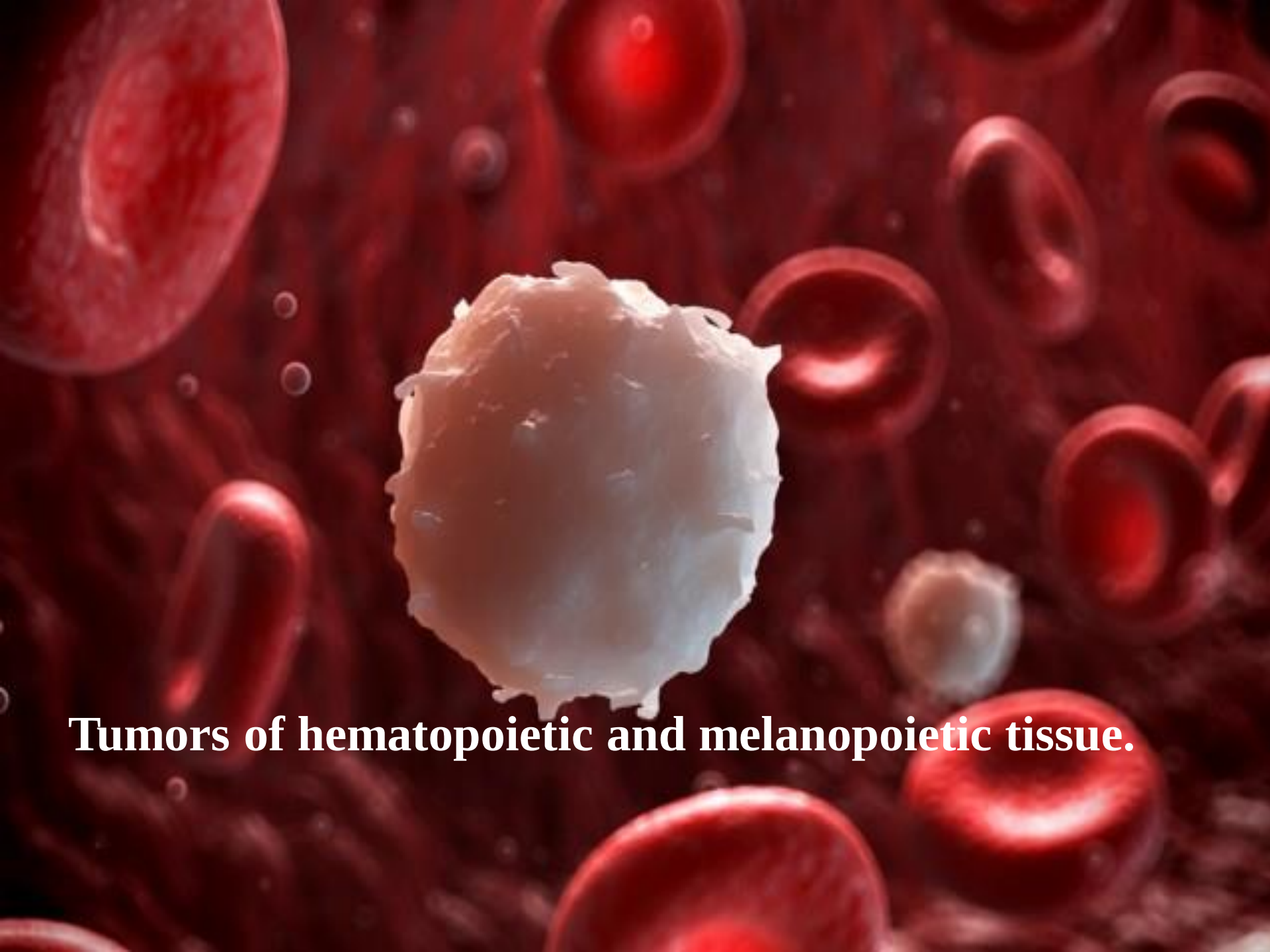


Tumors of hematopoietic and melanopoietic tissue.

Tumors of hematopoietic and melanopoietic tissue.

