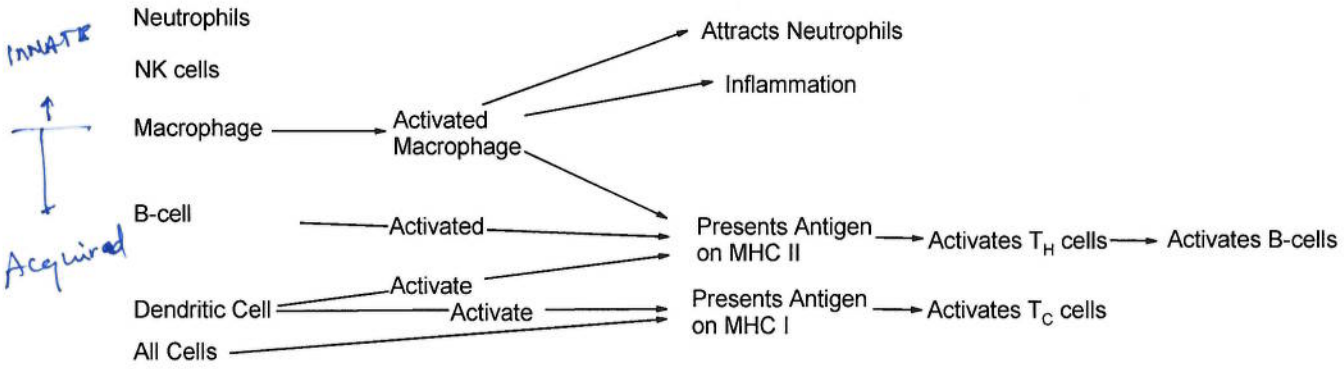
Lecture 5: Introduction to Acquired Immunity

Suggested reading Ch 3

Key concepts: Immuno-surveillance & Enhanced Probability of Rare Events, Clonal selection.

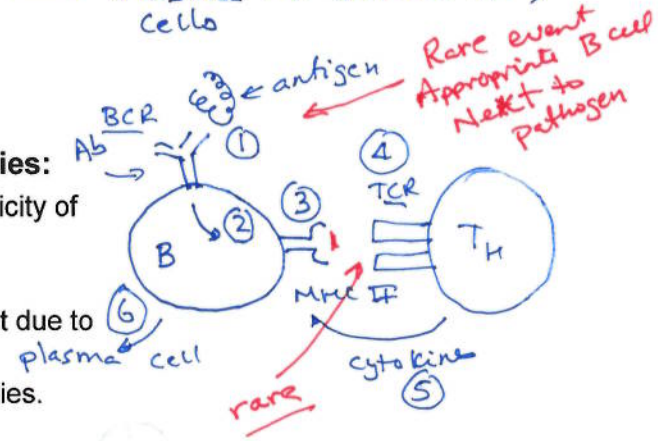
Interplay between Innate and Acquired:



Types of Acquired Immunity:

Humoral Immunity: Antibodies (B $\xrightarrow{T_H}$ Plasma cells → secrete Ab)

Cellular Immunity:

