Hematology Introduction

Organization of blood and blood forming organs

What is hematology?

- Hematology is the study of blood which is composed of plasma (~55%), and the formed elements which are:
  - The erythrocytes (RBCs) (~45%)
    - Contain hemoglobin
    - Function in the transport of O_2 and CO_2
  - The Leukocytes (WBCs) and platlets (thrombocytes) (~1%)
    - Leukocytes are involved in the body's defense against the invasion of foreign antigens.
    - Platlets are involved in hemostasis which forms a barrier to limit blood loss at an injured site.

What is hematology?

- Hematology is primarily a study of the formed cellular elements.
- Alterations in the formed elements in the blood are usually a result of disease rather than being the primary cause of disease.
  - In fact, variations in the formed elements in the blood are often the first sign that disease is occurring in the body.
  - The changes caused by disease may be detected by lab tests that measure deviations of the blood constituents from the normal values. These lab test may include:

What is hematology?

- RBC count
- WBC count
- Platlet count
- Hematocrit (packed cell volume)
- Mean corpuscular volume (MCV)
- Mean corpuscular hemoglobin concentration (MCHC)

- Under normal conditions the production, release, and survival of blood cells is a highly regulated process. Quantitative and/or qualitative hematologic abnormalities may result when there is an imbalance between cell production, release, and/or survival.

What is hematology?

- Age, sex, and geographic location are involved in physiologic changes in normal values of the formed cellular elements
- Pathologic changes in the values of the formed cellular elements occur with disease or injury.
- Normal values for a group are determined by calculating the mean for healthy individuals of the group and reporting the normal range as the mean +/- 2 standard deviations

What is hematology?

- Hematopoiesis is a term describing the formation and development of blood cells.
  - Cells of the blood are constantly being lost or destroyed. Thus, to maintain homeostasis, the system must have the capacity for self renewal. This system involves:
    - Proliferation of progeny stem cells
    - Differentiation and maturation of the stem cells into the functional cellular elements.
    - In normal adults, the proliferation, differentiation, and maturation of the hematopoietic cells (RBCs, WBCs, and platlets) is limited to the bone marrow and the widespread lymphatic system and only mature cells are released into the peripheral blood.

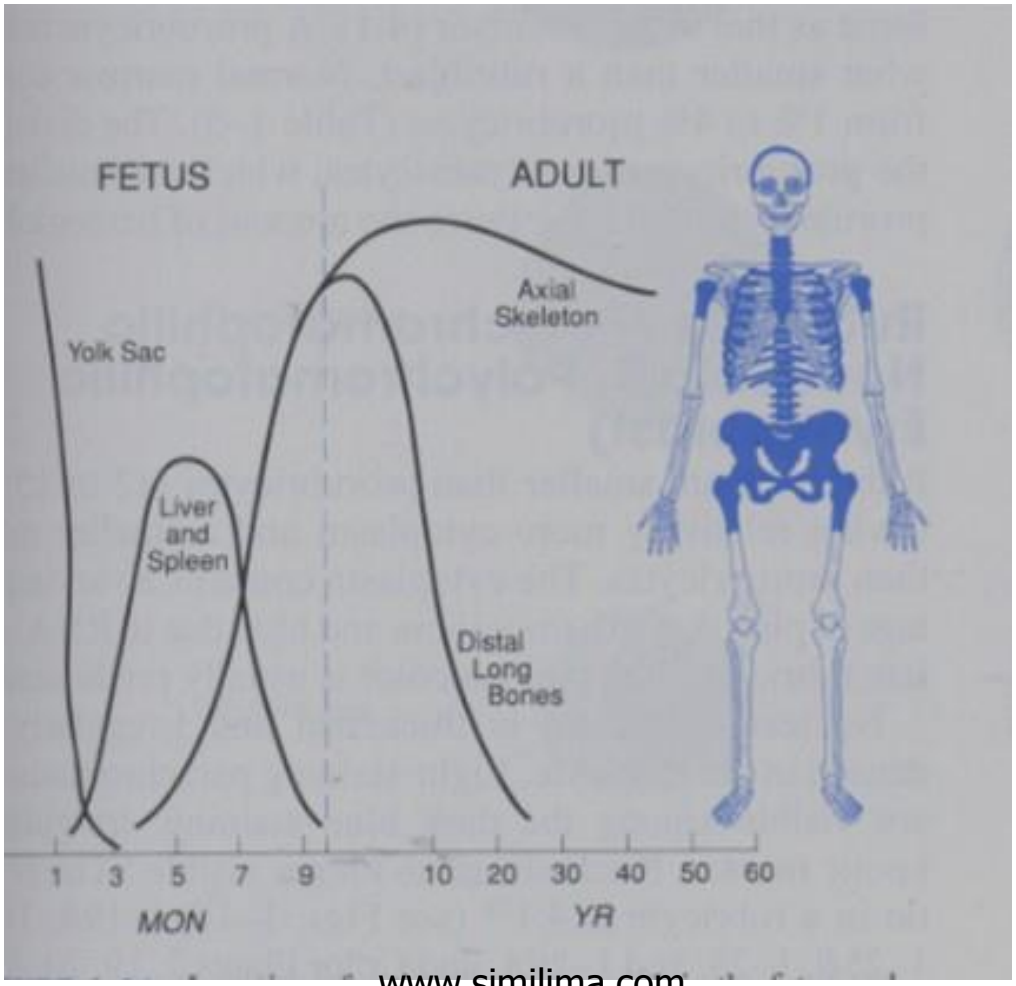
What is hematology?

