino acids, also recognised.

→ Two major theory for antibody specificity.

Selective theory (Paul Ehrlich) (1900):

Explained origin of Serum antibody.

(i) cells in blood has variety of receptors called side-chain receptors, which bind to infectious agents and inactivate them.

(ii) Receptor-infection agent is like fit between Lock and Key model.

(iii) interaction b/w infectious agent and receptor helps cell to produce more receptors with same specificity.

cells → pluripotent, expressing no of different receptors. of which individually will be selected.

(iv) Antigen selected the appropriate receptor.

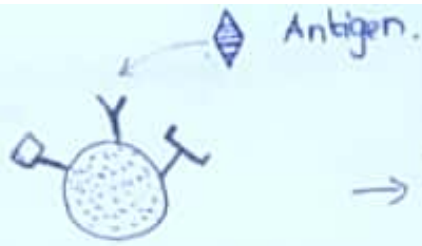
→ All are proven correct except, (in which one cell making many receptors, each cell makes many copies of just one membrane bound receptor (one specificity).

→ selected B-cells, triggers proliferated and produces, many copies of receptor, ~~cell~~ Antibody are produced.

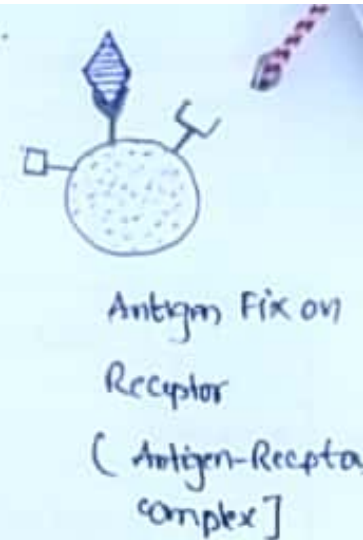




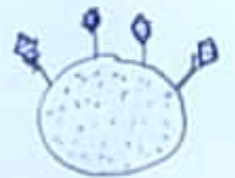
Different specific Receptors  
or side chains.



Specific Antigen find  
Specific receptor on  
cell. (good fit).



Antigen Fix on  
Receptor  
(Antigen-Receptor  
complex]



Synthesis of  
Specific Receptor is  
Triggered.

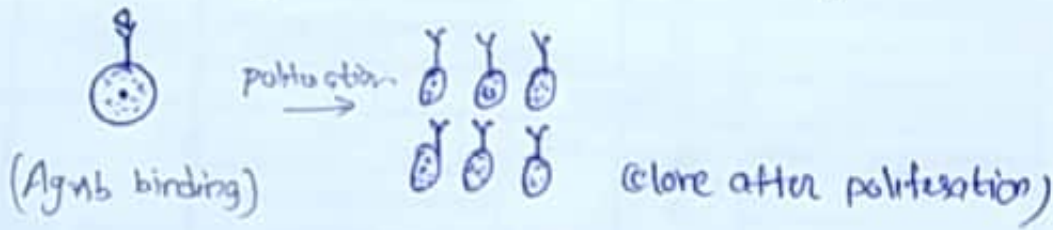
### Instructional theory:

Antigen played an important role in determining antibody specificity. Antigen would serve as a template, around which antibody, would fold.

Antibody is assumed to be complementary configuration to Antigen. Postulated by F. Bering, Felix Hausrowitz in 1930, redefined in terms of protein folding by Linus Pauling.

→ Clonal Selection: Niels Jerne, David Talmadge, Burnet. redefined selection theory. called clonal selection.

A single B, T cells expresses many copies of a membrane receptor. that specific to single Antigen. Antigen binding triggers to specific receptor activates cell, causes to proliferate in to clone of daughter cell have same receptor.



pathogen must breach Natural Barriers.

microenvironment influence the outcome. pathogen may be treated differently, depending up on the context / surroundings.

→ Some foreign compounds, and some commensal microbes that enter via digestive tract, help us to digest food are tolerated

→ Same foreign entered via blood treated (or) destroyed.

→ different strategies based on nature of invader / and microenvironment in which engagement occurs