I. Microspecimens:

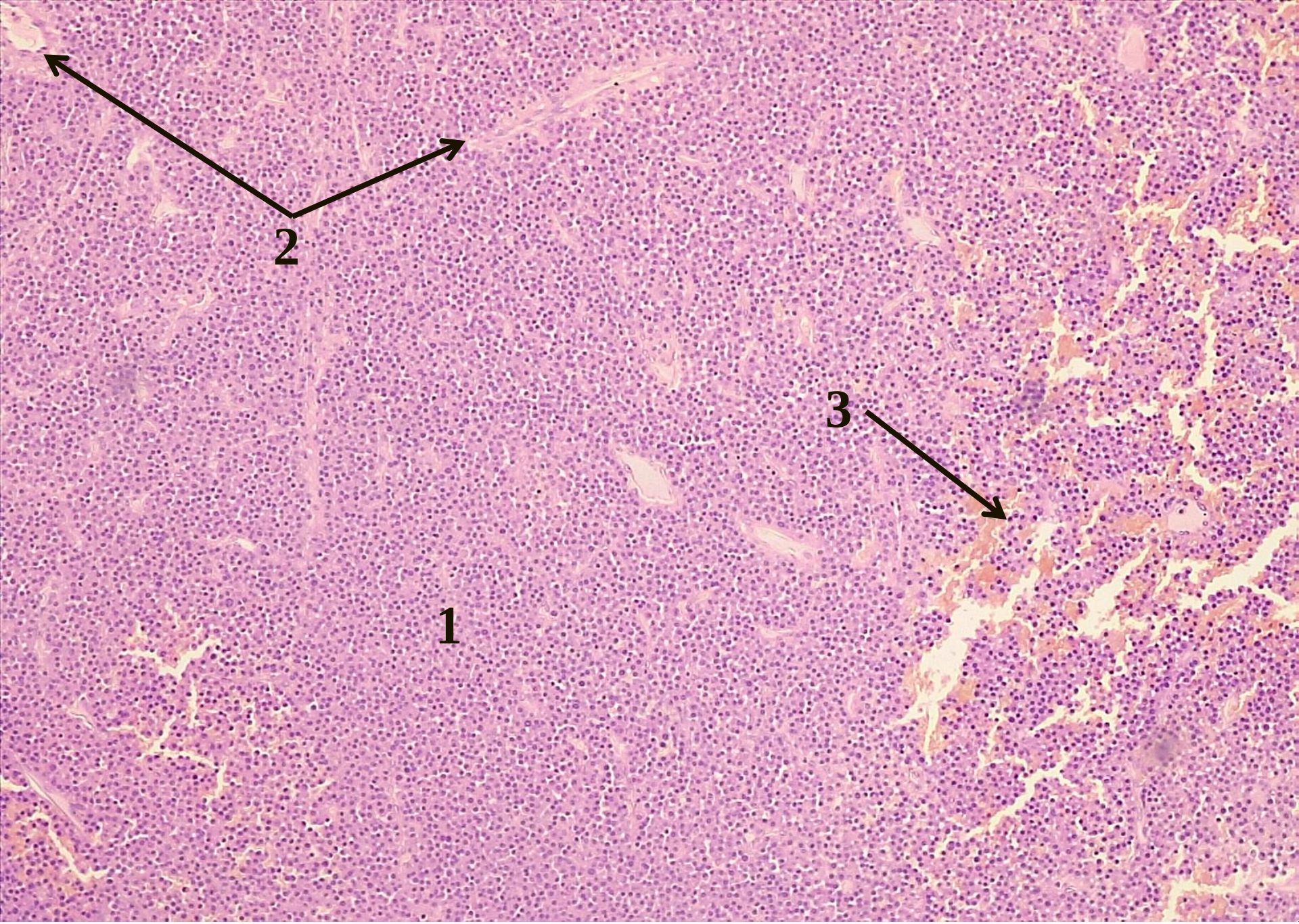
№ 145. Solitary plasmacytoma of bone. *(H-E stain).*

Indications:

1. Polymorphic tumoral cells of plasmo cytic 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-Jonce 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.