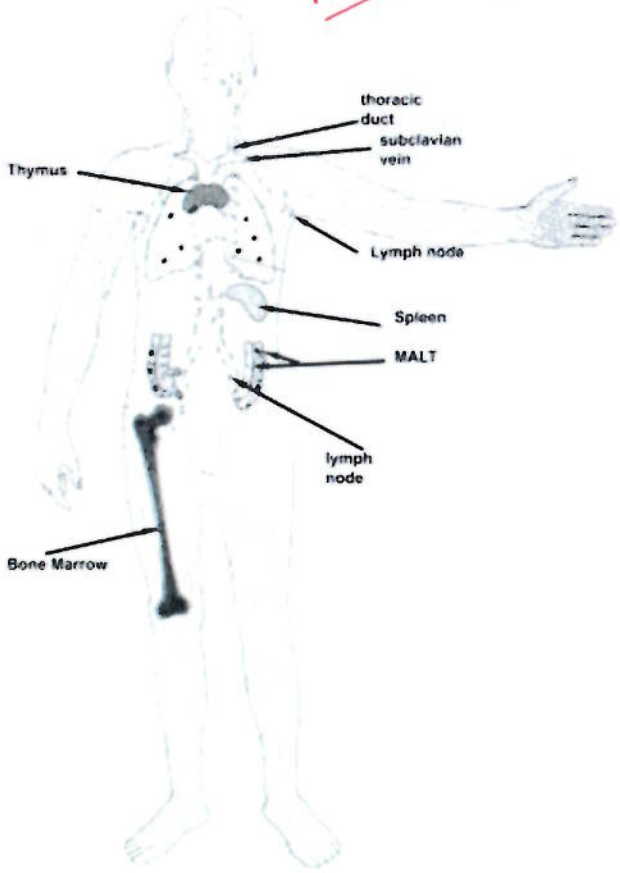


Fundamental Immune process to generate antibodies:

1) B-cell recognizes antigen, rare event due to high specificity of antibodies.
2) B-cell presents peptides on MHC class II.
3) Peptide-MHC complex recognized by T_H cell, rare event due to high specificity of the T-cell receptor.
4) B-cells develop into plasma cells which secrete antibodies.

Primary Immune organs:

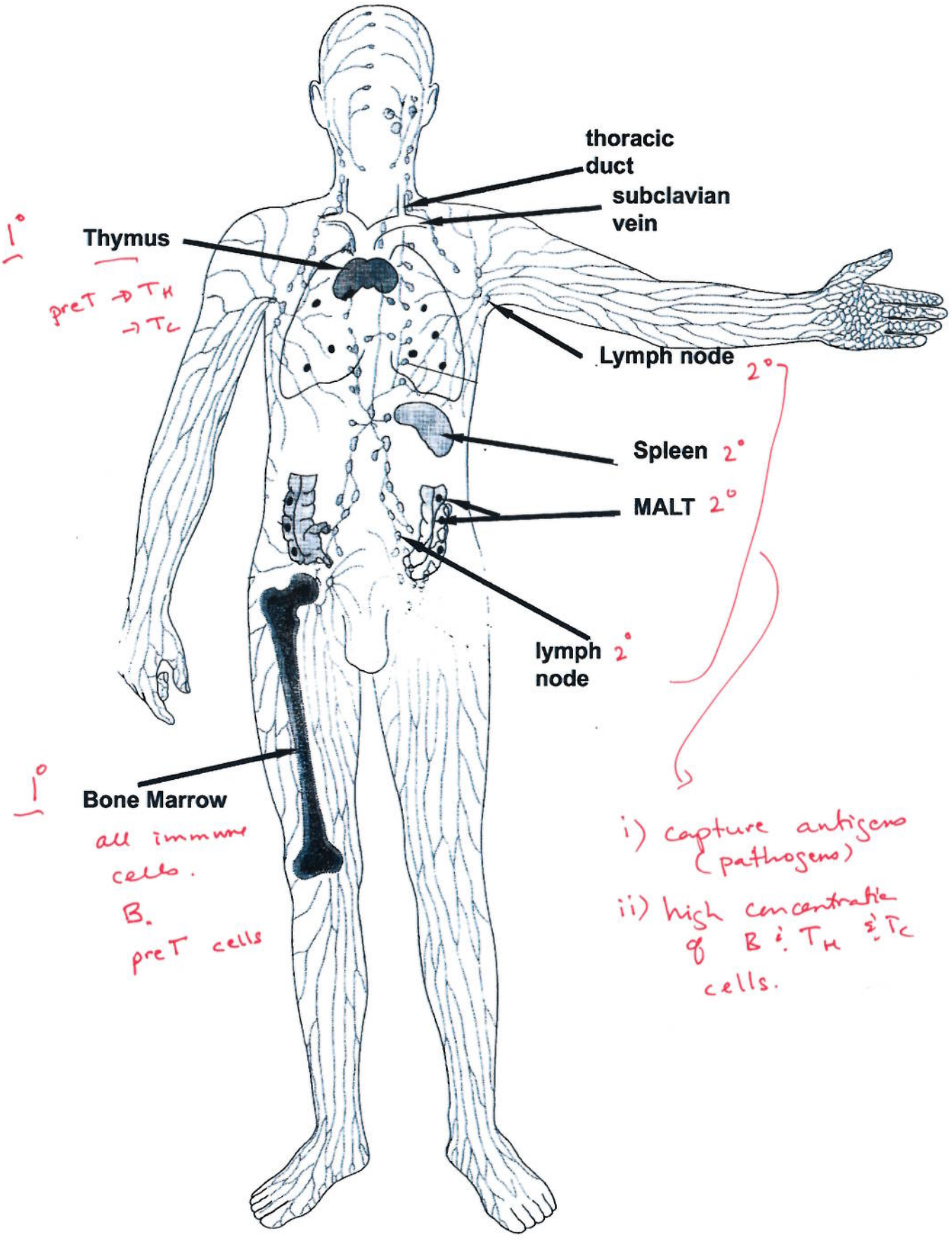
- Bone Marrow: Responsible for initial development of T cells and maturation of B cells. Only B cells that express an *intact immunoglobulin* that recognizes *foreign* molecules are allowed to leave the bone marrow. B-cells that recognize self are either destroyed or are non-functional.
- Thymus: Responsible for maturation of the T cells. Only T-cells that can recognize *foreign* peptides *in complex with self MHC* are allowed to leave the thymus. All others are destroyed.



