TDC 5TH SEM MAJOR :5.3

COMPONENTS OF IMMUNESYSTEM

BY: DR. LUNA PHUKAN

The main parts of the immune system are:

white blood cells.

antibodies.

complement system.

lymphatic system.

spleen.

bone marrow.

thymus.

Immune responses are mediated by leukocytes, which derive from precursors in the bone marrow. A pluripotent hematopoietic stem cell gives rise to the lymphocytes responsible for adaptive immunity, and also to myeloid lineages that participate in both innate and adaptive immunity.

Neutrophils, eosinophils, and basophils are collectively known as granulocytes; they circulate in the blood unless recruited to act as effector cells at sites of infection and inflammation. Macrophages and mast cells complete their differentiation in the tissues where they act as effector cells in the front line of host defense and initiate inflammation.

Macrophages phagocytose bacteria, and recruit other phagocytic cells, the neutrophils, from the blood. Mast cells are exocytic and are thought to orchestrate the defense against parasites as well as triggering allergic inflammation; they recruit eosinophils and basophils, which are also exocytic. Dendritic cells enter the tissues as immature phagocytes where they specialize in ingesting antigens. These antigen-presenting cells subsequently migrate into lymphoid tissue.

There are two major types of lymphocyte: B lymphocytes, which mature in the bone marrow; and T lymphocytes, which mature in the thymus. The bone marrow and thymus are thus known as the central or primary lymphoid organs. Mature lymphocytes recirculate continually from the bloodstream through the peripheral or secondary lymphoid organs, returning to the bloodstream through the lymphatic vessels.

Most adaptive immune responses are triggered when a recirculating T cell recognizes its specific antigen on the surface of a dendritic cell. The three major types of peripheral lymphoid tissue are the spleen, which collects antigens from the blood; the lymph nodes, which collect antigen from sites of infection in the tissues; and the mucosal-associated lymphoid tissues (MALT), which collect antigens from the epithelial surfaces of the body.

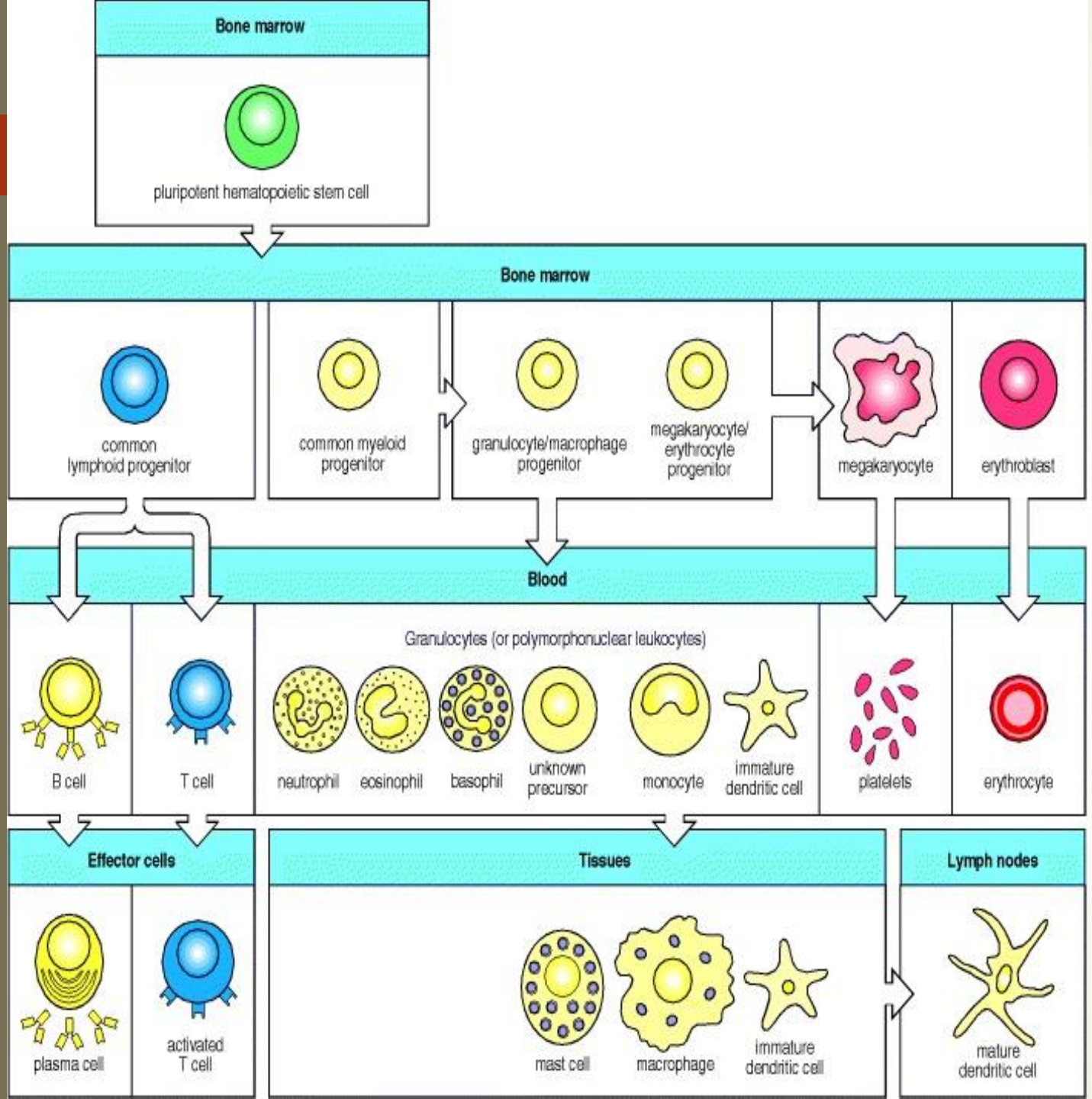
Adaptive immune responses are initiated in these peripheral lymphoid tissues: T cells that encounter antigen proliferate and differentiate into antigen-specific effector cells, while B cells proliferate and differentiate into antibody-secreting cells.

The components of the immune system

The cells of the immune system originate in the **bone marrow**, where many of them also mature. They then migrate to guard the peripheral tissues, circulating in the blood and in a specialized system of vessels called the lymphatic system.

The white blood cells of the immune system derive from precursors in the bone marrow

All the cellular elements of blood, including the red blood cells that transport oxygen, the platelets that trigger blood clotting in damaged tissues, and the white blood cells of the immune system, derive ultimately from the same progenitor or precursor cells—the hematopoietic stem cells in the bone marrow.

