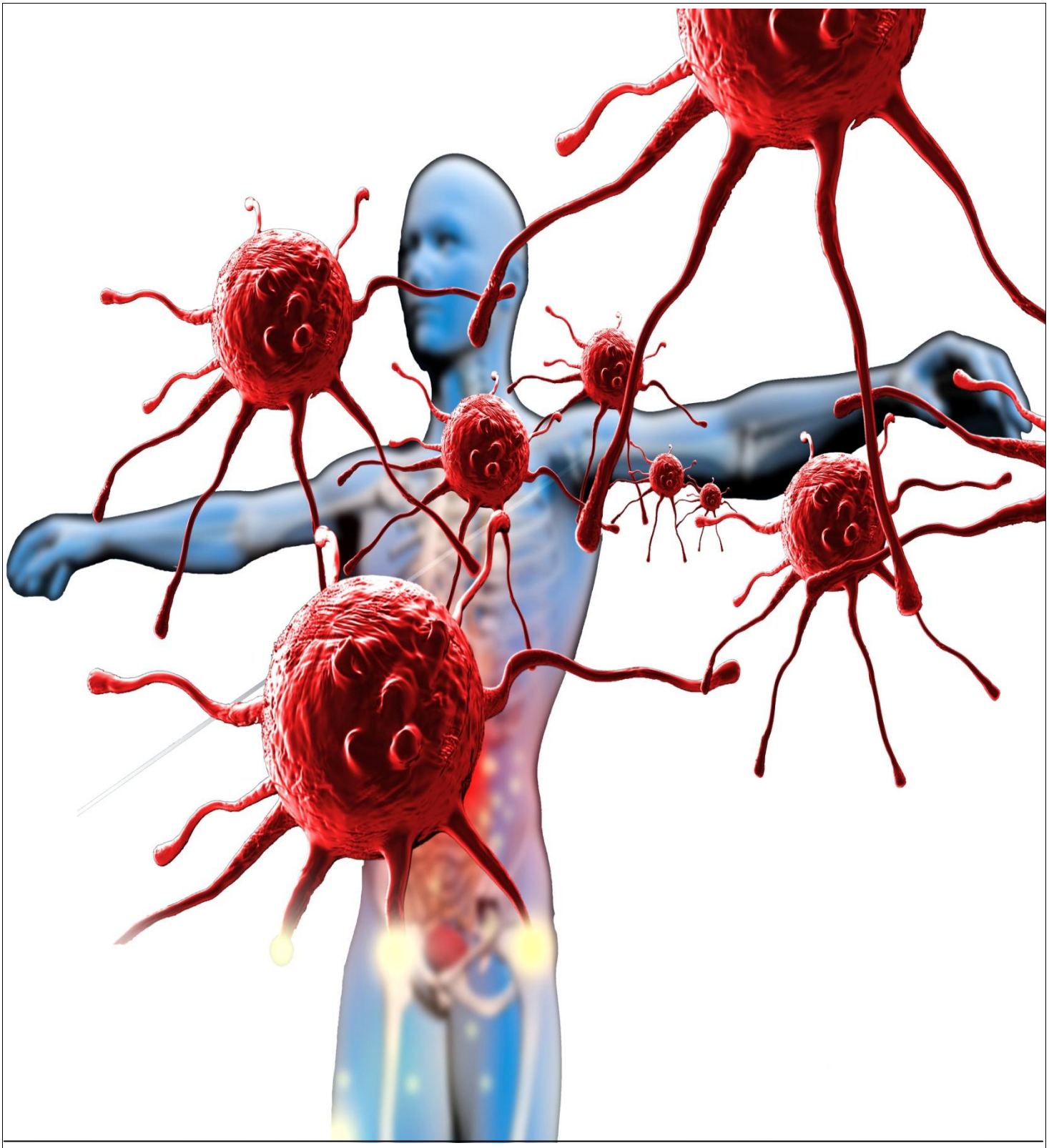


IMMUNOLOGY

Done By: Rashid Dahabreh

2

Dr. Hassan Abu Al-Ragheb

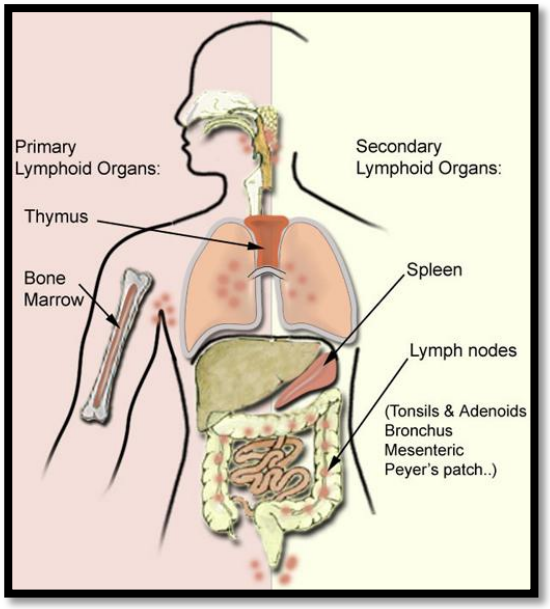
By Mohammed Nawasreh

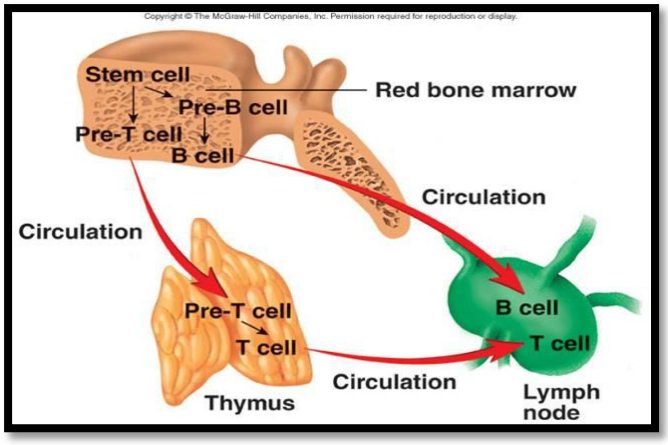
Lymphoid Organs

The lymphoid tissue in the body is classified into:

1)Primary lymphoid organs (Considered as sites of lymphoid cell development): These include the **bone marrow** and the **Thymus**