Circulation Though the Lymphatic System.

- A naive lymphocyte in the blood will enter the lymphatic system 2-12 hours after it is released from the bone marrow or thymus. Passage across the endothelial wall similar to that used by neutrophils in inflammation, except a different cytokine/cytokine receptor is used.

Lymphatic System:



1°

Thymus

preT → T_H
→ T_C

2°

Spleen 2°

MALT 2°

lymph node 2°

1°

Bone Marrow

all immune cells.

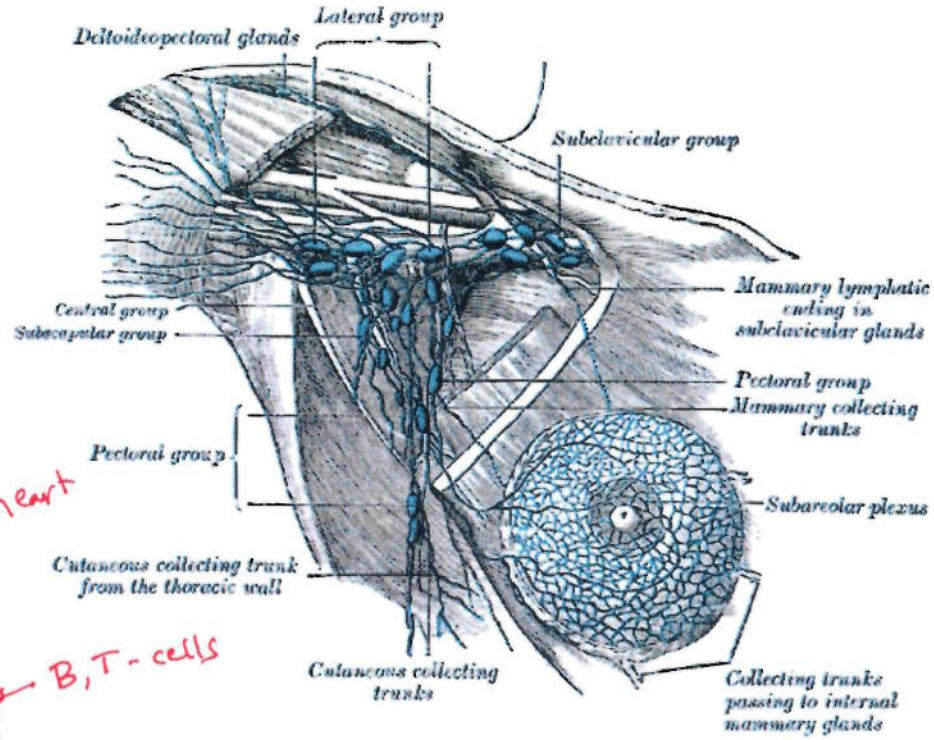
B.