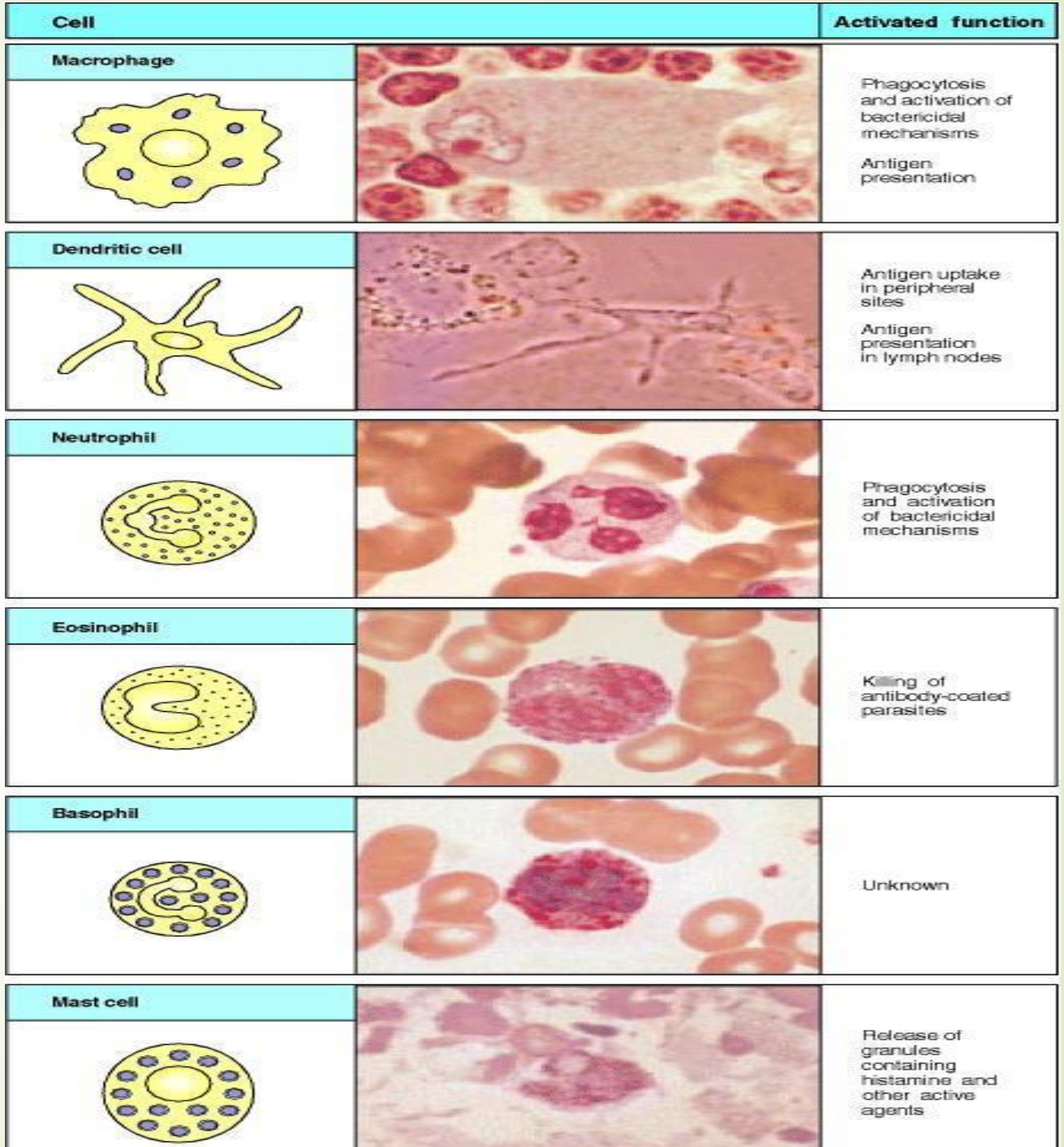


All the cellular elements of blood, including the lymphocytes of the adaptive immune system, arise from hematopoietic stem cells in the bone marrow. These pluripotent cells divide to produce two more specialized types of stem cells, a common lymphoid

As these **stem cells** can give rise to all of the different types of blood cells, they are often known as pluripotent hematopoietic stem cells. Initially, they give rise to stem cells of more limited potential, which are the immediate progenitors of red blood cells, platelets, and the two main categories of white blood cells. The different types of blood cell and their lineage relationships are summarized in We shall be concerned here with all the cells derived from the common lymphoid progenitor and the myeloid progenitor, apart from the megakaryocytes and red blood cells.

The myeloid progenitor is the precursor of the granulocytes, macrophages, dendritic cells, and mast cells of the immune system. Macrophages are one of the three types of phagocyte in the immune system and are distributed widely in the body tissues, where they play a critical part in innate immunity. They are the mature form of monocytes, which circulate in the blood and differentiate continuously into macrophages upon migration into the tissues. Dendritic cells are specialized to take up antigen and display it for recognition by lymphocytes. Immature dendritic cells migrate from the blood to reside in the tissues and are both phagocytic and macropinocytic, ingesting large amounts of the surrounding extracellular fluid. Upon encountering a pathogen, they rapidly mature and migrate to lymph nodes.

Myeloid cells in innate and adaptive immunity. Cells of the myeloid lineage perform various important functions in the immune response. The cells are shown schematically in the left column in the form in which they will be represented throughout the res



Mast cells

Mast cells are large cells found in connective tissues throughout the body, most abundantly in the submucosal tissues and the dermis. They contain large granules that store a variety of mediator molecules including the vasoactive amine histamine. Mast cells have high-affinity Fcε receptors (FcεRI) that allow them to bind IgE monomers. Antigen-binding to this IgE triggers mast-cell degranulation and mast-cell activation, producing a local or systemic immediate hypersensitivity reaction.

Mast cells have a crucial role in allergic reactions. Mastocytosis indicates an overproduction of mast cells.