2)Secondary lymphoid organs (considered as sites of antigen exposure): These include the **lymph nodes**, the **spleen**, And **MALT** (Mucosa Associated Lymphoid tissue).



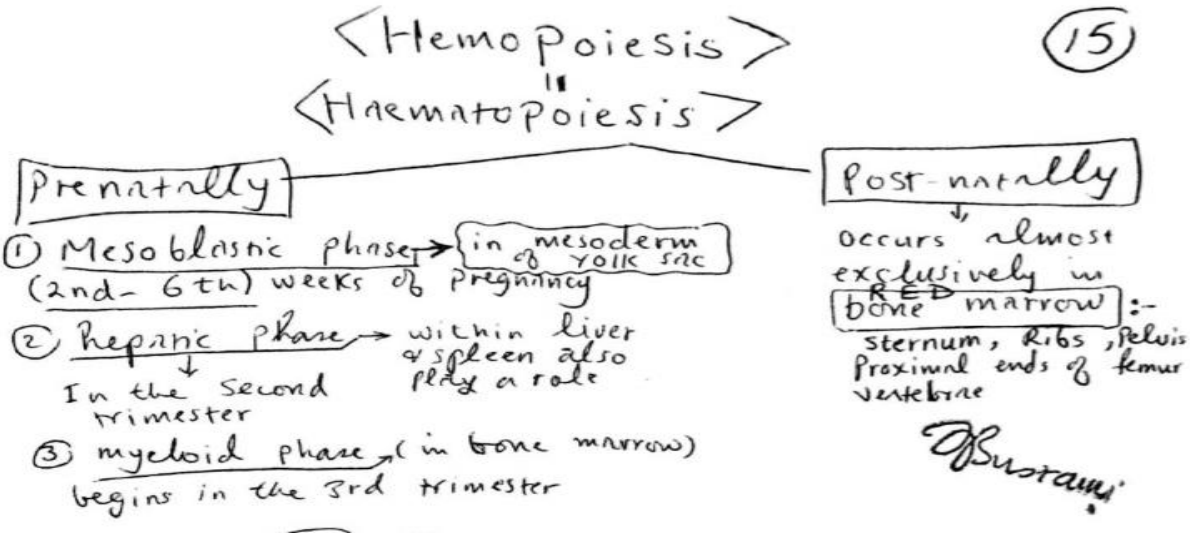


General concept: After lymphocytes develop in the primary lymphoid organs and become immunocompetent, they leave the primary lymphoid organs to the circulation in order to reach the secondary lymphoid organs searching for an antigen to become in contact with , recognize it, and then induce a specific immune response towards it.