preT cells

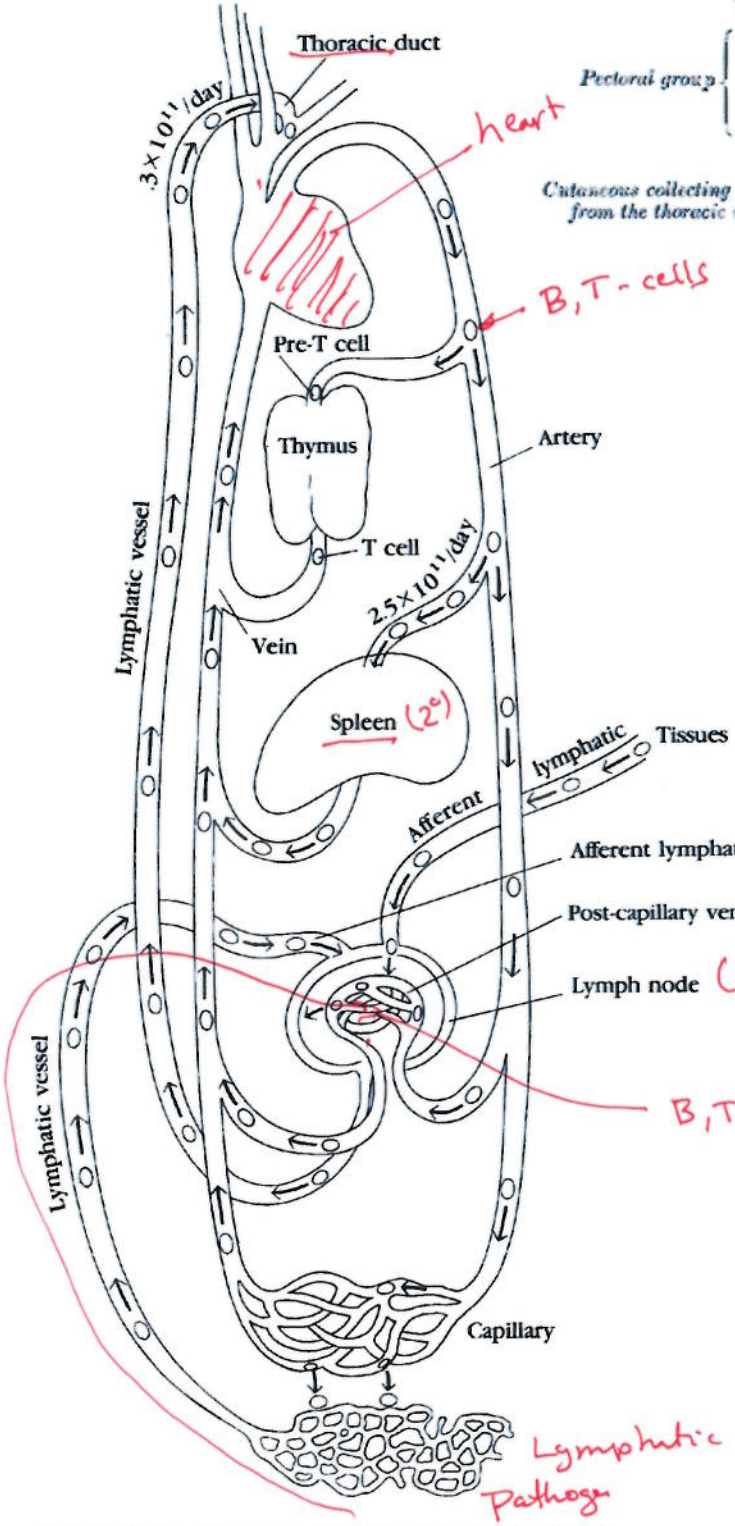
i) capture antigens (pathogens)

ii) high concentration of B & T_H & T_C cells.

Lymphatic system of Breast (Grays Anatomy, 1918)



Lymphatic Circulatory System



circulation increases chance of the rare event

- B - antigen
- B - T_H

FIGURE 3-23 Diagram of lymphocyte recirculation through the blood (purple) and lymph vasculature (gray) to the major organs of the lymphatic system.

- Approximately $3x10^{11}$ lymphatic cells flow through the system on a given day.
- A similar number are processed through the spleen.
- This high flux of cells insures that a foreign antigen will meet the appropriate B and T cells within a short period of time.
- If the naive lymphocyte does not encounter an antigen to which it can bind, it dies in a few days.
- Memory lymphocytes (B, T_H, and T_C) cells circulate for years to decades.