- Hematopoiesis begins as early as the nineteenth day after fertilization in the yolk sac of the embryo
  - Only erythrocytes are made
  - The RBCs contain unique fetal hemoglobins
- At about 6 weeks of gestation, yolk sac production of erythrocytes decreases and production of RBCs in the human embryo itself begins.

What is hematology?

- The fetal liver becomes the chief site of blood cell production.
  - Erythrocytes are produced
  - The beginnings of leukocyte and thrombocyte production occurs
- The spleen, kidney, thymus, and lymph nodes serve as minor sites of blood cell production.
- The lymph nodes will continue as an important site of lymphopoiesis (production of lymphocytes) throughout life, but blood production in the other areas decreases and finally ceases as the bone marrow becomes the primary site of hematopoiesis at about 6 months of gestation and continues throughout life.
  - When the bone marrow becomes the chief site of hematopoiesis leukocyte and thrombocyte production become more prominent.

Hematopoiesis



What is hematology?

- Hematopoiesis in the bone marrow is called medullary hematopoiesis
- Hematopoiesis in areas other then the bone marrow is called extramedullary hematopoiesis
  - Extramedullary hematopoiesis may occur in fetal hematopoietic tissue (liver and spleen) of an adult when the bone marrow cannot meet the physiologic needs of the tissues. This can lead to hepatomegaly and/or splenomegaly (increase in size of the liver or spleen because of increased functions in the organs).
- Hematopoietic tissue includes tissues involved in the proliferation, maturation, and destruction of blood cells

What is hematology?

- The mononuclear phagocytic system (also called the reticular endothelial system or RES) is involved in cellular destruction and it includes:
  - Circulating blood monocytes
  - Fixed macrophages in the bone marrow, liver, spleen, and lymph nodes
  - Free macrophages
    - These cells are involved in:
      - Engulfing particulate matter
      - Processing of antigens for lymphocyte presentation
      - Removal of damaged or senescent cells

What is hematology?

- Spleen – contains the largest collection of lymphocytes and mononuclear phagocytes in the body. The spleen functions in:
  - Filtering and destruction of senescent (aged) or damaged RBS – also called culling
  - Removal of particles (are found in some types of anemia) from RBC membranes – also called pitting – this causes a decrease in the surface to volume ratio of the RBC resulting in spherocytes (more on this later)
  - Enforcing close contact of blood borne antigens with lymphocytes and phagocytic cells – this is more important in children particularly in protection of the host from infections due to enveloped organisms

What is hematology?