Mast cells, whose blood-borne precursors are not well defined, also differentiate in the tissues. They mainly reside near small blood vessels and, when activated, release substances that affect vascular permeability. Although best known for their role in orchestrating allergic responses, they are believed to play a part in protecting mucosal surfaces against pathogens

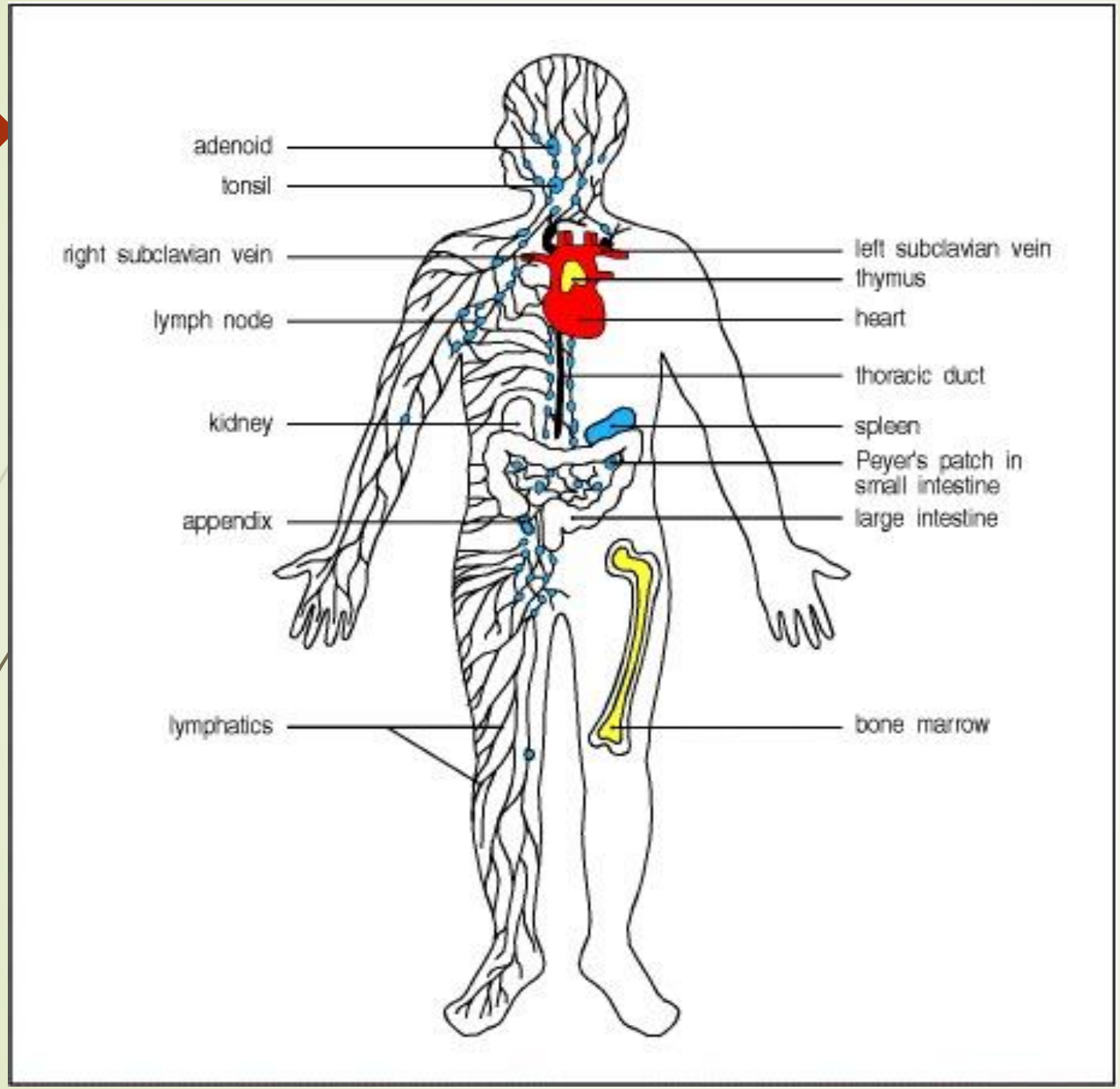
The granulocytes are so called because they have densely staining granules in their cytoplasm; they are also sometimes called polymorphonuclear leukocytes because of their oddly shaped nuclei.

There are three types of granulocyte, all of which are relatively short lived and are produced in increased numbers during immune responses, when they leave the blood to migrate to sites of infection or inflammation.

Neutrophils, which are the third phagocytic cell of the immune system, are the most numerous and most important cellular component of the innate immune response: hereditary deficiencies in neutrophil function lead to overwhelming bacterial infection, which is fatal if untreated. **Eosinophils are thought to be important chiefly** in defense against parasitic infections, because their numbers increase during a parasitic infection. **The function of basophils is probably similar** and complementary to that of eosinophils and mast cells;

The common lymphoid progenitor gives rise to the lymphocytes, with which most of this book will be concerned. There are two major types of lymphocyte: B lymphocytes or B cells, which when activated differentiate into plasma cells that secrete antibodies; and T lymphocytes or T cells, of which there are two main classes. One class differentiates on activation into cytotoxic T cells, which kill cells infected with viruses, whereas the second class of T cells differentiates into cells that activate other cells such as B cells and macrophages.

Most lymphocytes are small, featureless cells with few cytoplasmic organelles and much of the nuclear chromatin inactive, as shown by its condensed state . This appearance is typical of inactive cells and it is not surprising that, as recently as the early 1960s, textbooks could describe these cells, now the central focus of immunology, as having no known function. Indeed, these small lymphocytes have no functional activity until they encounter antigen, which is necessary to trigger their proliferation and the differentiation of their specialized functional characteristics.



The distribution of lymphoid tissues in the body. Lymphocytes arise from stem cells in bone marrow, and differentiate in the central lymphoid organs (yellow), B cells in bone marrow and T cells in the thymus. They migrate from these tissues and are carried