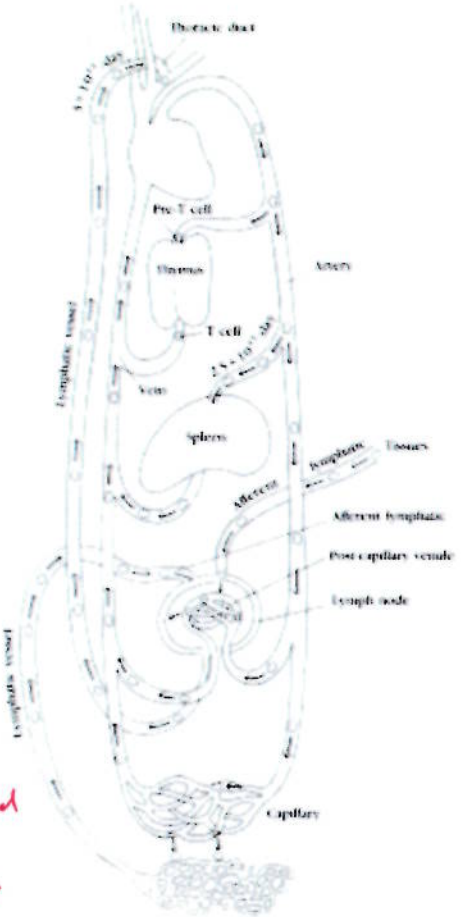


FIGURE 3-23 Diagram of lymphocyte recirculation through the blood (purple) and lymph vasculature (gray) to the major organs of the lymphatic system.

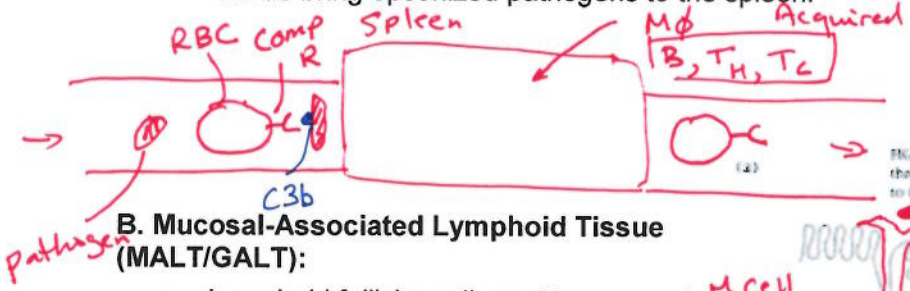
Secondary organs:

The secondary organs of the immune system serve two purposes:

- First, they trap foreign material. This trapped material is processed by dendritic cells as well as other antigen presenting cells, such as macrophages.
- Second, they provide a high density of B- and T-cells, such that the appropriate cell pairings can occur between antigen presenting cells and T_H-cells. This is facilitated by circulation of B and T cells through the lymphatic system.

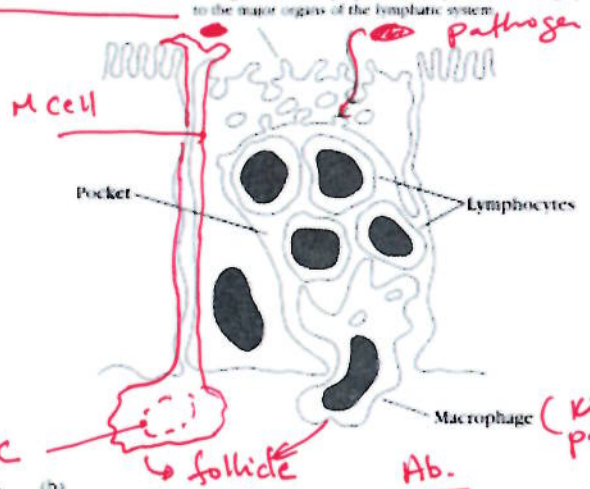
A. Spleen:

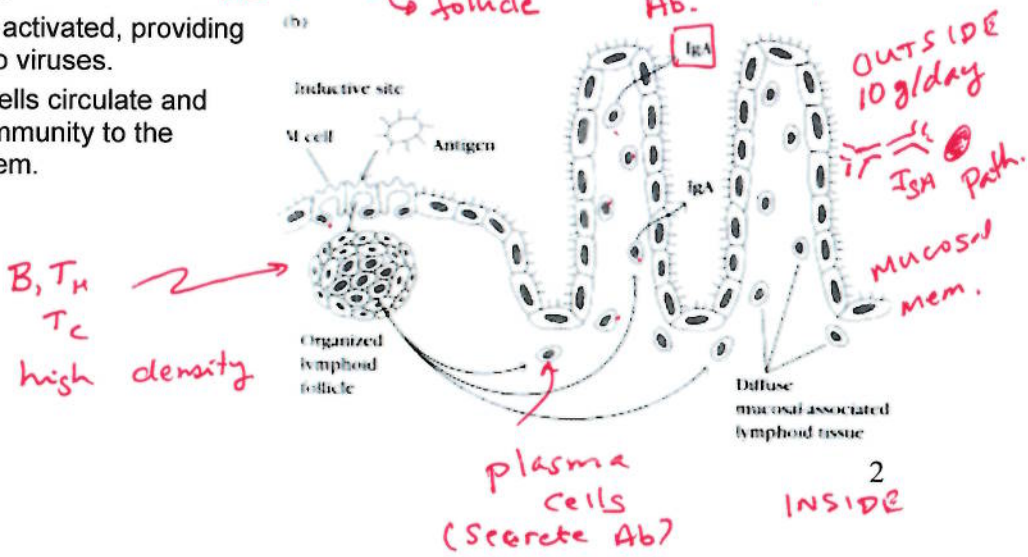
- Traps foreign particles from the blood via dendritic cells & macrophages. T-cells activated by dendritic cells and macrophages. B-cells activated in a manner similar to lymph nodes.
- RBCs bring opsonized pathogens to the spleen.



B. Mucosal-Associated Lymphoid Tissue (MALT/GALT):

- Lymphoid follicles adjacent to mucosal membranes (e.g. tonsils, Peyer's patches).
- Specialized M-cell in wall of mucus membrane entraps foreign particle, delivering it to lymphocytes on the other side of the mucosa. This leads to activation of B-cells which migrate to the mucosa and deliver antibodies of a specific class (IgA class) across the mucosal membrane.
- T_c cells can also be activated, providing mucosal immunity to viruses.
- Activated immune cells circulate and provide protective immunity to the entire mucosal system.



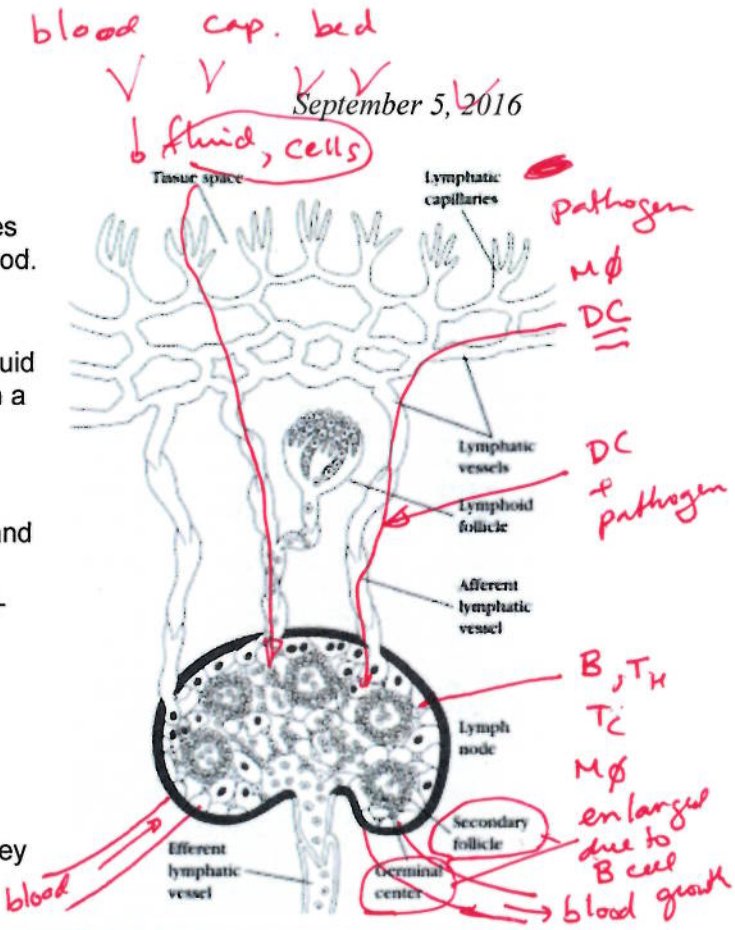


C. Lymphatic system & Lymph Nodes:

- Traps local foreign bodies near the source of infections. Drains fluid from cells to lymph nodes and follicles, eventually returning fluid to the blood. Nodes and follicles contain B-cells, T-cells, macrophages, and dendritic cells.
- Lymphocytes can entire either from the lymph fluid or cross the endothelial wall of a blood vessel in a manner similar to neutrophils.