The main site in adults where lymphocytes are produced in the process of hematopoiesis (formation of all Blood cells from pluripotent stem cells) is in the bone marrow .In fetal life, the yolk sac was responsible for that process ,then both the liver and the spleen became in charge and then comes the bone marrow to take over the wheel.

Written by Rashid Dahabreh

Reminder from Doctor Faraj's Hand out:

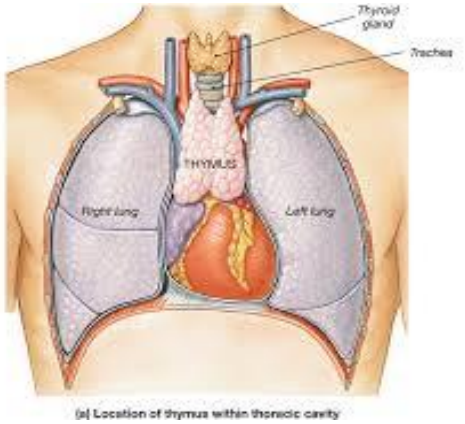


Note: In adults, Hemopoiesis is active in flat bones (such as sternum, the iliac crest, the vertebra, and some parts of the skull) and there would be no or little activity in long bones whereas Hemopoiesis in children takes place in all bones including long bones

When you want to take a sample of the bone marrow, from where do you take it?
Either from the Sternum or The iliac crest, those are the easiest places to deal with. Examining the sample would show you that there are a certain sense of **compartmentalization** within the bone marrow where each lineage of development takes places in its own compartment. Meaning that, red blood cells development Erythropoiesis) is going to be separated from White blood cells development (Granulopoiesis)

The Thymus:

T lymphocytes are produced in the bone marrow and then they leave the bone marrow and proceed to the thymus to finish their development and maturation in order to become immunocompetent (Having the ability to recognize an antigen and attacking it).



(a) Location of thymus within thoracic cavity

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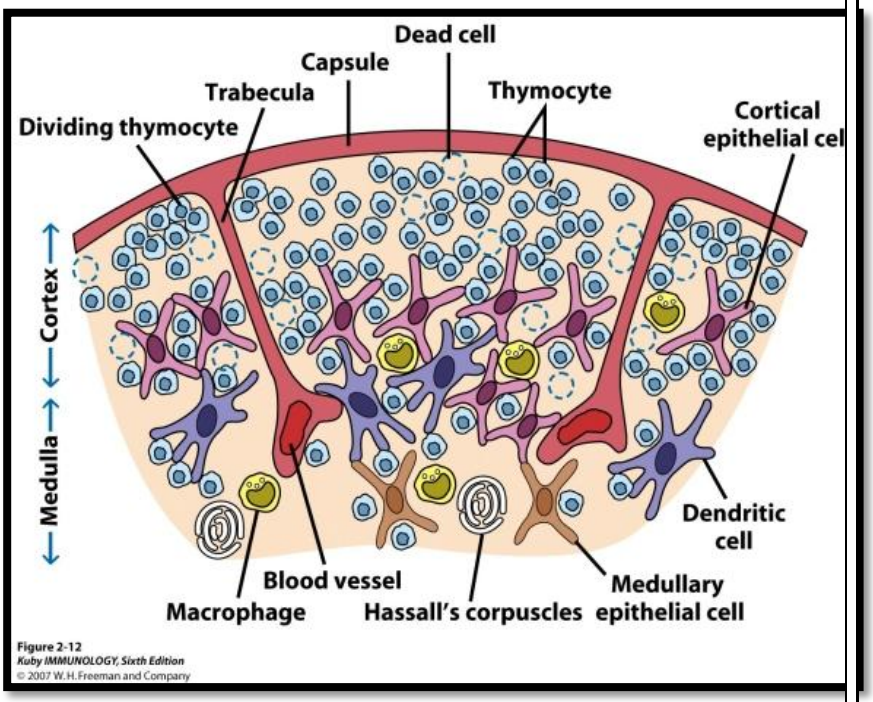
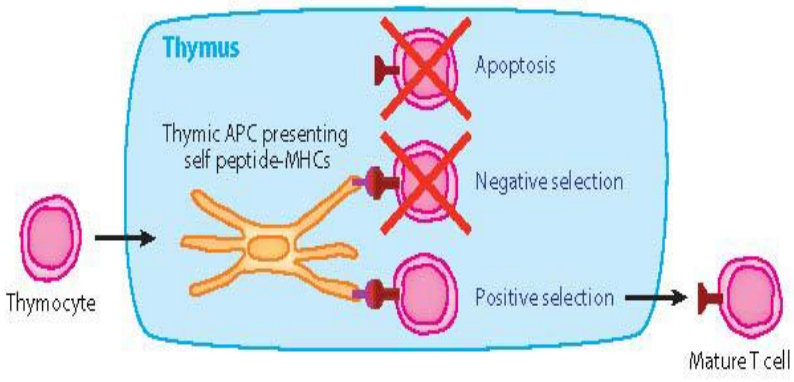
The thymus is a bilobed structure ,derived from the endoderm of the 3rd and 4th pharyngeal pouches, And located above the heart (it's a retrosternal structure). It gets atrophied after the age of puberty .