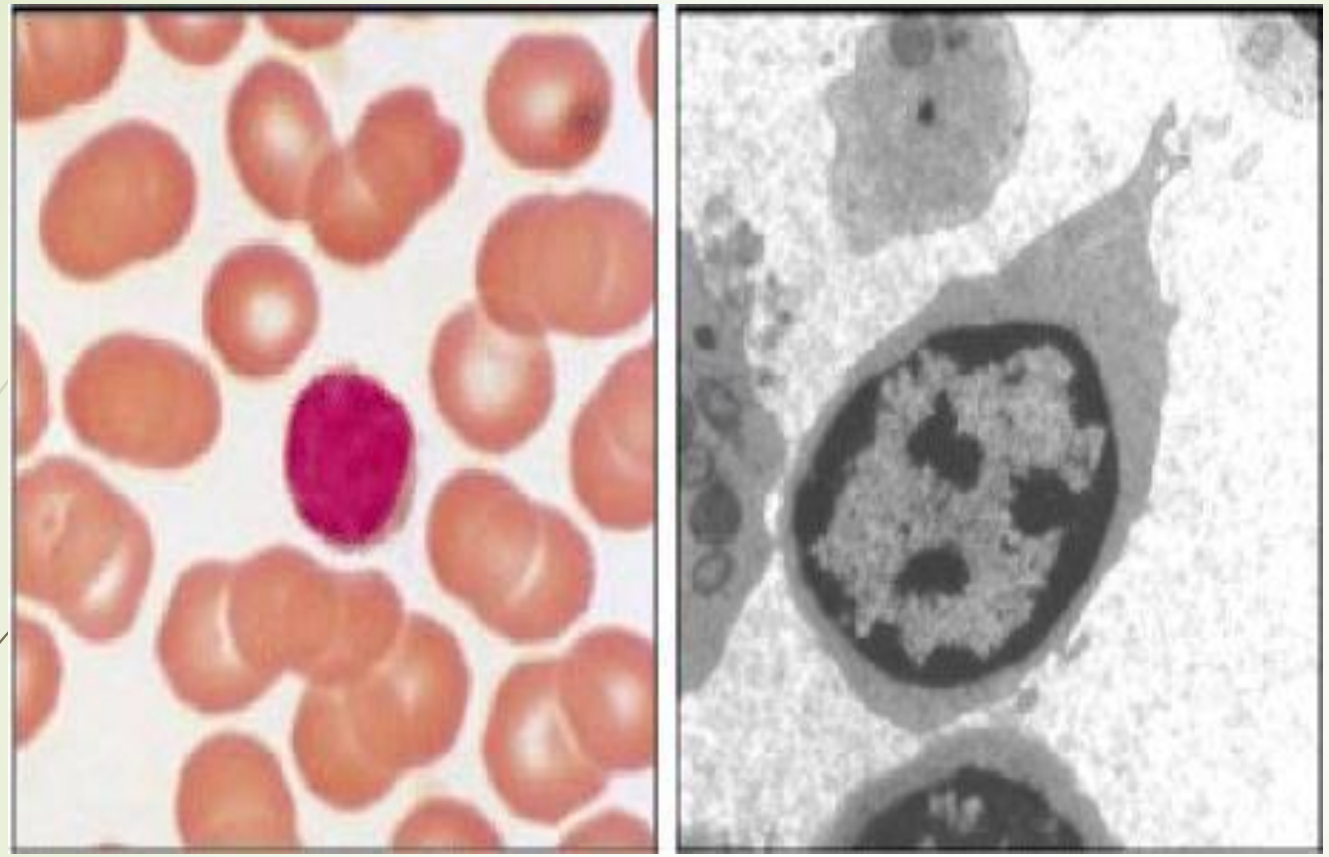
Lymphocytes are remarkable in being able to mount a specific immune response against virtually any foreign antigen. This is possible because each individual lymphocyte matures bearing a unique variant of a prototype antigen receptor, so that the population of T and B lymphocytes collectively bear a huge repertoire of receptors that are highly diverse in their antigen-binding sites. The B-cell antigen receptor (BCR) is a membrane-bound form of the antibody that the B cell will secrete after activation and differentiation to plasma cells. Antibody molecules as a class are known as immunoglobulins, usually shortened to Ig, and the antigen receptor of B lymphocytes is therefore also known as membrane immunoglobulin (mIg). The T-cell antigen receptor (TCR) is related to immunoglobulin but is quite distinct from it, as it is specially adapted to detect antigens derived from foreign proteins or pathogens that have entered into host

A third lineage of lymphoid cells, called natural killer cells, lack antigenspecific receptors and are part of the innate immune system. These cells circulate in the blood as large lymphocytes with distinctive cytotoxic granules . They are able to recognize and kill some abnormal cells, for example some tumor cells and virus-infected cells, and are thought to be important in the innate immune defense against intracellular pathogens

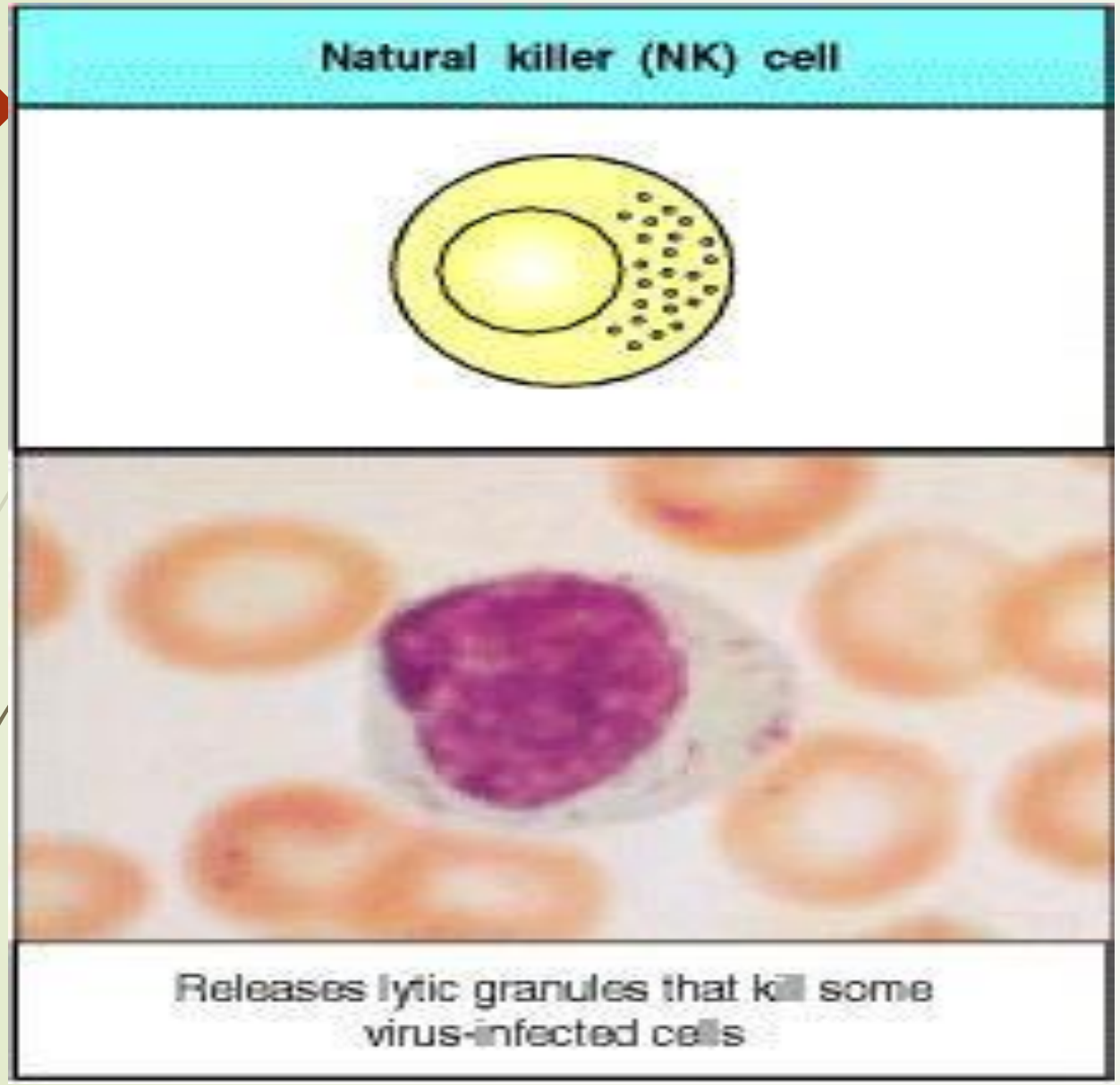
Natural killer (NK) cells. These are large granular lymphocyte-like cells with important functions in innate immunity. Although lacking antigen-specific receptors, they can detect and attack certain virus-infected cells

