



Tumors of hematopoietic and melanopoietic tissue.

Tumors of hematopoietic and melanopoietic tissue

I. Microspecimens:

№ 145. Solitary plasmacytoma of bone. (H-E stain). Indications:

1. Polymorphic tumoral cells of plasmocytic origin.
2. Tumoral stroma with blood vessels.
3. Hemorrhagic foci.

The biopsy was taken from a solitary tumoral node from the region of the mandible. Microscopically there is a cell mass, composed predominantly of tumoral plasma cells, most of them similar to normal plasma cells, with eccentric nucleus, hyperchrome, chromatin arranged "in wheel spokes", rich cytoplasm, basophilic, with perinuclear halo, absent nucleoli, larger plasmoblasts are observed, the nucleus with a well-defined nucleoli, the tumor stroma is poor, there are foci of plasmorrhagia and hemorrhage.

Solitary plasmacytoma (localized) and multiple myeloma are the main diseases in the group of plasma cell neoplasms, the morphological substrate of which is the excessive, neoplastic proliferation of plasma cells. The lesions begin in 95% of cases in the medullary cavity of the bones and gradually erode the spongy bone tissue, and later the compact one, causing pathological fractures. In solitary plasmacytoma, a single bone is affected, and in multiple myeloma the lesions are multifocal, involving bones with active hematopoiesis: spine, ribs, skull, pelvic bones and a. Solitary plasmacytoma is an early stage of multiple myeloma, progressing within 5-10 years from monoosal to polyosal lesions. The affected bones take on a "moth-eaten" appearance, with defects having a diameter of 1-4 cm. The cellularity of the bone marrow is increased, over 30% being the plasma cells. Tumor cells secrete an immunoglobulin, usually IgG (monoclonal secretion) or light chains of immunoglobulins, which are excreted in the urine - the Bence-Jonck protein. Very important is myelomatous nephropathy, which is manifested by deposits of protein cylinders in the distal tubules and collecting ducts, necrosis of the epithelium of the twisted tubules, metastatic calcinosis, bacterial pyelonephritis, AL amyloidosis. In the terminal stage, the multiple plasmacytoma / myeloma acquires a leukemic appearance. Complications: bone fractures, anemia. Causes of death: renal failure, infectious complications.

№ 58. Lymphatic node in Hodgkin's disease. (H-E stain). Indications:

1. Giant polynuclear Reed-Sternberg cells.
2. Lymphocytes.
3. Bundles of newly formed connective tissue.

The microspecimen reveals tumor nodules, consisting of different cellular elements: 1) giant Reed-Sternberg cells, up to 45 μ in diameter, binucleated, with 2 nuclei arranged symmetrically as in a mirror, with prominent nucleoli with a clear perinucleolar halo "owl eyes", 2) large mononuclear Hodgkin cells, 3) lacunar cells (mononuclear cells, with multilobate nucleus, multiple nucleoli and abundant, pale cytoplasm), 4) non-tumoral inflammatory infiltrate with lymphocytes, histiocytes, eosinophils, neutrophils and plasmocytes in various proportions; tumor nodules are separated by collagen bundles of different thickness.

LH is a neoplasm that develops from B lymphocytes in germinal centers. It constitutes on average ~ 30% of the total number of lymphomas. There are 4 classic histological forms (subtypes) of LH: 1) with nodular sclerosis, 2) with mixed cellularity, 3) with lymphocyte predominance and 4) with lymphocyte depletion. The most common are the first 2 - with nodular sclerosis ~ 65-75% and with mixed cellularity ~ 25%. The morphological substrate consists in the proliferation of pathognomonic tumor cells - Reed-Sternberg (RS) cells and their derivatives: lacunar cells, which are a particular form of RS cells and Hodgkin cells, which are the precursors of RS cells. These tumor cells represent only 1-5% of the total cell mass, the other cellular elements are of reactive, inflammatory origin. Immunohistochemical studies have demonstrated with certainty the B lymphocyte origin of RS cells. Although the number of specific tumor cells is so small, the definite diagnosis of LH is established only on the basis of the identification of RS cells or their variants in the biopsy or necropsy material.

No OP 25. Intramucosal nevus of the oral cavity (H-E stain). Indications:

1. Superficial epithelium.
2. Nests of nevus cells arranged subepithelially.
3. Fibrous bands.

Microscopically, it is characterized by a proliferation of nevus cells arranged subepithelially, in the form of nests separated by fibrous bands. Tumor cell nests can be arranged in the chorion (intramucosal nevus), at the junction with the epithelium (junctional nevus) or located both in the chorion and at the junction with the epithelium (compound nevus). Nevic cells are uniform, small, ovoid, with small and uniform nuclei and a moderate amount of eosinophilic cytoplasm, with indistinct cell boundaries. The melanin pigment is brown in color and is present in varying amounts intracytoplasmically or in the adjacent stroma. The junctional and the compound nevus have a tendency to malignant transformation.

Macroscopically, it has different sizes, is flat or slightly prominent, brown, rarely achromatic (white).

The melanocytic nevus is an acquired benign tumor lesion that originates in melanic cells arranged in the basal layer of the Thyndalli epithelium. It is located more frequently in the palate and gums. It occurs with predisposition in women, around the age of 35. As variants of melanocytic env are described: congenital malanocytic nevus (larger than the acquired diameter) and blue nevus (benign proliferation of melanocytic cells, most commonly located in the palate, the cells being fusiform, with high melanin content, deeply located in the lamina propria, which determines the blue color of the tumor - Tyndall effect).

No OP 26. Melanoma of the oral cavity (*H-E stain*). Indications:

1. Ulcerated superficial epithelium.
2. Nests of malignant melanotic cells

In the microspecimen, multiple nests of malignant melanic cells with vertical development are revealed, which extend both in the surface epithelium and in the underlying connective tissue. Malignant cells have variable shape and size, with pronounced cellular and nuclear polymorphism, hyperchromic nuclei, obvious nucleoli, in the cytoplasm deposits of melanin granules.

Macroscopically, they are tumors with inhomogeneous pigmentation, brown, black, blue or red, asymmetrical and with irregular edges.

Melanoma is a malignant neoplasm of melanocytic origin that develops de novo or on the background of a benign melanocytic lesion. It occurs in both sexes, with frequent localization in the hard palate, jaw, as well as the gums, lips or oral mucosa. The microscopic appearance is comparable to that of similar skin lesions, at the level of the oral mucosa there is nodular melanoma, melanoma with superficial extension and lentiginous melanoma of the mucosa. The prognosis of tumors depends on the type of melanoma, the age of the patient (young patients have a better prognosis), but also the deep invasion. Mucosal tumors have a much worse prognosis than skin tumors. It is extremely aggressive, a tumor with a thickness of only a few mm can produce multiple metastases. Lymphogen metastases in regional lymph nodes, and more frequently hematogenously in the liver, lungs, brain and other organs, can be metastases in virtually any region of the body. In most cases the metastases are black due to the melanin content.

II. Macrospecimens:

№ 145. Bone marrow in leukemia.

Longitudinal section of the femoral bone, the osteomedullary tissue is homogeneous, juicy, the division into red and yellow marrow is absent, the adipose tissue in the diaphysis region is replaced by active hematopoietic tissue, the color is gray-yellow, has a purulent appearance ("pious bone marrow").

In leukosis the bone marrow is affected primarily, namely in the marrow the tumor process begins, and the peripheral blood and other organs are involved secondarily. The neoplastic proliferation of a cell series takes place in the spinal cord, which gradually replaces the other components of the hematopoietic tissue, and from the spinal cord leukemic cells enter the blood and infiltrate other organs, primarily the organs / tissues of the lymphoid system, but also the central parenchymal organs. , skin, etc. Microscopically in the marrow is revealed the increase of cellularity, which can reach the level of 100%, the norm being 50% hematopoietic tissue / 50% adipose tissue. These changes in the hematopoietic marrow are observed in both acute leukosis and chronic leukosis in their accelerated phase and blastic crises.

№ 84. Kidney in leukemia.

The kidney is enlarged in size, the capsule is relaxed, the consistency is dense, on the cut section the borders between the layers are absent, have a whitish-gray color, with punctiform hemorrhages. Kidney damage can occur in any form of leukosis and is caused by infiltration of the organ with neoplastic elements from the spinal cord, which is initially located perivascular, and later leukemic infiltrates may become more or less extensive.

Due to this fact and circulatory disorders caused by leukemic infiltration of the vascular walls and increased blood viscosity, dystrophic changes of the renal parenchyma occur, there may be foci of necrosis and hemorrhage.

№ 142. Spleen in CML (chronic myeloid leukemia).

The spleen is considerably enlarged in size, sometimes 20-30 times, the mass reaching a few kg (norm ~ 180 gr), per section reddish-gray color, homogeneous, dense consistency, there may be foci of ischemic infarction and hemorrhage.

Massive splenomegaly, which is revealed in chronic myeloid leukosis is caused by intense leukemic infiltration, diffuse with cells from the myeloid series, predominantly with myelocytes and metamyelocytes; Outbreaks of infarction are caused by increased blood viscosity, which can sometimes lead to leukemic thrombi. Fibrin deposits (perisplenitis), cracks may be deposited on the spleen capsule, it is possible to rupture the capsule with lethal intraperitoneal hemorrhage.

№ 143. Mesenterial lymph node in CLL (chronic lymphoid leukemia).

The lymph nodes are uniformly enlarged in size, dense-elastic consistency, whitish color, form tumor conglomerates, which compress the adjacent organs.

Generalized lymphadenopathy is the predominant clinical-morphological sign of chronic lymphoid leukosis. The lymph nodes are symmetrically enlarged in size, microscopically reveals diffuse infiltration with small mature, uniform lymphocytes, without atypia; foci of proliferation are also observed with larger, mitotically active lymphocytes, without precise limits. 80% of chronic lymphocytic leukosis comes from B-lymphocytes. Although the number of neoplastic lymphocytes is considerably increased, they are immunologically inactive, leading to hypogammaglobulinemia, decreased humoral immunity with infectious complications, and autoimmune reactions, primarily hemolytic anemias and autoimmune thrombocytopenias.

№ 146. Lymphatic nodes in Hodgkin's disease.

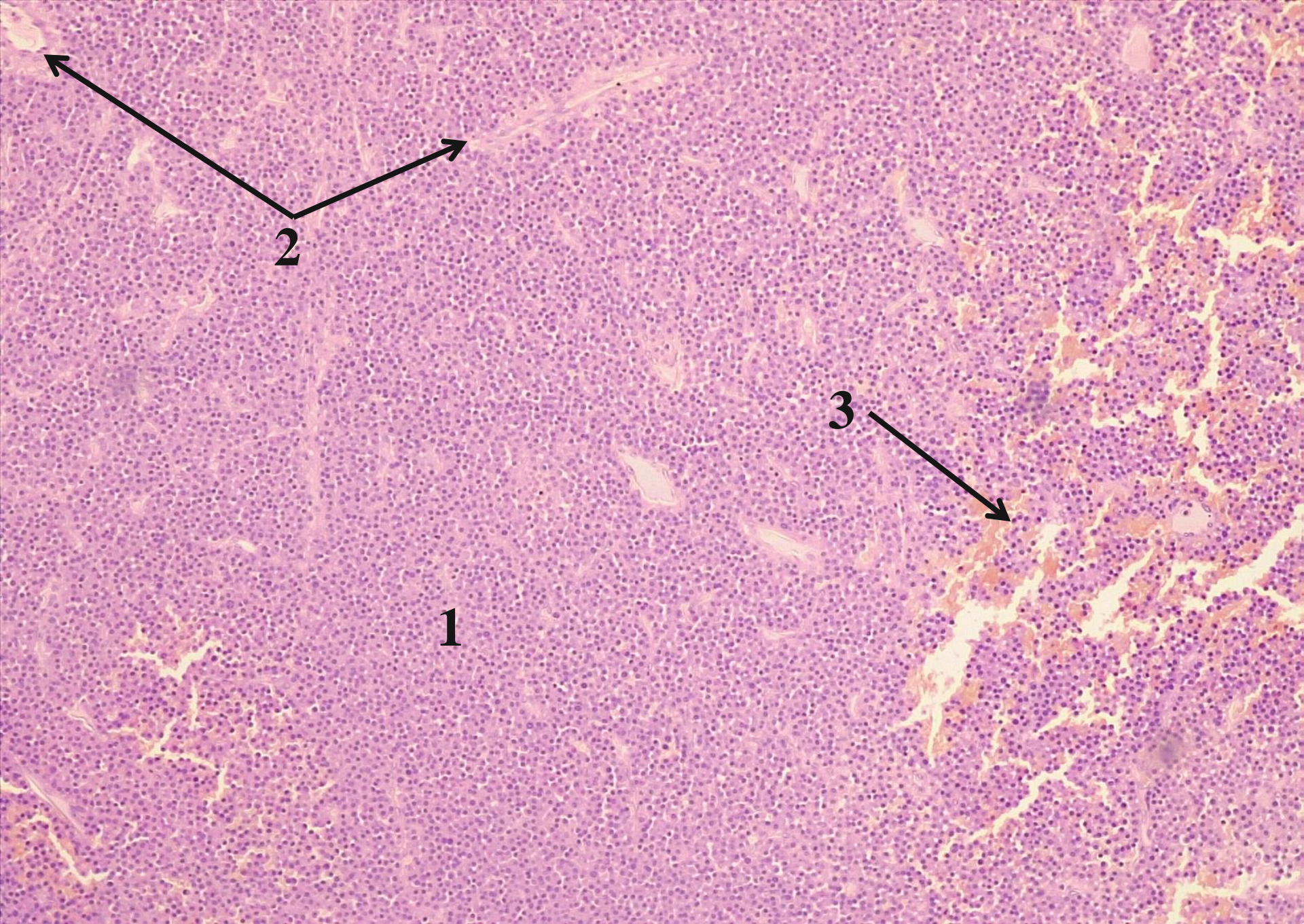
The lymph nodes are unevenly enlarged in size, of dense consistency, light-whitish color, adhere to each other due to infiltration of perinodular connective tissue, on a motley-looking section, white-yellow foci of necrosis and fibrosis.

Hodgkin's lymphoma begins in a single lymph node or in a group of lymph nodes, usually cervical, supraclavicular, or axillary. Subsequently, the tumor process progresses, gradually involving other groups of lymph nodes on the same side of the diaphragm, on both sides of the diaphragm or extralymph (extranodal) tissues / organs. At first the lymph nodes are separated, and later they become adherent, forming tumor conglomerates, which compress the adjacent tissues / organs.

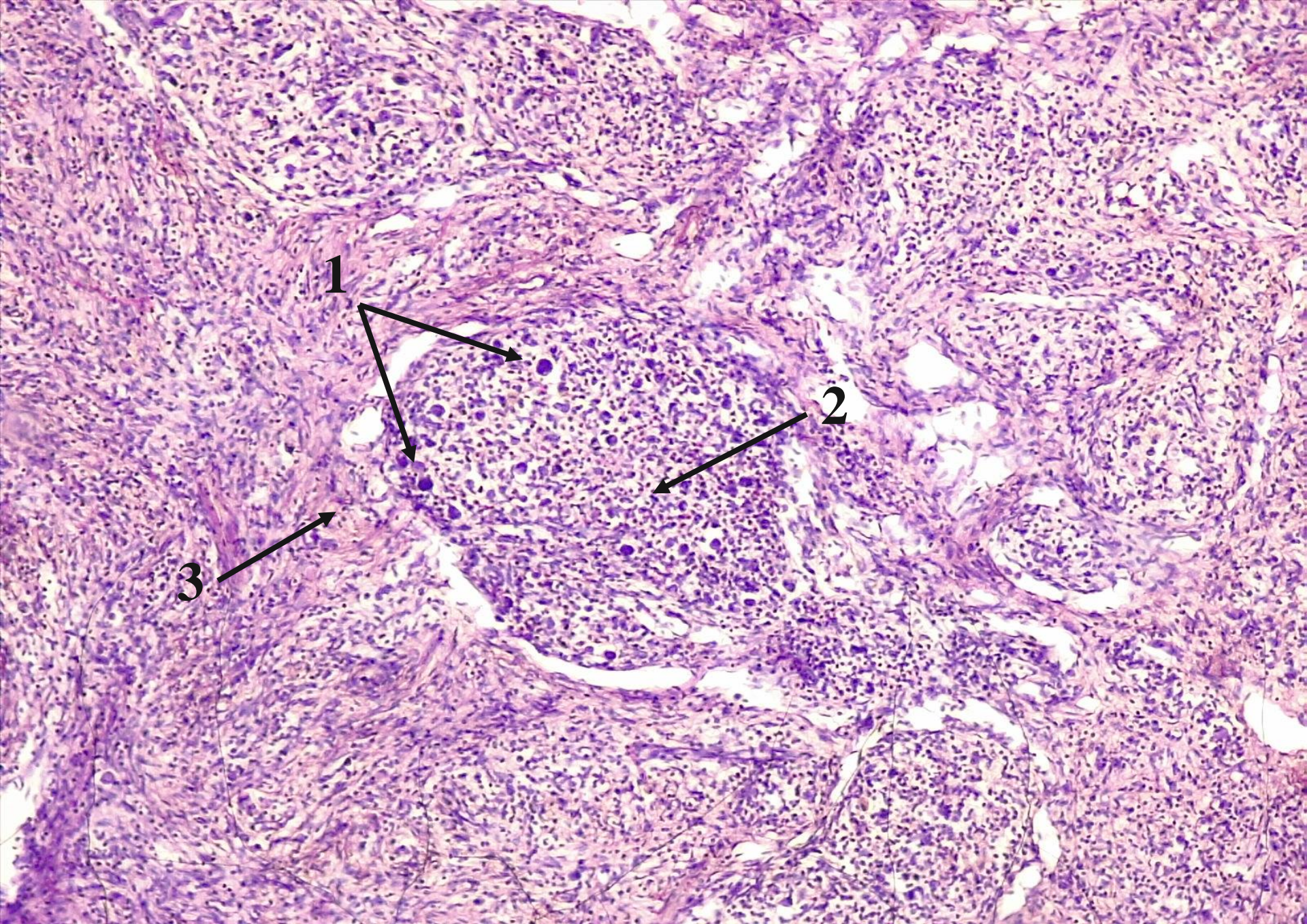
№ 147. Spleen in Hodgkin's disease.

The spleen is enlarged in size 3-5 times, the mass reaching up to 1 kg, dense consistency, on a motley-looking section due to the alternation of white-yellowish proliferative foci and necrosis with whitish sclerosis foci on the background of the red pulp, which gives the splenic tissue an appearance similar to porphyry granite ('porphyry spleen') [the motley appearance is poorly pronounced due to the action of formalin].

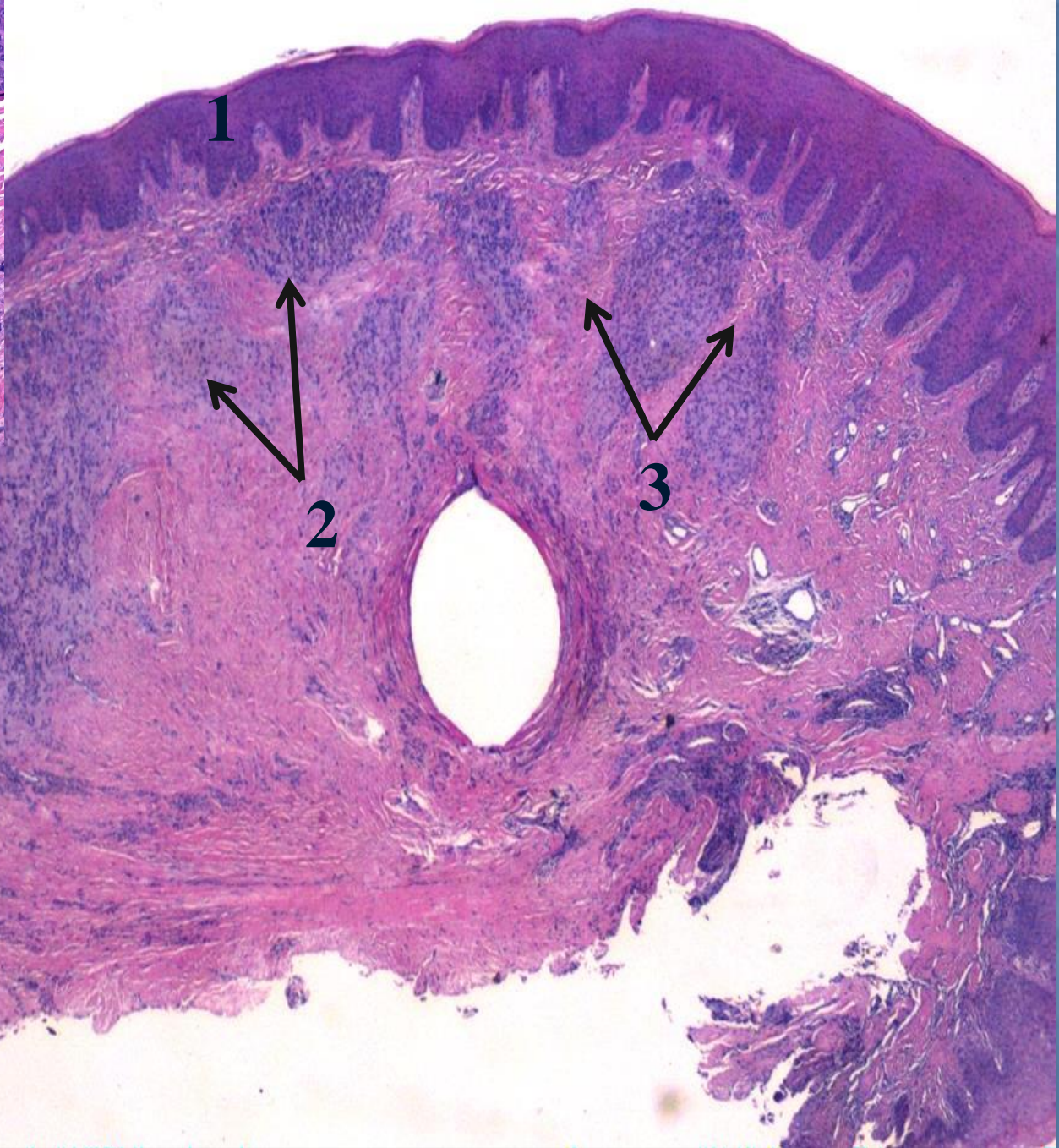
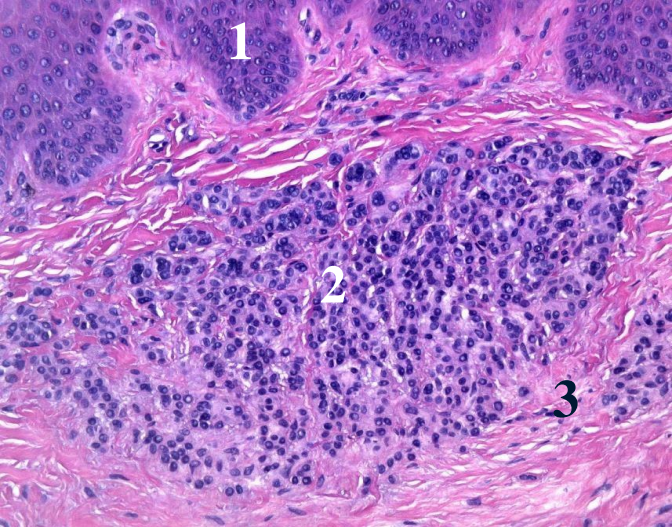
Splenomegaly in Hodgkin's lymphoma is an expression of tumor progression, in the first stage being affected lymph nodes, and later other extranodal organs, primarily the spleen. Spleen damage is observed in about half of patients, being a process of metastasis from the primary focus of the lymph nodes. Histologically, tumor nodules consisting of a mixture of Reed-Sternberg cells and reactive cells (eosinophils, plasma cells, neutrophilic leukocytes, macrophages), foci of necrosis, sometimes caseous, and fibrosis are revealed.



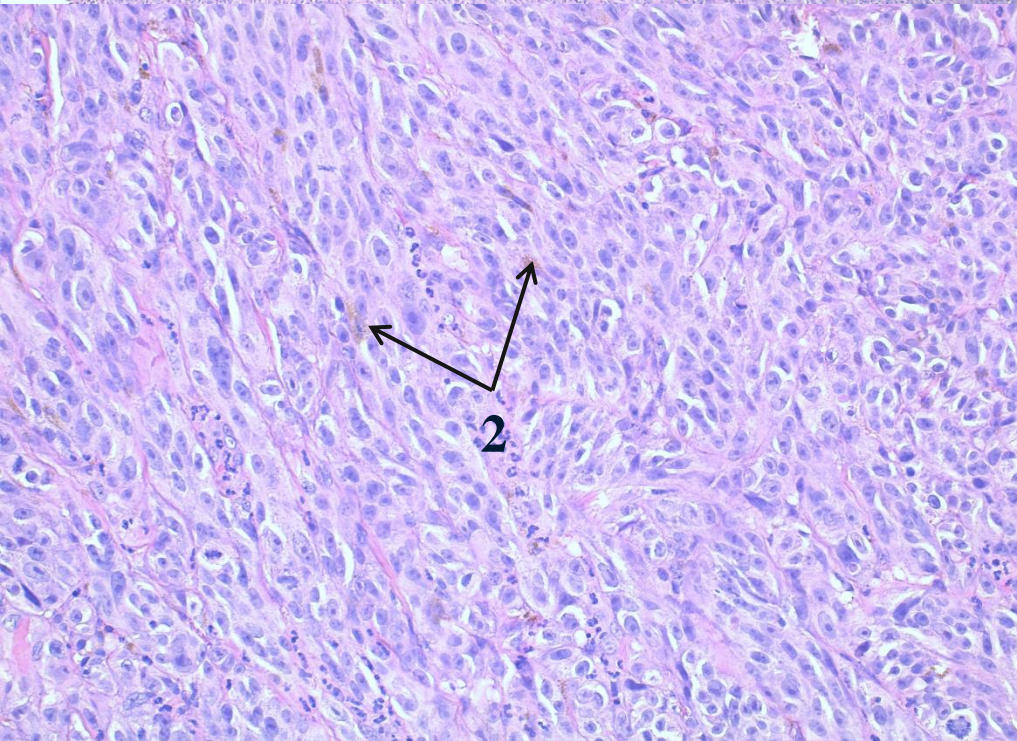
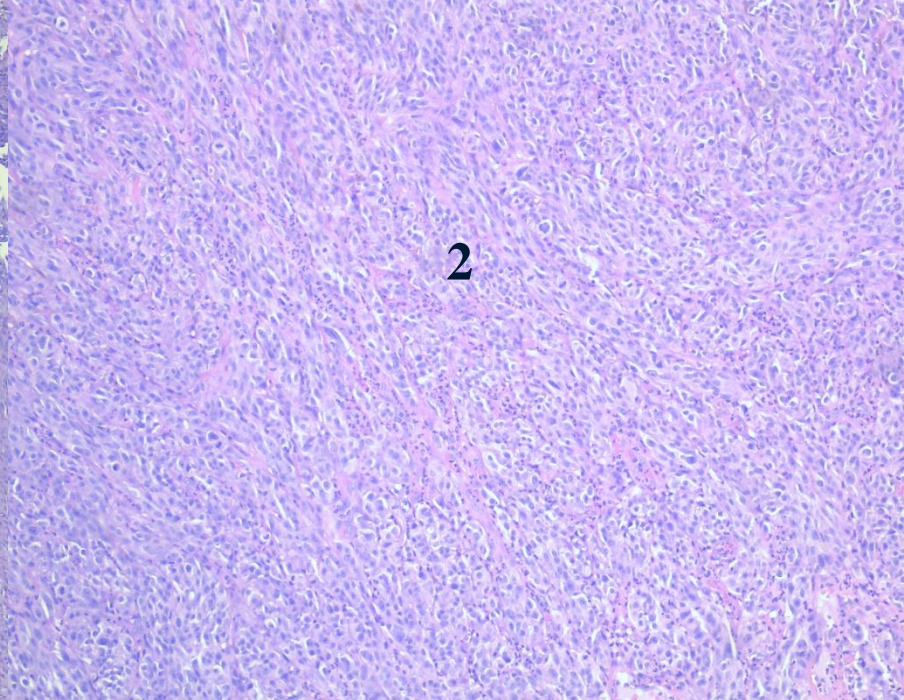
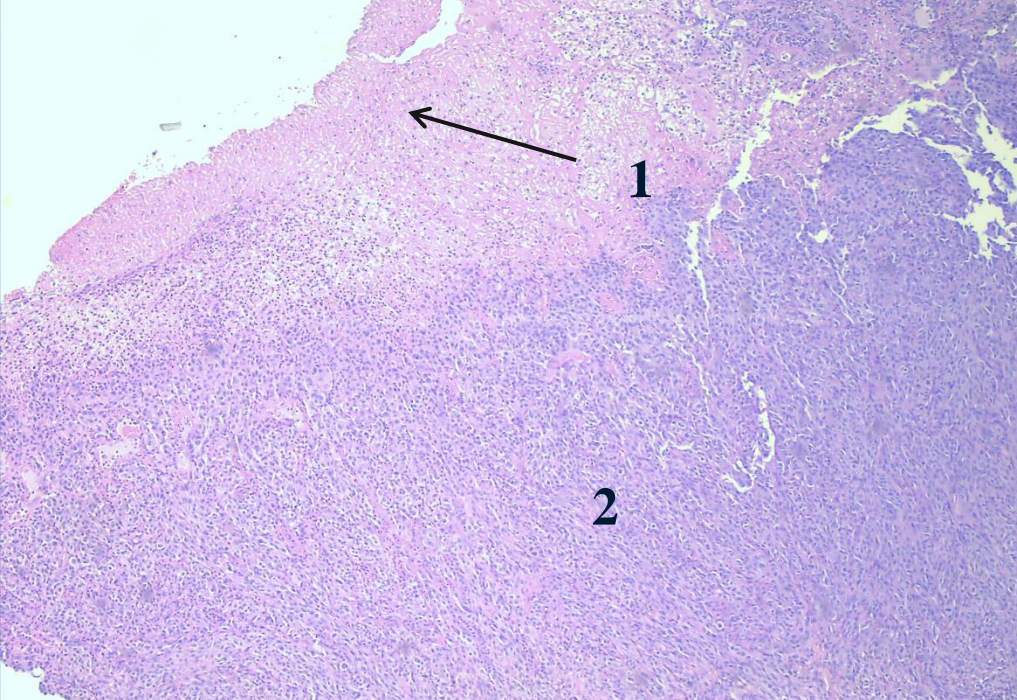
№ 145. Plasmocytoma. (H-E stain).