- Dendritic cells in tissue engulf foreign particles, migrate to the lymph node, activating T_H cells (and potentially T_C cells.)
- Antigen trapped in lymph node activates both B- and T-cells.
- B-cells activated by T_H cells, form a **germinal center**

- Plasma cells release antibody into circulation. (Plasma cells may migrate to bone marrow.)
- Activated T-cells migrate to site of infection. They secrete **INF-γ,** which recruits macrophages.



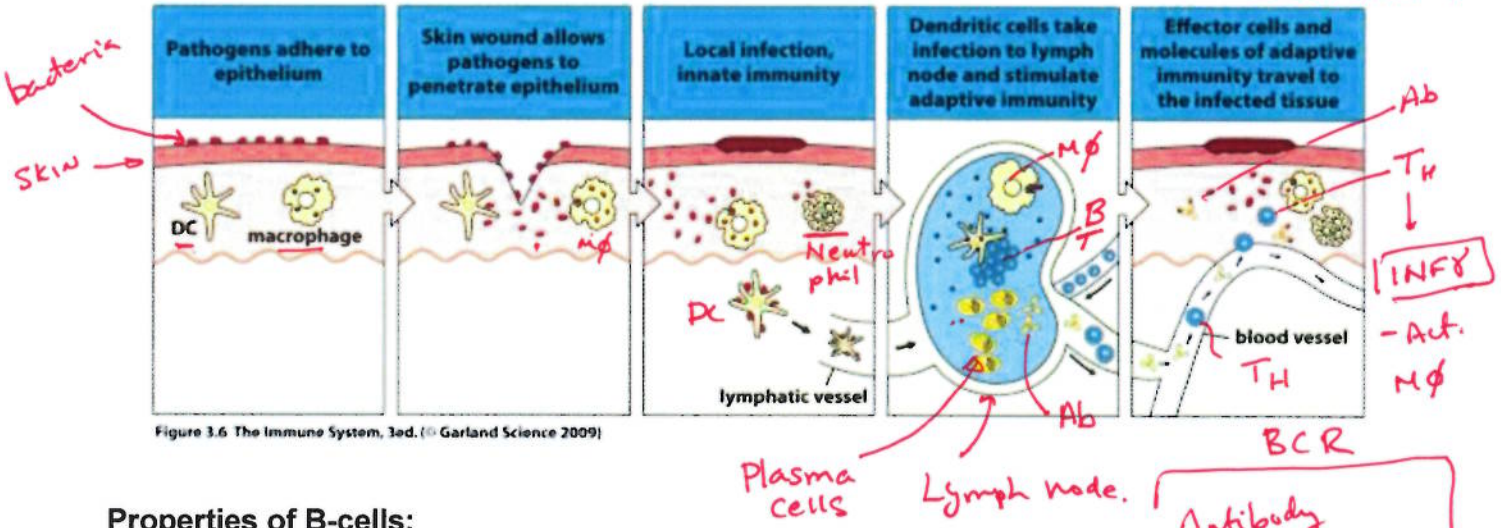


Figure 3.6 The Immune System, 3ed. (© Garland Science 2009)

Properties of B-cells:

i) Mature in the bone marrow.

ii) **B-cell receptor** binds *foreign* material (e.g. proteins, carbohydrates.) via antibody component. Highly specific interaction. In addition to the antibody component, the receptor also contains signaling chains.