Lymphocytes mature in the bone marrow or the thymus

The lymphoid organs are organized tissues containing large numbers of lymphocytes in a framework of nonlymphoid cells. In these organs, the interactions lymphocytes make with nonlymphoid cells are important either to lymphocyte development, to the initiation of adaptive immune responses, or to the sustenance of lymphocytes



Lymphocytes are mostly small and inactive cells. The left panel shows a light micrograph of a small lymphocyte surrounded by red blood cells. Note the condensed chromatin of the nucleus, indicating little trans-criptional activity, the relative absence



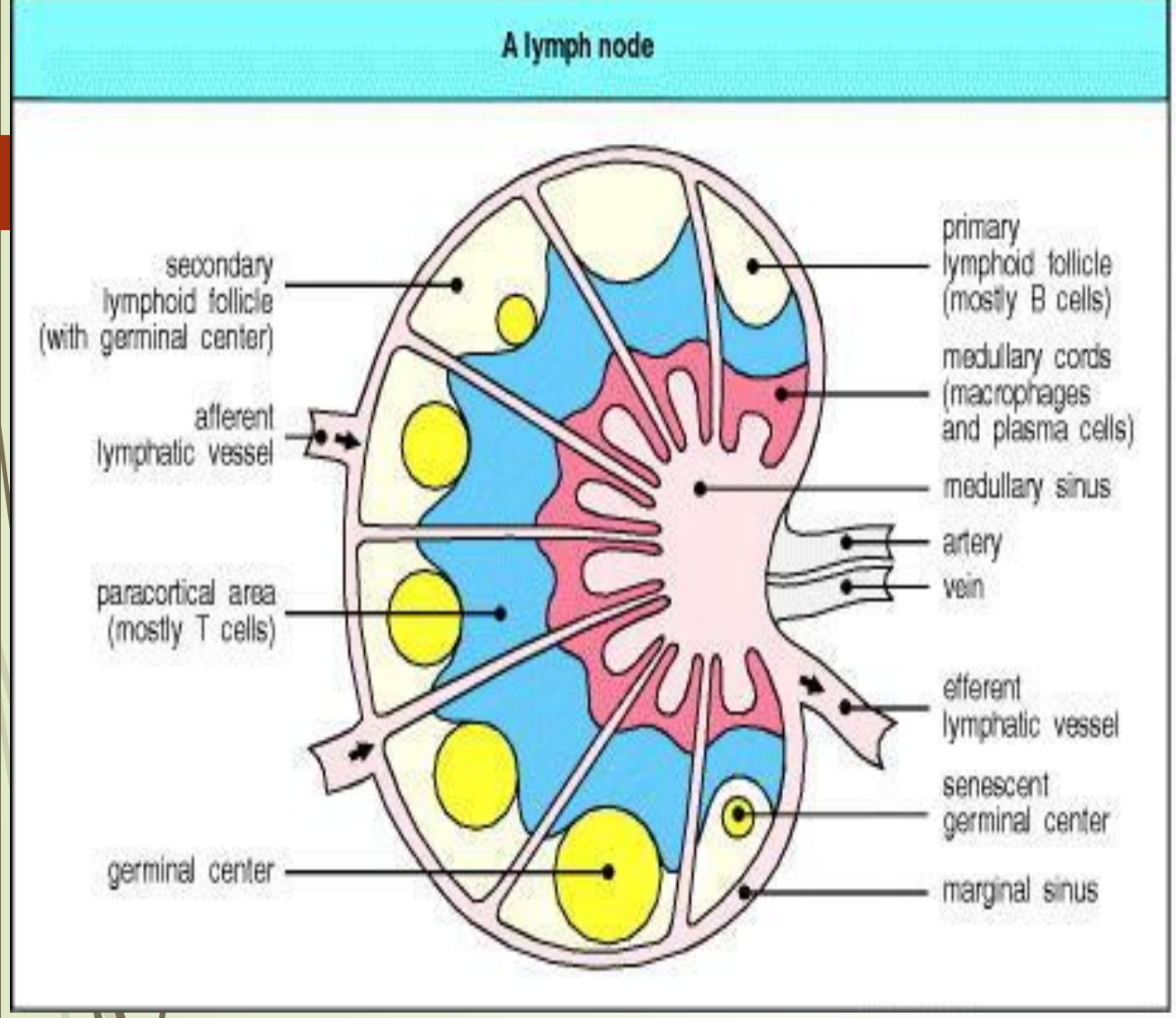
Natural killer (NK) cells

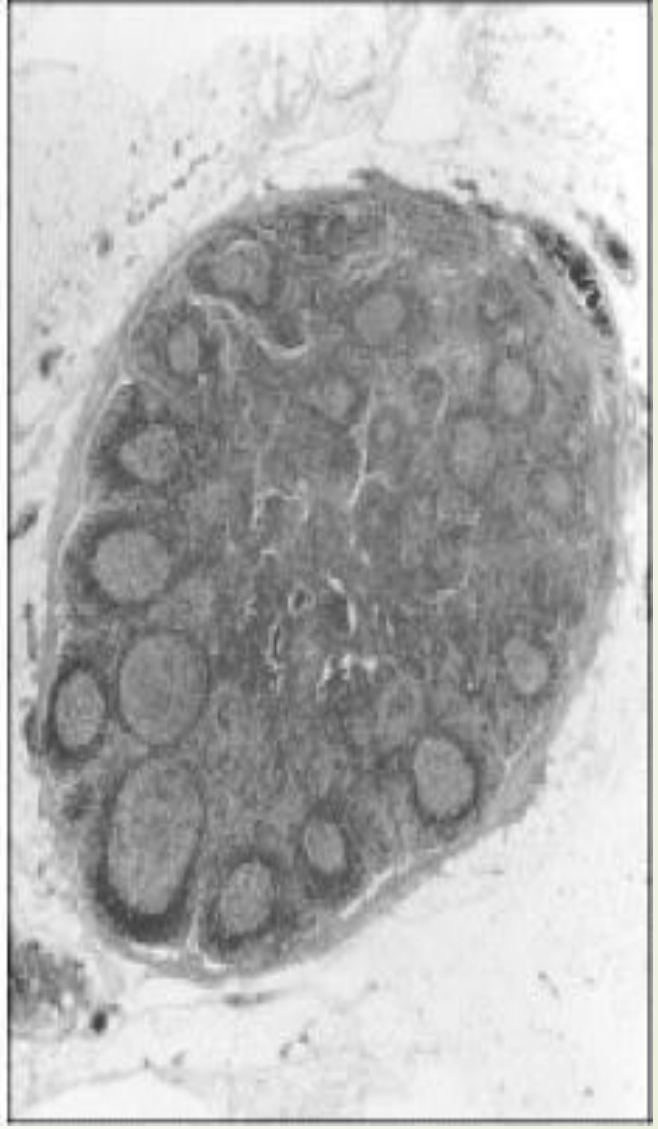
These are large granular lymphocyte-like cells with important functions in innate immunity.

Although lacking antigen-specific receptors, they can detect and attack certain virus-infected cells.

Lymphoid organs can be divided broadly into central or primary lymphoid organs, where lymphocytes are generated, and peripheral or secondary lymphoid organs, where adaptive immune responses are initiated and where lymphocytes are maintained. The central lymphoid organs are the bone marrow and the thymus, a large organ in the upper chest; the location of the thymus, and of the other lymphoid organs,

Both B and T lymphocytes originate in the bone marrow but only B lymphocytes mature there; T lymphocytes migrate to the thymus to undergo their maturation. Thus B lymphocytes are so-called because they are bone marrow derived, and T lymphocytes because they are thymus derived. Once they have completed their maturation, both types of lymphocyte enter the bloodstream, from which they migrate to the peripheral lymphoid organs.