№ 58. Lymphatic node in Hodgkin's disease. (*H-E stain*).



№ OP25. Intramucosal nevus of the oral cavity (H-E stain).



№ OP 26. Melanoma of the oral cavity
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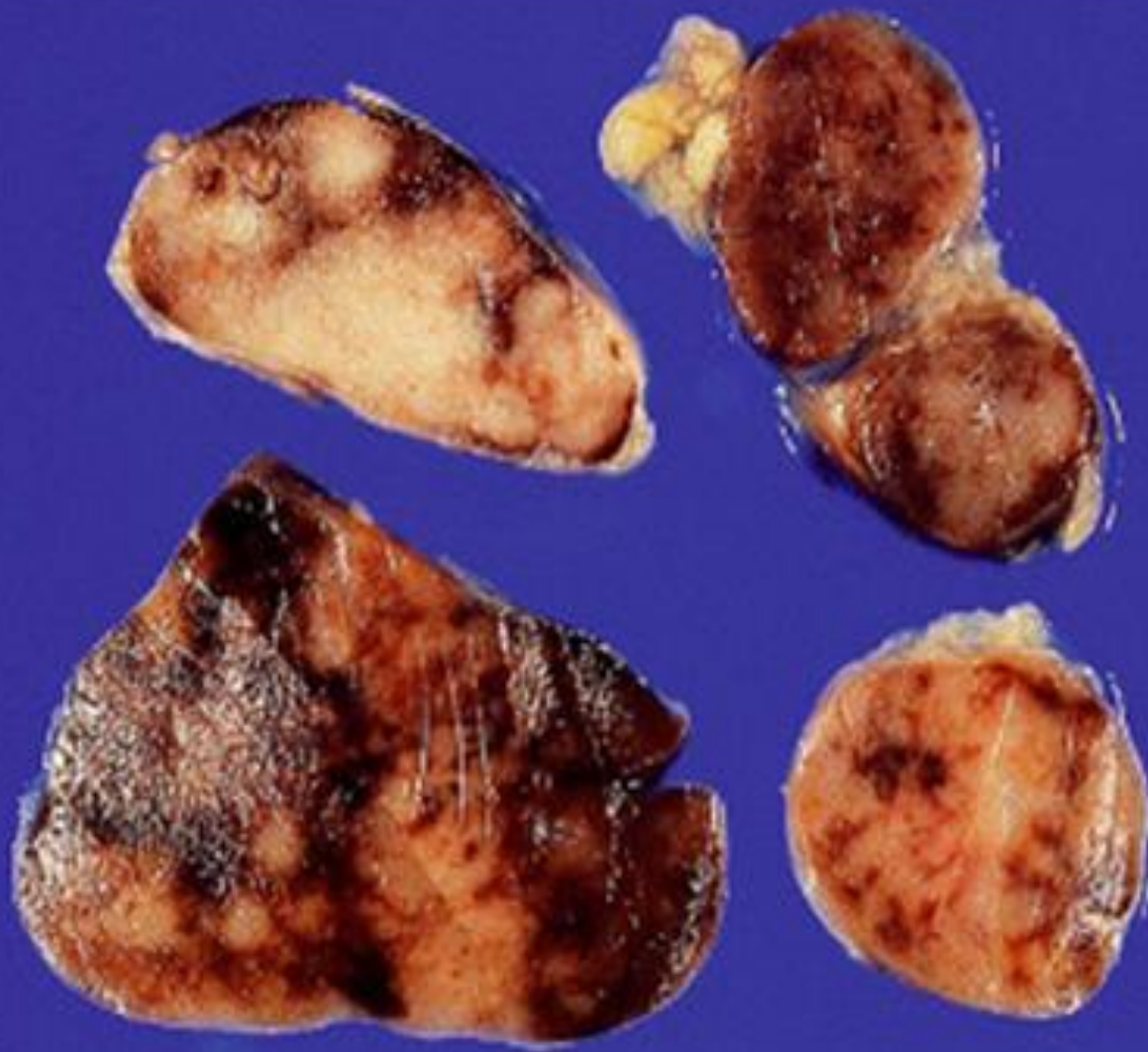
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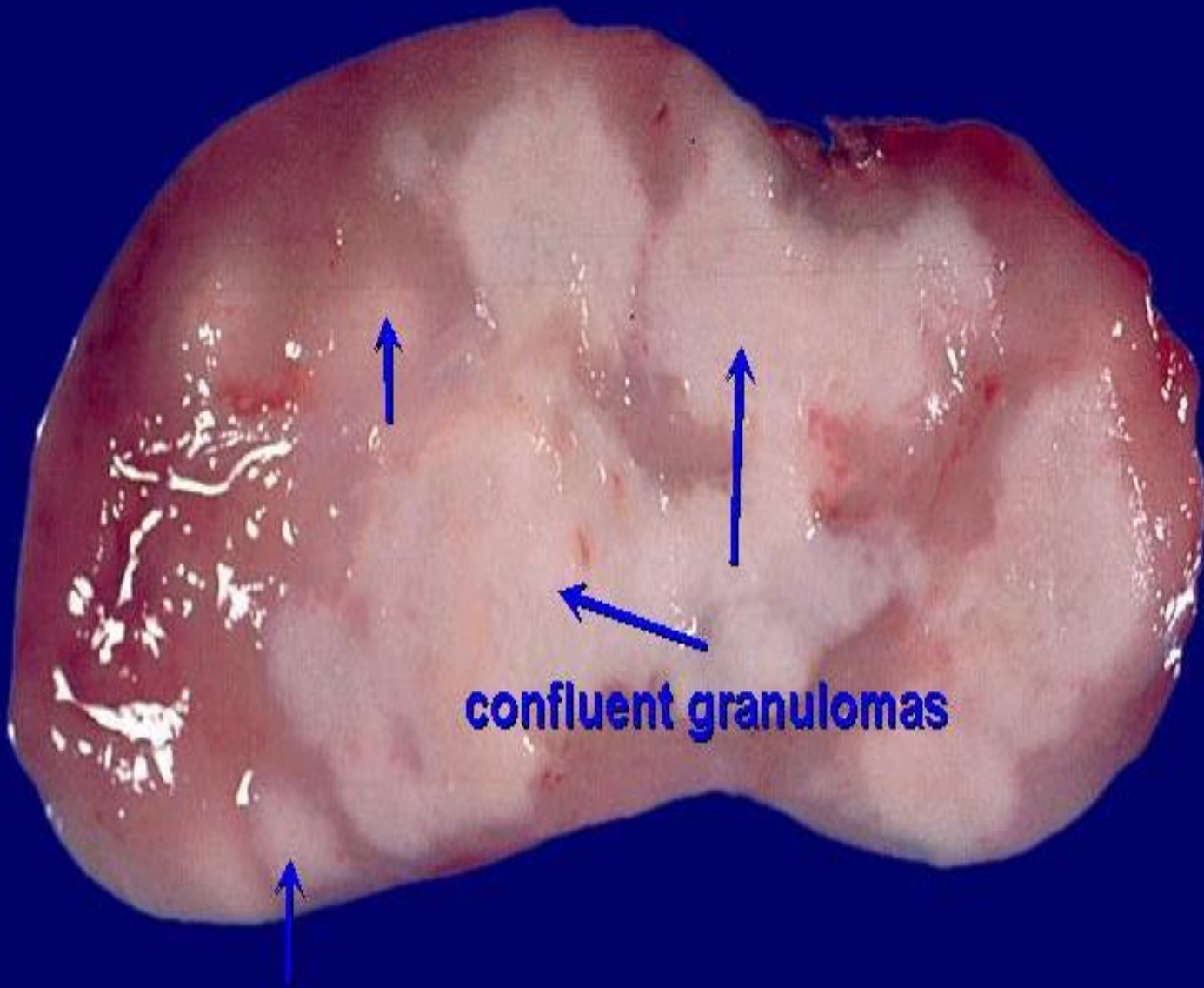
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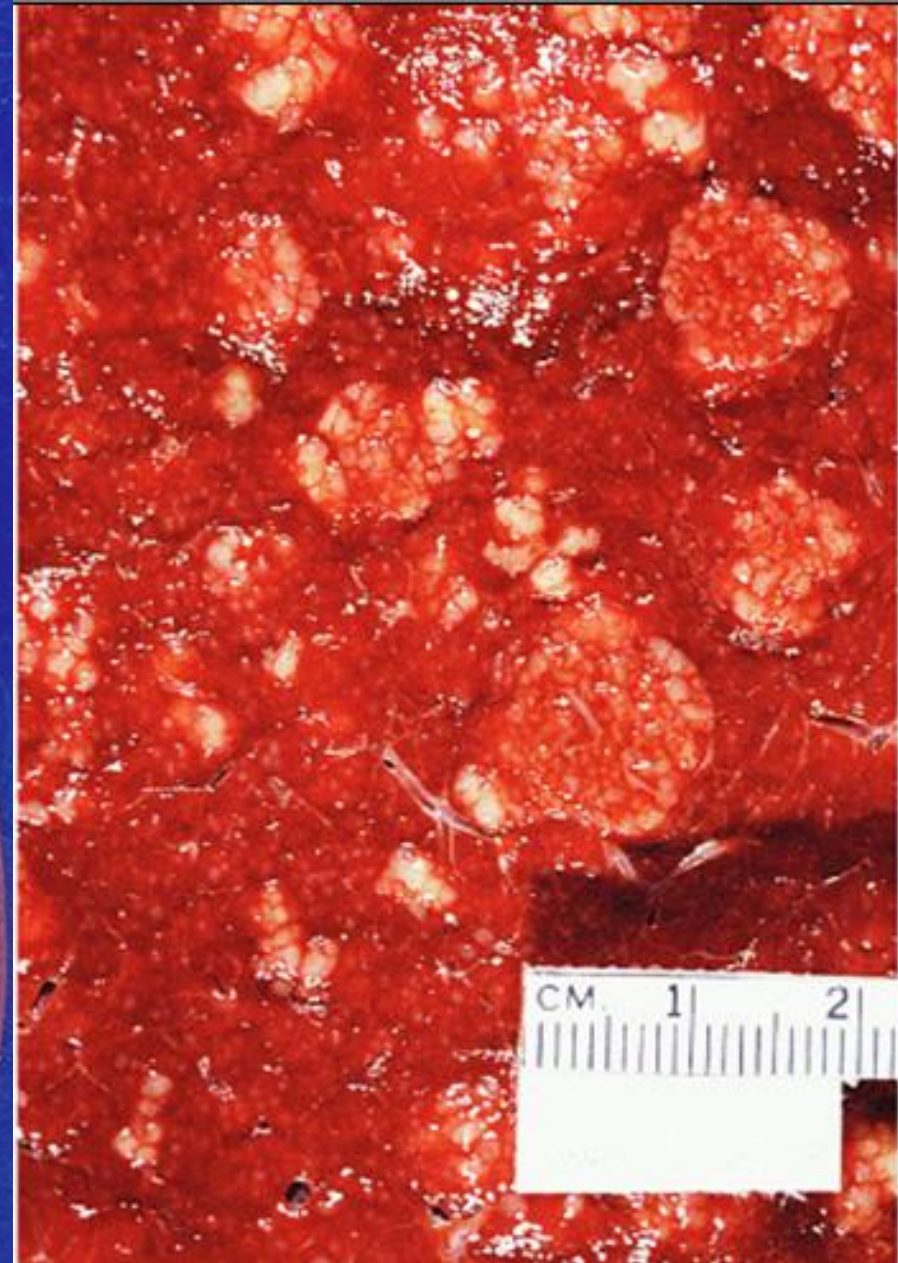
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Pathology of the hematopoietic system.

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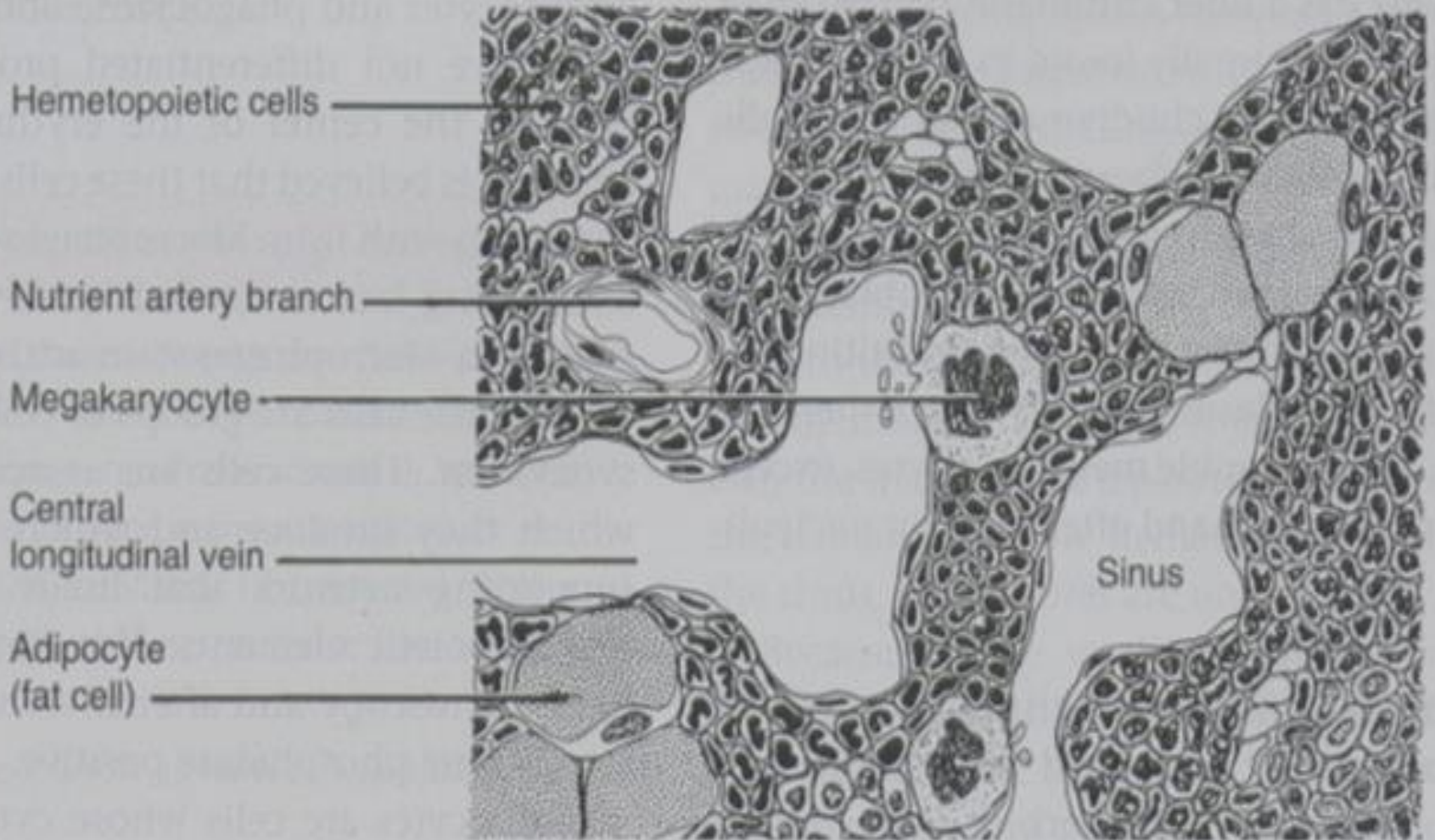
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A microscopic view of blood cells, showing a large orange-red cell on the left and several smaller purple and pink cells on the right, all set against a dark background. The text is overlaid on this image.

BLOOD AND LYMPHATIC DISORDERS

STRUCTURE OF BONE MARROW



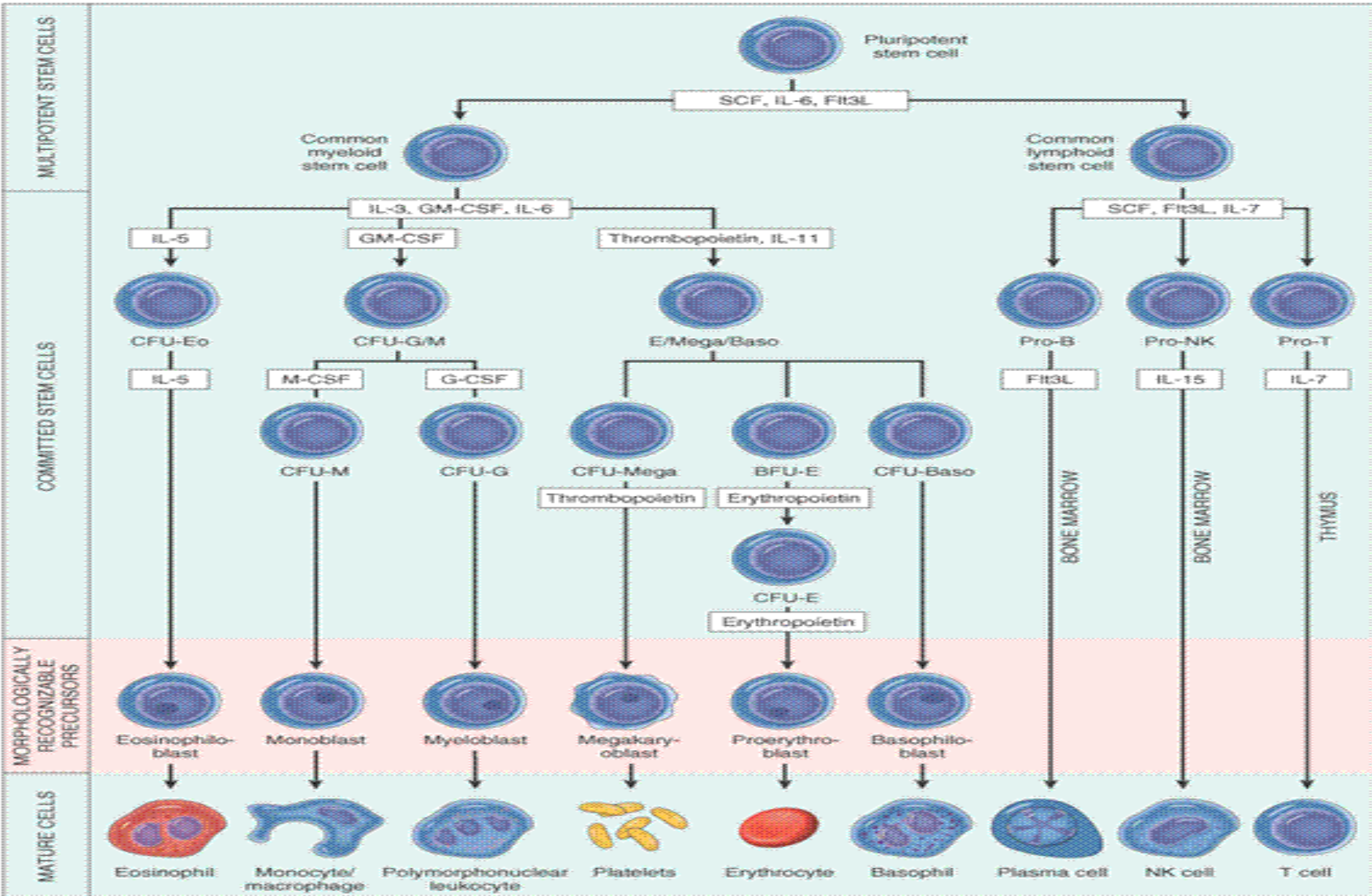
WHERE is MARROW?

- **Yolk Sac: very early embryo**
- **Liver, Spleen: NEWBORN**
- **BONE**
 - **CHILDHOOD: AXIAL SKELETON & APPENDICULAR SKELETON BOTH HAVE RED (active) MARROW**
 - **ADULT: AXIAL SKELETON RED MARROW, APPENDICULAR SKELETON YELLOW MARROW**

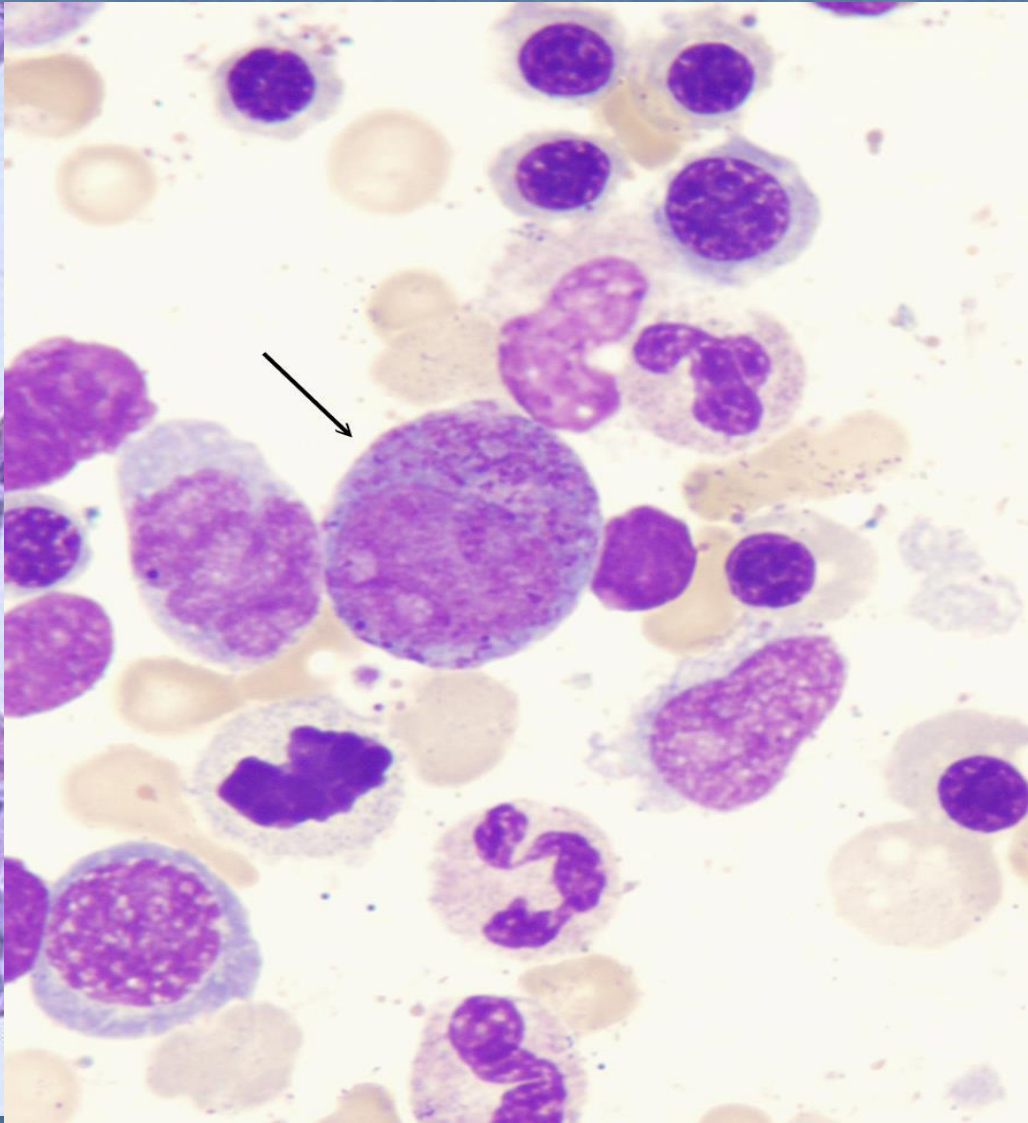
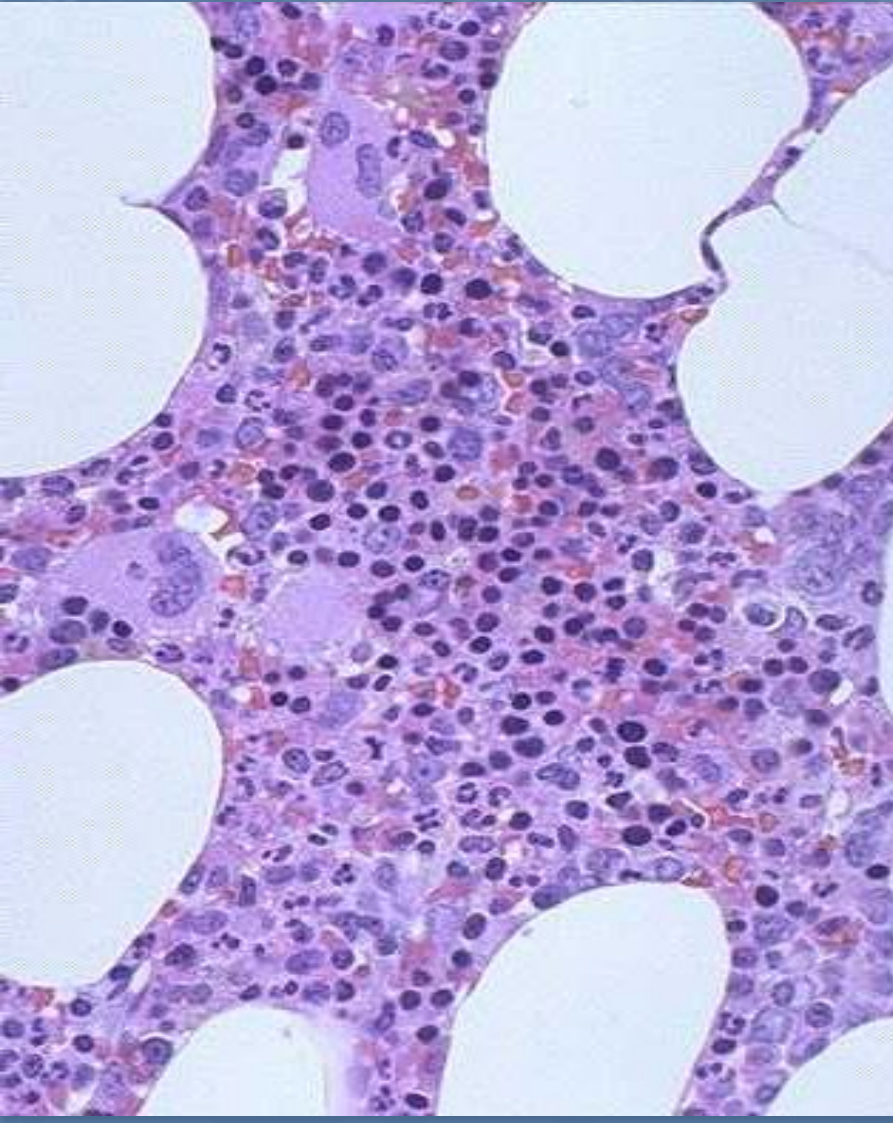
MARROW FEATURES

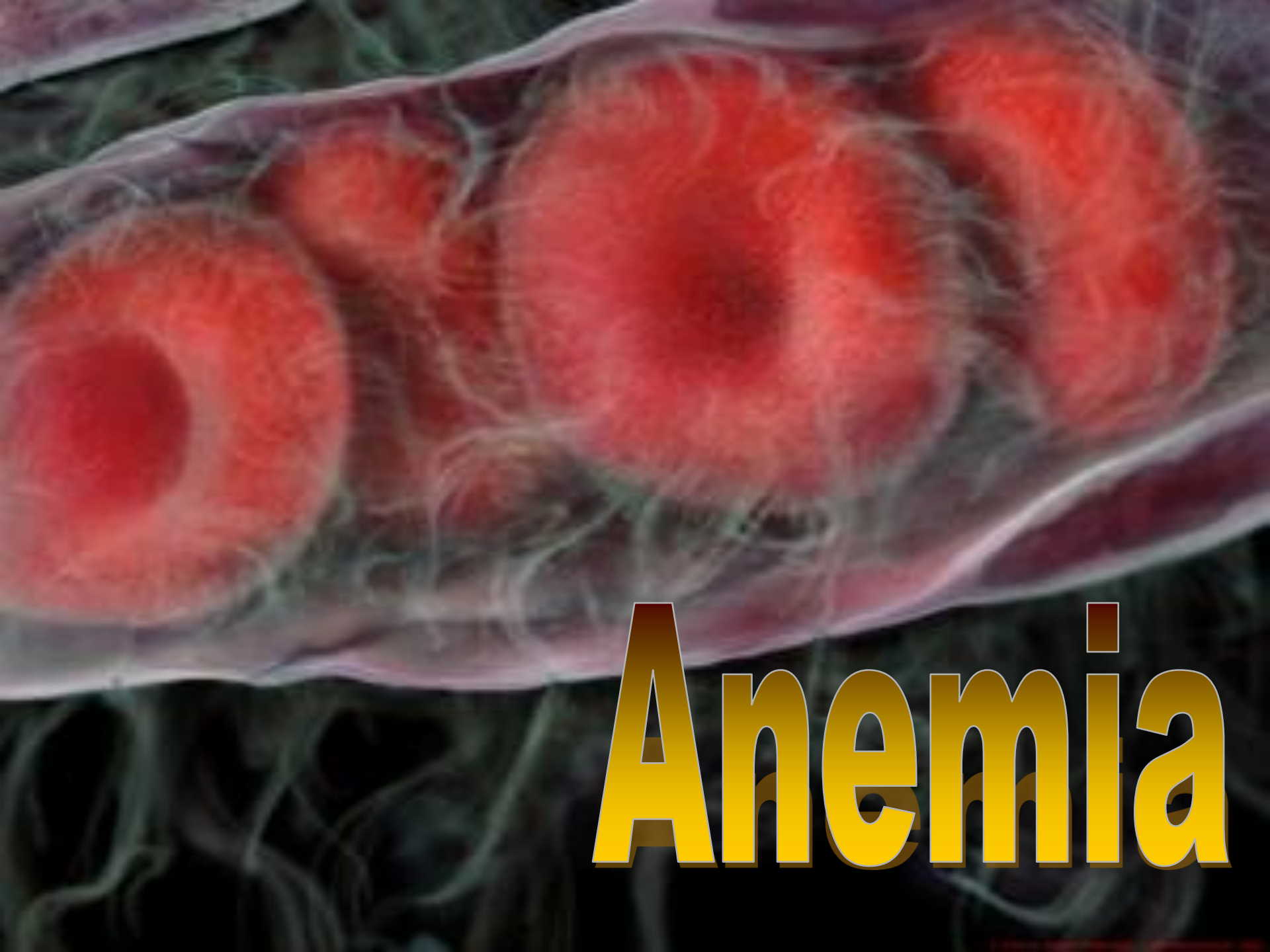
- CELLULARITY
- MEGAKARYOCYTES
- M:E RATIO
- MYELOID MATURATION
- ERYTHROID MATURATION
- LYMPHS, PLASMA CELLS
- STORAGE IRON, i.e.,
HEMOSIDERIN
- "FOREIGN CELLS"

MARROW "DIFFERENTIATION"



BONE MARROW



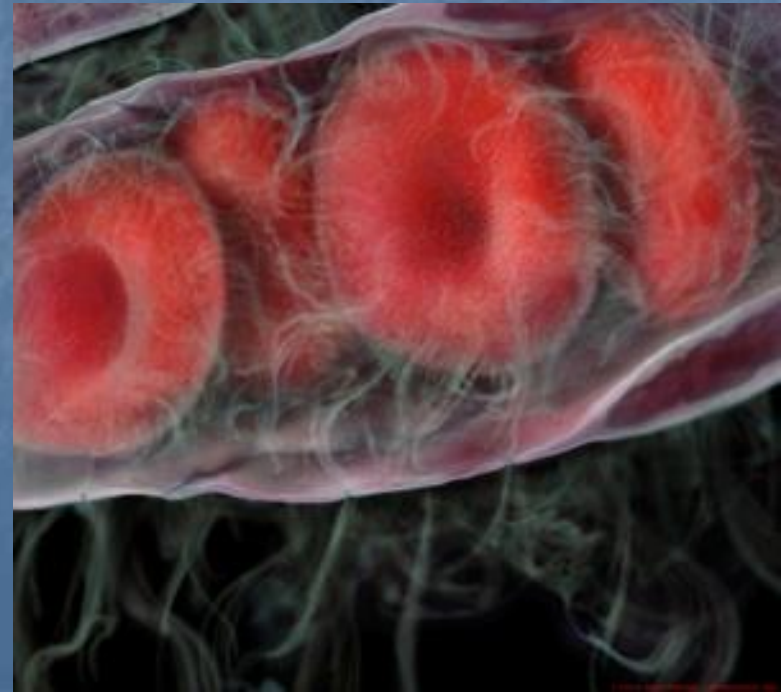


Anemia

ANEMIAS

A good definition would be a decrease in **OXYGEN CARRYING CAPACITY**, rather than just a decrease in red blood cells, because you need to have enough blood cells **THAT FUNCTION**, and not just enough blood cells.

