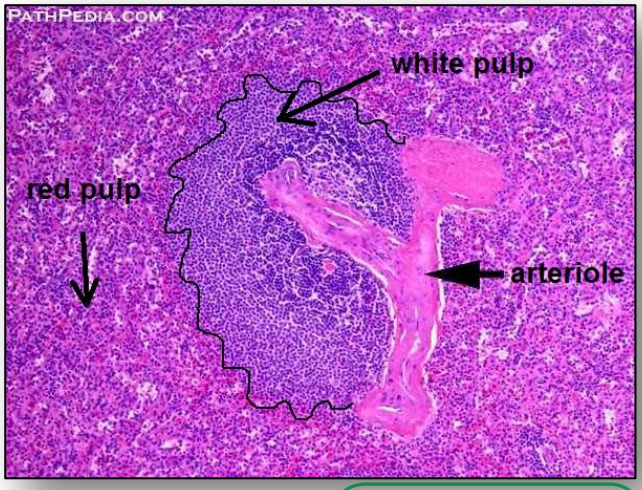
LYMPHOID TISSUE

- primary : thymus , bone marrow
- secondary : lymph nodes , MALT , spleen

SPLEEN:

there are 2 main types of tissues in the spleen :

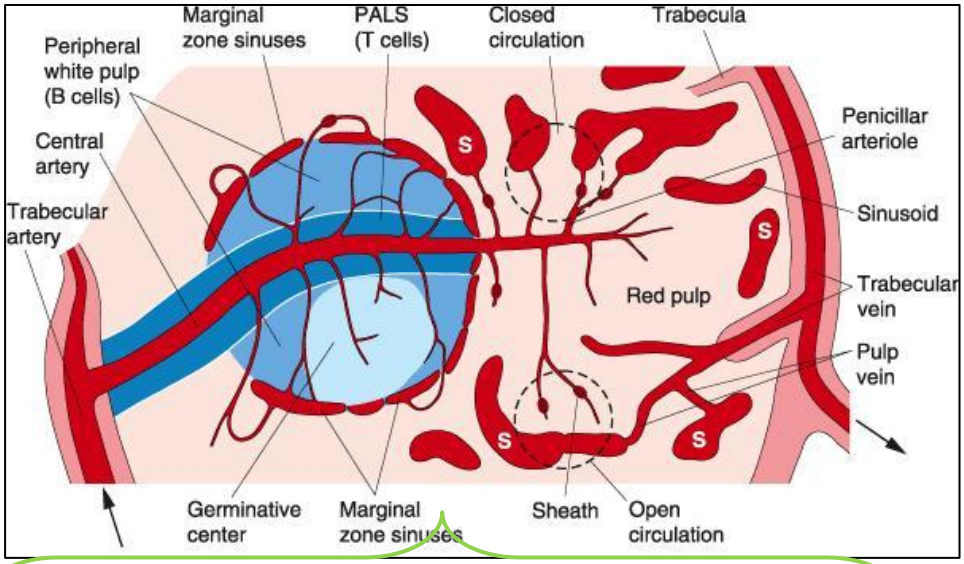
1. white pulp (gray area) : contains lymphoid tissue
2. red pulp: is vascular , has sinusoids filled with blood



the artery that enters the spleen branches into arterioles. arterioles give rise to distal branches called **penicillar arterioles**, which eventually give rise to terminal capillaries. around these arterioles theres aggregations of lymphocytes that make a sheath around these arteriole called *periarteriolar lymphoid sheath*(PALS)

SO periarteriolar lymphoid sheath = the lymphoid tissue present in the spleen

- just like lymph nodes; the spleen has follicles that have germinal centers populated by B-cells , and the rest of the spleen has T-cells .
- without the spleen you can survive but your immunity will be affected negatively



THE

IMMUNITY

Innate **Acquired**

Innate Immunity (non-specific immune system): consists of :

1) **physiological barriers:** barriers that stops the organisms from coming in.
   - **A. skin:** it prevents bacteria from coming in, so if u get cut it u'll be infected
   - **B. sweat, sebum :** has antibacterial effect that reduce the bacterial growth.
   - **C. mucous membranes:** they're not effective as the skin , but the mucus traps bacteria , and then it either get passed by the GIT or it goes up by the cilia in the respiratory tract.
   - D. **secretions (saliva , tears):** they contain lysozyme that breaks down the peptidoglycan bridges in gram +ve bacteria
   - **E. digestive enzymes of the intestines**
   - **F. acidity of the stomach and vagina (lactobacilli that produces lactic acid)**
   - **G. normal flora:** it's the nonpathogenic bacteria present in GIT or on skin , they protect us by:
     1. competing with pathogenic bacteria for nutrients
     2. might produce some kinds of antibiotics called bacteriocins .

bacteriocins: are chemicals produced by some bacteria to kill other bacteria

- so taking antibiotics might be harmful to us because they kill the normal flora. e.g: taking broad-spectrum antibiotics can kill all normal flora in GIT giving chance to clostridium difficile (for example) to overgrow causing pseudomembranous colitis.