The thymus consists of an **outer cortex** that has the developing immature T cells (**Thymocytes**) and an inner medulla which cells pass into as they mature (There are also epithelial cells there called medullary epithelial cells). Cells of the cortex of the thymus are **epithelial reticular cells** that are in contact with the developing thymocytes and aid in the development process by running a selection process (To select which T cell is good and acceptable to be released to the circulation to start searching for antigens). The process is going to be discussed in details later on but as a general idea keep in mind that the epithelial reticular cells of the thymus expose the developing thymocytes to self antigens and check if they're going to react with it or not, if they don't react with them then that means it's acceptable to release them to the circulation as they won't be recognizing normal body cells (that's called positive selection) but if they do react with self antigen then they undergo programmed cell death/ Apoptosis because if they got released from the thymus, they're going to react with normal body cells and cause autoimmuno diseases (that's called Negative selection). Therefore, only 5-10% of T cells that enter the thymus mature and then get released to the circulation .





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Note: Both the cortex & the medulla contain a network of epithelial cells, dendritic cells, and macrophages that interact with the developing T cells (thymocytes) and aid in their development.

As the T cell develop in the thymus, it would acquire its own markers that are going to specify its type and function, whether it's going to be a cytotoxic T cell or a helper T cell. A cytotoxic T cell is always CD4+ (it has a marker on its surface called CD4) and a helper T cell is always CD8+ (it has a marker on its surface called CD8).

WAIT A MINUTE!..... If the thymus gets atrophied after the age of puberty then how is the body supposed to produce more lymphocytes after puberty? Many explanations could be presented and here are some of them:

1) the first explanation suggests that The body doesn't have to produce more T cells because by the age of puberty, there will be a huge mass of T memory cells that are going to live along in the body for a long time and play the role of responding to an antigen .

2) A second explanation says that even after being atrophied, some cells of the Thymus that are found In the fatty tissue continue their Job in the maturation and selection of developing T cells but at a lower level this time.

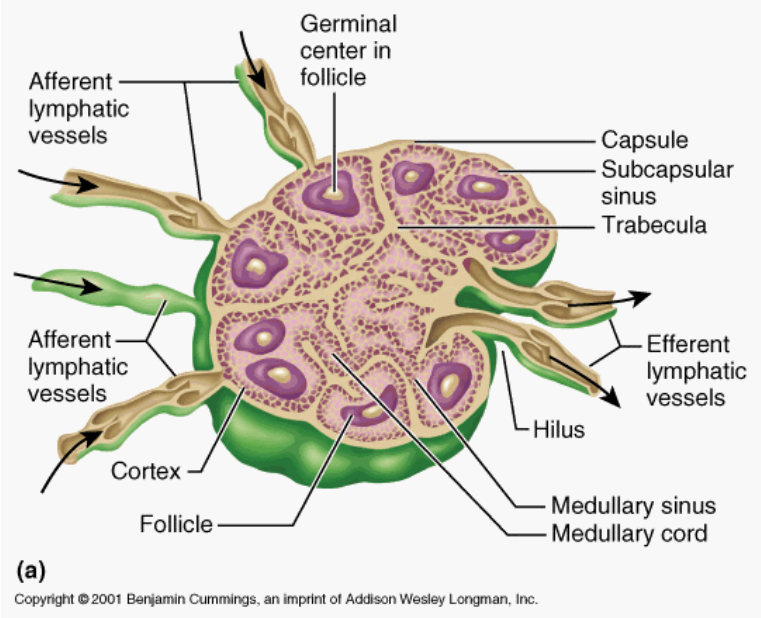
3) A third explanation suggests that the role of the thymus after it gets atrophied is taken over by MALT of the gastrointestinal tract (MALT: Mucosa Associated Lymphoid Tissue)

Lymph nodes:

- They're kidney shaped and recognized as small nodular aggregates of secondary lymphoid tissue .