Organization of a lymph node. As shown in the diagram on the left, a lymph node consists of an outermost cortex and an inner medulla. The cortex is composed of an outer cortex of B cells organized into lymphoid follicles, and deep, or paracortical, area

The peripheral lymphoid organs are specialized to trap antigen, to allow the initiation of adaptive immune responses, and to provide signals that sustain recirculating lymphocytes The lymph nodes are highly organized lymphoid structures located at the points of convergence of vessels of the lymphatic system, an extensive system of vessels that collects extracellular fluid from the tissues and returns it to the blood. This extracellular fluid is produced continuously by filtration from the blood, and is called lymph. The vessels are lymphatic vessels or lymphatics .

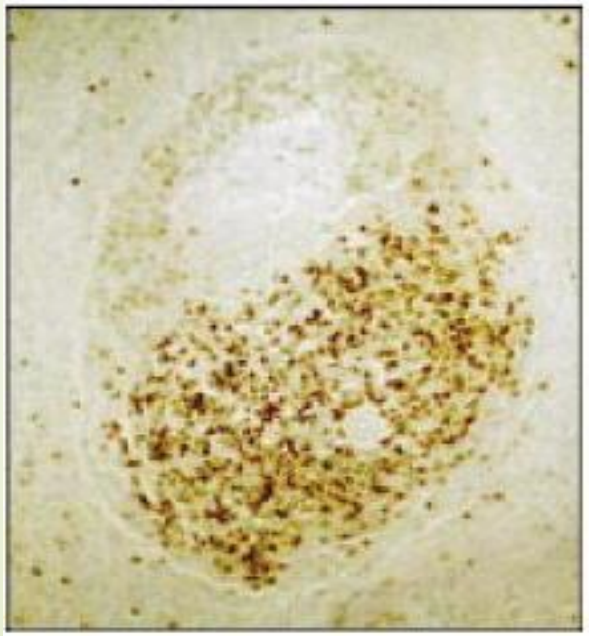
Afferent lymphatic vessels drain fluid from the tissues and also carry antigen-bearing cells and antigens from infected tissues to the lymph nodes, where they are trapped. In the lymph nodes, B lymphocytes are localized in follicles, with T cells more diffusely distributed in surrounding paracortical areas, also referred to as T-cell zones. Some of the B-cell follicles include germinal centers, where B cells are undergoing intense proliferation after encountering their specific antigen and their cooperating T cells.

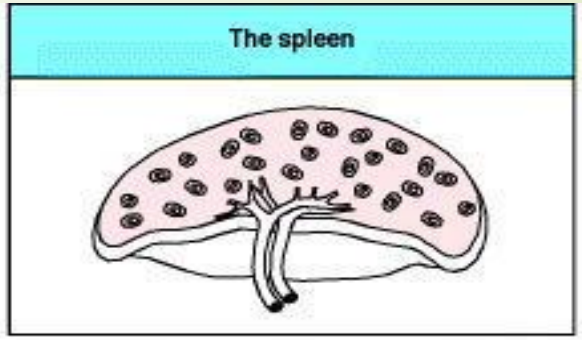
B and T lymphocytes are segregated in a similar fashion in the other peripheral lymphoid tissues, and we shall see that this organization promotes the crucial interactions that occur between B and T cells upon encountering antigen.