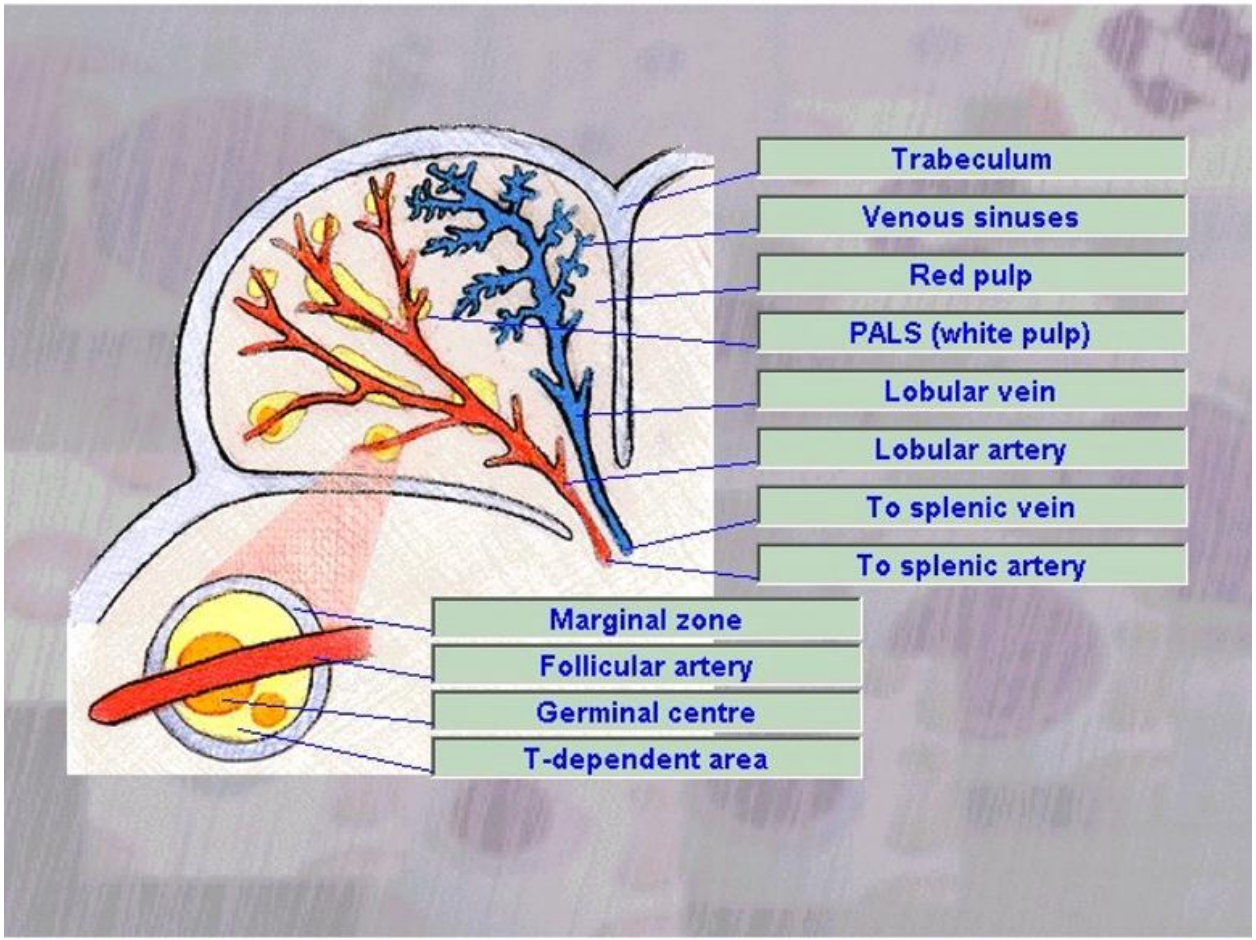
- Sequestering 1/3 of the platlet mass – in massive splenomegaly this can lead to peripheral thrombocytopenia (decrease in platlets in the blood)
- After a splenectomy (removal of the spleen), RBC inclusions and abnormal RBC shapes are seen. Culling is taken over by the liver which is less effective in performing all of the splenic functions
- Hypersplenism (splenomegaly) – in a number of conditions the spleen may become enlarged and through an exaggeration of its normal functions of filtering, and destruction and sequestering, it may cause anemia (may be caused by decreased RBCs), leukopenia (decreased WBCs), or thrombocytopenia or combinations of these cytopenias. When all three cell types are decreased this is called pancytopenia. There are two types of hypersplenism:

What is hematology?

- Primary – no underlying disease has been identified
- Secondary – caused by an underlying disorder such as:
  - Inflammatory diseases
  - Infectious diseases
  - Blood disorders that cause compensatory or workload hypertrophy of the organ such as:

    Abnormal blood cells, antibody coated blood cells, hereditary spherocytosis, idiopathic throbocytopenic purpura (ITP)
  - The effects of these are relieved by splenectomy

Structure of the spleen



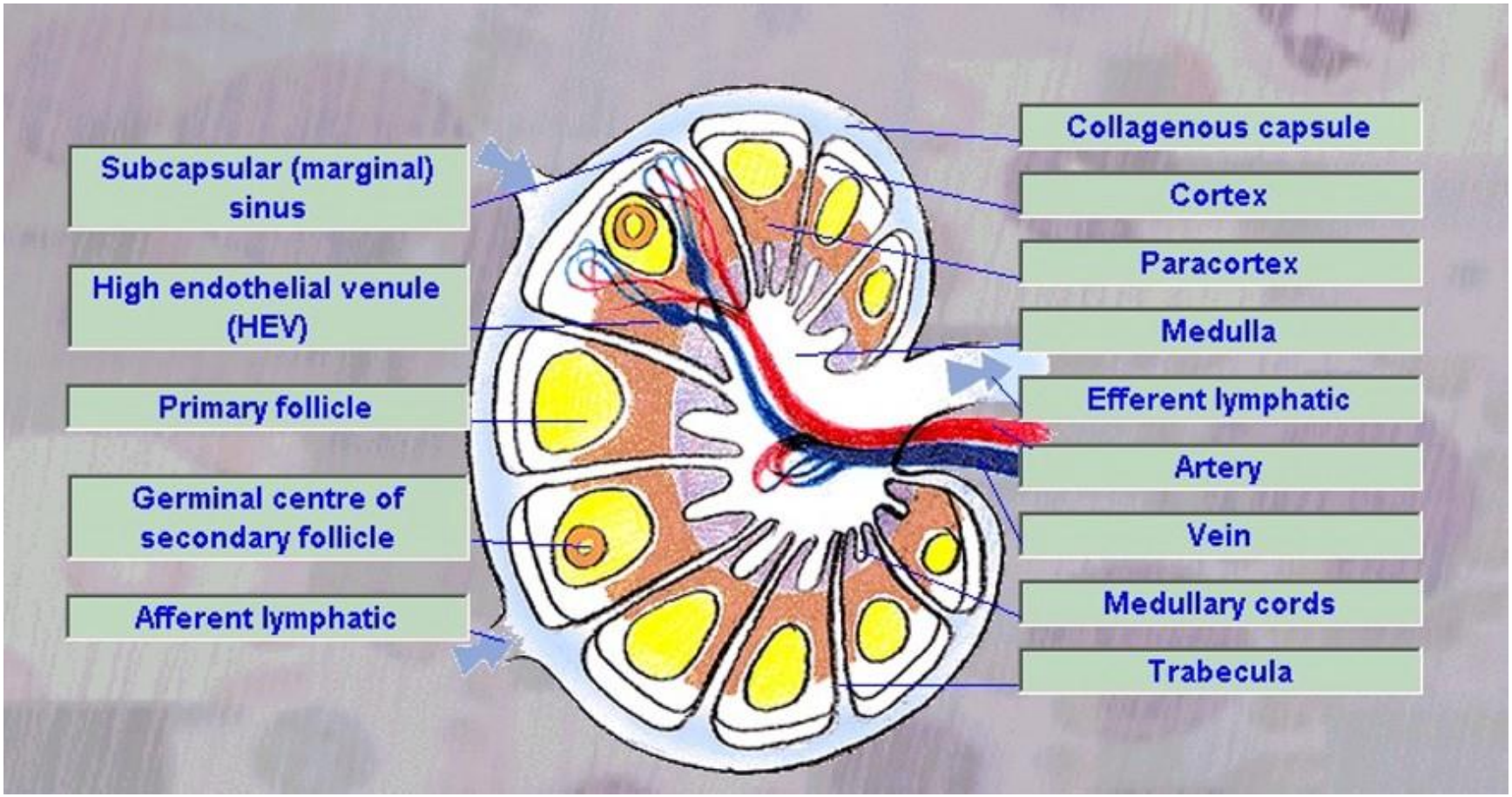
What is hematology?