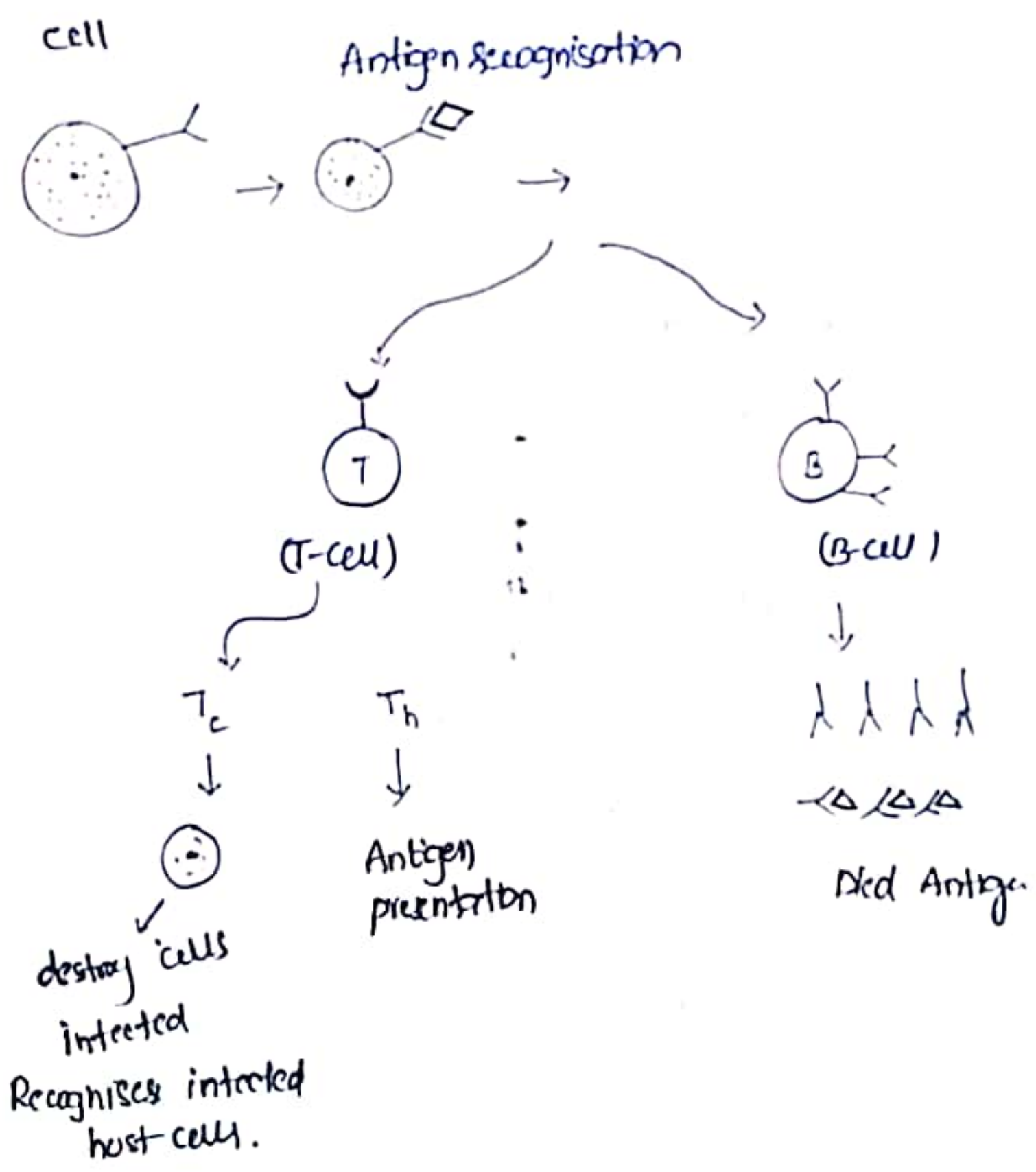
commensable microbe → through food → Tolerated

→ through blood → destroyed.

→ immune system act when foreigner breach natural barrier

Skin, Mucous membrane.

acidity of stomach, vagina → low pH.



→ viruses, small and tiny infection. immune cell must recognise infected cell and find surface of pathogen.

$T_c$  → cytotoxic T-cell  
↓  
identity infected host cell.

$T_H$  → guides the other immune cell B-cells, T-cells.

→ Extracellular pathogen bacteria, fungi.

cell surface antigen recognised by B-cells.

large parasitic worm → affects growth, development of individuals.

Tapeworm, Ringworm, Helminths worm etc.

cells, organs & microenvironment of immune system

primary lymphoid organs - Bone marrow, Thymus.

cell mediated immunity (CMI), cells played an main role. lymphoid system → primary lymphoid cells  
→ lymphoid organs

lymphoid organs → primary L.O  
→ Secondary L.O

→ primary lymphoid organs, in which precursor lymphocytes proliferate, develop and acquire immunological capacity.

Thymus, Bursa of Fabricius in bird.

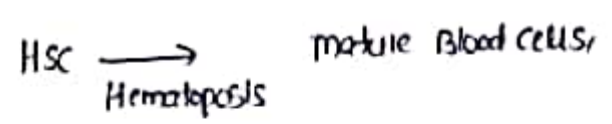
↓  
equivalent in humans is

Bone marrow.

Primary lymphoid organs:

immune cell proliferate & activated. Regulate development of immune cells from immature precursor.

All mature blood cells (RBC, WBC etc) arise from Hematopoietic stem cell (HSC). The process called Haematopoiesis



→ P. organs, where stem cells mature to immune cells.

Bone marrow  $\rightarrow$  HSC resides, and give rise to all cell types.

Thymus  $\rightarrow$  T-cell maturation completed.

→ stem cells properties (i) ability to regenerate

(ii) ability to differentiate into all cell types

Embryonic stem cells  $\rightarrow$  pluripotent

differentiate into any cell in organism.

Adult stem cell  $\rightarrow$  give rise to diverse cell types that specify a particular tissue.

HSC  $\rightarrow$  Adult stem cell  $\rightarrow$  to all types of blood cells.