- designed to initiate immune responses to **tissue-Borne antigens**

- Basic structure: Lymph nodes are covered by a capsule of dense connective tissue which sends septa called trabeculae which forms partitions within the lymph node.



-Lymph comes to the lymph node by **afferent lymphatics** , the fluid percolates through an outer cortex area where there are aggregates of cells called follicles. There are two types of follicles:

1)Primary follicles containing **Resting/ inactivated B cells**. Thus, primary follicles appear blue when dyed because they contain B cells that are inactivated, meaning there's little cytoplasm and (That's why there's a little red color) a larger nucleus .

2) Secondary Follicles contain a germinal center: When B cells get activated by antigens, they migrate to the center of follicle and form a germinal center where they proliferate and differentiate into active B cells/plasma cells and B memory cells (**A primary follicle will become a secondary follicle upon immunological stimulation**).

When secondary follicles are stained, the periphery of the follicles would stain blue because cells there aren't activated whereas the center of the follicle would stain more pinkish/reddish as cells there are activated, proliferating and differentiating.

Written by Rashid Dahabreh

NOTE: Secondary follicles appear upon recognizing an antigen and inducing an immunological response against it. That's why you wouldn't see secondary follicles in a newborn, only primary follicles, because newborns haven't been exposed to infections (antigens) or vaccinations (dead antigens) yet .

-The Paracortical region: between the cortex and the medulla, It contains **resting/ inactivated T cells**. T cells of this region also help the B cells of follicles to proliferate and produce antibodies when stimulated.

-Medulla:

-Innermost portion of a lymph node

- most cells here are activated plasma cells

- keep in mind that the lymph inside the lymph node reaches it by afferent lymphatics, percolated through an outer cortex, and then passes into the inner medulla and then it leaves the node through the hilum in an efferent lymphatic vessels. Lymph carries the antigen to the secondary lymphoid organs (lymph nodes) where antigen recognition by lymphocytes occur.

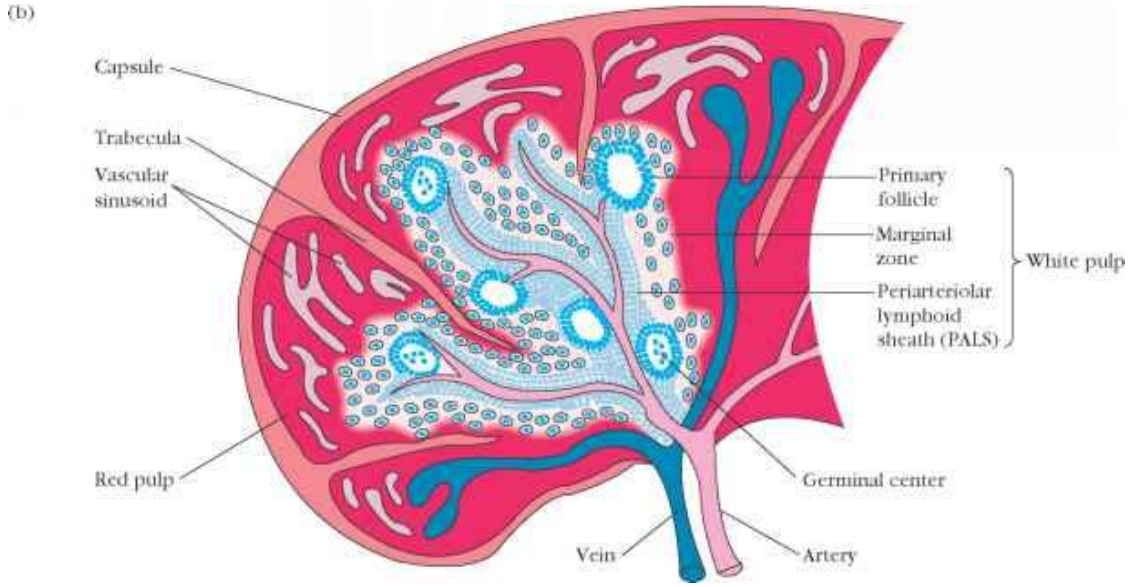
MAlT (Mucosa associated lymphoid tissue):

- a lymph tissue that's not quite organized or compartmentalized in a certain architecture as lymph nodes are. Nevertheless, they contain T cells and follicles of B cells, primary and secondary ones.