- **BLOOD LOSS**
 1. acute
 2. chronic
- **IN-creased destruction (HEMOLYTIC)**
- **DE-creased production**



Features of ALL anemias

- Pallor, where?
- Tiredness
- Weakness
- Dyspnea, why?
- Palpitations
- Heart Failure (high output), why?

Blood Loss

Acute: trauma

Chronic: lesions of gastrointestinal tract, gynecologic disturbances. The features of chronic blood loss anemia are the same as iron deficiency anemia, and is defined as a situation in which the production cannot keep up with the loss

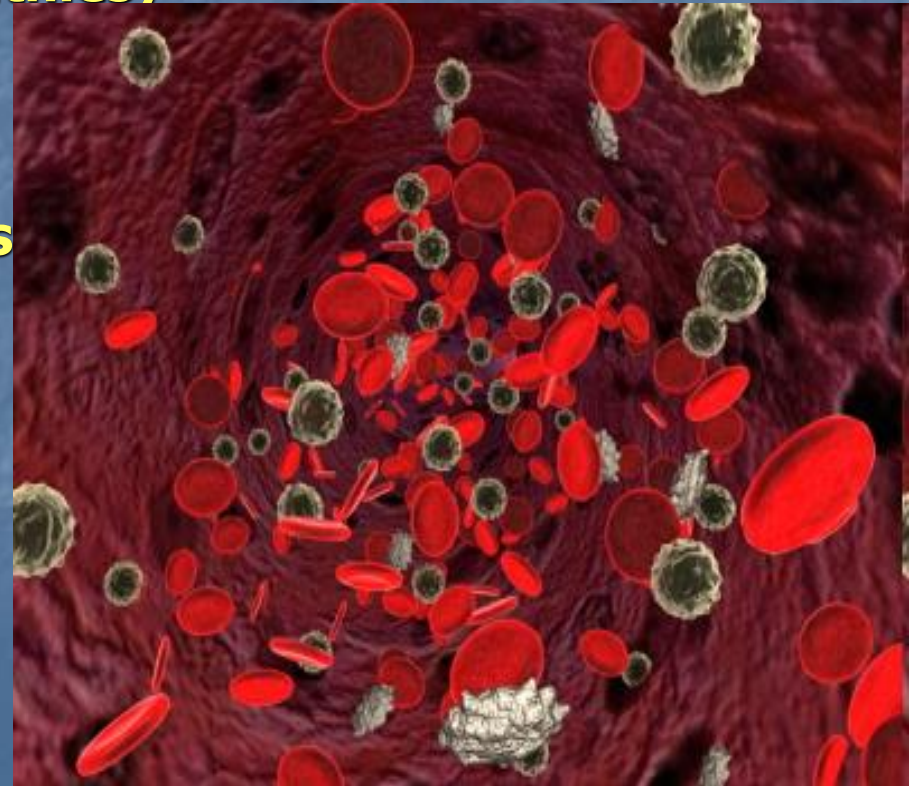
HEMOLYTIC

■ HEREDITARY

- MEMBRANE disorders: e.g., spherocytosis
- ENZYME disorders: e.g., G6PD deficiency
- HGB disorders (hemoglobinopathies)

■ ACQUIRED

- MEMBRANE disorders (PNH)
- ANTIBODY MEDIATED, transfusion related
- or autoantibodies
- MECHANICAL TRAUMA
- INFECTIONS
- DRUGS, TOXINS
- HYPERSPLENISM



IMPAIRED PRODUCTION

- **Disturbance of proliferation and differentiation of stem cells: aplastic anemias, pure RBC aplasia, renal failure**
- **Disturbance of proliferation and maturation of erythroblasts**
- **Defective DNA synthesis: (Megaloblastic)**
- **Defective heme synthesis: (Fe)**
- **Deficient globin synthesis: (Thalasseмии)**

MODIFIERS

- **MCV, microcytosis, macrocytosis**
- **MCH**
- **MCHC, hypochromic**
- **RDW, anisocytosis**

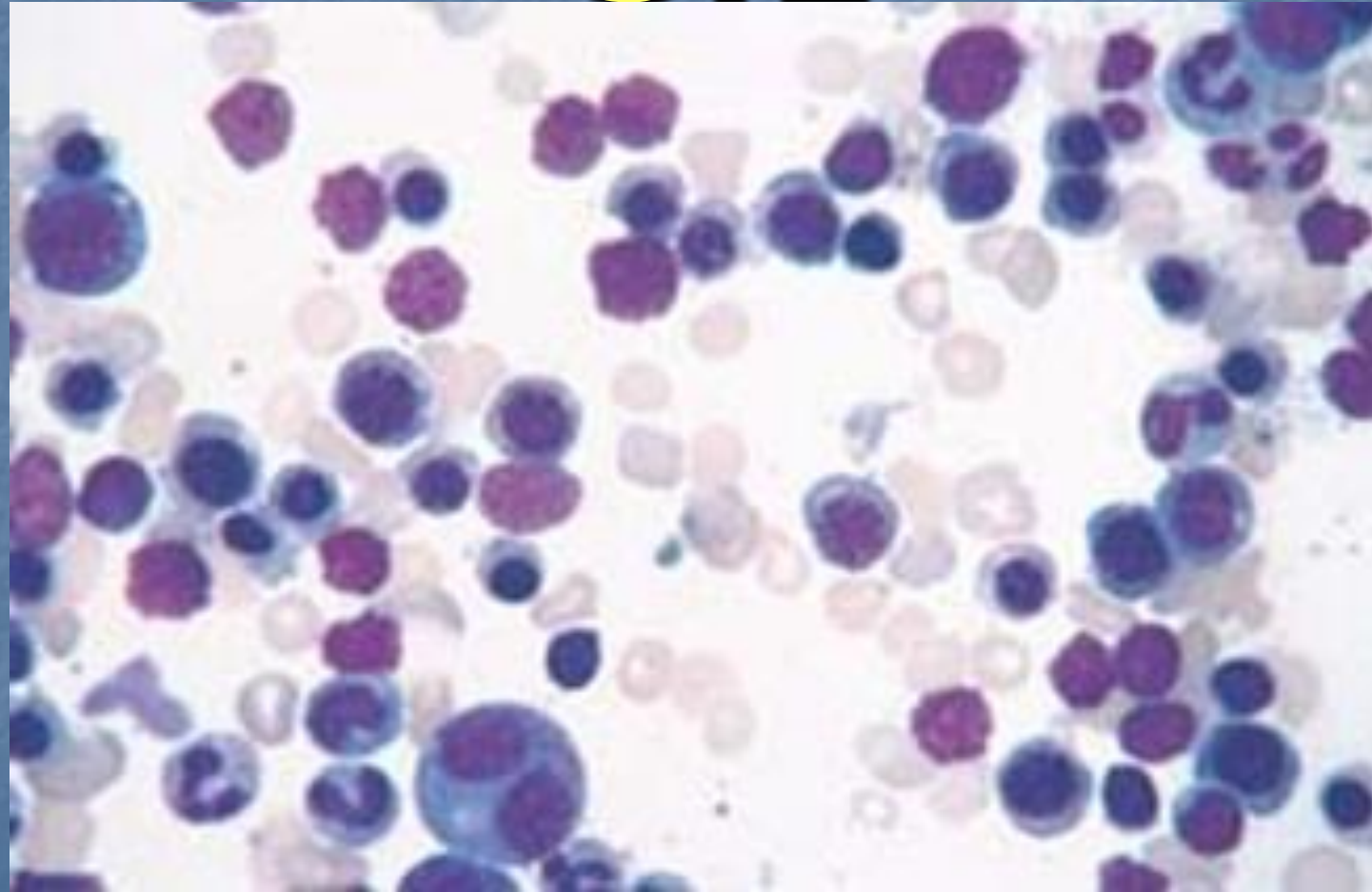
HEMOLYTIC ANEMIAS

- Life span LESS than 120 days
- Marrow hyperplasia (M:E), EPO+
- Increased catabolic products, e.g., bilirubin, serum HGB, hemosiderin

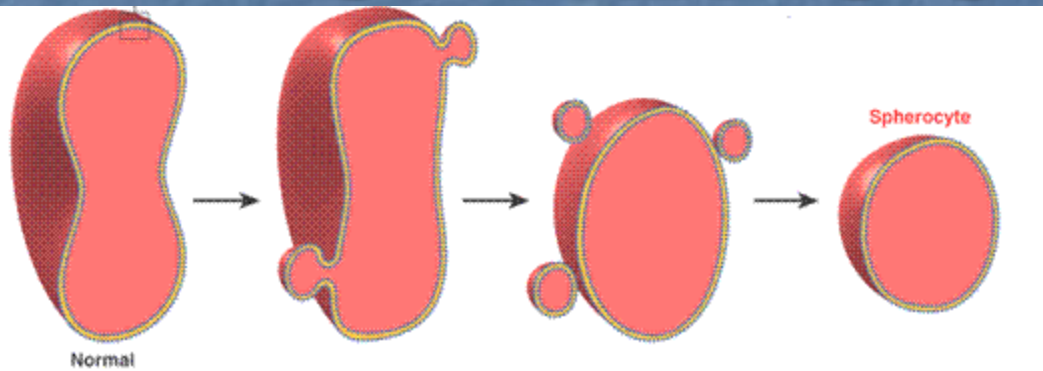
HEMOLYSIS

- **INTRA-vascular (vessels)**
- **EXTRA-vascular (spleen)**

M:E Ratio normally 3:1



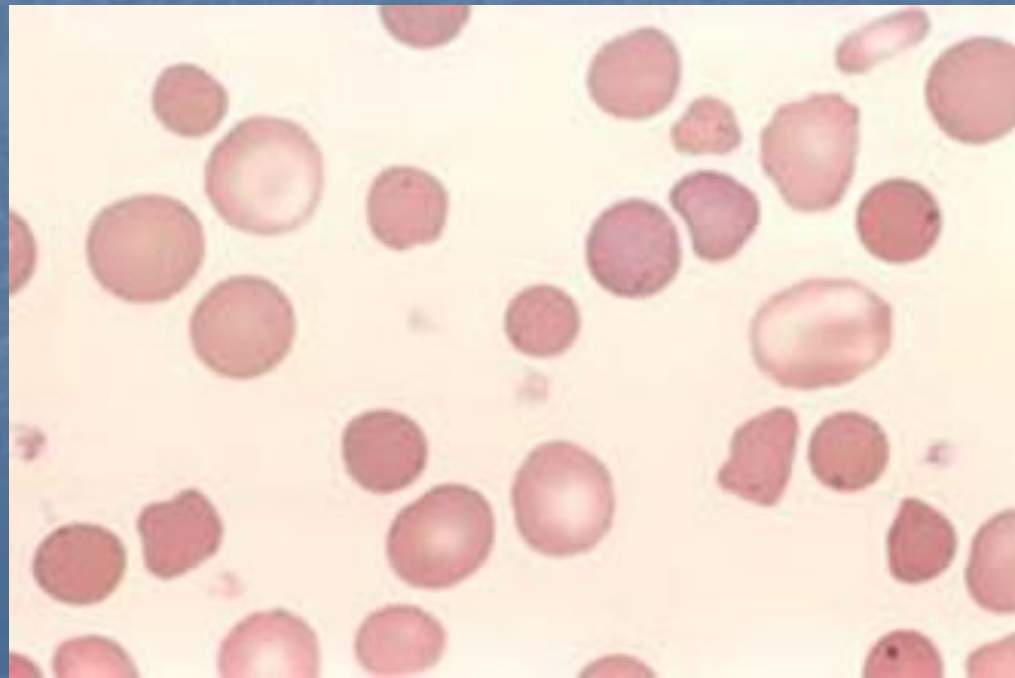
HEREDITARY SPHEROCYTOSIS



Genetic defects affecting ankyrin, spectrin, usually autosomal dominant

Children, adults

Anemia, hemolysis, jaundice, splenomegaly, gallstones (what kind?)

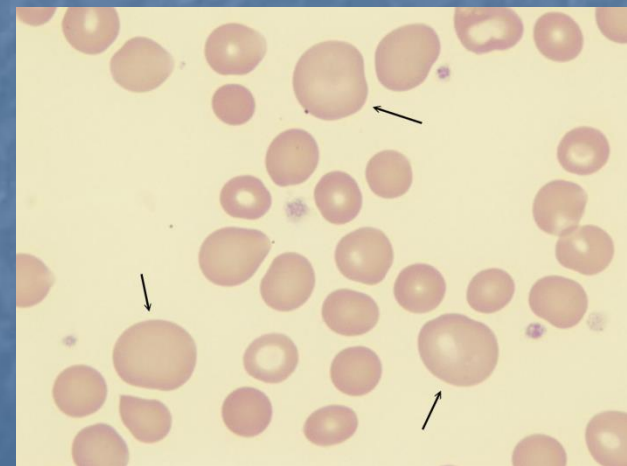
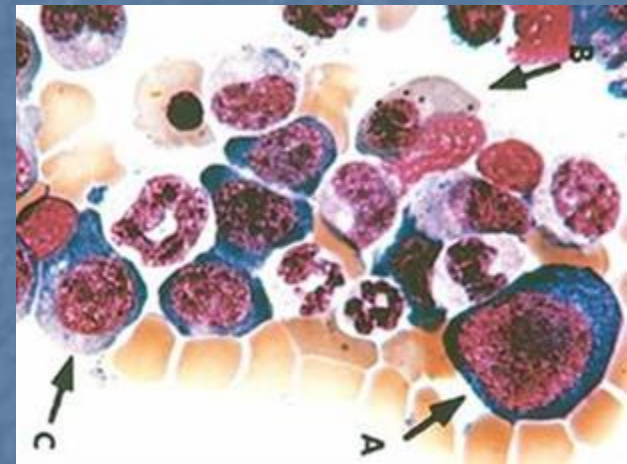


NON-Hemolytic Anemias: i.e., DE-creased Production

- **“Megaloblastic” Anemias**
- **B12 Deficiency (Pernicious Anemia)**
- **Folate Deficiency**
- **Iron Deficiency**
- **Anemia of Chronic Disease**
- **Aplastic Anemia**
- **“Pure” Red Cell Aplasia**
- **OTHER forms of Marrow Failure**

MEGALOBLASTIC ANEMIAS

- Differentiating megaloblasts (marrow) from macrocytes (peripheral smear, $MCV > 94$)
- Impaired DNA synthesis
- For all practical purposes, also called the anemias of B12 and FOLATE deficiency



etiology

Decreased intake

Inadequate diet, vegetarianism

Impaired absorption

Intrinsic factor deficiency

Pernicious anemia

Gastrectomy

Malabsorption states

Diffuse intestinal disease, e.g., lymphoma, systemic sclerosis

Ileal resection, ileitis

Competitive parasitic uptake

Fish tapeworm infestation

Bacterial overgrowth in blind loops and diverticula of bowel

Increased requirement

Pregnancy, hyperthyroidism, disseminated cancer

Vit-B12 Physiology

- **Oral ingestion**
- **Combines with INTRINSIC FACTOR in the gastric mucosa**
- **Absorbed in the terminal ileum**
- **DEFECTS at ANY of these sites can produce a MEGALOBLASTIC anemia**

Please remember that ALL megaloblastic anemias are also MACROCYTIC (MCV>94 or MCV~100), and that not only are the RBC's BIG, but so are the neutrophils, and neutrophilic precursors in the bone marrow too, and even more so, HYPERSEGMENTED!!!

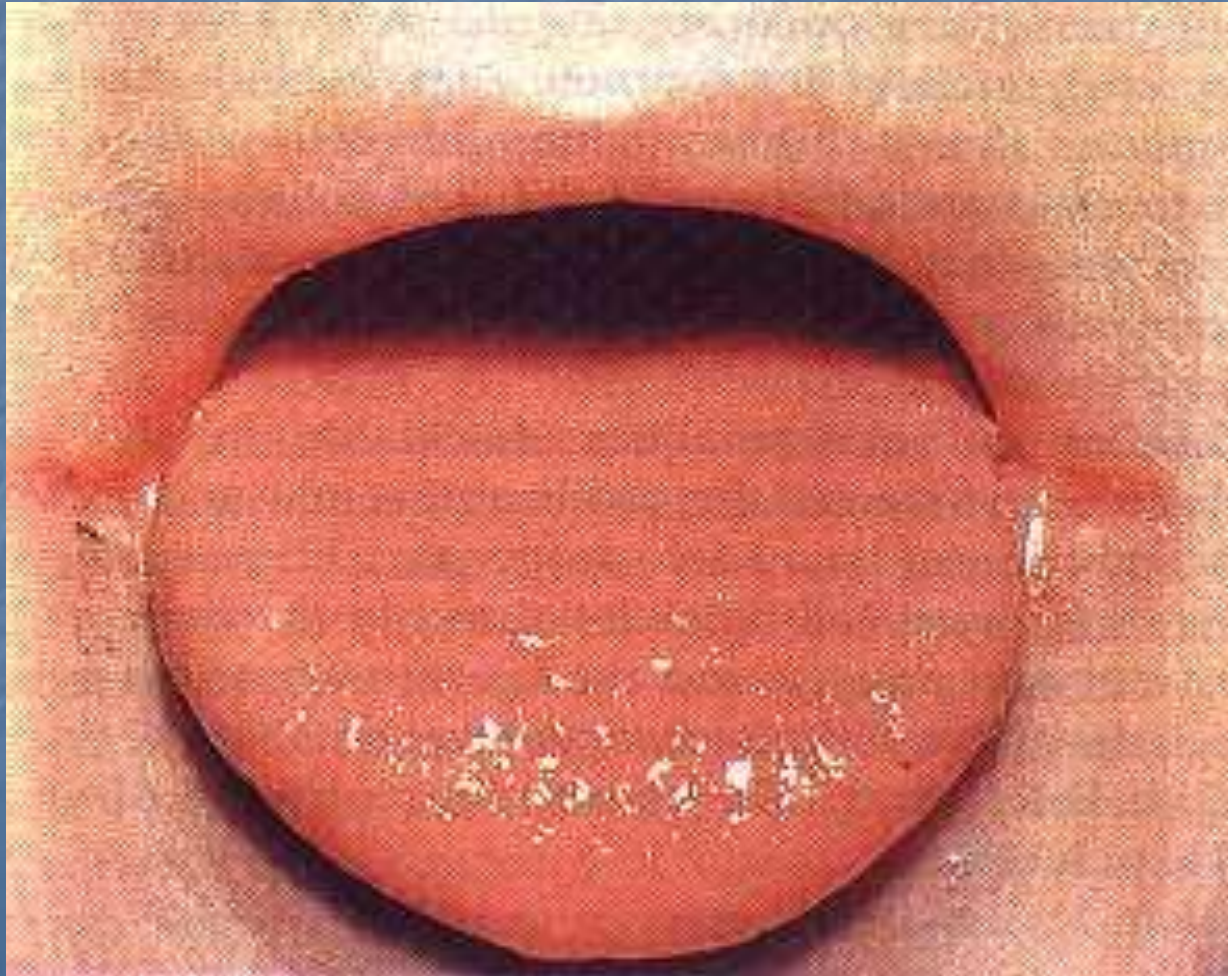
FOLATE DEFICIENCY MEGALOBLASTIC ANEMIAS

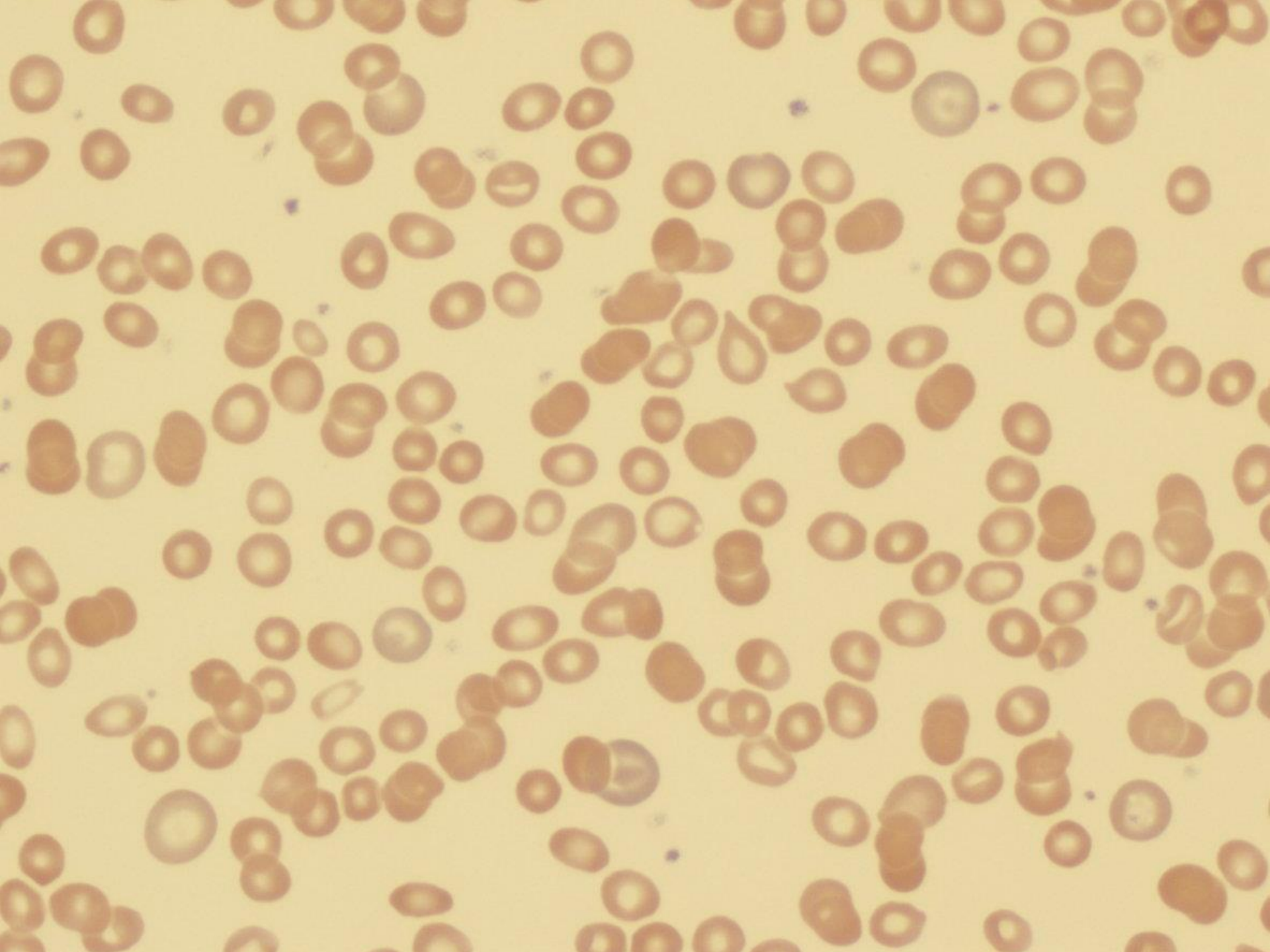
- **Decreased Intake: diet, etoh-ism, infancy**
- **Impaired Absorption: intestinal disease**
- **DRUGS: anticonvulsants, BCPs, CHEMO**
- **Increased Loss: Hemodialysis**
- **Increased Requirement: Pregnancy, infancy**
- **Impaired Usage**