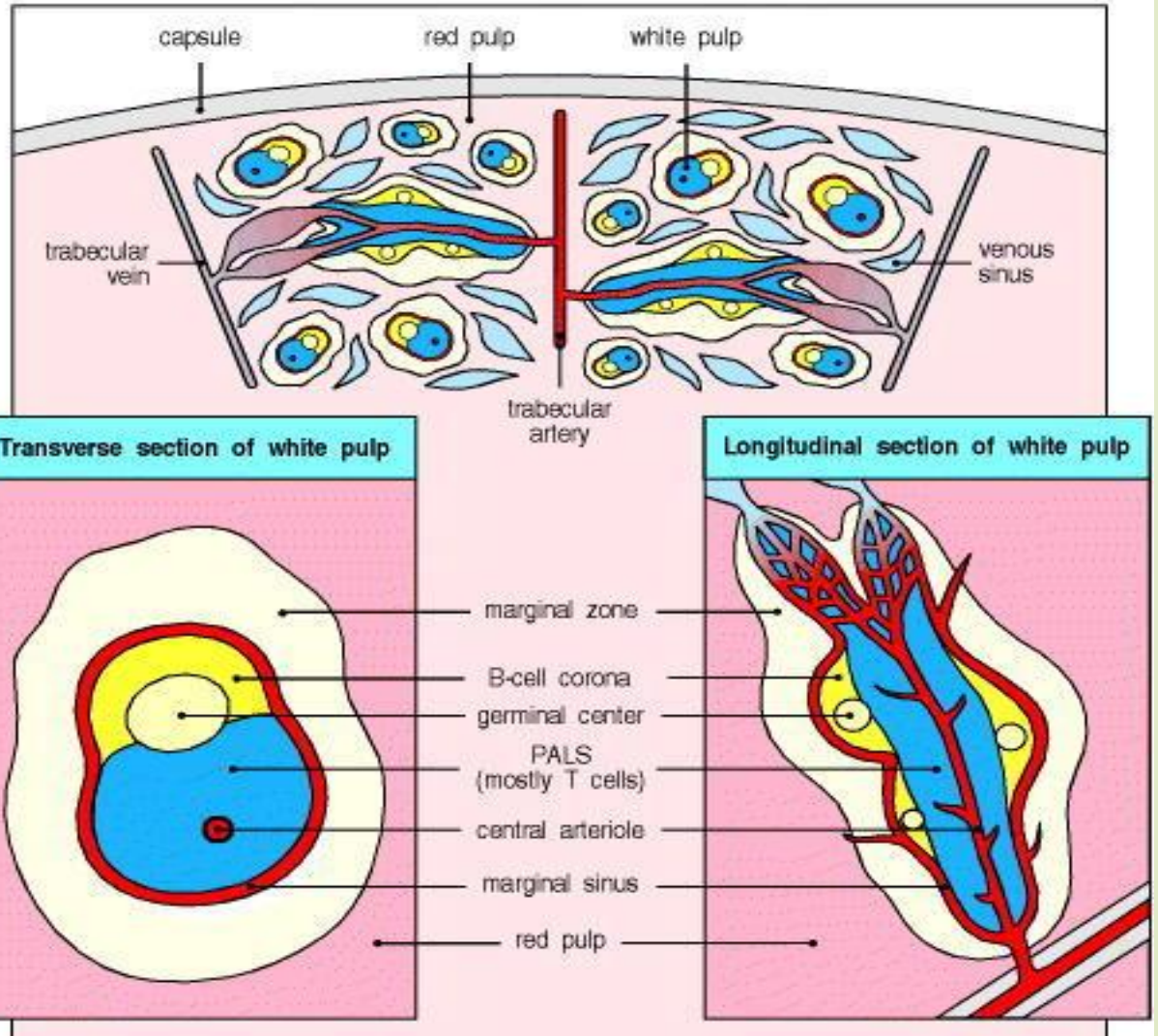
The spleen is a fist-sized organ just behind the stomach that collects antigen from the blood. It also collects and disposes of senescent red blood cells. The bulk of the spleen is composed of red pulp, which is the site of red blood cell disposal. The lymphocytes surround the arterioles entering the organ, forming areas of white pulp, the inner region of which is divided into a periarteriolar lymphoid sheath (PALS), containing mainly T cells, and a flanking B-cell corona.

Organization of the lymphoid tissues of the spleen

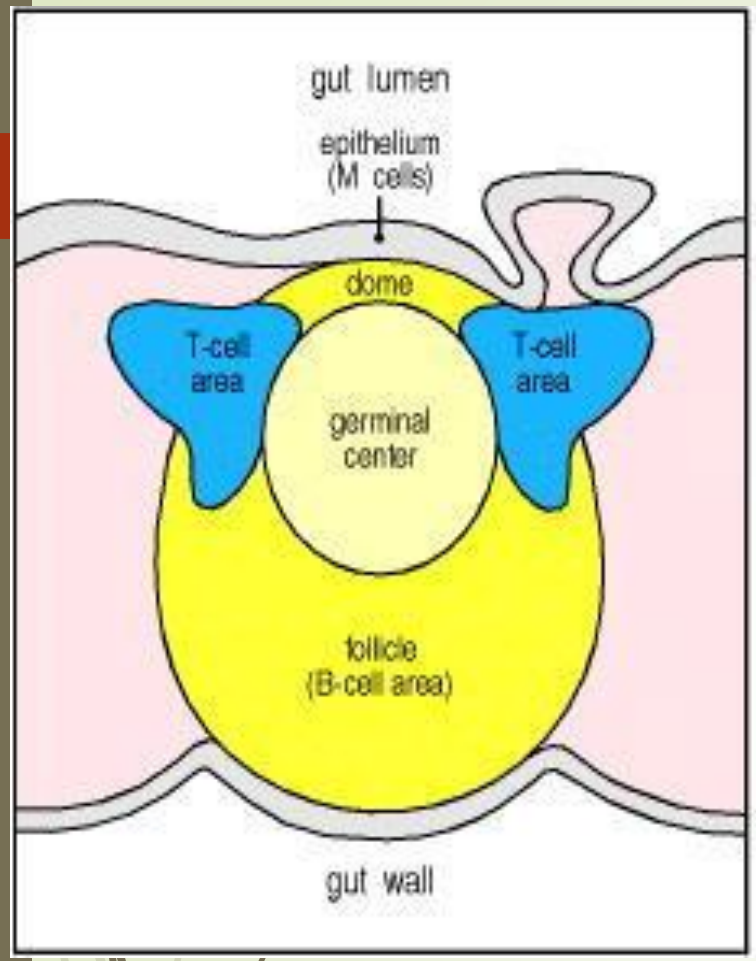
The schematic at top right shows that the spleen consists of red pulp (pink areas in the top panel), which is a site of red blood cell destruction,