- Lymph nodes – the lymphatic system is composed of lymph nodes and lymphatic vessels that drain into the left and right lymphatic duct. Lymph is formed from blood fluid that escapes into the connective tissue.
  - Lymph nodes are composed of lymphocytes, macrophages, and a reticular network.
  - They act as filters to remove foreign particles by phagocytic cells
  - As antigens pass through the lymph nodes, they come into contact with and stimulate immunocompetent lymphocytes to proliferate and differentiate into effector cells.

What is hematology?

- The structure of the lymph node consists of :
  - An inner area called the medulla which contains plasma cells
  - An outer area called the cortex which contains follicles with B lymphocytes surrounded by T lymphocytes and macrophages

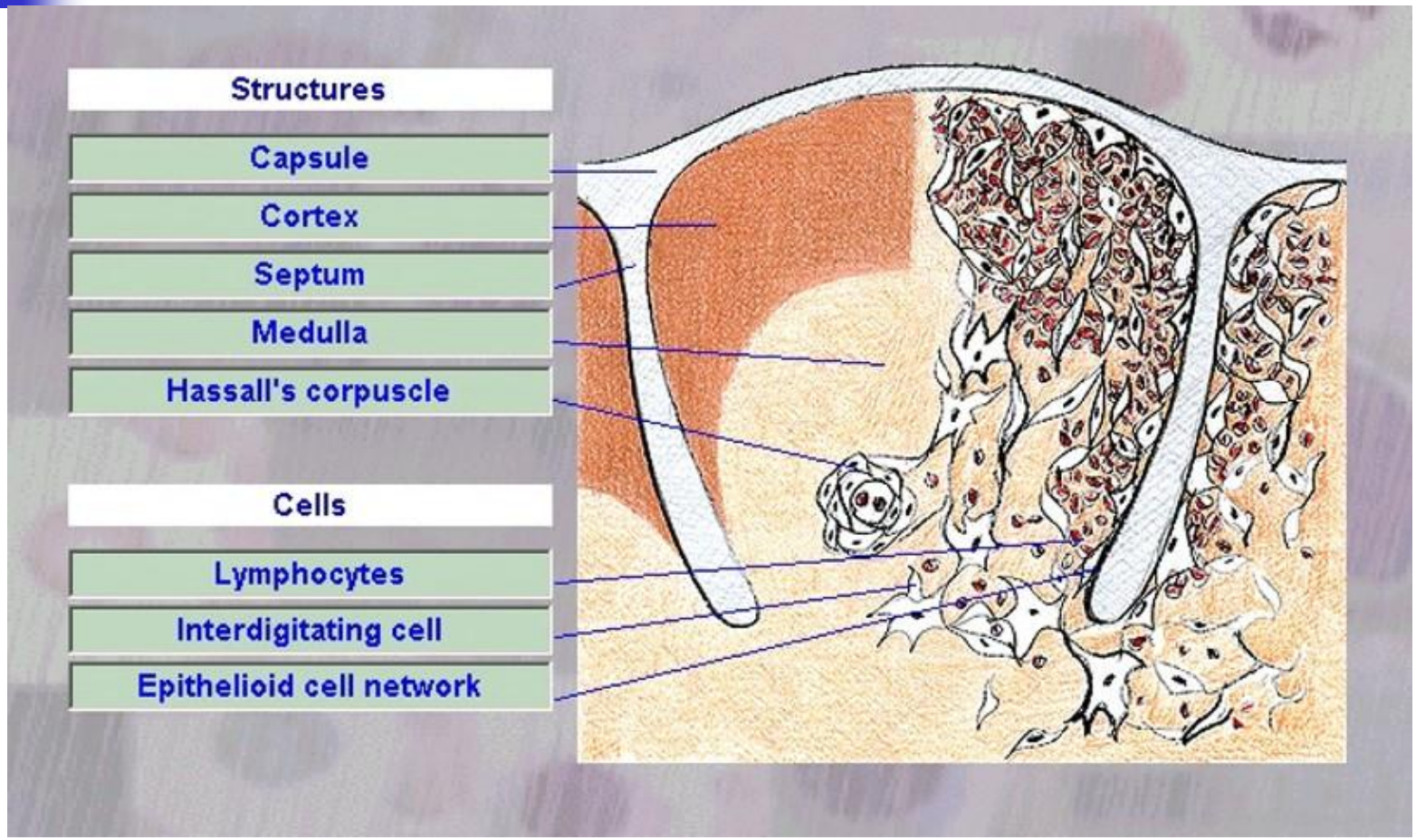
Lymph node structure



What is hematology?

- Thymus – this organ is well developed at birth and increases in size until puberty at which time it starts to decrease in size.