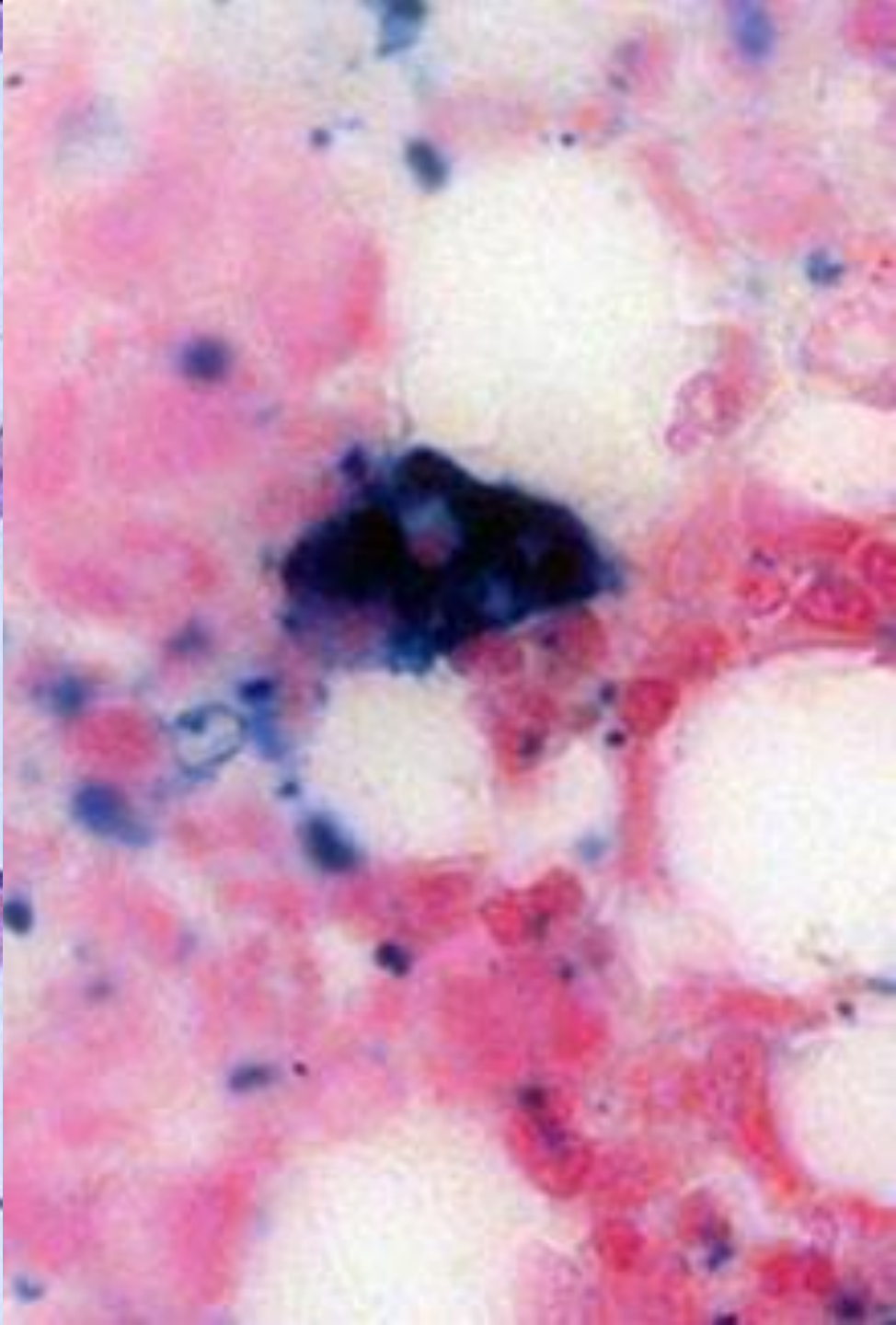
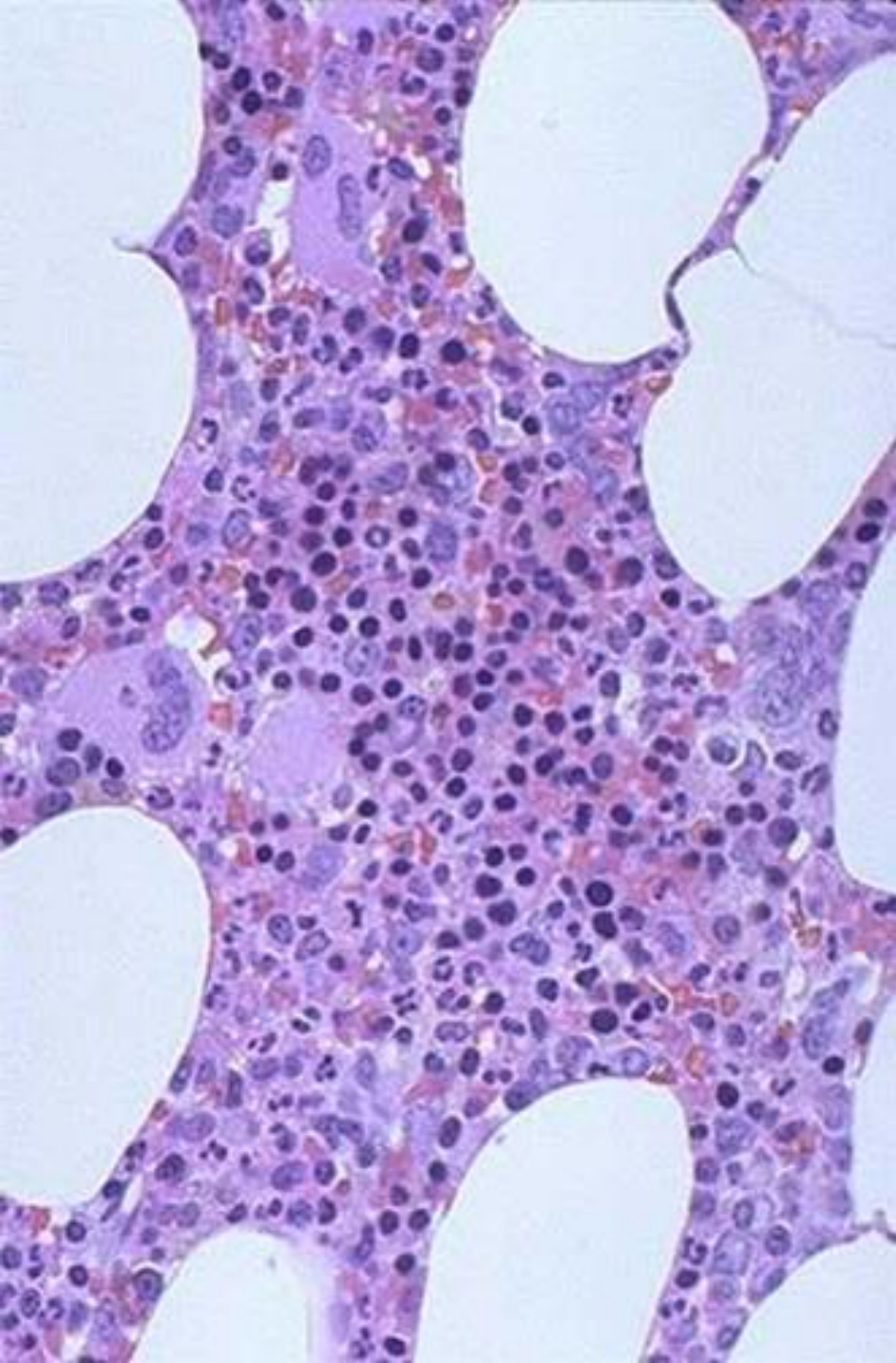
Clinical Fe-Defic- Anemia

- **Adult men: GI Blood Loss**
- **PRE menopausal women: menorrhagia**
- **POST menopausal women: GI Blood Loss**

Clinical Fe-Defic- Anemia







Anemia of Chronic Disease*

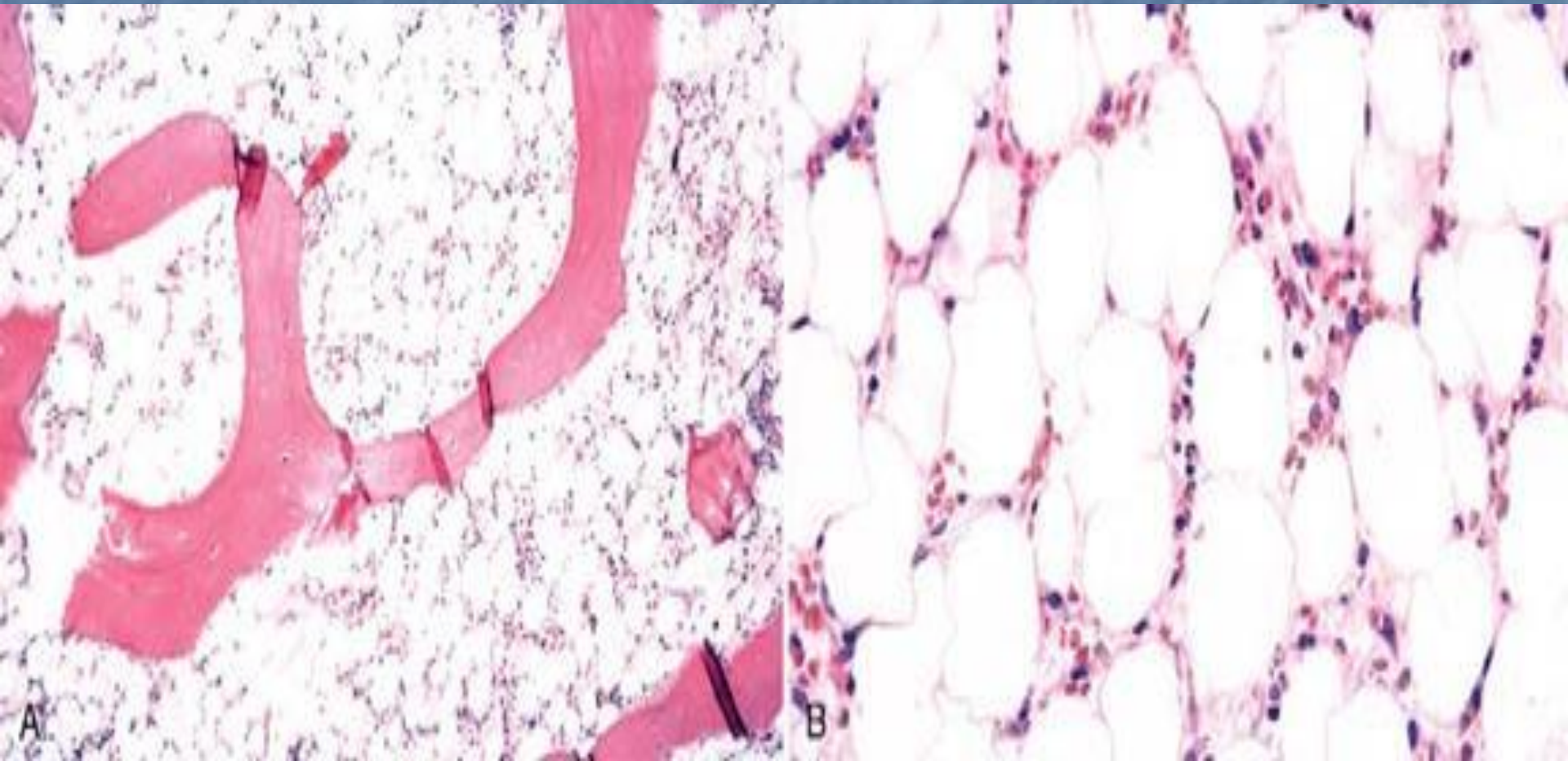
- CHRONIC INFECTIONS**
- CHRONIC IMMUNE DISORDERS**
- NEOPLASMS**
- LIVER, KIDNEY failure**

* Please remember these patients may very very much look like iron deficiency anemia, BUT, they have **ABUNDANT STAINABLE HEMOSIDERIN** in the marrow!

APLASTIC ANEMIAS

- **ALMOST ALWAYS** involve platelet and WBC suppression as well
- Some are idiopathic, but **MOST** are related to drugs, radiation
- **FANCONI'S ANEMIA** is the only one that is inherited, and **NOT** acquired
- Act at **STEM CELL** level, except for "pure" red cell aplasia

APLASTIC ANEMIAS

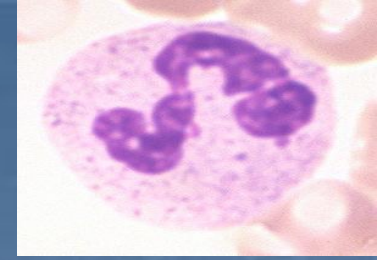
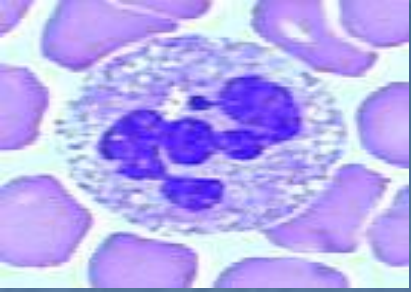


APLASTIC ANEMIAS

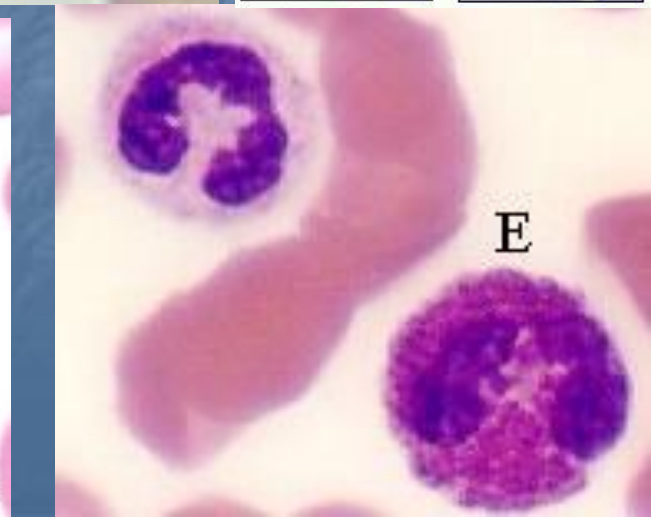
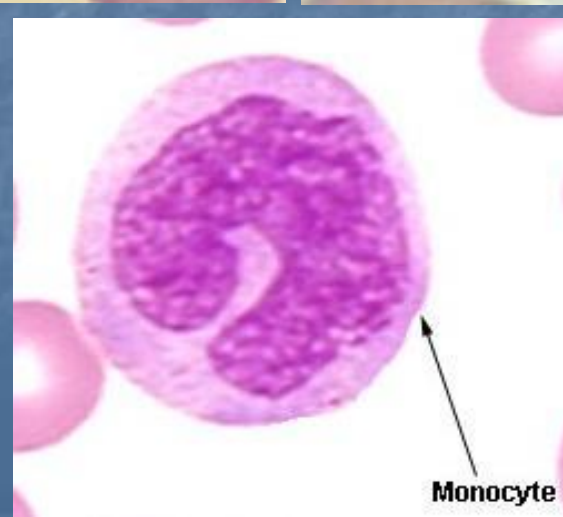
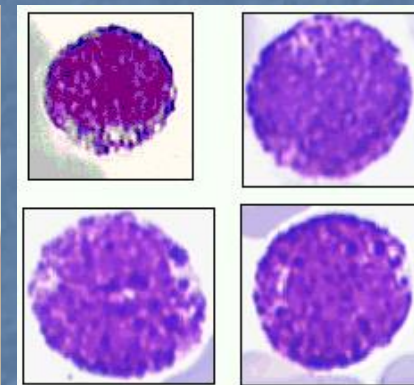
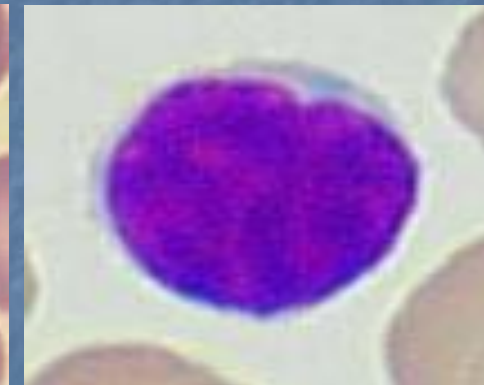
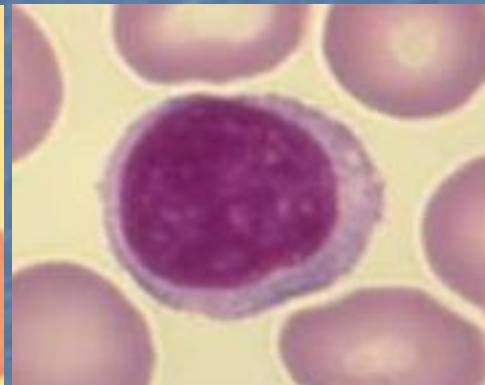
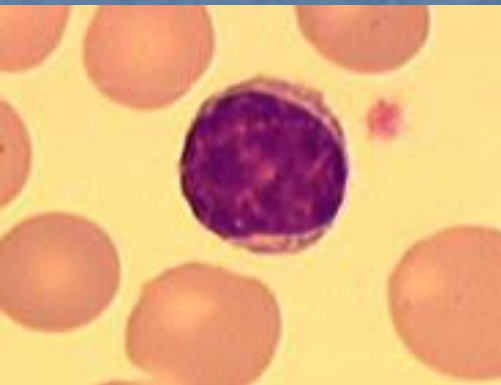
- **CHLORAMPHENICOL**
- **OTHER ANTIBIOTICS**
- **CHEMO**
- **INSECTICIDES**
- **VIRUSES**
 - **EBV**
 - **HEPATITIS**

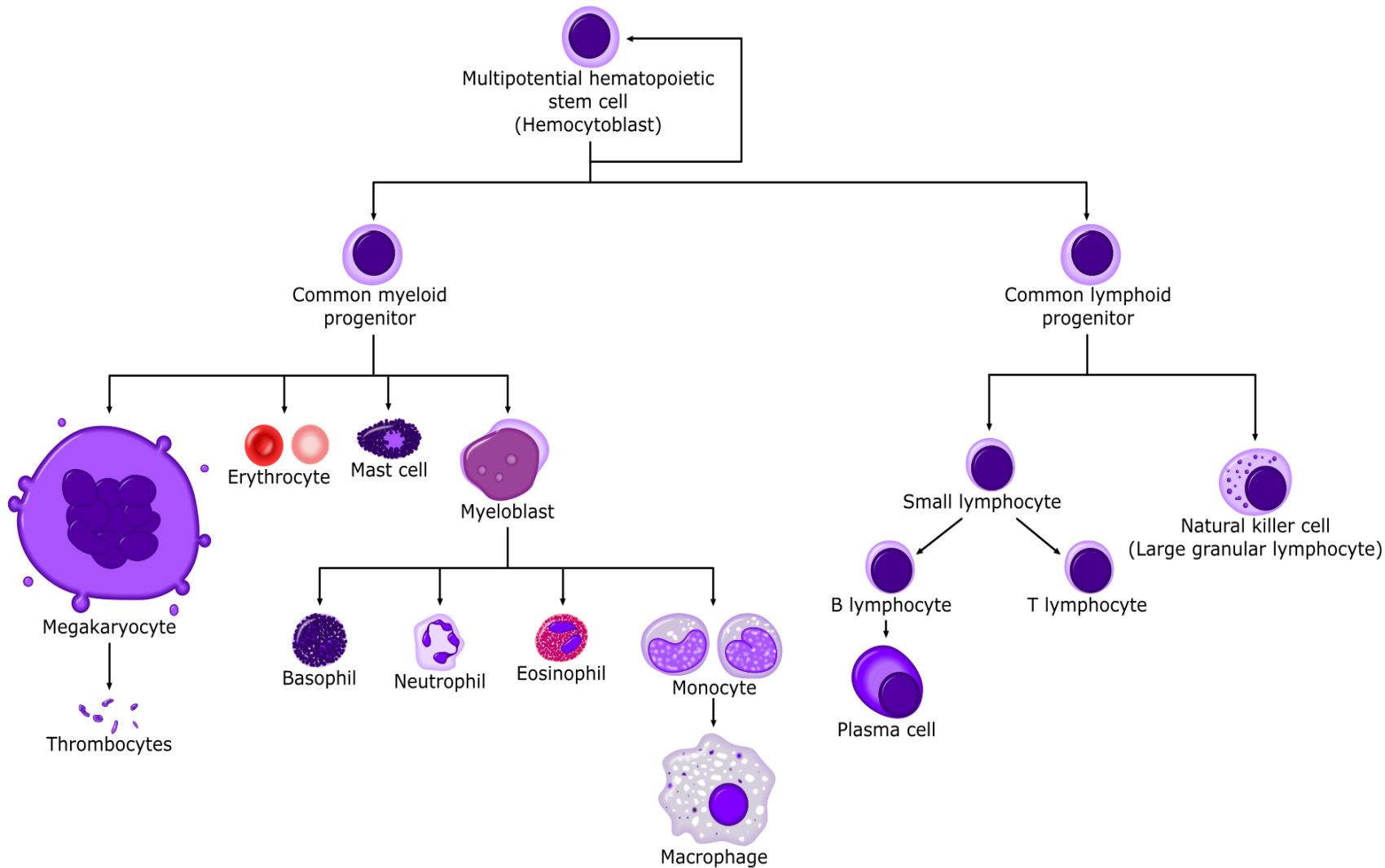
MYELOPHTHISIC ANEMIAS

- **Are anemias caused by metastatic tumor cells replacing the bone marrow extensively**



DISEASES OF WHITE CELLS AND LYMPHOID TISSUE





Myeloid

Lymphoid

NEUTROPHIL



Neutrophil

**Polymorphonuclear
Leukocyte, PMN, PML**

“Leukocyte”

**Granulocyte, Neutrophilic
granulocyte**

“Poly-”

Polymorph

LEUKOPENIA/NEUTRO- penia

Neutropenia/Agranulocytosis

- INADEQUATE ^S PRODUCTION
- INCREASED DESTRUCTION

- 500-1000/mm³ is the
DANGER zone!

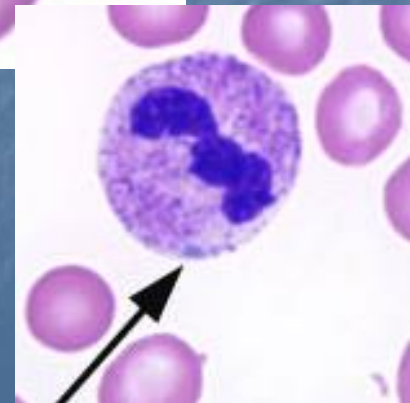
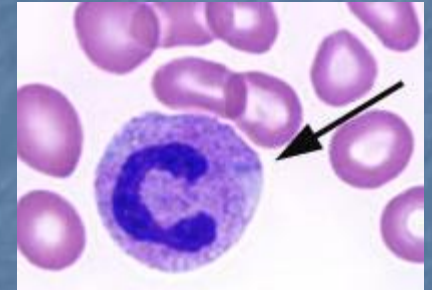
Leukocytosis/Neutrophilia

a

- Marrow and splenic pool size
- Rate of release between pool and circulation
- Marginating pool
- Rate of WBCs (neutrophils/monocytes) leaving the vascular compartment
- NON-vascular pools FIFTY times larger than the vascular pools
- TNF/IL-1/cytokines stimulate T-cells to produce CSF, the WBC equivalent of EPO

NEUTROPHIL INCREASES (e.g., "NEUTROPHILIA")

- BACTERIA
- TISSUE NECROSIS, e.g., MI
- DÖHLE BODIES (e.r. remnants) and TOXIC GRANULES are often seen with NEUTROPHILIA
- Accompanied by a "LEFT" shift



LEUKEMIAS

- **MALIGNANT PROLIFERATIONS of WHITE BLOOD CALLS**
- **In the case of neutrophilic precursors, the primary process is marrow and peripheral blood, but can involve any organ or tissue which receives blood**
- **In the case of lymphocytes, there is an intimate concurrence with malignant lymphomas**

LEUKEMIAS

These are composed of two major groups: myeloid (granulocytic) and lymphoid.

Causes: The cause is unknown but some predisposing factors have been recognized:

1. Myelodysplastic syndromes precede the onset of leukemia
2. Genetic factors may play a role, chromosomal syndromes (Downs, etc.) are associated with increased risk of leukemias.
3. Ionizing radiation; there is increased incidence in those exposed to radiation for treatment or otherwise.
4. Alkylating agents used in chemotherapy are associated with increased risk
5. Viruses: Human T-cell lymphocytic virus-1 (HTLV-1) is an RNA oncogenic virus that causes T-cell leukemias
6. Endogenous oncogenes play a role and are associated with chromosomal breaks, translocations or deletions. The Philadelphia chromosome (translocation of fragments of chromosomes 9 & 22) is associated with the formation of an oncogene (a proto-oncogene on #22 separates from its expression control) and are associated with the development of CML (also ALL & AML to a lesser extent).

Leukemias vs. Lymphomas

- All leukemias of lymphocytes have lymphoma counterparts
- Primary lymphomas can have “leukemic” phases, including multiple myelomas
- Any myeloid leukemia can infiltrate a lymph node, or any other site, but if/when it does it is NOT called a lymphoma, but simply a myeloid infiltrate INTO a lymph node
- ALL lymphomas are malignant proliferations of lymphocytes
- ALL leukemias involve bone marrow changes

LYMPHOMAS

- **NODAL or EXTRANODAL**
- **T or B**
- **SMALL or LARGE CELLS**
- **FOLLICULAR or DIFFUSE**
- **Hodgkins or NON-Hodgkins**
- **“F.A.B. classification” is currently popular this week**

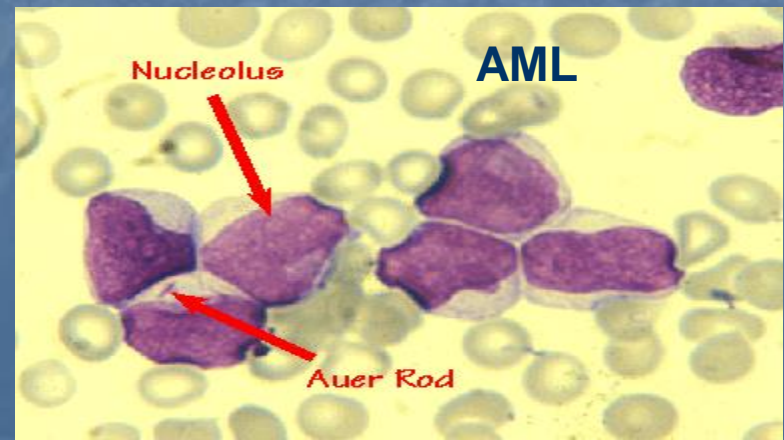
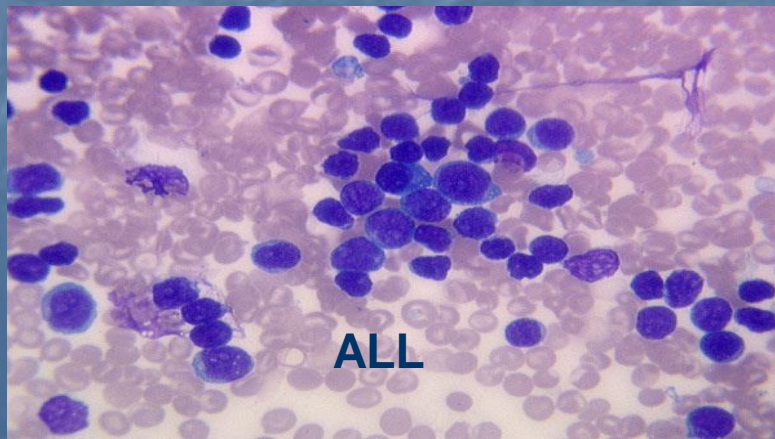
(French American British), for the NON-Hodgkins lymphomas

LEUKEMIAS

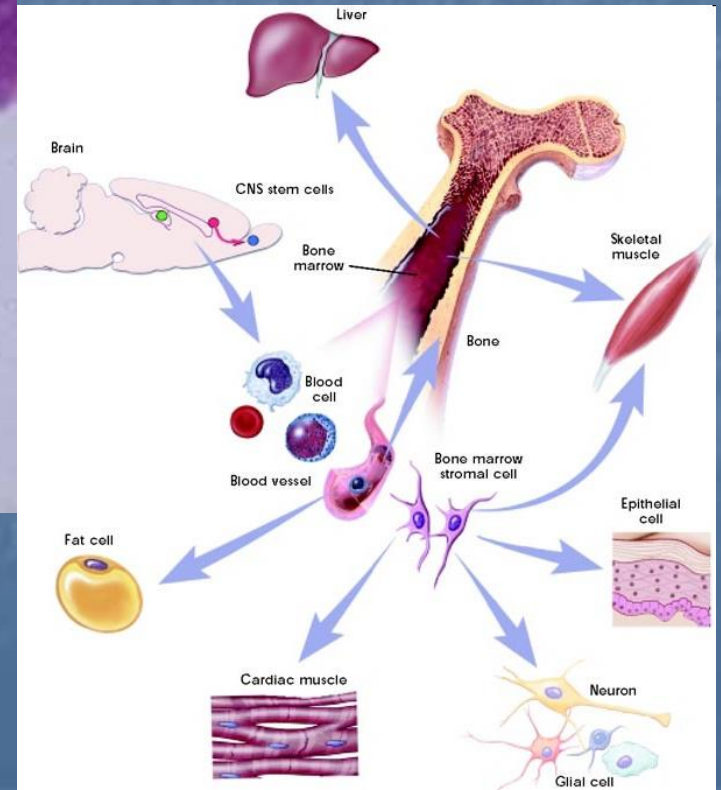
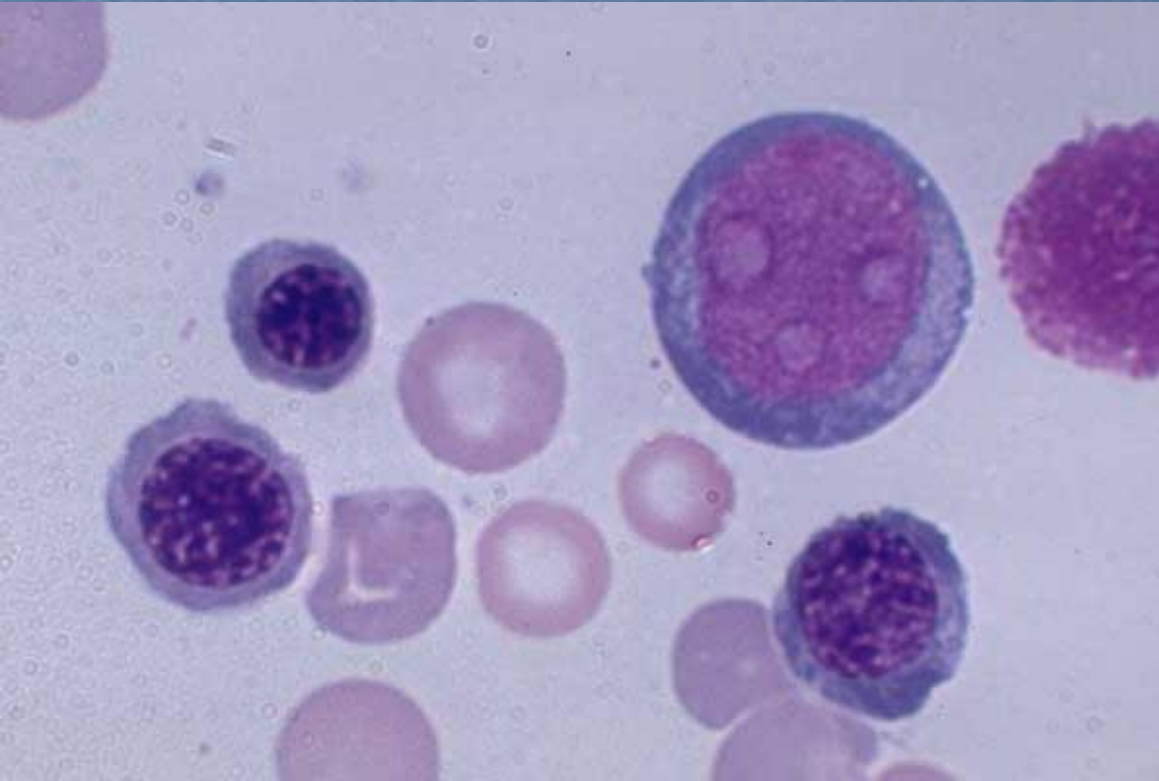
- **Acute or Chronic**
- **Myeloid or Lymphocytic**
- **Childhood or Adult**
- **All involve marrow**
- **All ACUTE leukemias suppress normal hematopoiesis, i.e., have anemia, thrombocytopenia**
- **Most have chromosomal aberrations**
- **Some can respond DRASTICALLY to chemo, most notably ALL in children, even be cured!!!!**

Types of Leukemias

1. **Acute Lymphoblastic leukemia (ALL)** ~30% of all leukemias, the most common among children under 5 years old a second peak occurs after age 60. The marrow contains more than 30% lymphoblasts. The prognosis is inversely proportional to age, responds remarkably well to chemotherapy & marrow transplant, 85% long term survival in 1-10 year olds, ~50% in adults.
2. **Acute myelogenous leukemia (AML)** ~80% of acute leukemias in adults. Marrow has >20% myeloblasts. Overall prognosis is poor with relapse after chemotherapy and most do not survive more than 5 years after diagnosis. Two forms; acute denovo AML(better prognosis ~70% 5 year (especially acute promyelocytic~90% 5 year) or as an end-stage of CML and myelofibrosis (poorer prognosis~15% 5 year).