2) **phagocytosis:** the plasma membrane of the phagocytic cells (macrophage or neutrophil) stick to the bacteria and starts surrounding it --> form phagosome --> the phagosome fuses with the lysosome --> form phagolysosome and kill the bacteria.
   - ✓ the recognition of foreign bodies is nonspecific by certain receptors on the phagocytes , these receptors bind to some molecules on the bacteria that don't change (ya3ni these molecules don't change from one type of bacteria to another) like:
     1. peptidoglycans: they're essential for the bacteria and don't change by mutations (not variable)
     2. LPS
     3. lipoteichioc acid: on gram +ve bacteria
     4. flagellin

5. mannose sugars

- ✓ they all present only on bacterial cells not on mammalian cells, so phagocytes don't attack our own cells
- ✓ these receptors on phagocytic cells used to be known as "**scavengers** receptors" but now they're referred to as **Toll-like receptors**.or **pattern recognition receptors**.
- ✓ Toll is actually a gene in dorsophila fly, but they found that these receptors on phagocytes are similar to the proteins produced by Toll gene.
- ✓ Toll like receptors are 14 in number , some of them recognize LPS others recognize the peptidoglycans .. etc

- ❖ In capsulated bacteria it's hard for the phagocytes receptors to bind to peptidoglycans , why? Its hard for the phagocytic cell to get near enough to the bacteria because the capsule has -ve charge and the phagocytic cell is also negatively charged --> repulsion ... so how to phagoctose them?
  1) by producing Ab's against the capsule
  2) by activation of the complement system and then the break down products of the complement system will bind to the capsule.

  macrophages and neutrophils has receptors for IgG (Fc receptors) and also receptors for complement (CR1) break down product. now by these receptors phagocytosis could occur. this process is known as opsonisation.

opsonisation: the process by which the phagocytosis is made possible specially with capsulated bacteria

Abs and complement break down product = **opsonins**

so as we can see there's interaction or overlap between innate and acquired immunity, and we can't separate them

3) **The complement**: is a system in the body that consists of several proteins which activate each other (one after the other) so it's a chain reaction or cascade reaction.

- the complement system has: inflammatory function, opsonising function and it lyses the cells . all functions together can cause damage to the bacteria and leads to death.

- the complement is considered as part of innate and acquired immunity.

4) **Fever (pyrexia) :** when we have infection we get rise in body temperature, why it's beneficial to the body when there is infection ?
    1. because bacteria can't grow at high temperature, they prefer the normal body temperature to grow in
    2. (more reasonable explanation) the supply or availability of iron is reduced (and this iron is very essential for bacterial growth and metabolism of bacteria)

5) **Interferons:** they're cytokines , produced by any kind of cells in the body that's infected by virus. they shut off the metabolism (no proteins) of the cell so the virus won't be able to replicate.
    - IFN $_{\gamma}$ has antiviral activity and is also a cytokine .

6) **Acute phase proteins:** are proteins synthesized de novo at greater magnitude than the normal under the effect of IL-1 and IL-6 mainly by liver or sometimes by macrophages. the level of these proteins increases with infection. e.g:
    1) **C-reactive protein** , why is it called like that? this protein was discovered when it reacted with C-polysaccharide component of streptococcus pneumonia. it acts like an Ab , but it's not an Ab .... (remember: Ab are specific but this protein is not specific and binds to many types of bacteria)
    2) **mannan-binding protein (manose-binding protein)**: it binds to manose sugars on bacteria , also acts like an Ab.

    (they act like an Ab by activating the complement system and they rise in 1 day)

7) **Defensins:** are small peptides that act like Antibiotics, produced by neutrophils. they can be inside the lysosomes or can be secreted to kill the bacteria by making holes in them --> the bacteria swells up --> lysis
    - ✓ they work on plasma membranes that don't have steroids (all bacteria don't have steroids except for mycoplasma , our cells have steroids so they can't harm our cells)

8) **NK cells:** they non-specifically recognize cells which are abnormal or stressed. they have receptors on their surface, some are inhibitory and others are activating receptors.

stressed cell (tumor cells , infected with virus)

has molecules on its surface
(MIC A & MIC B)

NK cell

has receptors
(NKG2D)

when the receptor reacts with the molecules , it inhibits the cell growth.

the other control the NK cell is done according to the presence or absence of MHC class I molecules. if they present on the cell in large number, then the cell is healthy and NK cell won't kill it. But if MHC disappears or become few in number, NK cell realizes that there's sth wrong with cell and kills it.

NK cells also work through antibodies, they have receptors for IgG (Fc receptor) ... this' s called ADCC (antibody dependent cell-mediated cytotoxicity) they use granzymes and perforins

ADCC can occur in macrophages and eosinoplils in killing parasites

- ✓ SO; NK cells can kill by binding to the cell (nonspecifically) or it can use the acquired immune system to work.

Acquired Immunity:

humoral immunity

mediated by soluble molecules in the serum (Ab) that are produced by plasma cells

cell-mediated immunity

T-lymphocytes CD4 and CD8

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