  - It serves as a compartment for the maturation of T lymphocytes into immunocompetent T cells. The hormone thymosin plays a role in this process.
  - The structure of he thymus consists of:
    - An outer area called the cortex which is densely packed with small lymphocytes and macrophages
    - An inner area called the medulla which is less cellular with a few lymphocytes, macrophages, and epithelial cells.

Structure of the thymus



What is hematology?

Bone marrow – is located inside spongy bone

- In a normal adult, ½ of the bone marrow is hematopoietically active (red marrow) and ½ is inactive, fatty marrow (yellow marrow).
- The marrow contains both Erythroid (RBC) and leukocyte (WBC) precursors as well as platlet precursors.
- Early in life most of the marrow is red marrow and it gradually decreases with age to the adult level of 50%.
- In certain pathologic states the bone marrow can increase its activity to 5-10X its normal rate.
  - When this happens, the bone marrow is said to be hyperplastic because it replaces the yellow marrow with red marrow.

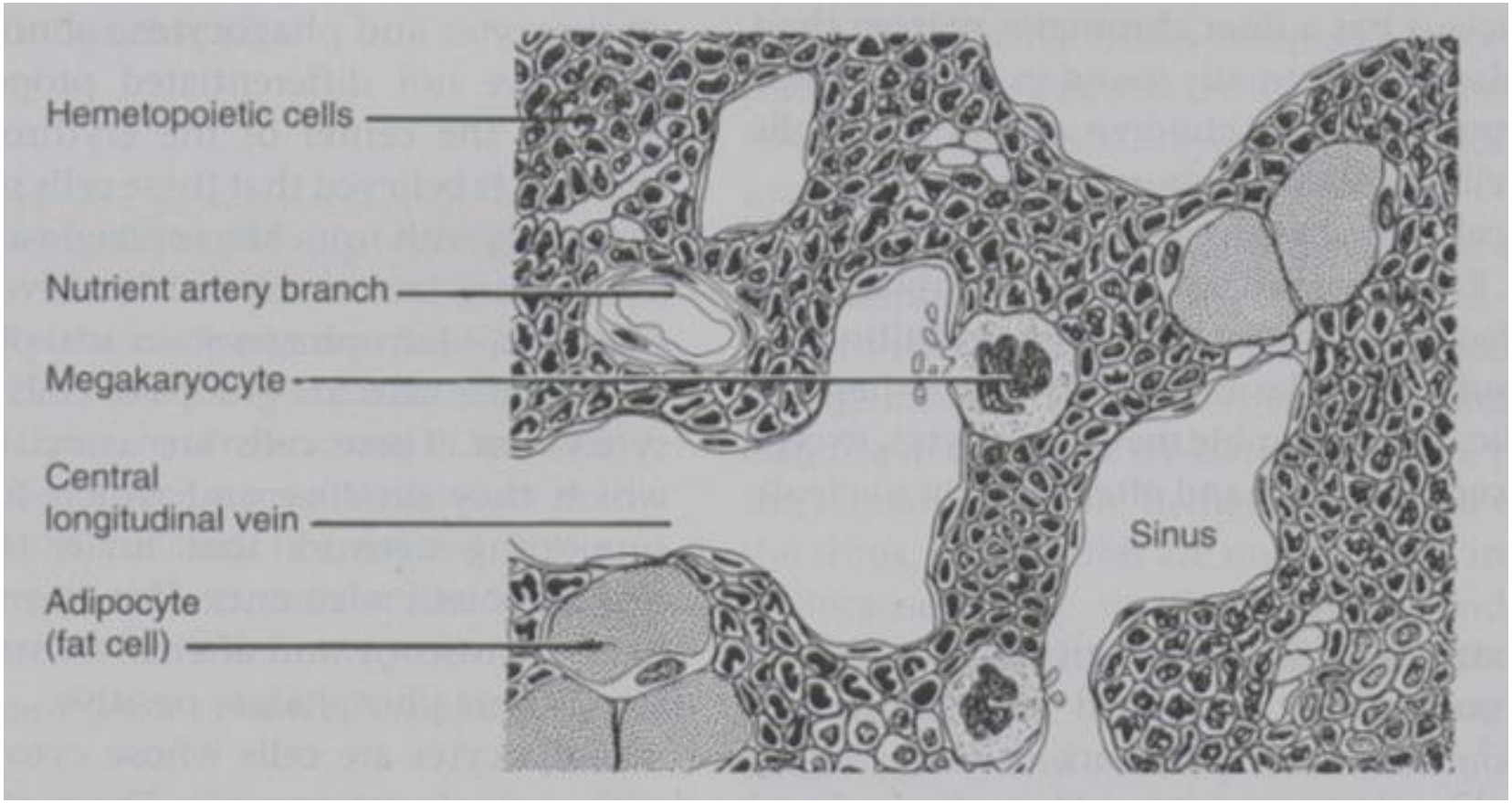
What is hematology?