BLAST



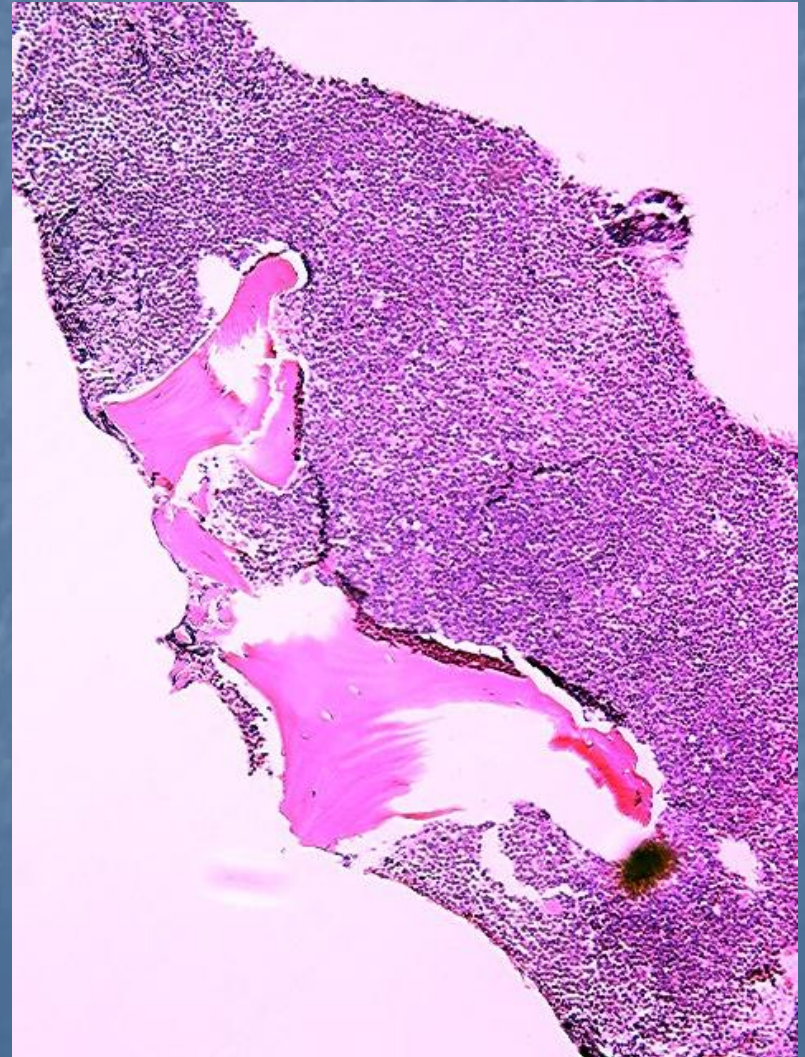
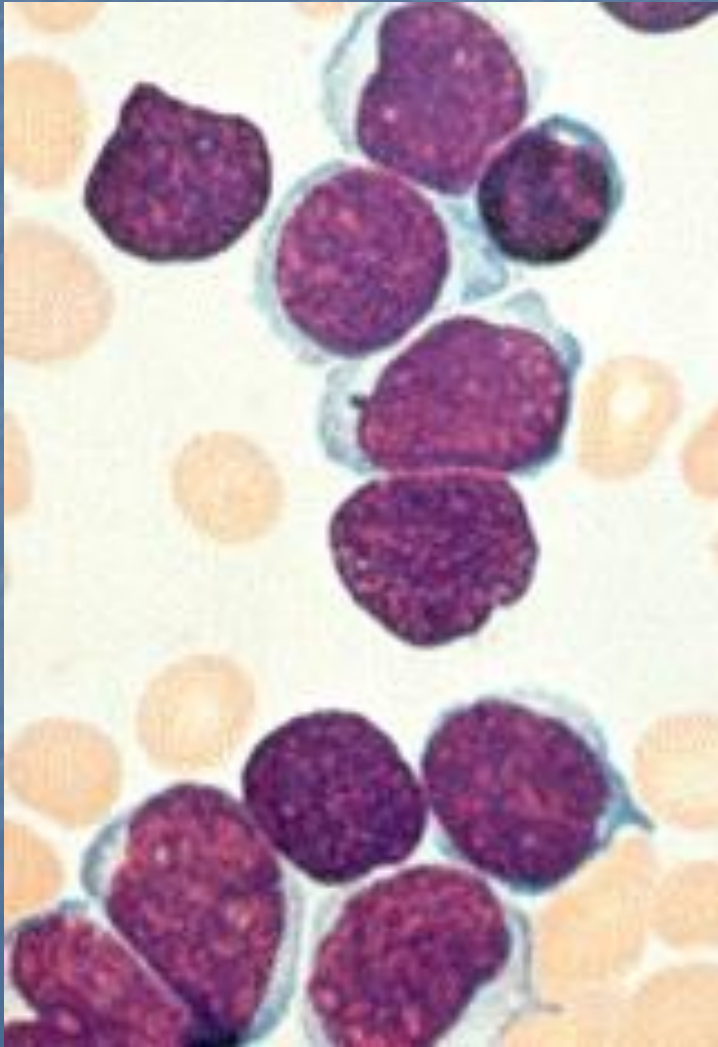
Types of Leukemias

- 3. Chronic lymphocytic leukemia (CLL)** Peak incidence is in elderly males >60 years old. Bone marrow has >40% lymphoid cells, peripheral blood has >150,000. Neoplastic cells resemble B-lymphocytes and infiltrate marrow, spleen, liver & nodes. CLL has an indolent course over 7-10 years, it responds poorly to chemotherapy. It is closely related to small cell lymphoma and lymphadenopathy is common.
- 4. Chronic myelogenous leukemias (CML)** Peak incidence is 35-50 years old. Symptoms are related to loss of normal marrow functioning; anemia, bleeding & infection. Associated with the presence of the Philadelphia chromosome. Peripheral WBC counts in the 20-50,000 range with large component of "more mature" myeloid precursors. Prominent splenomegaly, greater than hepatomegaly or adenopathy. Frequently terminates in a "blast" crisis with peripheral WBCs of >100,000 with immature myeloid cells. Prognosis is poor despite chemotherapy.

ORGANOMEGALY



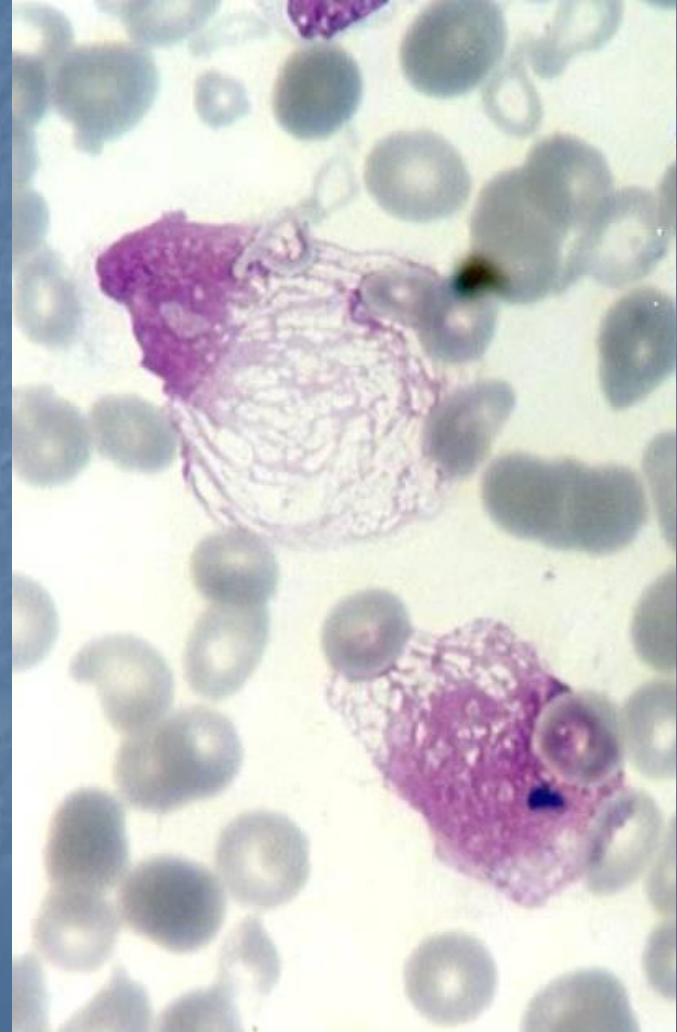
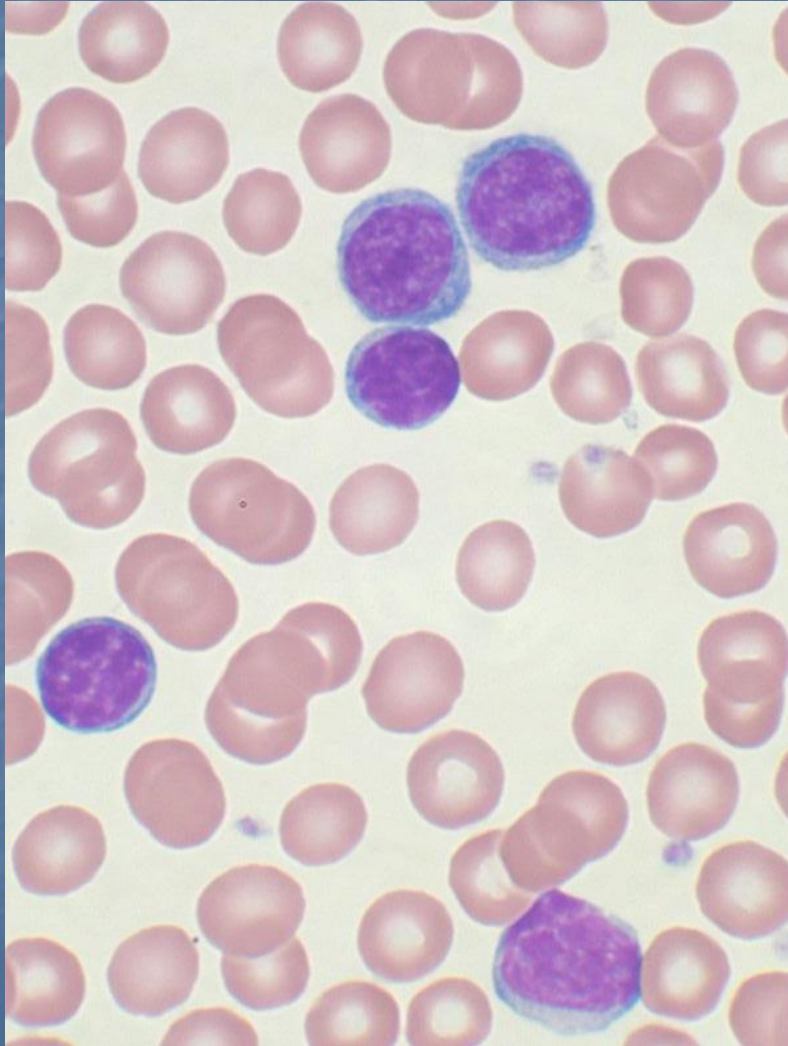
A.L.L.



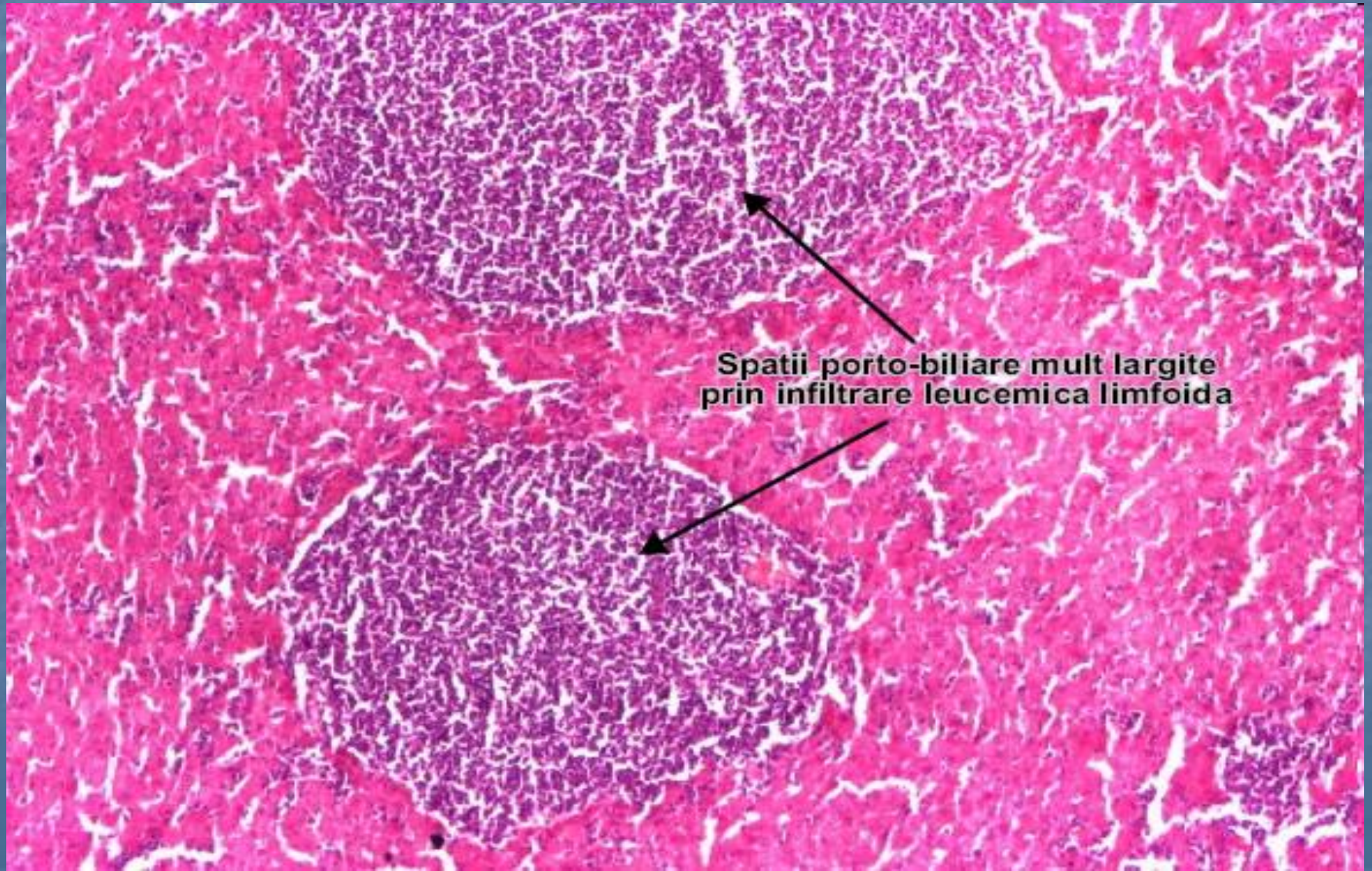
C.L.L.

- Unexplained sustained (months) lymph count of $> 4000/\text{mm}^3$ is CLL, usually picked up on CBC
- M > F
- Lymphs look normal and are NOT blasts
- No need for marrow exam for dx, but progressive involvement of marrow, nodes, and other organs is the usual biologic behavior
- Liver can be involved portally or sinusoidally
- Translocations RARE, but trisomies and deletions common

C.L.L.



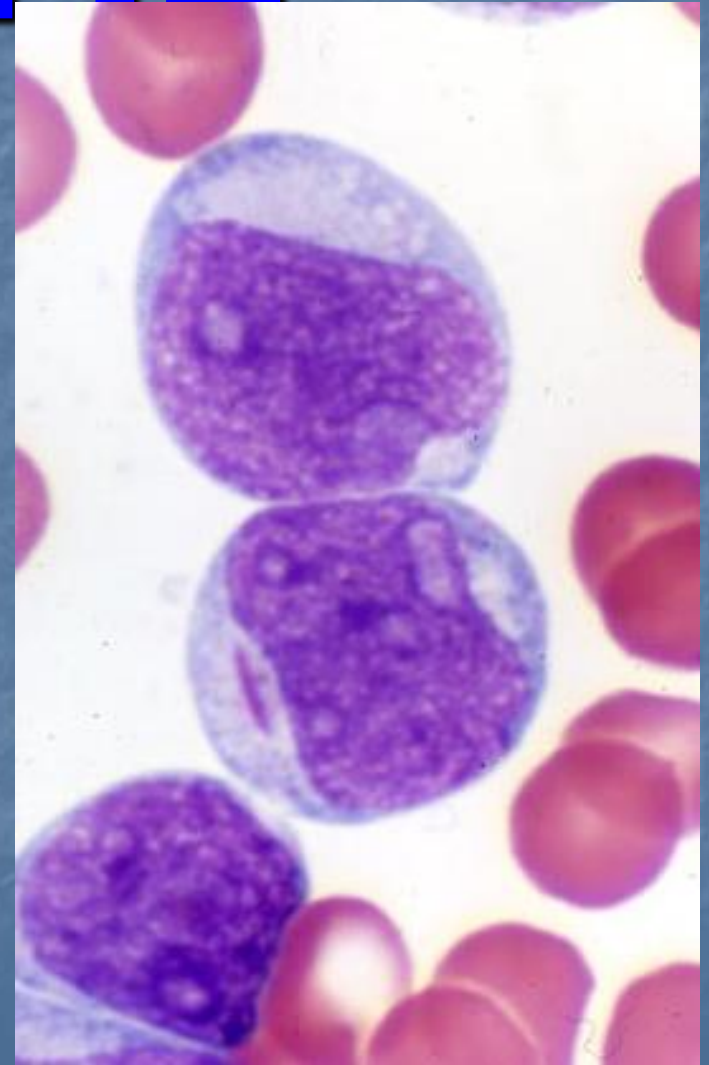
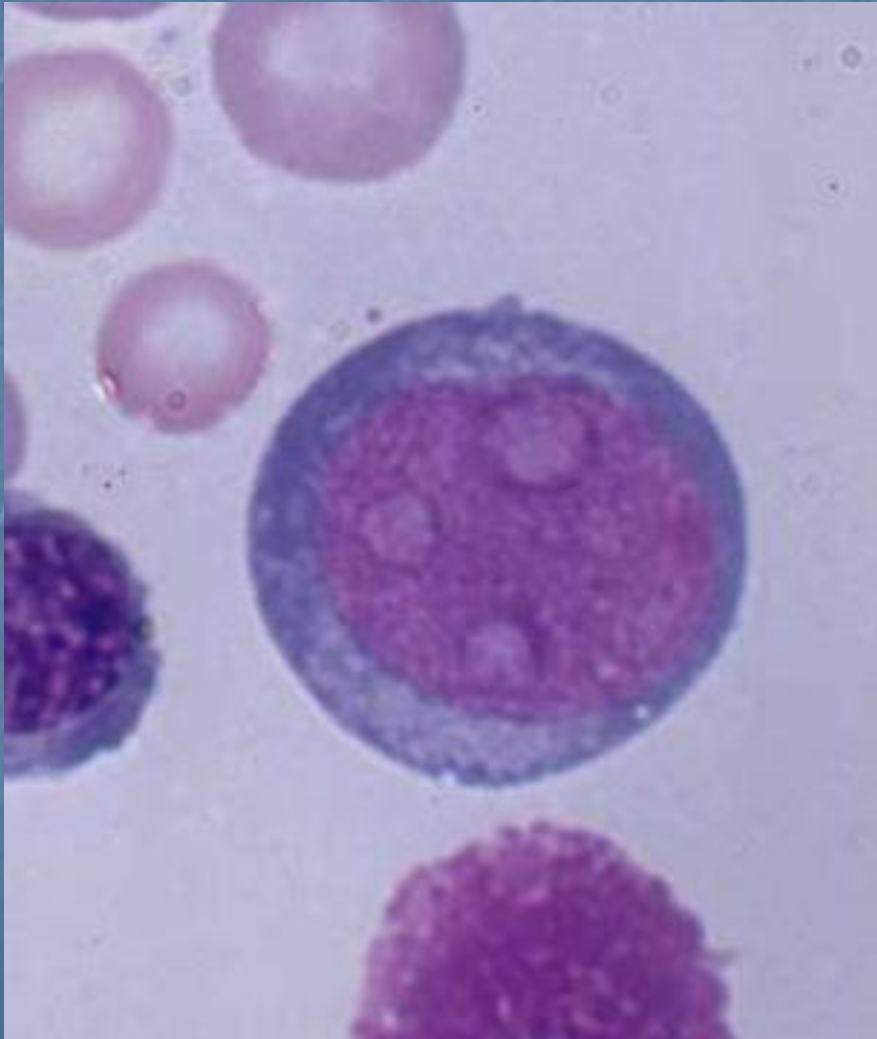
CLL



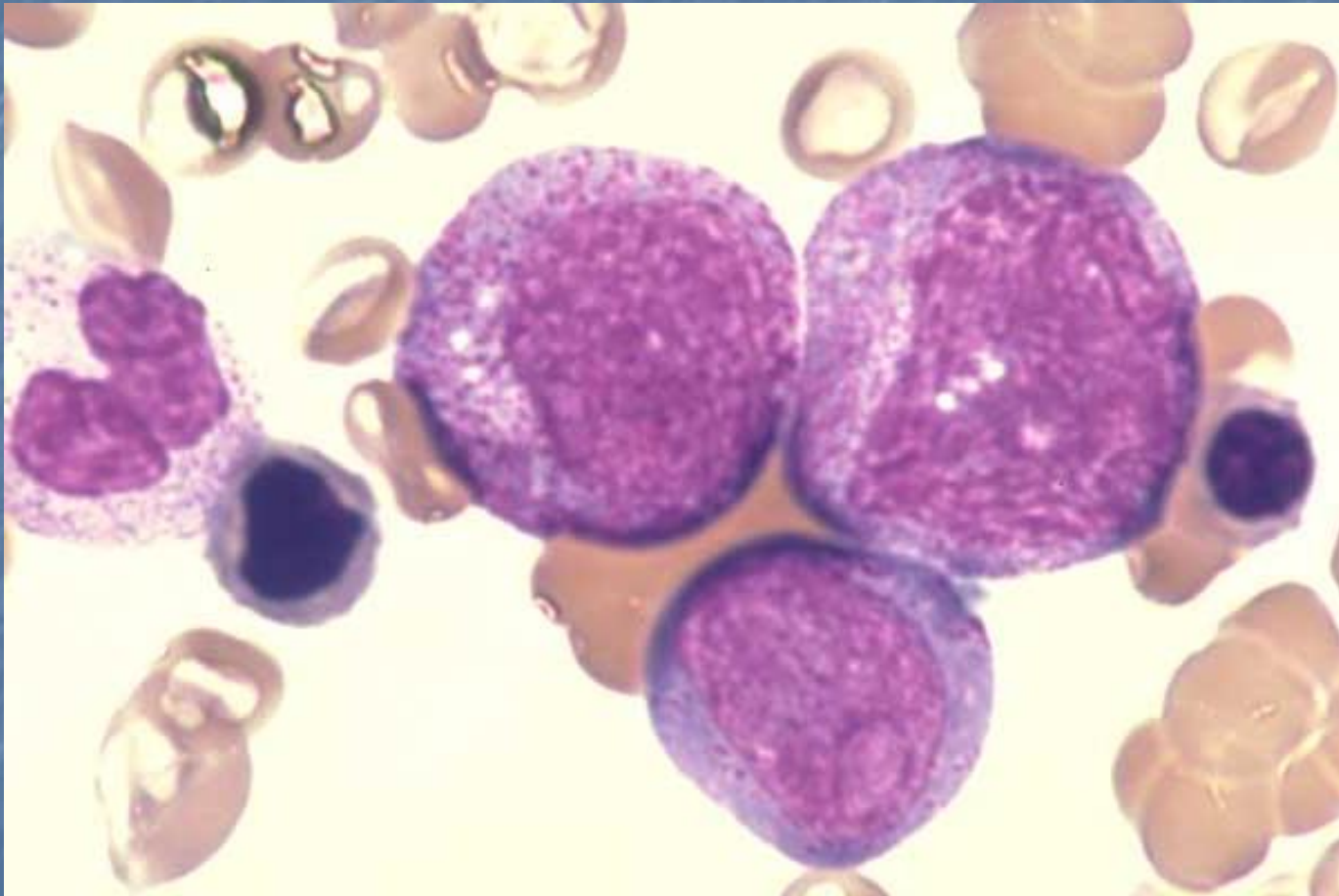
A.M.L.

- **GENETIC ABERRATIONS INHIBIT DIFFERENTIATION**
- **Many have various TRANSLOCATIONS**
- **F.A.B. classifies them as M0 → M7**
- **MORE than 20% of BLASTS are needed in the marrow for a diagnosis of acute leukemia!!! (i.e., ANY kind of BLAST**
- **NORMALLY, a marrow should have only about 1-2 % blasts**

M0 → M2



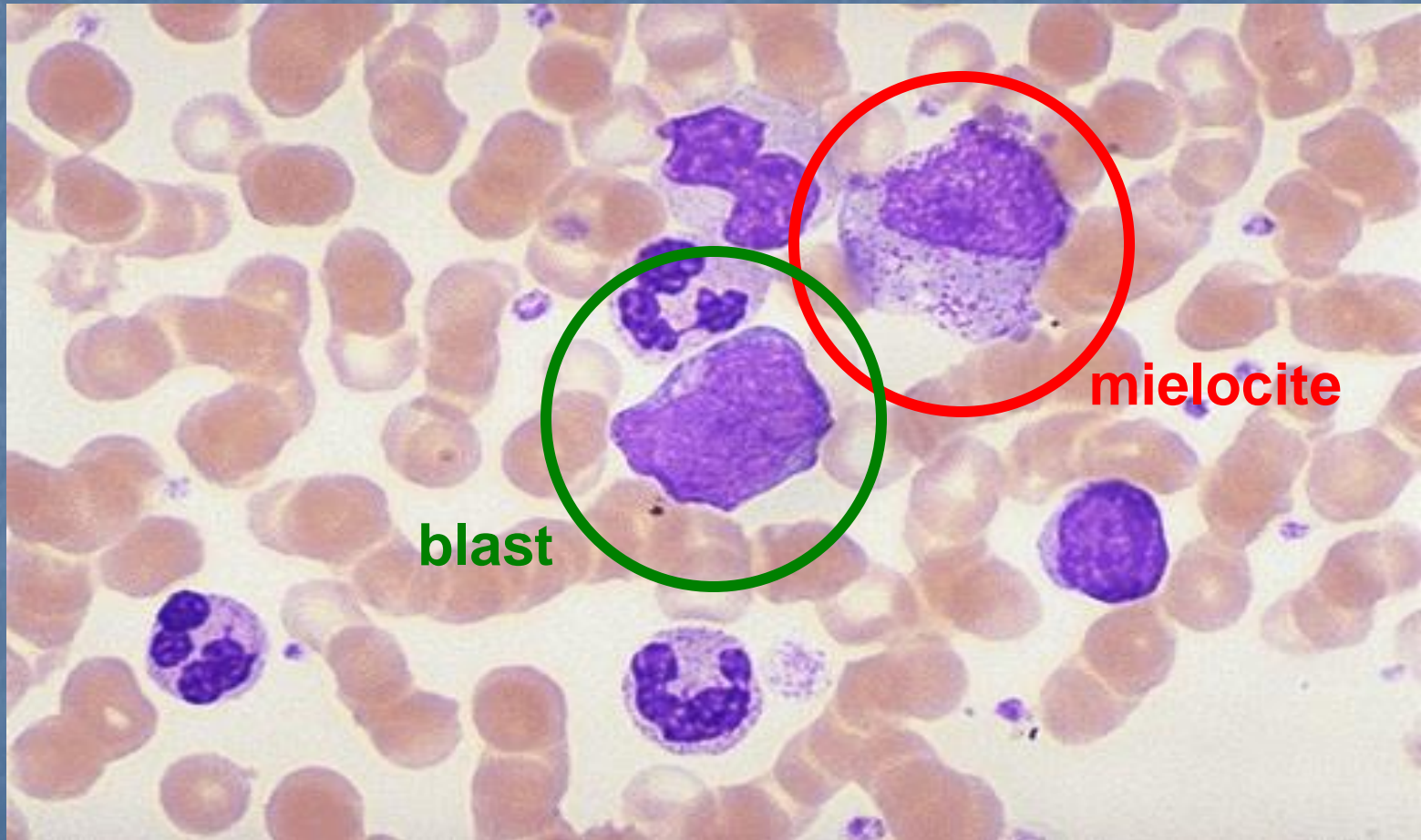
M3



A.M.L.

- Anemia
- Thrombocytopenia (bleeding)
 - Petechiae
 - Ecchymoses
- Fever
- Fatigue
- Lymphadenopathy
- 60% respond, BUT only 20 % are free of remission after 5 years, WORSE than A.L.L.