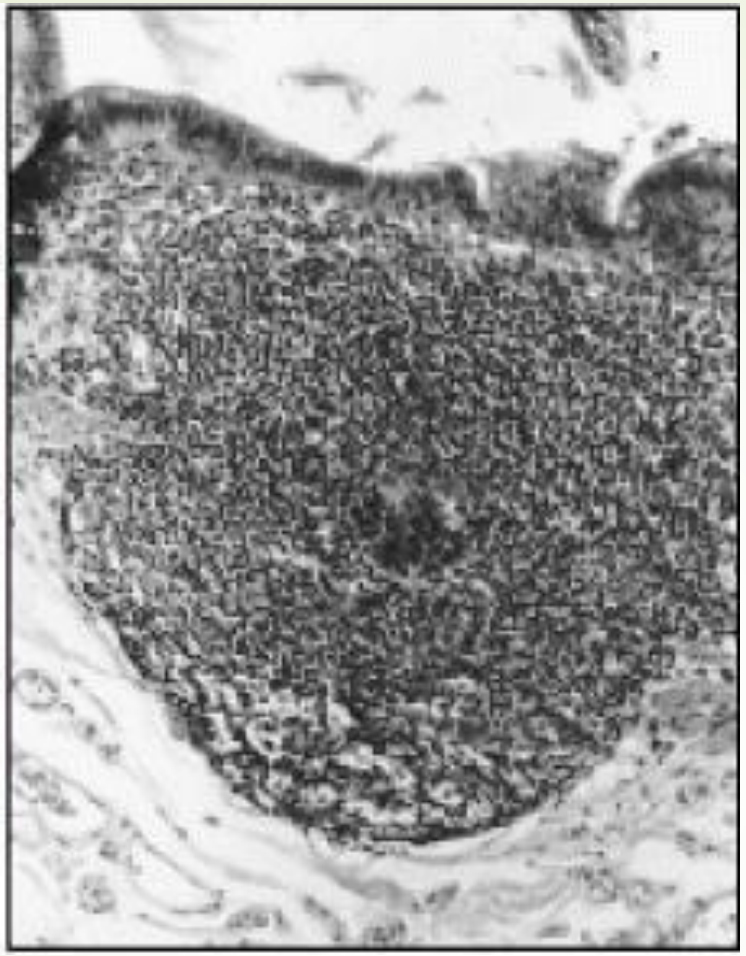






The gut-associated lymphoid tissues (GALT), which include the tonsils, adenoids, and appendix, and specialized structures called Peyer's patches in the small intestine, collect antigen from the epithelial surfaces of the gastrointestinal tract. In Peyer's patches, which are the most important and highly organized of these tissues, the antigen is collected by specialized epithelial cells called multi-fenestrated or M cells. The lymphocytes form a follicle consisting of a large central dome of B lymphocytes surrounded by smaller numbers of T lymphocytes . Similar but more diffuse aggregates of lymphocytes protect the respiratory epithelium, where they are known as bronchial-associated lymphoid tissue (BALT), and other mucosa, where they are known simply as mucosal-associated lymphoid tissue (MALT). Collectively, the mucosal immune system is estimated to contain as many lymphocytes as all the rest of the body, and they form a specialized set of cells obeying somewhat different rules.





Organization of typical gut-associated lymphoid tissue

As the diagram on the left shows, the bulk of the tissue is B cells, organized in a large and highly active domed follicle. T cells occupy the areas between follicles. The antigen enters across a specialized epithelium made up of so-called M cells. Although this tissue looks very different from other lymphoid organs, the basic divisions are maintained. The light micrograph shows a section through the gut wall. The dome of gut-associated lymphoid tissue can be seen lying beneath the epithelial tissues.

spleen

The spleen is an organ in the upper left side of the peritoneal cavity containing a red pulp, involved in removing senescent blood cells, and a white pulp of lymphoid cells that respond to antigens delivered to the spleen by the blood.

spleen, and mucosal-associated lymphoid tissues all share the same basic architecture. Each of these tissues operates on the same principle, trapping antigen from sites of infection and presenting it to migratory small lymphocytes, thus inducing adaptive immune responses. The peripheral lymphoid tissues also provide sustaining signals to the lymphocytes that do not encounter their specific antigen, so that they continue to survive and recirculate until they encounter their specific antigen. This is important in maintaining the correct numbers of circulating T and B lymphocytes, and ensures that only those lymphocytes with the potential to respond to foreign antigen are sustained.

Lymphocytes circulate between blood and lymph

Small B and T lymphocytes that have matured in the bone marrow and thymus but have not yet encountered antigen are referred to as naive lymphocytes. These cells circulate continually from the blood into the peripheral lymphoid tissues, which they enter by squeezing between the cells of capillary walls.

They are then returned to the blood via the lymphatic vessels or, in the case of the spleen, return directly to the blood. In the event of an infection, lymphocytes that recognize the infectious agent are arrested in the lymphoid tissue, where they proliferate and differentiate into effector cells capable of combating the infection.

When an infection occurs in the periphery, for example, large amounts of antigen are taken up by dendritic cells which then travel from the site of infection through the afferent lymphatic vessels into the draining lymph nodes . In the lymph nodes, these cells display the antigen to recirculating T lymphocytes, which they also help to activate. B cells that encounter antigen as they migrate through the lymph node are also arrested and activated, with the help of some of the activated T cells. Once the antigen-specific lymphocytes have undergone a period of proliferation and differentiation, they leave the lymph nodes as effector cells through the efferent lymphatic vessel ..

Because they are involved in initiating adaptive immune responses, the peripheral lymphoid tissues are not static structures but vary quite dramatically depending upon whether or not infection is present. The diffuse mucosal lymphoid tissues may appear in response to infection and then disappear, whereas the architecture of the organized tissues changes in a more defined way during an infection. For example, the B-cell follicles of the lymph nodes expand as B lymphocytes proliferate to form germinal centers and the entire lymph node enlarges, a phenomenon familiarly known as swollen glands.