- This occurs in conditions where there is increased or ineffective hematopoiesis.
- The degree to which the the bone marrow becomes hyperplastic is related to the severity and duration of the pathologic state.
- Pathologic states that cause this include:
  - Acute blood loss in which there is a temporary replacement of the yellow marrow
  - Severe chronic anemia – erythropoiesis (RBC production) may increase to the extent that the marrow starts to erode the bone itself.
  - Malignant disease – both normal red marrow and fatty marrow may be replaced by proliferating abnormal cells.

What is hematology?

- The hematopoietic tissue may also become inactive or hypoplastic. This may be due to:
  - Chemicals
  - Genetics
  - Myeloproliferative disease that replaces hematopoietic tissue with fiberous tissue

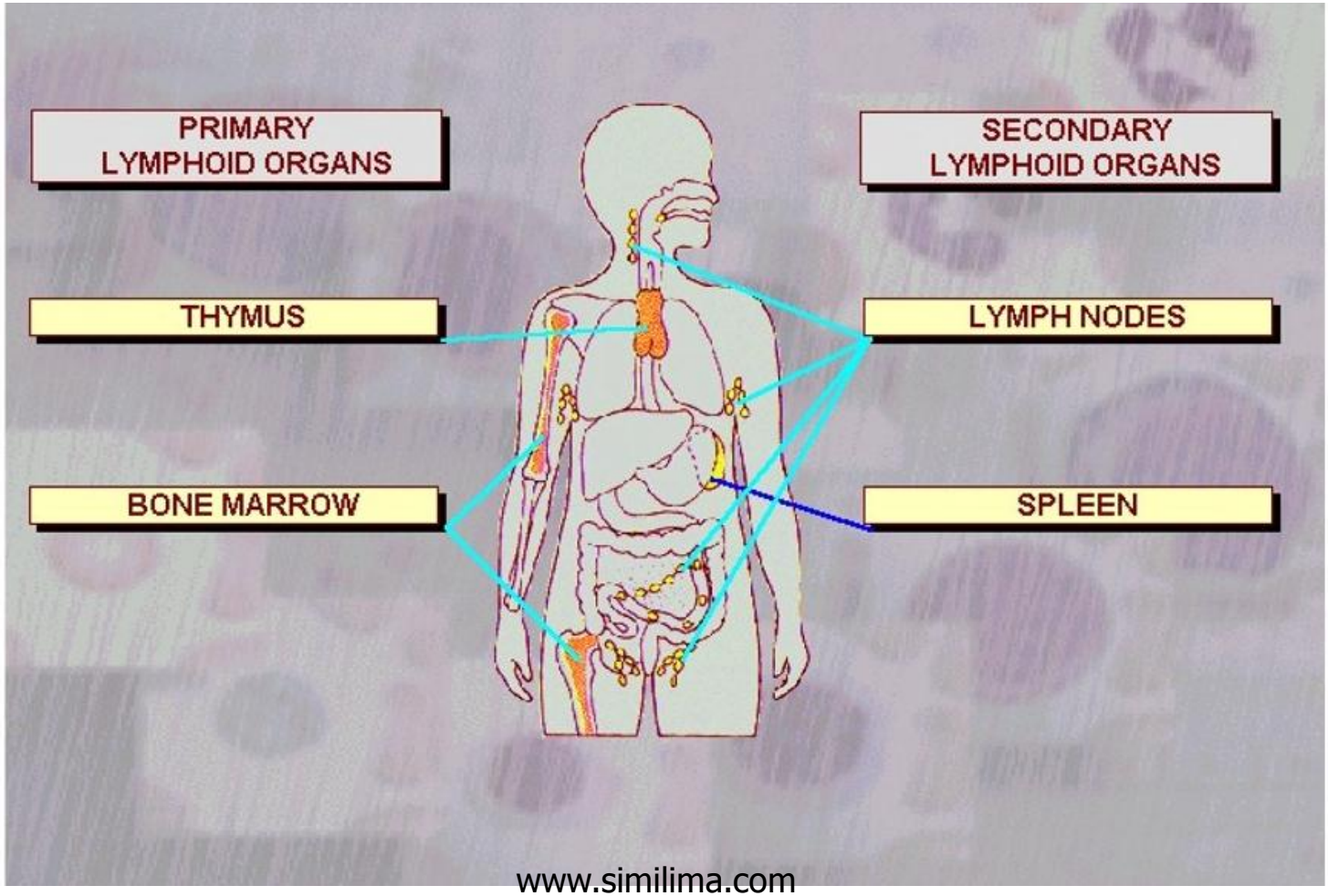
Structure of bone marrow



What is hematology?