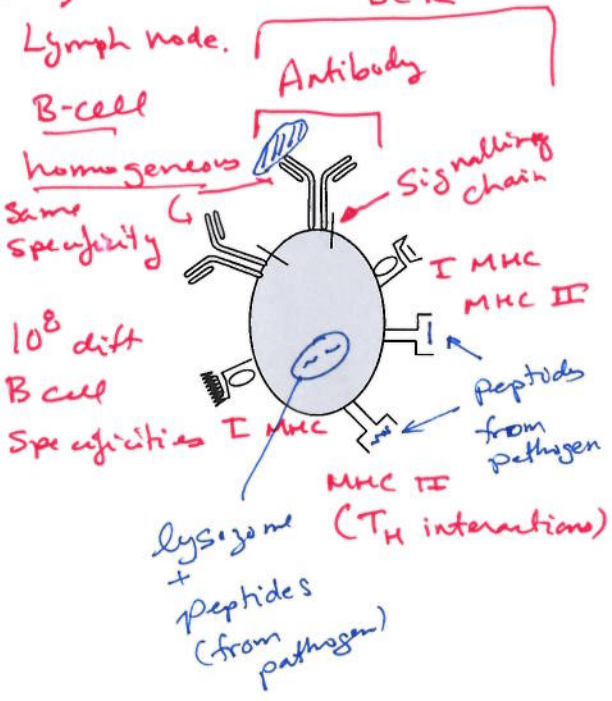
iii) All **B-cell receptors are identical on a *single* B-cell,** but diversity is on the order of 10^8 different B-cells within an individual. Genetic diversity in population is low – we all have the same germ line DNA.

iv) Antibody component of the BCR receptor is the IgM & IgD isotype in naïve B-cells.

v) Self-reactive B-cells are eliminated.

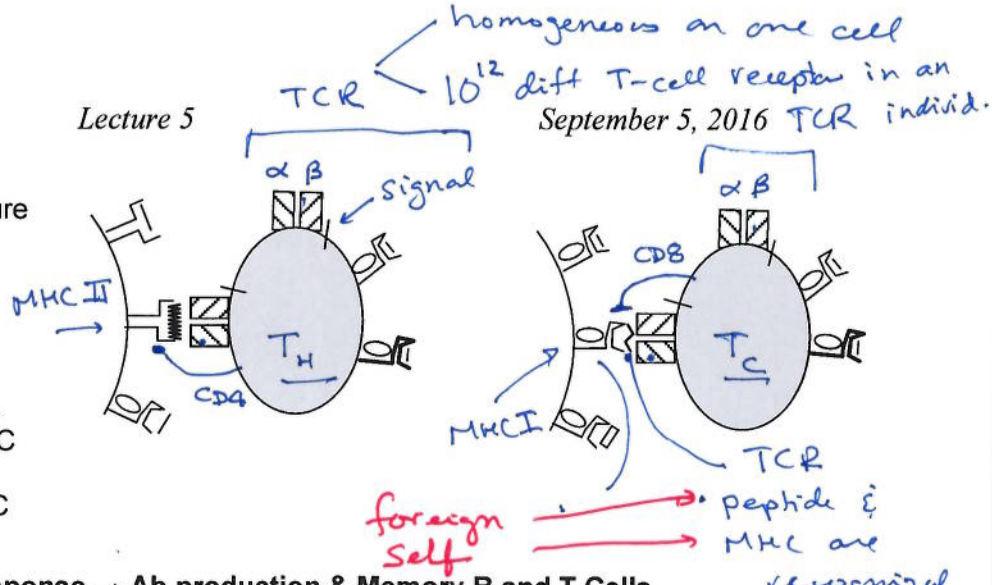
vi) Activation leads to expansion of specific B-cell population and generation of plasma and memory cells. This is the basis of the **clonal selection theory.**

vii) Memory B-cells & plasma cells often produce a different type of antibody (but same specificity).



Properties of αβ-T-Cells

i) Arise in the bone marrow, mature in the thymus.
ii) Recognize foreign peptide on self-MHC via T-cell receptor (TCR) α and β chains.
iii) **TCR** is **homogenous** on one cell, ~10^{12} different specificities.
iii) T_H cells recognize class II MHC via CD4 co-receptor.
iv) T_C cells recognize class I MHC via CD8 co-receptor.



Overview of Acquired B-cell Response → Ab production & Memory B and T Cells

i) antigen binds to B-cell receptor (membrane bound antibody).
ii) Antigen internalized, digested,
iii) Peptides from antigen displayed (presented) on class II MHC.
iv) MHC-peptide recognized by a specific T_H cells, activating the T_H cell.
v) Population of B-cells expanded **(clonal selection)**
vi) Activated T_H cells activate B-cells →Plasma cells (Ab secreting)
vii) Memory T and B cells formed, which will produce a faster and more intense secondary response due to the higher number of cells that recognize a particular antigen.