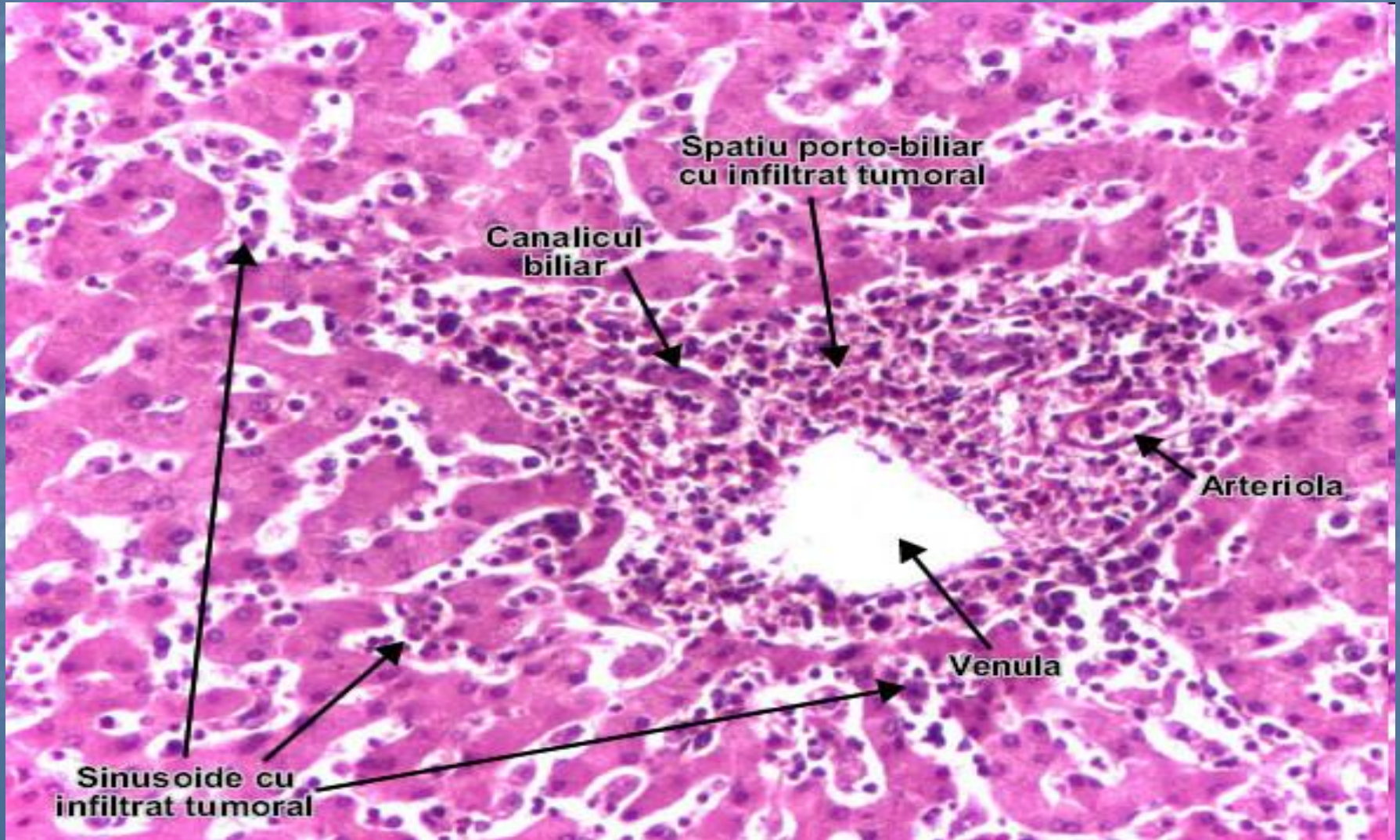
CML high-power



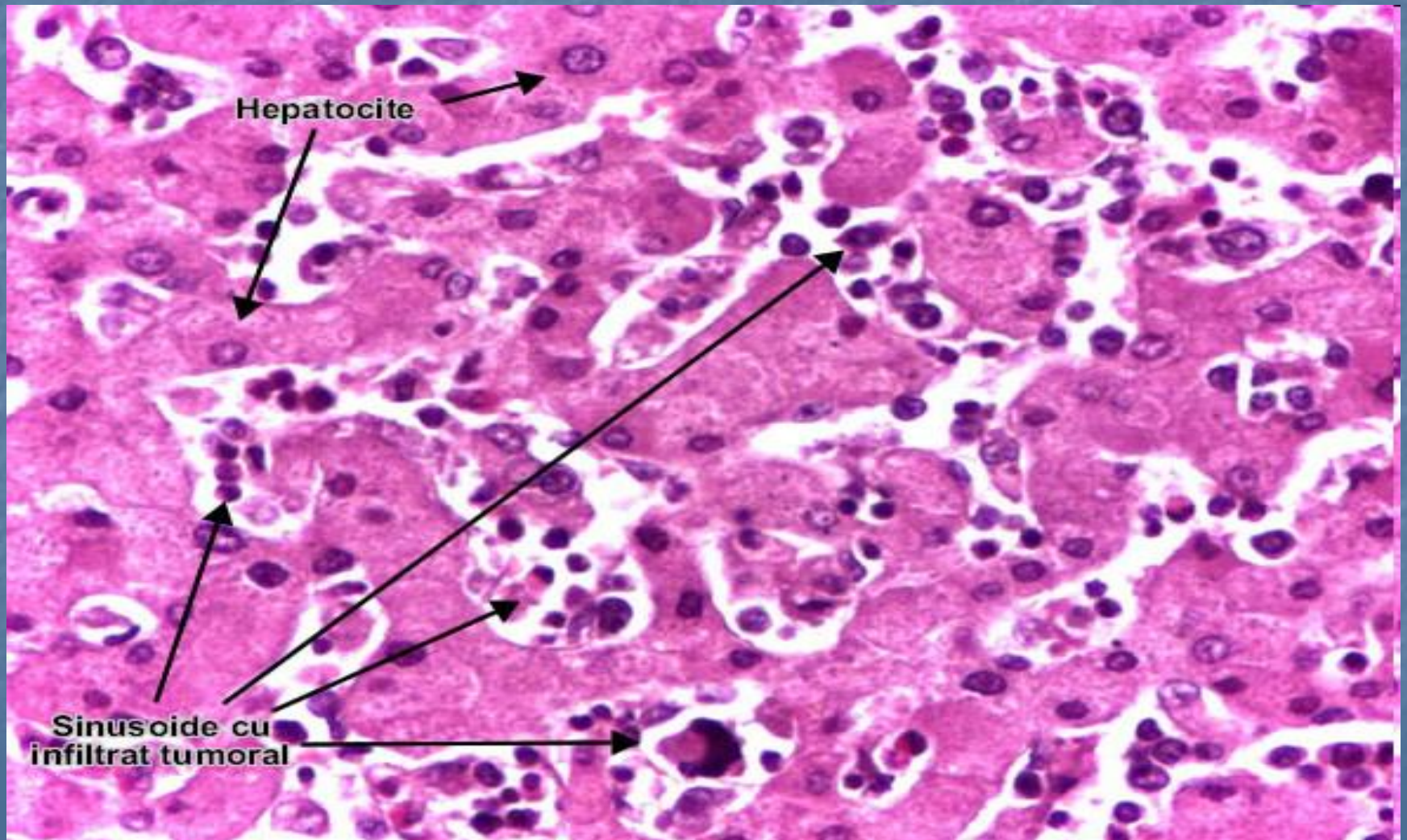
Massive splenomegaly in CML



CLL



CML



PLASMA CELL DISORDERS

Main types

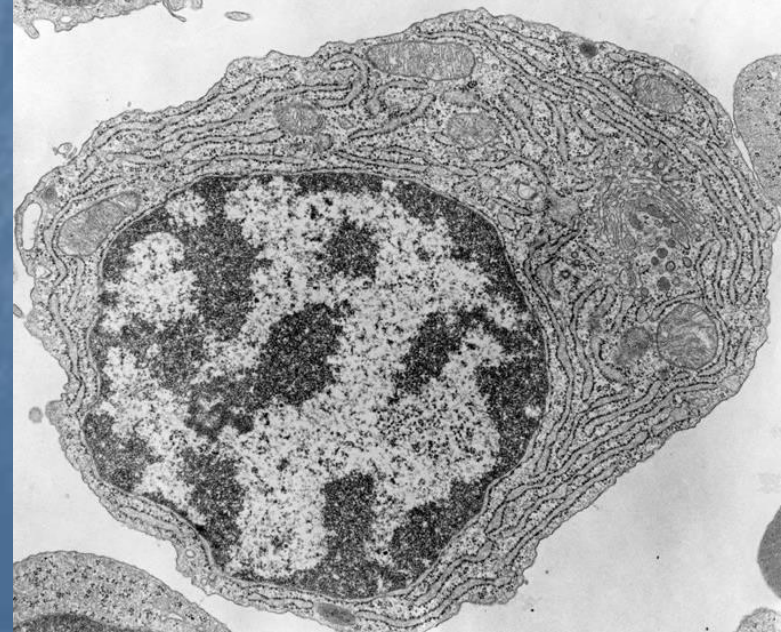
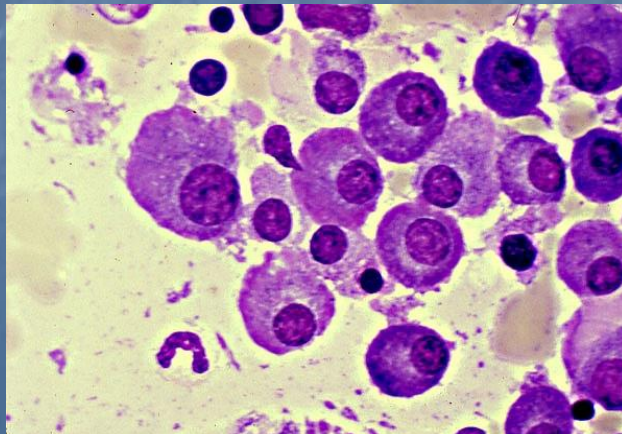
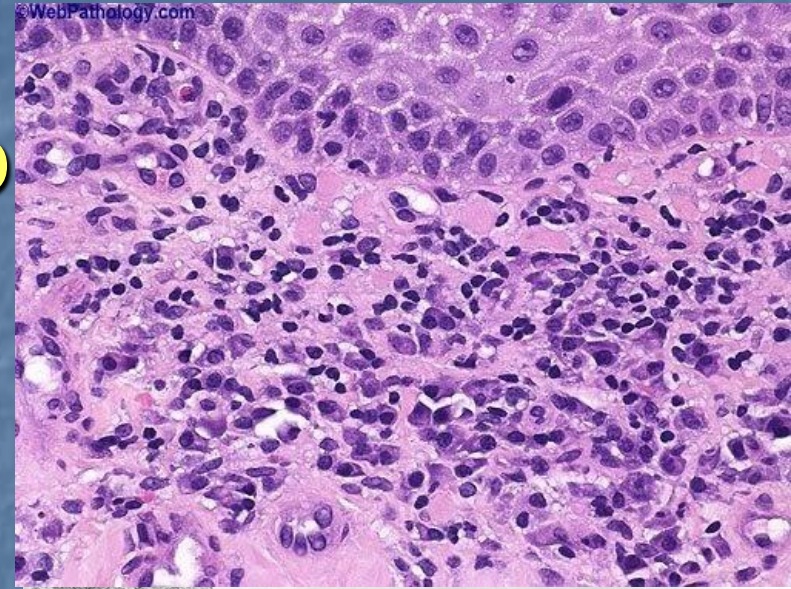
- **Multiple myeloma**
- **Waldenstrom macroglobulinemia:** A malignancy of plasmacytoid lymphocytes that secrete IgM resulting in a hyperviscosity syndrome with renal, retinal and cerebral ischemia as a result of microvascular occlusion. Infiltration of plasmacytoid cells in the marrow, spleen and nodes.
- **Monoclonal gammopathy of unknown significance:** often diagnosed in asymptomatic elderly patients. It is present in ~1% of patients over 60 years old and 3% of patients over 70. There is a 1% risk of developing multiple myeloma. The vast majority suffer no ill effects.

Clinical features

- Tend to occur in those >45 years old.
- Neoplastic plasma cells produce a monoclonal immunoglobulin component that can be identified by serum electrophoresis
- Deposition of light chain immunoglobulin may form amyloid deposits in the kidneys, vessels and other organs.

PLASMA CELL classic features

- **OVAL** cytoplasm, **ROUND** nucleus off to side
- **Cartwheel/Clockface** chromatin
- **Prominent Golgi** or "Hoff"

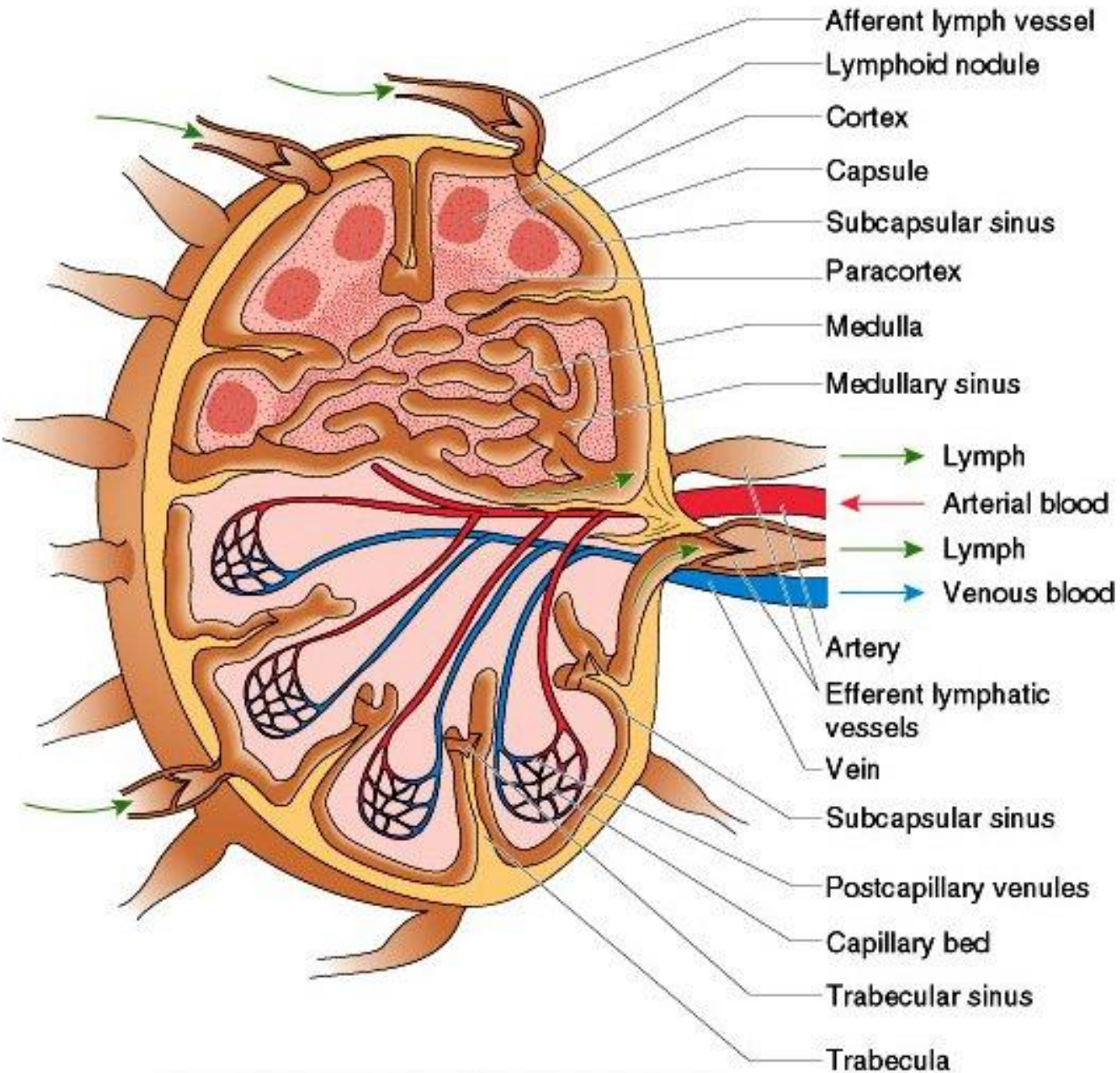


Multiple Myeloma: Skull X-ray

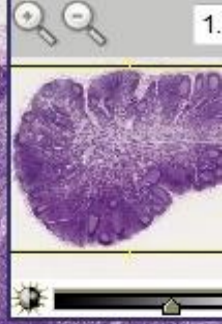
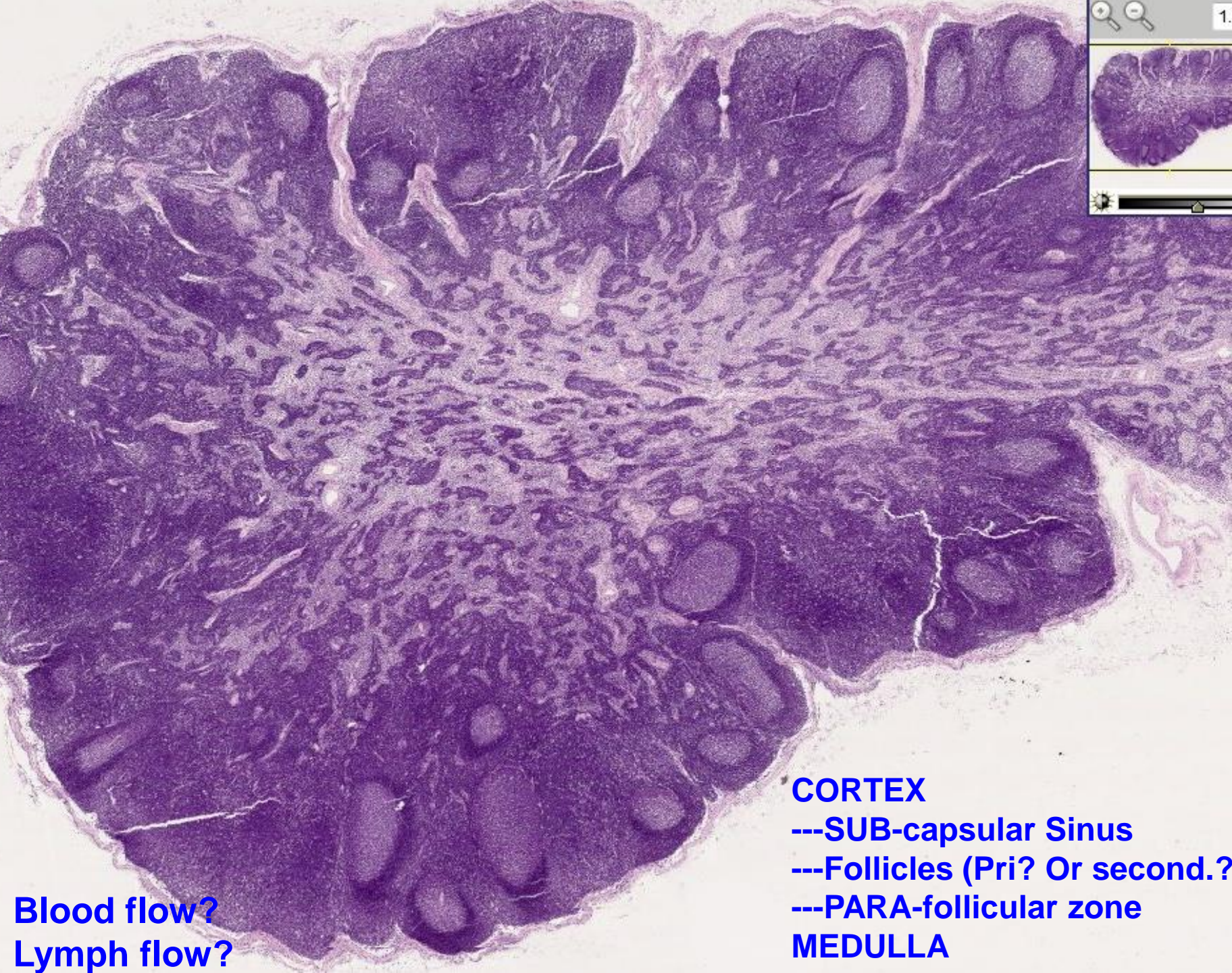


LYMPH NODES

- **Normal Structure, Function**
- **Benign enlargement/Benign disease**
 - **Acute**
 - **Chronic (follicular vs. "sinus histiocytosis")**
- **Lymphomas/Malignant Lymphomas**
 - **Adjectives of various classifications**
 - **Features**
 - **STAGING**
- **Metastatic disease TO lymph nodes**



- Afferent lymph vessel
- Lymphoid nodule
- Cortex
- Capsule
- Subcapsular sinus
- Paracortex
- Medulla
- Medullary sinus
- Lymph
- ← Arterial blood
- Lymph
- Venous blood
- Artery
- Efferent lymphatic vessels
- Vein
- Subcapsular sinus
- Postcapillary venules
- Capillary bed
- Trabecular sinus
- Trabecula



CORTEX

- SUB-capsular Sinus
- Follicles (Pri? Or second?)
- PARA-follicular zone

MEDULLA

Blood flow?

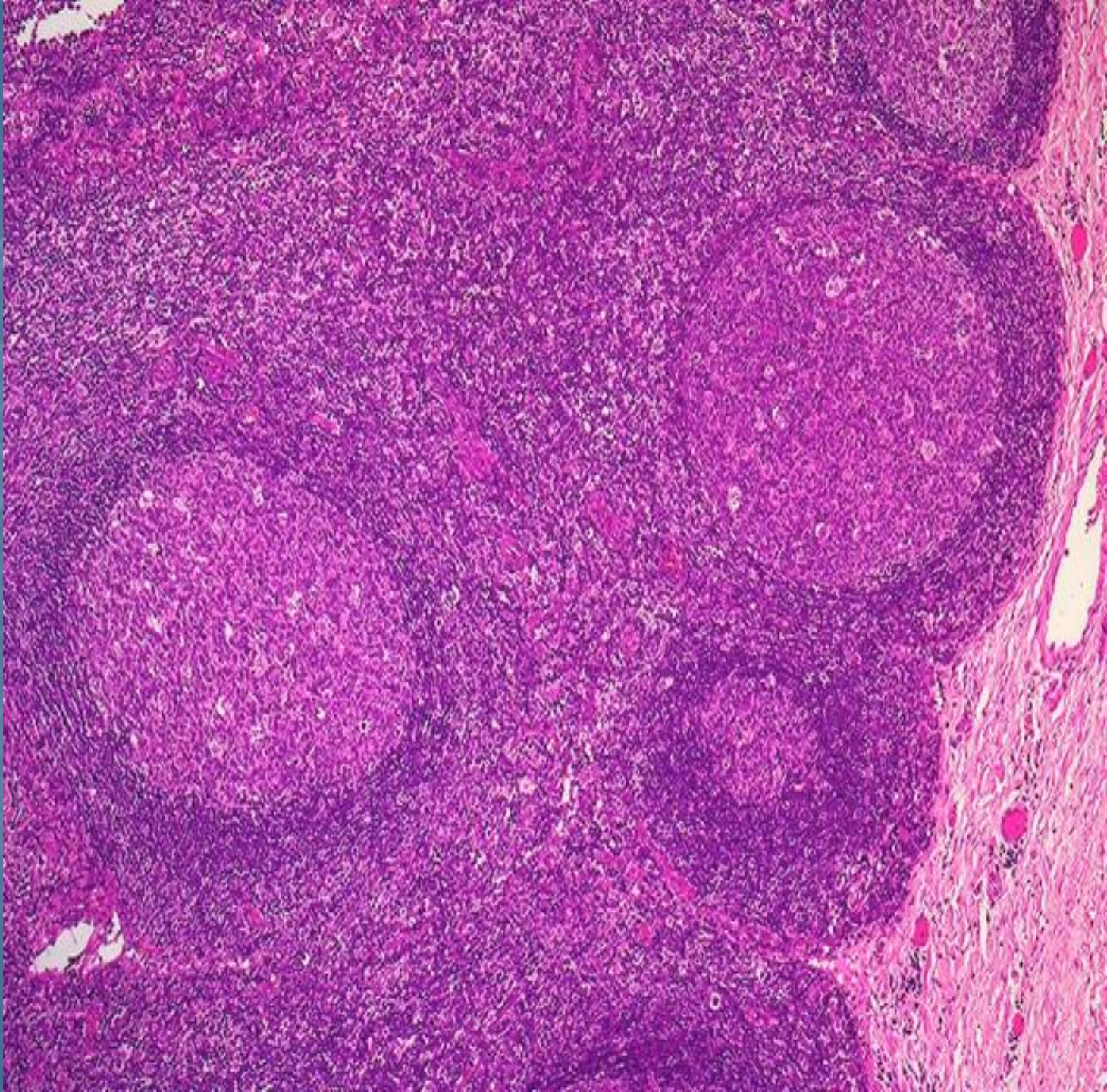
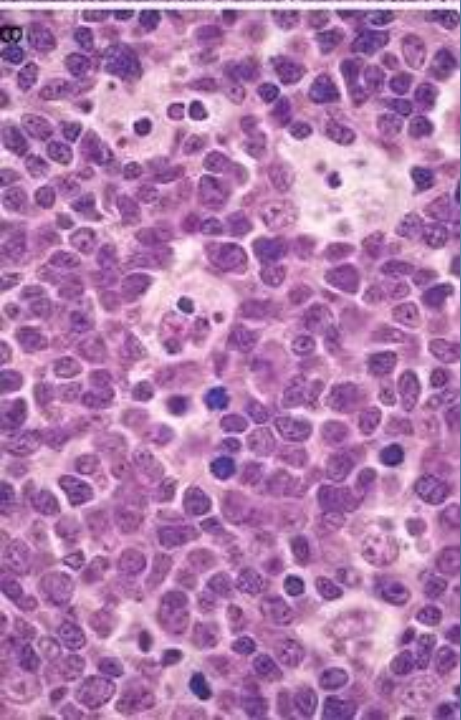
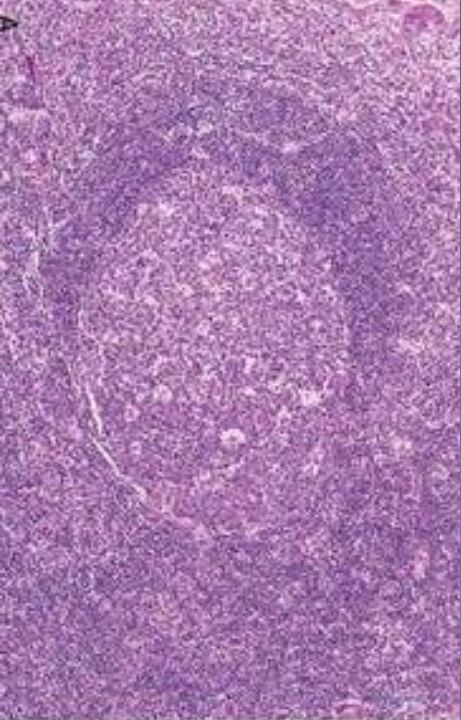
Lymph flow?