- Liver – contains phagocytic cells known as Kupffer cells that act as a filter for damaged or aged cells in a manner similar to, but less efficient than the phagocytic cells in the spleen.
  - If the bone marrow cannot keep up with the physiologic demand for blood cells, the liver may resume the production of blood cells that it began during fetal life

Summary of blood forming organs



Derivation of blood cells

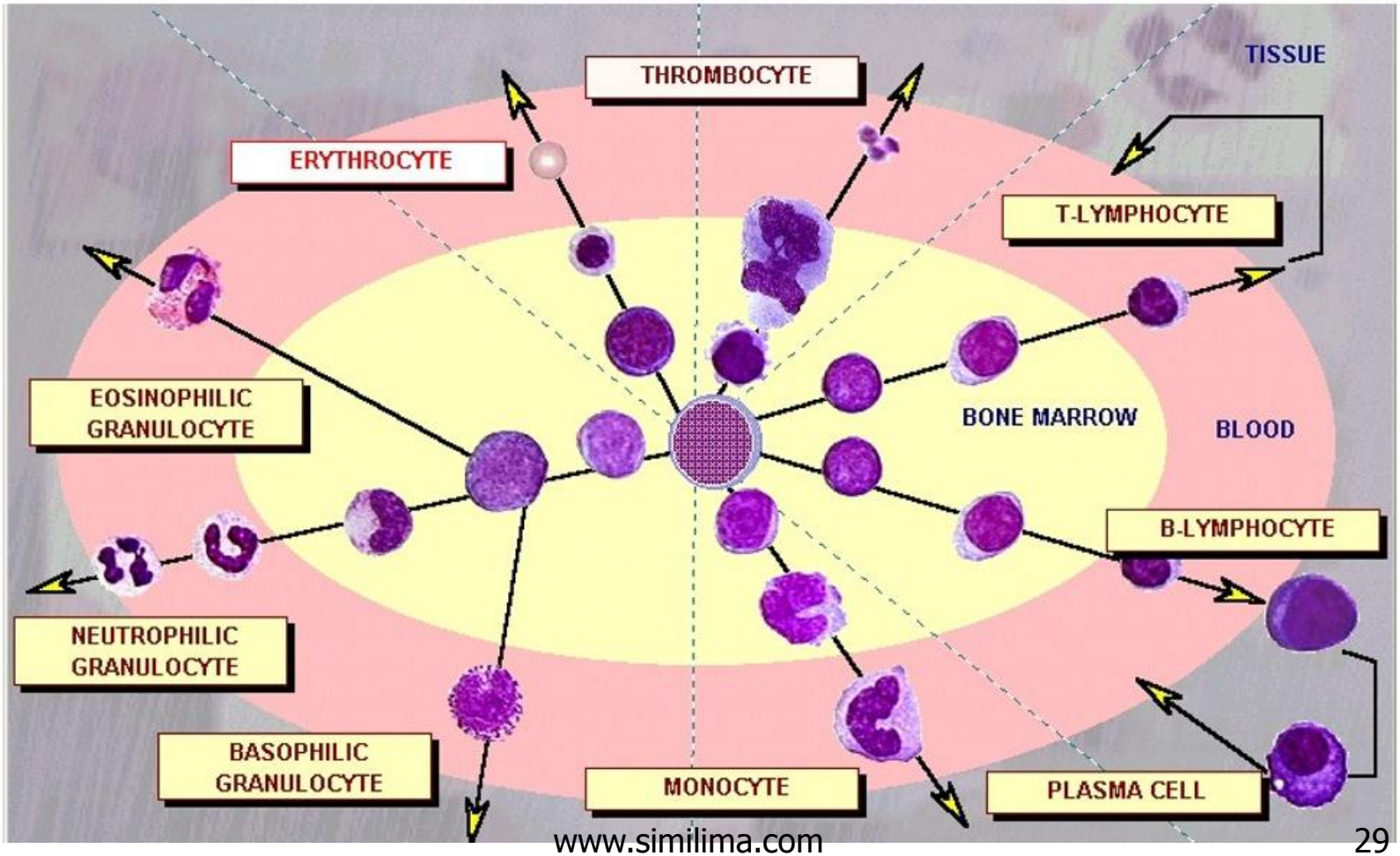
- Mature blood cells have a limited life span and with the exception of lymphocytes, are incapable of self-renewal.
  - Replacement of peripheral hematopoietic cells is a function of the pluripotential (totipotential) stem cells found in the bone marrow
    - Pluripotential stem cells can differentiate into all of the distinct cell lines with specific functions and they are able to regenerate themselves.
    - The pluripotential stem cells provide the cellular reserve for the stem cells that are committed to a specific cell line.