The spleen:

-secondary lymphoid organ designed to initiate immune response to **blood borne antigens**(It filters the blood).

- Basic structure: Capsule (Spleen is surrounded by a capsule of dense connective tissue) / Extensions of the capsule caked trabeculae that form partitions within the spleen/ Hilum/ The tissue inside the spleen is called the splenic pulp= It's divided into **white pulp** (lymphatic tissue) and **red pulp** (rich in blood)



- a single splenic artery enters the capsule at the hilum of the spleen and branches into arterioles, which become surrounded by cuffs of lymphocytes called the **periarteriolar lymphoid sheaths** (PALS). PALS are areas of T cells around central arterioles.

Spherical clusters of B cells (follicles- primary and secondary ones) are scattered throughout the PALS as well.

-Marginal zone is the region between the white and the red pulp, composed primarily of macrophages and dendritic cells (antigen presenting cells)

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-There are two arms for the immune System:

1) The innate (natural/ non specific) immune system:

Characteristics: Present intrinsically from birth/ nonspecific (direct against a broad group of antigens that have something in common) / no memory (not enhanced in activity by repeated exposure) / limited diversity of expression .

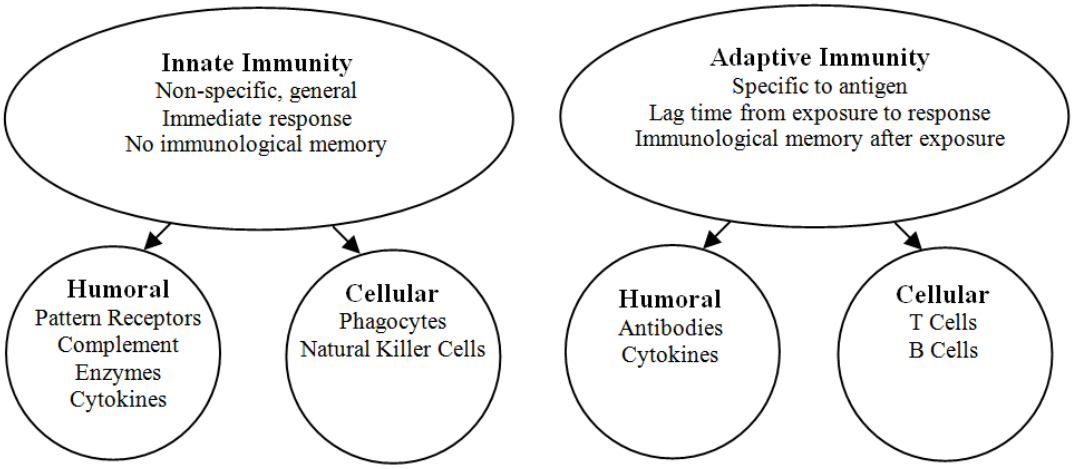
Cells involved here (such as Monocytes, neutrophils, and macrophages) have FIXED receptors on their surfaces that recognize fixed antigenic determinants found on the surface of the antigens (Those antigenic determinants are markers on the antigen surface that aren't found on the surface of normal cells. Example: Flagella of bacteria/ lipopolysaccharides of gram negative bacteria / peptidoglycans

2) The adaptive (acquired/ specific) Immune system:

Characteristics: Specific for particular antigens/ Diverse in their specificity- meaning that each lymphocyte would have SPECIFIC receptors to a SPECFIC antigen/ Memory (enhanced with each repeated exposure) / capable of self V.S. non-self recognition / self-limiting .

Note: The human body can deal with nearly 10* 10^9 different antigens since the adaptive immune system is capable of constantly providing new lymphocytes with new and different specificities towards different antigens

Once the barriers of the innate immune response have been defeated, the adaptive immune response is activated in an antigen specific manner for the elimination of antigen and lasting protection from repeated exposure through memory cells .



There's an overlap in the function of the innate and adaptive immune response, they're not separated from each other:

1) macrophages (a part of the innate immune system) process and present antigens to T lymphocytes (a part of the adaptive immune response)
2) Antibodies produced from plasma cells (adaptive) binds to pathogens and can activate the complement system (innate) to destroy those pathogens
3) T-helper cells produce Cytokines (adaptive) that enhance the bactericidal activity of phagocytes (innate) .

End of the sheet.

- Written by Rashid Dahabreh.