Definition of TERMS

- **Lymphadenopathy**
- **Lymphadenitis**
- **What to do if a lymph node is enlarged?**
- **Diffuse/Follicular**
- **T/B/NK, Small/Large, Cleaved/Non-cleaved**
- **Precursor/Peripheral**
- **HD/Non-HD**

BENIGN ENLARGEMENT

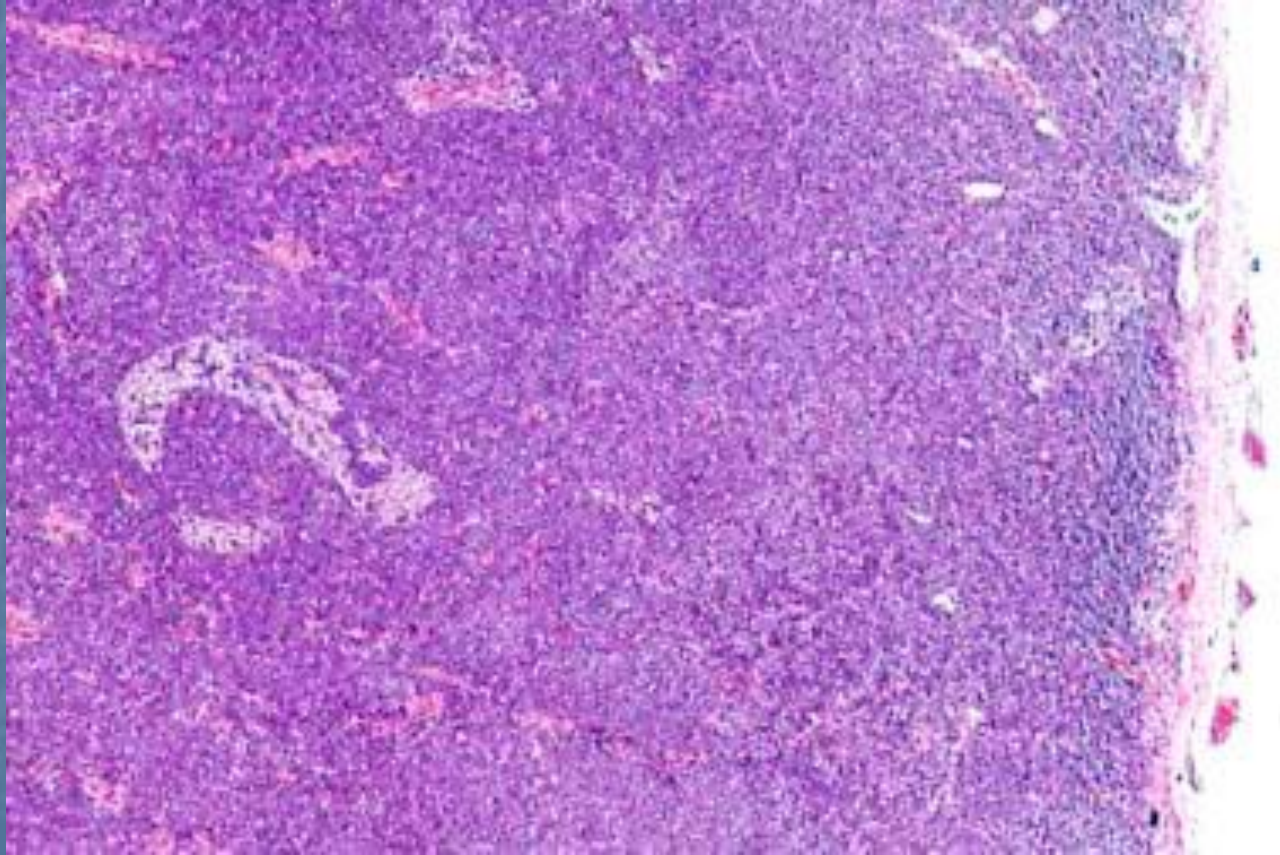
- Also called **LYMPHADENITIS**, and **HYPERPLASIA**
- Can be **ACUTE** (tender), or **CHRONIC** (non-tender)
- Usually **SUBSIDE** in, say, less than 6 weeks
- **FOLLICULAR HYPERPLASIA** is enlargement of the cortical secondary follicles and increase in number of the cortical secondary follicles
- **SINUS HISTIOCYTOSIS** is prominence in medullary sinuses (also called "reticular" hyperplasia)



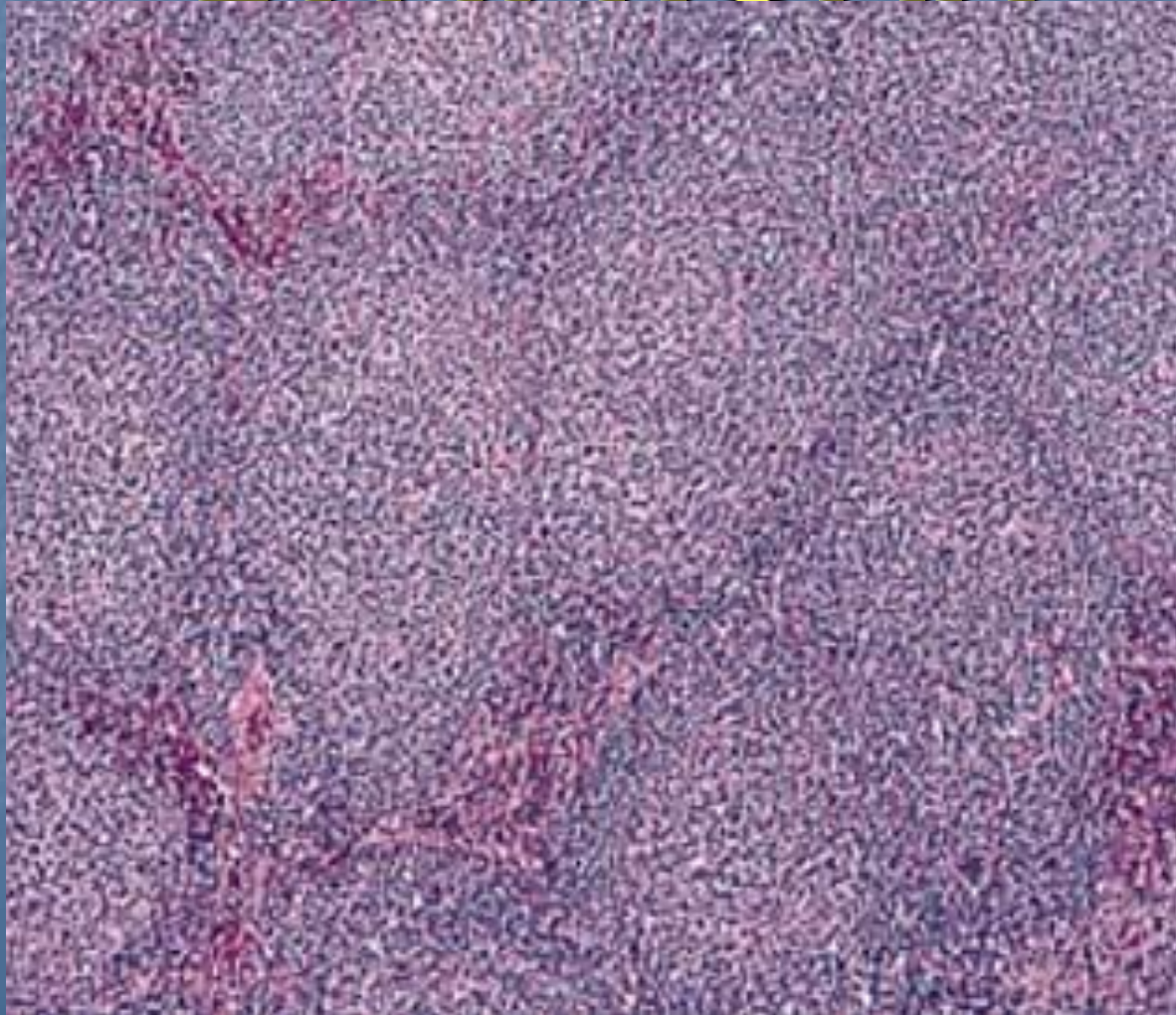
(MALIGNANT) LYMPHOMAS

- **Terms in historic classifications:**
 - **Diffuse/Follicular, Small/Large, Cleaved/Non-cleaved**
 - **Hodgkins /NON-Hodgkins**
 - **Lukes, Rappaport, etc.**
 - **Working Formulation, WHO, NIH, FAB, Intl., etc.**
 - **B**
 - **T**
 - **PRECURSOR (less mature looking)**
 - **PERIPHERAL (more mature looking)**

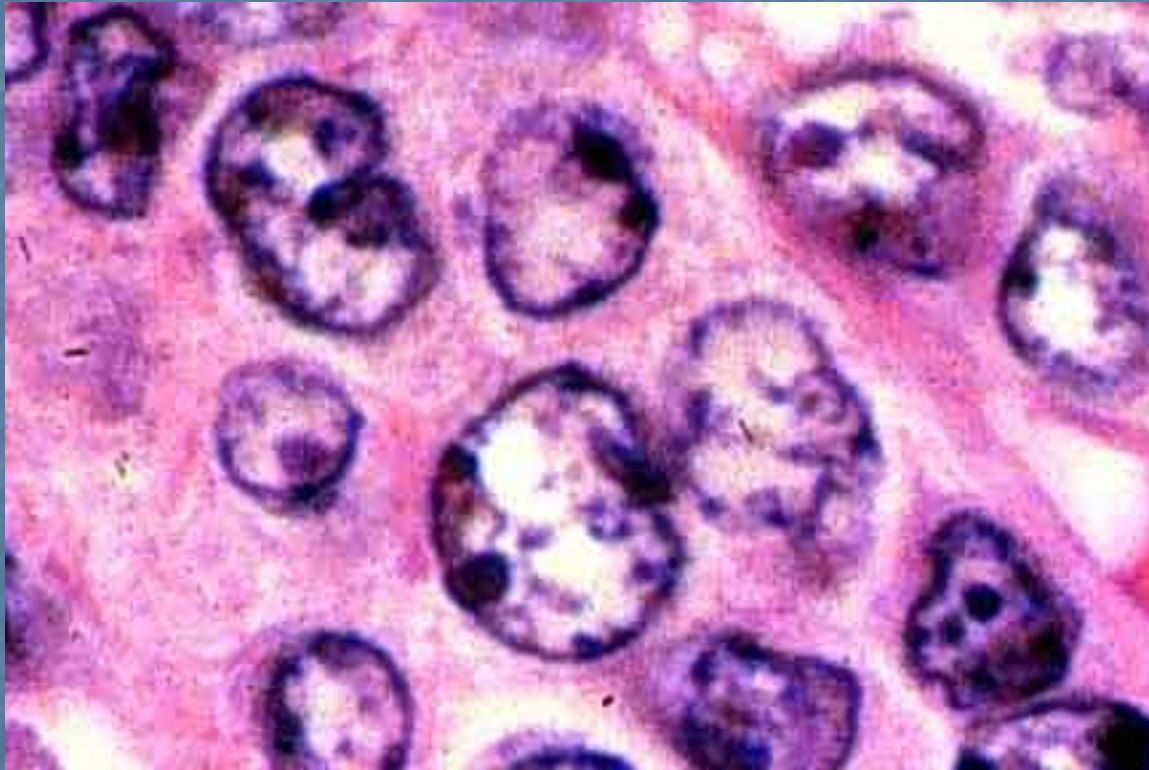
DIFFUSE LYMPHOMA



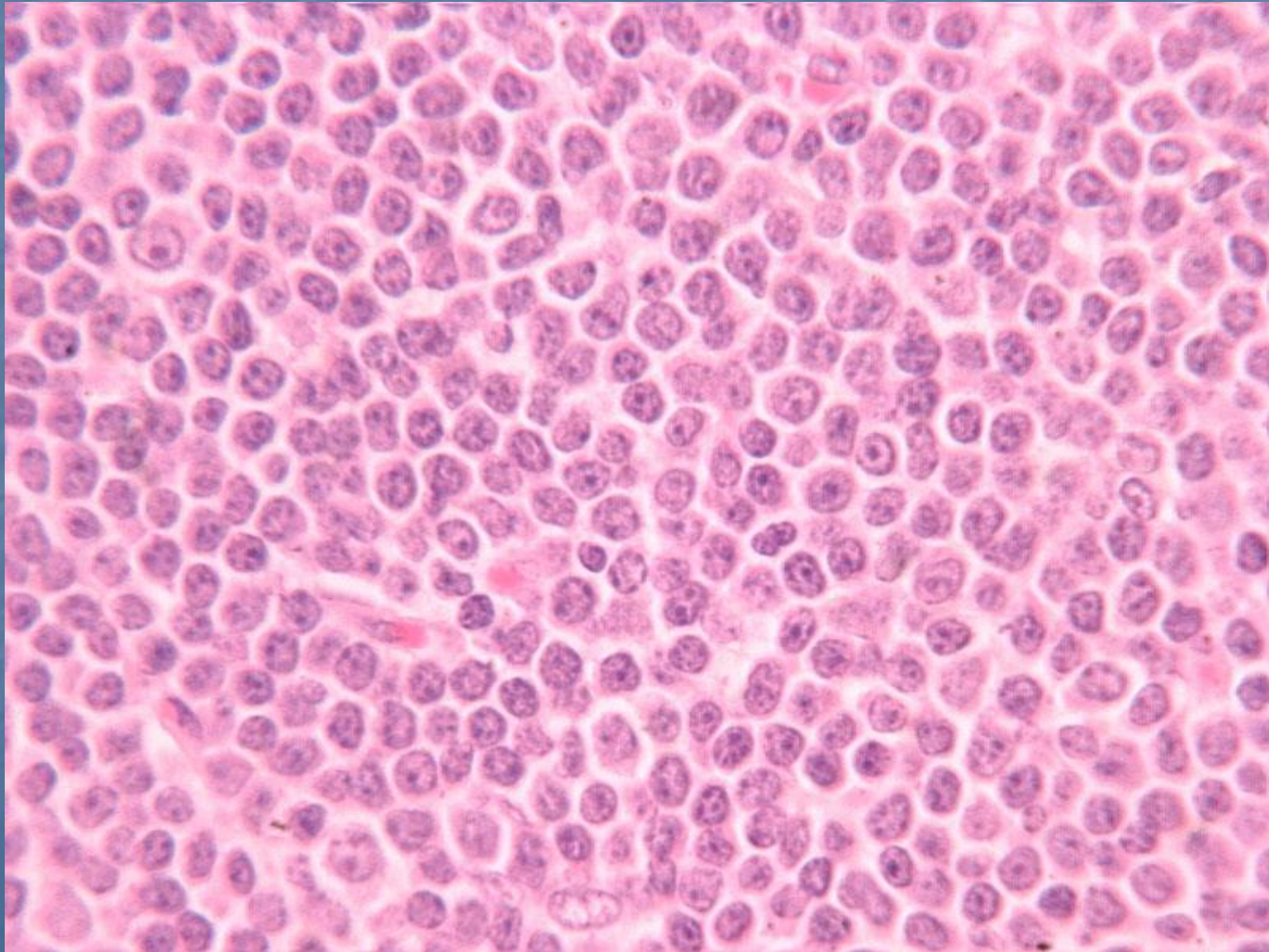
FOLLICULAR LYMPHOMA



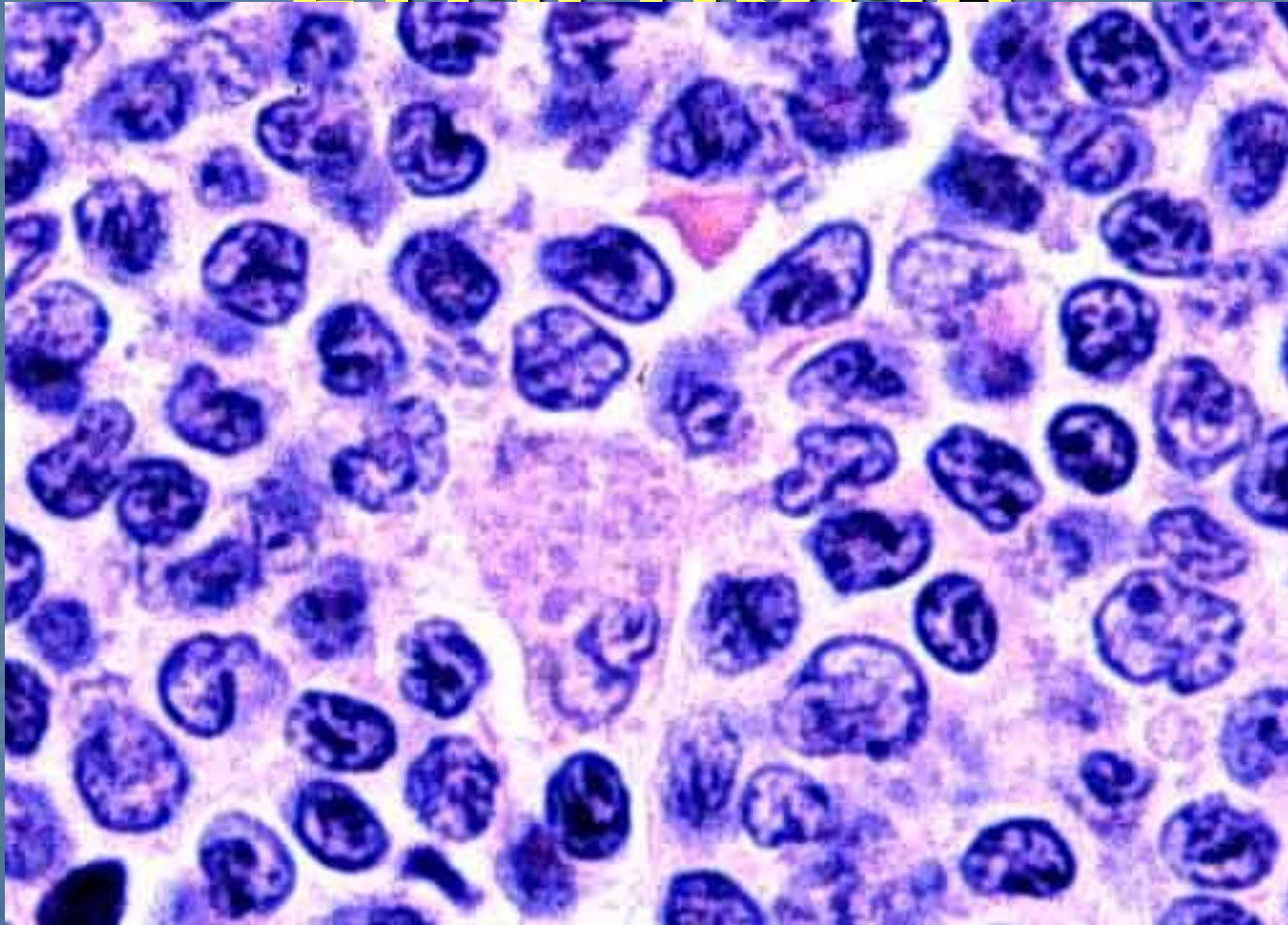
LARGE CELL LYMPHOMA



SMALL CELL LYMPHOMA



"CLEAVED" CELL LYMPHOMA



FEATURES of LYMPHOMAS

- The Antigen receptor genes re-arrangement **PRECEDES** malignant transformation, so the cells are **MONOCLONAL**, NOT the usual **POLYCLONAL**
- 85% B-cell, 15% T-Cell
- The tumor cells congregate wherever T and B cell congregate normally however
- **DISRUPTED** or “**EFFACED**” normal architecture, obliterated subcapsular sinus
- HD/Non-HD staging **CRUCIALLY IMPORTANT**, esp. HD. Why? HD grows more “linearly”

LATEST

CLASSIFICATION

- **NON-HODGKIN**

- **PRECURSOR B**

- **PERIPHERAL B**

- **PRECURSOR T**

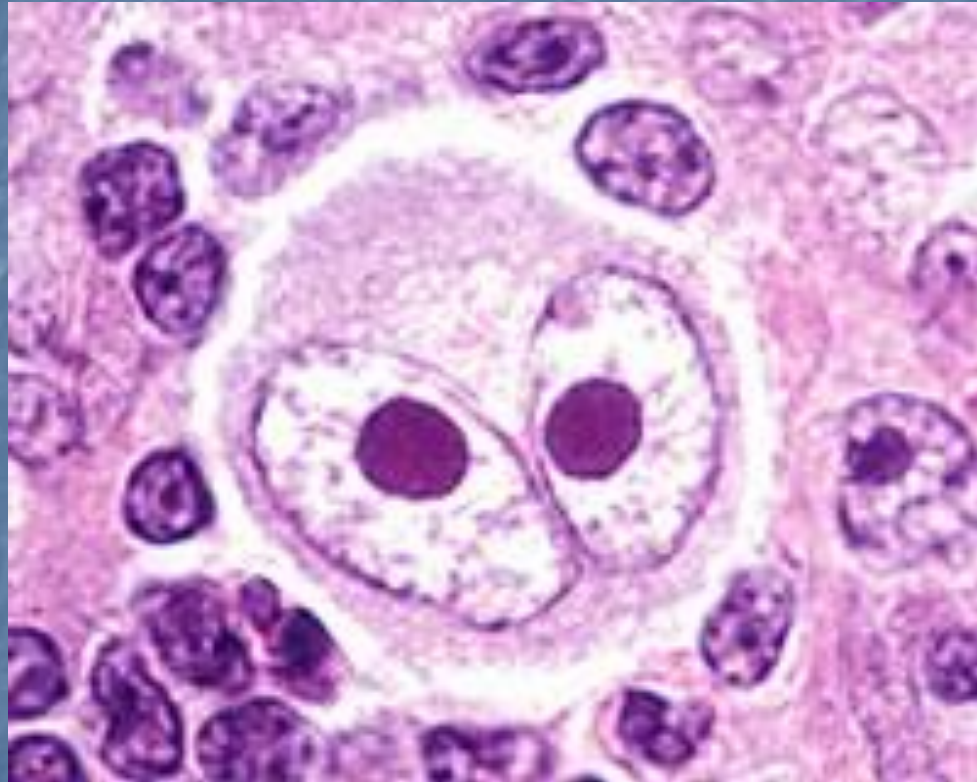
- **PERIPHERAL T**

- **HODGKIN'S DISEASE (i.e.,
HODGKINS LYMPHOMA)**

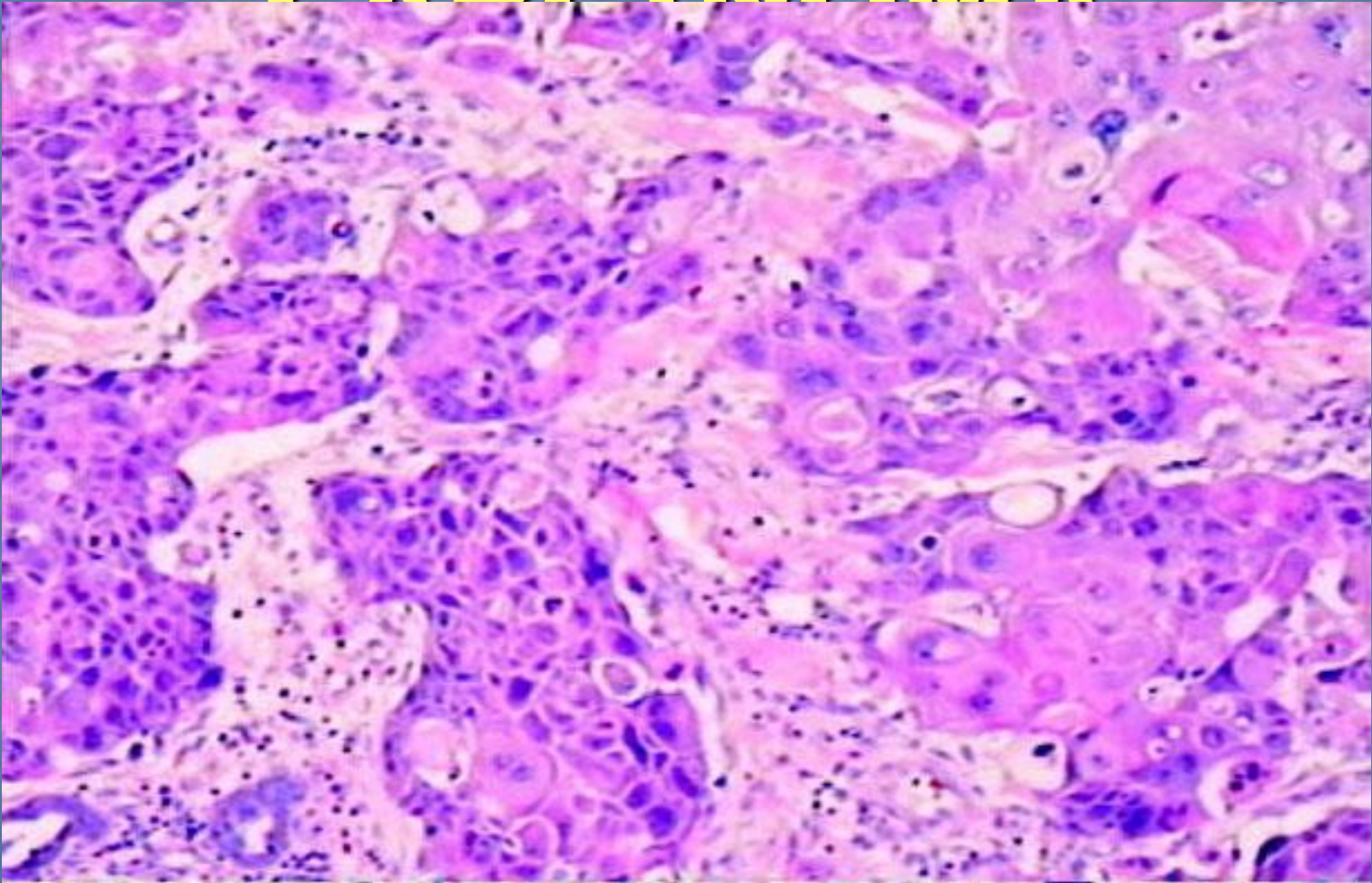
HODGKINS DISEASE

- **NEED R-S (Reed-Sternberg, or Sternberg-Reed) cells for correct diagnosis**
 - **NODULAR SCLEROSIS** (Young Women), the R-S cells may be called "LACUNAR" cells
 - **MIXED CELLULARITY**
 - Lymphocyte RICH
 - Lymphocyte POOR
 - Lymphocyte PREDOMONANCE

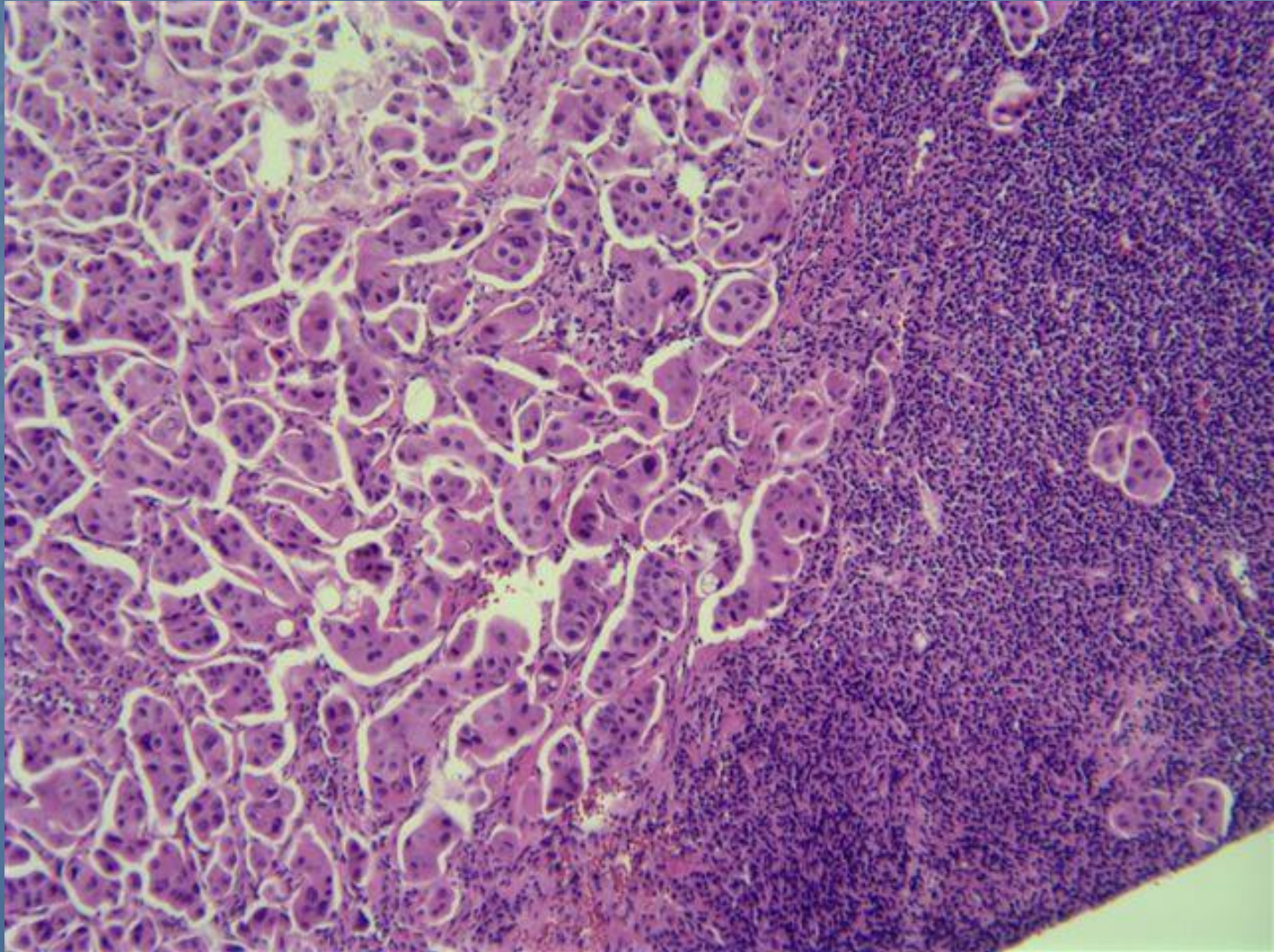
STERNBERG-REED CELL



METASTATIC SQUAMOUS CELL CARCINOMA

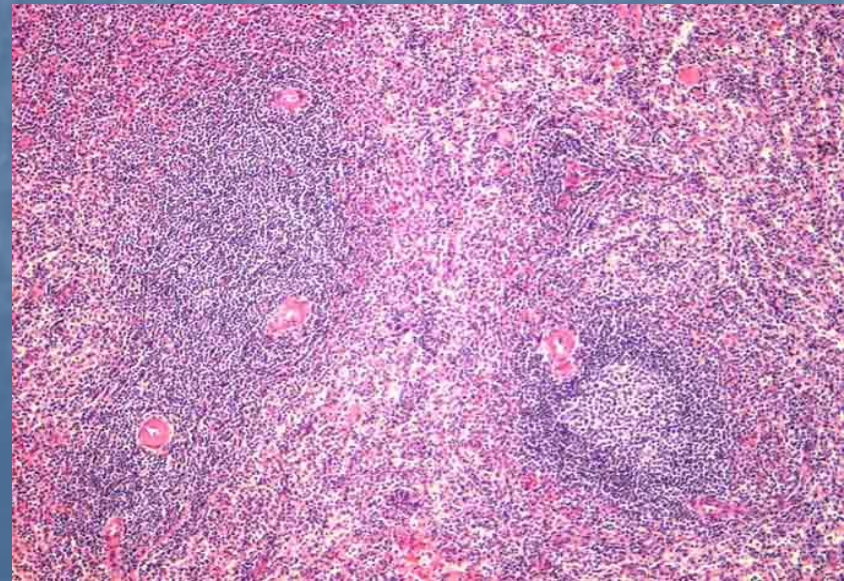
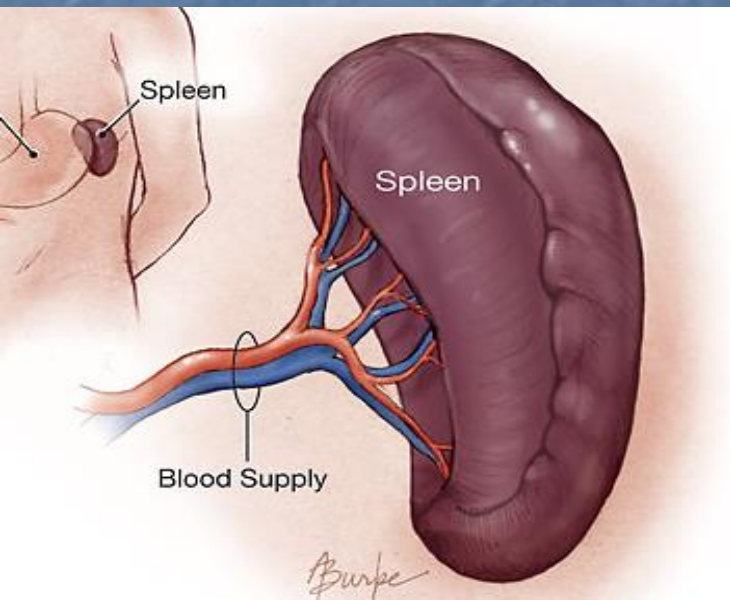