Derivation of blood cells

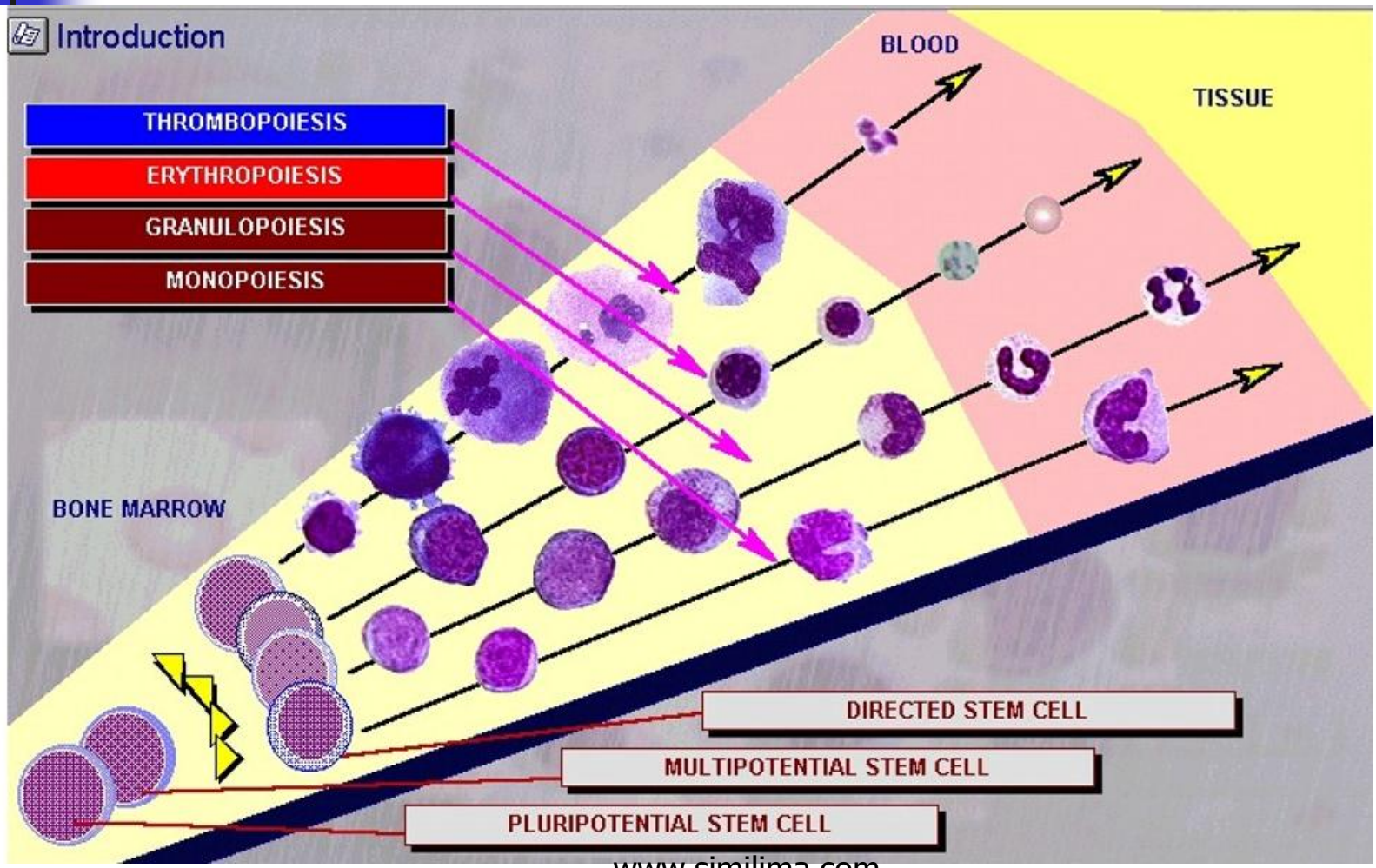
- The committed lymphoid stem cells will be involved in lymphopoiesis to produce lymphocytes
- The committed myeloid stem cell can differentiate into any of the other hematopoietic cells including erythrocytes, neutrophils, eosinophils, basophils, monocytes, macrophages, and platlets.

- Hematopoietic cells can be divided into three cellular compartments based on maturity:
  - Pluripotential stem cell capable of self-renewal and differentiation into all blood cell lines.
  - Committed proginator stem cells destined to develop into distinct cell lines
  - Mature cells with specialized functions

Hematopoiesis summary



Hematopoiesis



Hematopoiesis