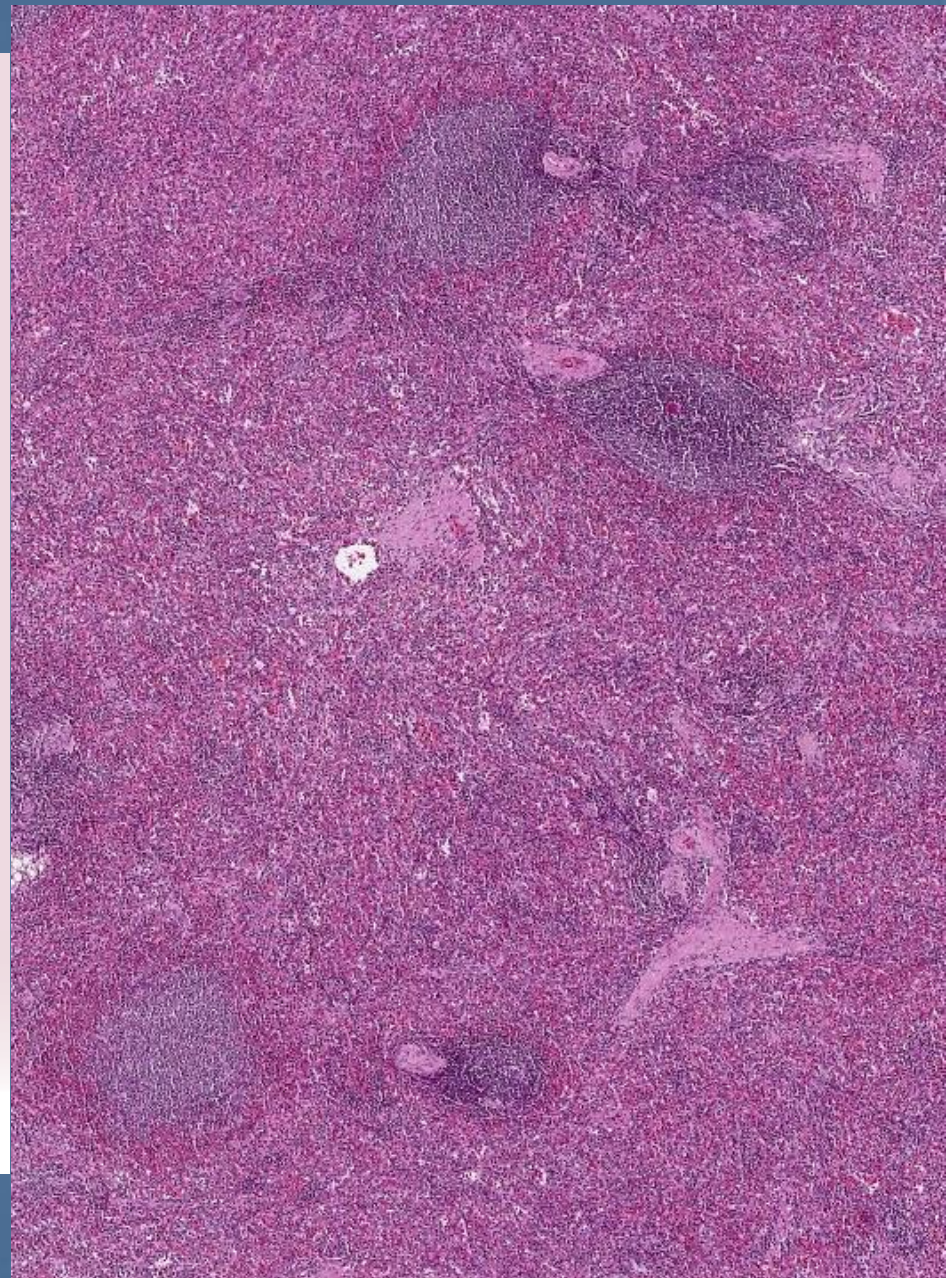
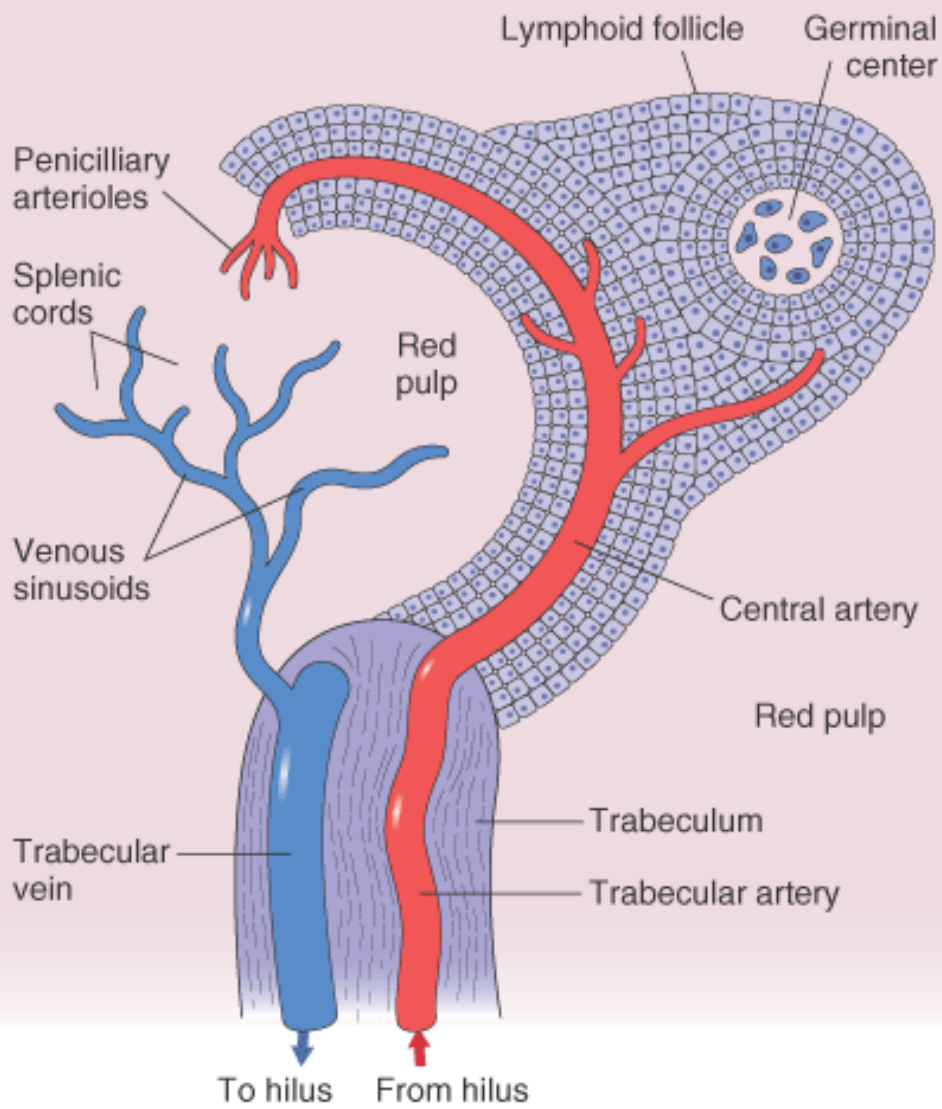
METASTATIC ADENOCARCINOMA



SPLEEN

- 150 grams POST-LUQ (just like kidney, 1/10 of liver)
- Bordered by diaphragm, kidney, pancreas, splenic flexure, stomach
- SMOOTH & GLISTENING capsule
- 50% RED pulp, 50% WHITE pulp

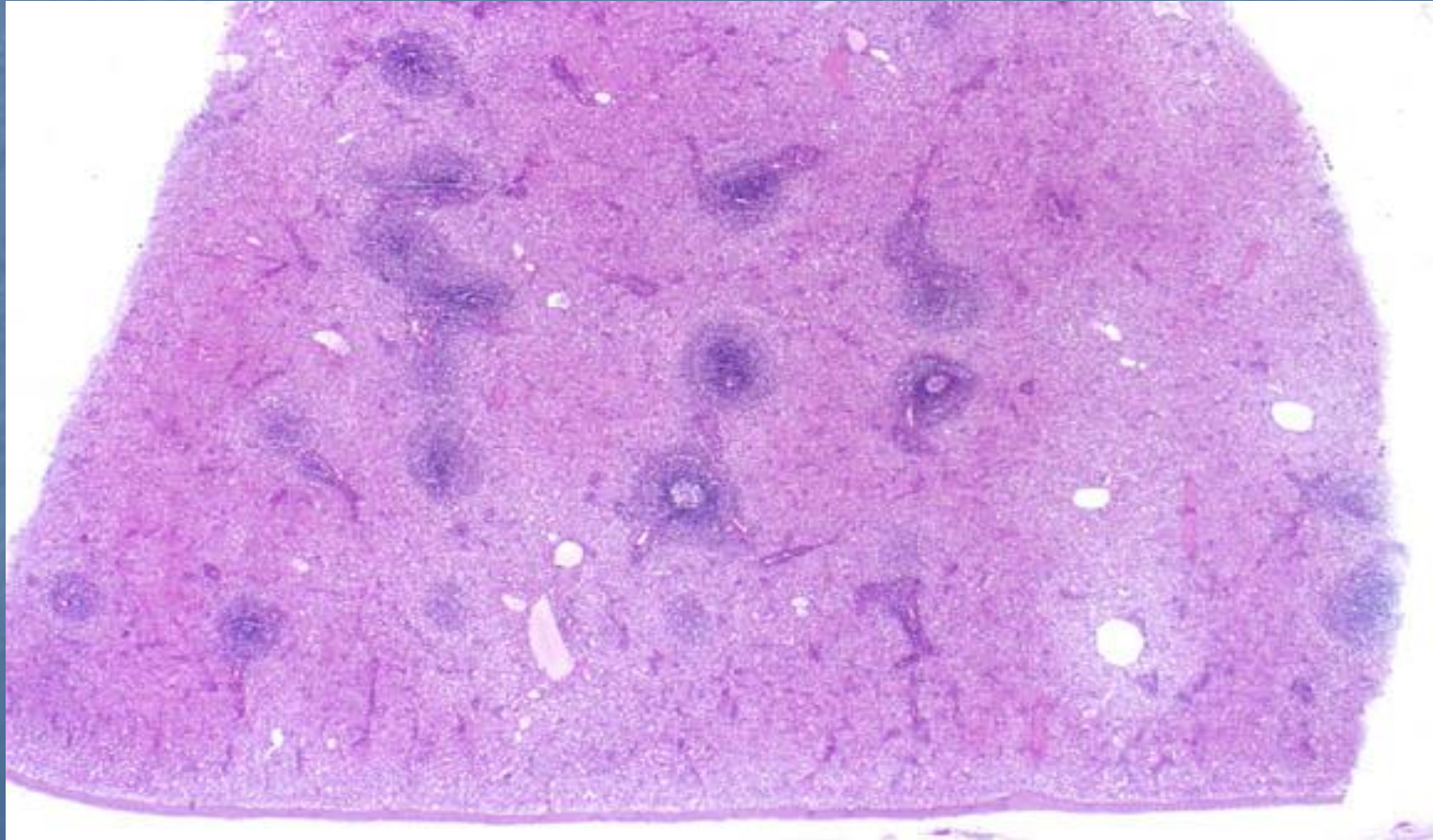




ABNORMAL SPLEEN



ABNORMAL SPLEEN



SPLENIC FUNCTION

- **REMOVE OLD BLOOD CELLS**
- **MAJOR SECONDARY ORGAN of the IMMUNE SYSTEM**
- **HEMATOPOIESIS**
- **SEQUESTER (POOL) BLOOD CELLS**
- **15% of body's PHAGOCYTIC activity is in the spleen (liver has >80)**

SPLENOMEGALY

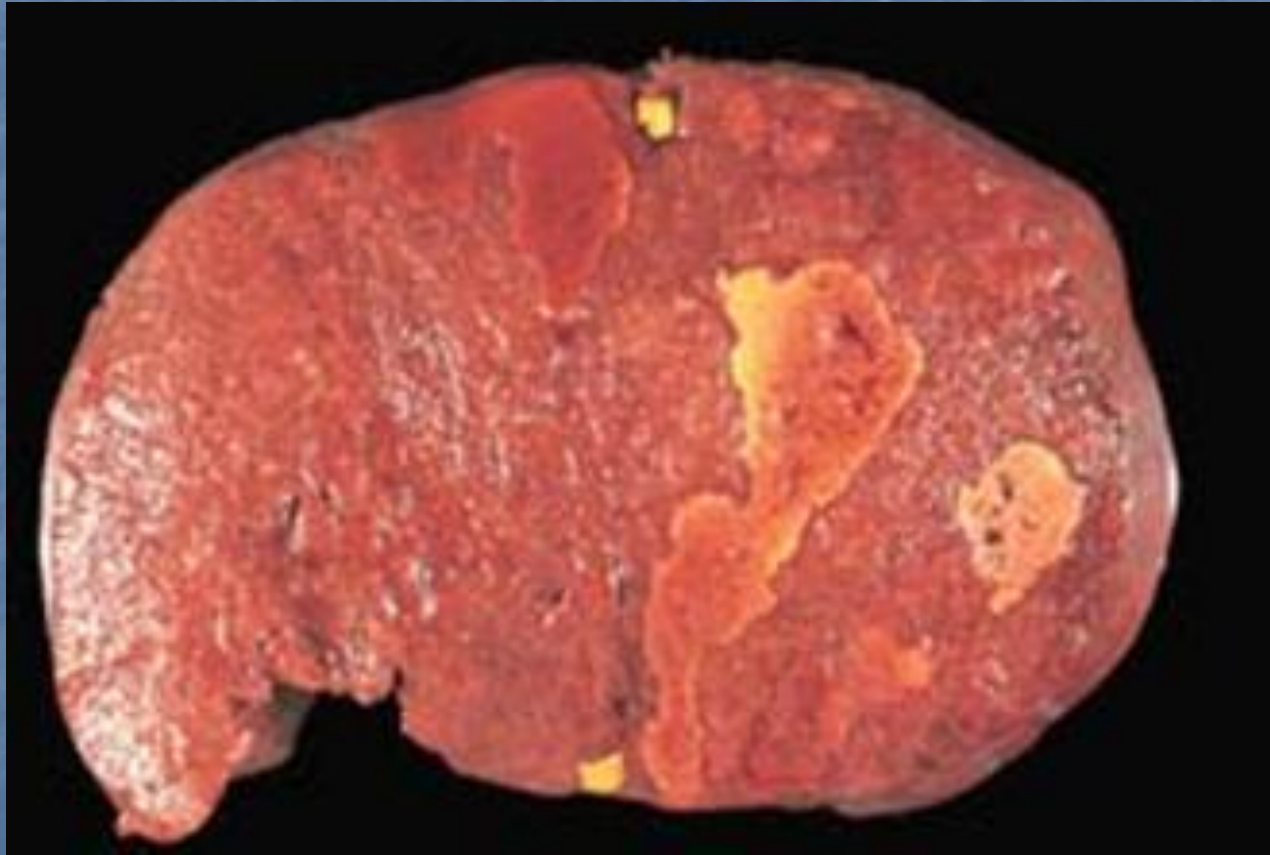
- **CONGESTIVE vs INFILTRATIVE**
- **HYPERSPLENISM**
 - **Anemia**
 - **Leukopenia**
 - **Thrombocytopenia**
- **DECISION for SPLENECTOMY**

SPLENOMEGALY

- **INFECTIONS:** TB, Mono, Malaria, Fungus
- **PORTAL HTN:** CHF, CIRRHOSIS, PV Thromb.
- **LYMPHOHEMATOGENOUS:** Leuk, Lymph
- **IMMUNE:** RA, SLE
- **STORAGE:** Gaucher, Niemann-Pick
- **MISC:** Amyloid, mets (melanoma, lymphoma, Germ cell tumors of testis)

LONG STANDING CONGESTION breeds FIBROSIS

INFARCT



PRIMARY TUMORS

(RARE)

- HEMANGIOMA

- LYMPHANGIOMA

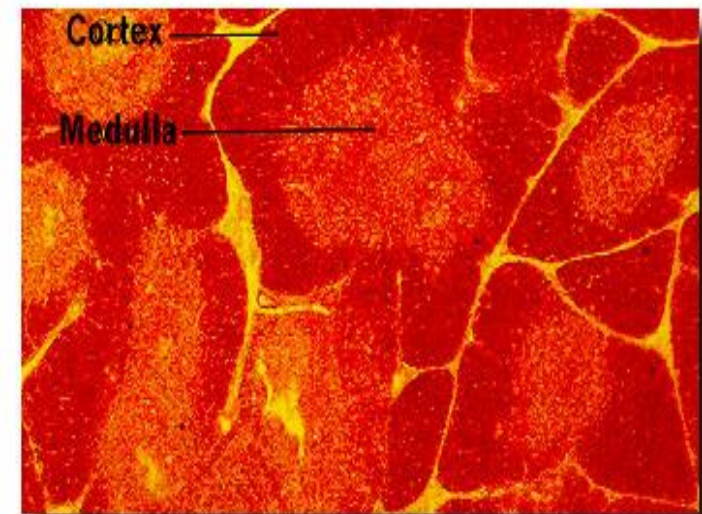
- fibroma

- osteoma

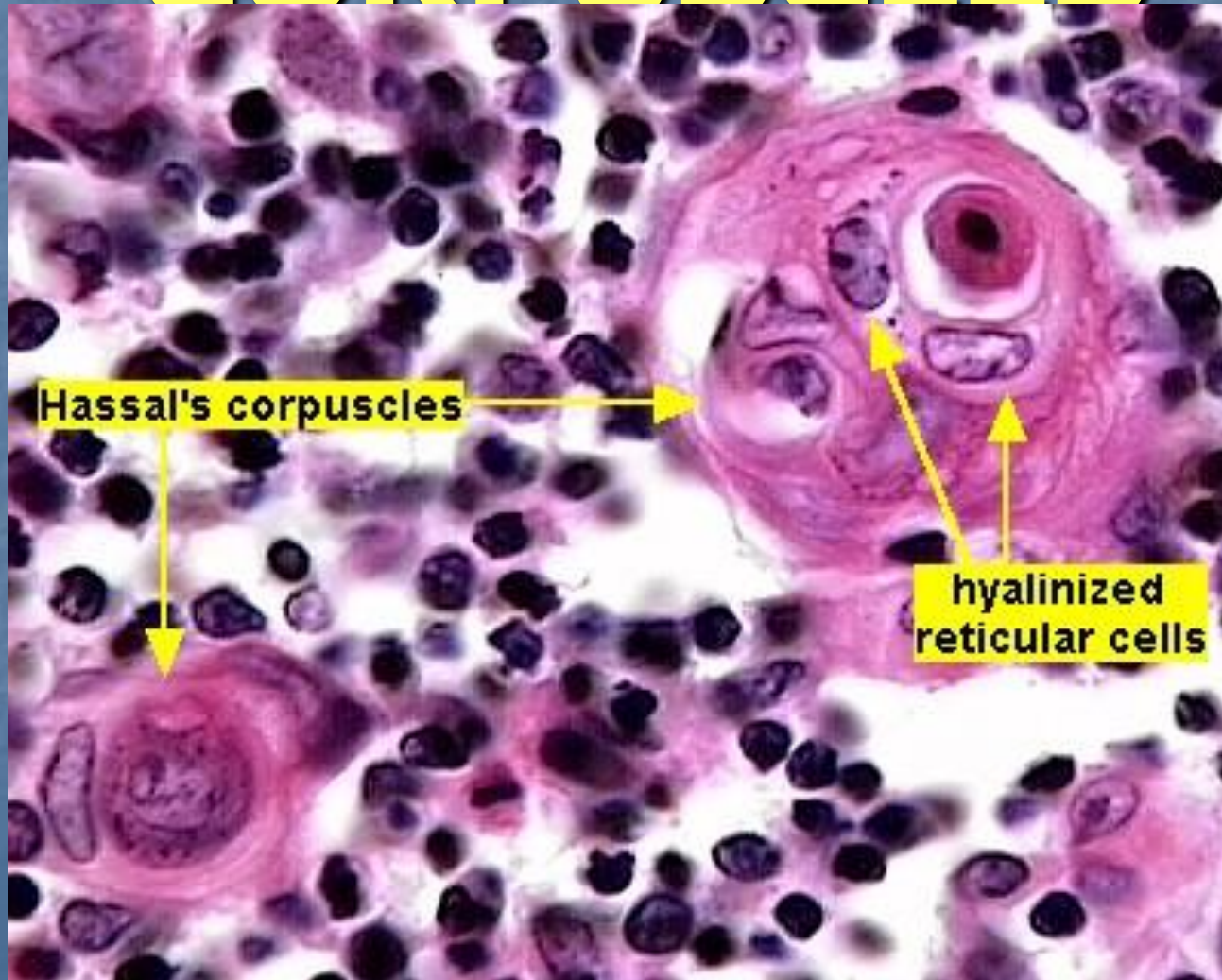
- chondroma

THYMUS

- Mother of all T-Cells
- Massive in newborns, virtually absent in the elderly, bilobed
- Under manubrium
- 1) Thymocytes
- 2) Epithelial Ret. Cells
- 3) Hassal's Corpuscles



HASSAL'S CORPUSCLES



DISEASES

■ HYPOPLASIA/APLASIA

A

- DiGeorge Syndrome

■ CYSTS (incidental)

■ THYMOMAS

Nevus

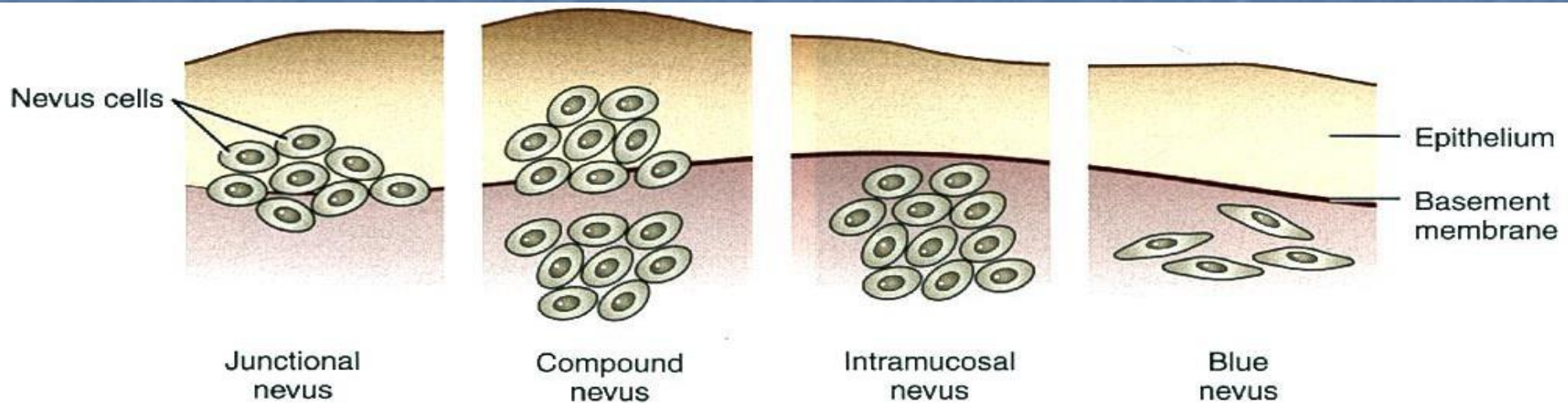
- They may be present at birth or may appear shortly after birth.
- About 15% of intramucosal nevi are not pigmented.
- Most frequently they appear on the hard palate (40%). The second most common location is the oral mucosa (20%), 10% of all types of oral nevi are found on the gums.
- About 75% of nevi are smaller than 0.6 cm.
- Slightly elevated papule or flat macula



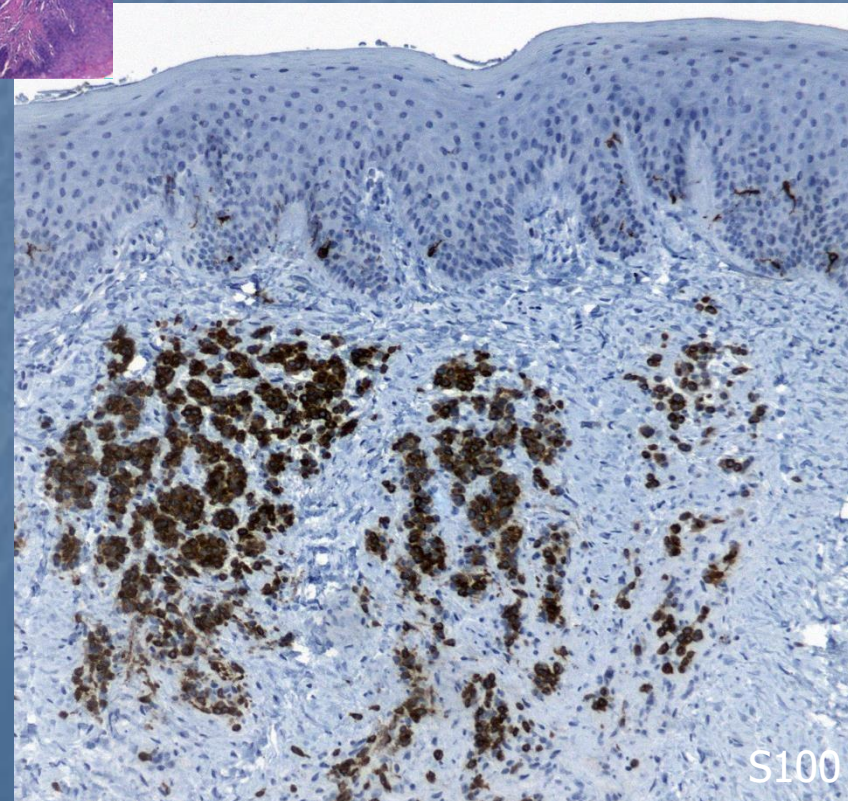
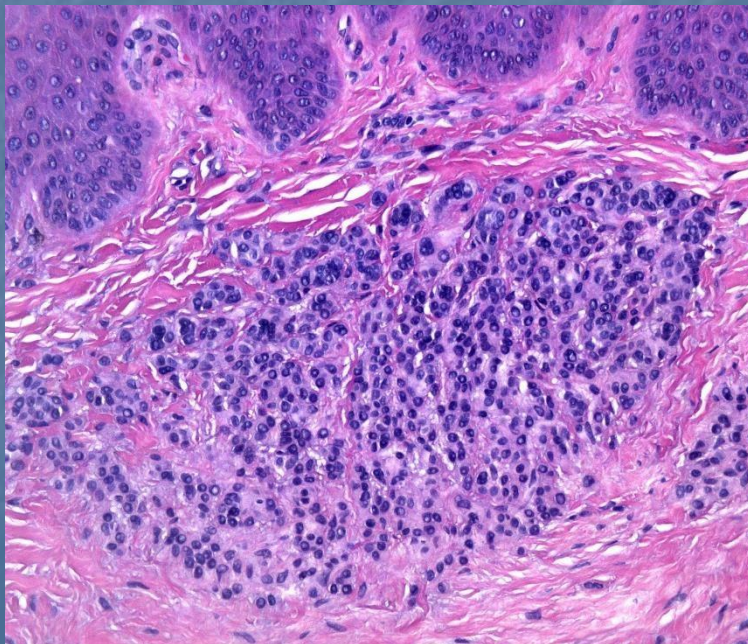
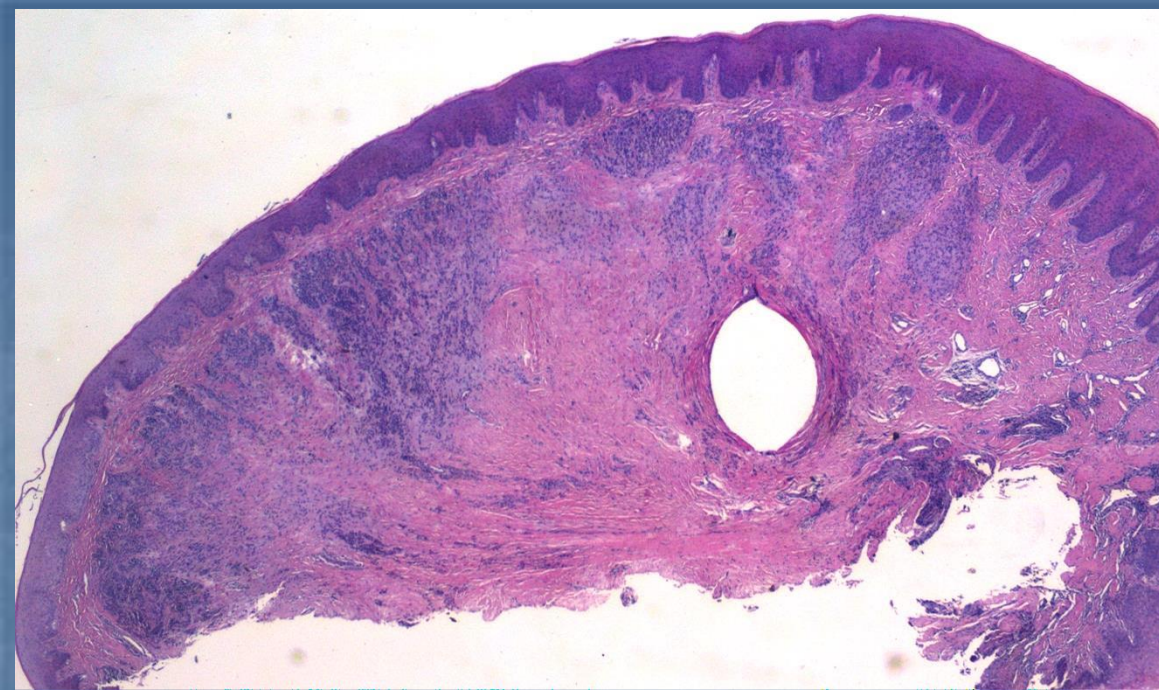
Nevus



Nevi - types



Intramucosal nevus



Melanoma is a malignant tumor of melanocytic origin, which is found on the skin, in the oral mucosa, anorectal, esophagus, meninges, eyeball. It is extremely aggressive, a tumor with a thickness of only a few mm can produce multiple metastases. Lymphogenous metastases in regional lymph nodes, and more frequently hematogenously in the liver, lungs, brain and other organs, can be metastases in virtually any region of the body. In most cases the metastases are black due to the melanin content.