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

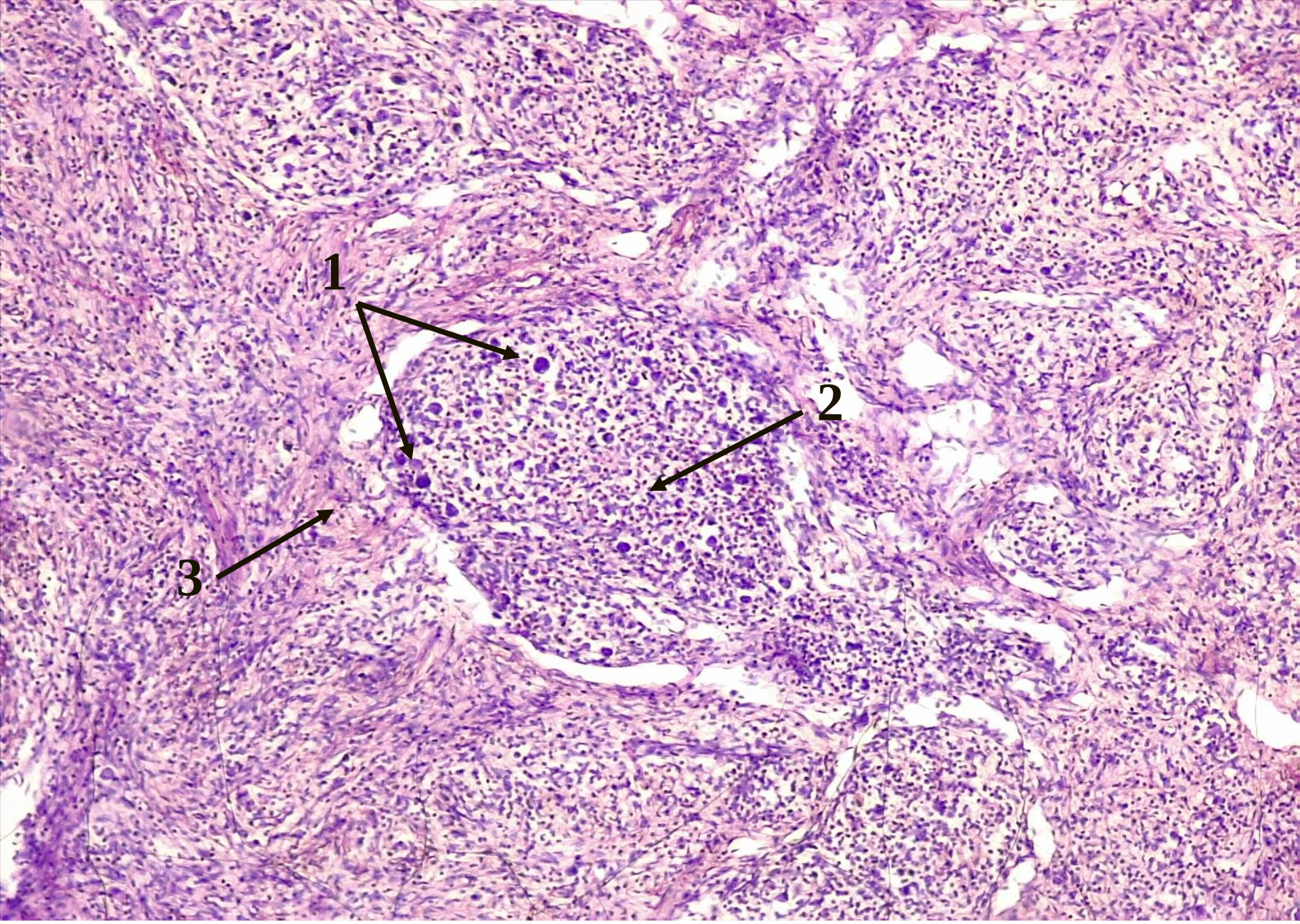
№ 58. Lymph node in Hodgkin's disease *(nodular sclerosis type).* *(H-E stain).*

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 45μ 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.



№ 58. Lymph node in Hodgkin's disease *(nodular sclerosis type).* *(H-E stain).*

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

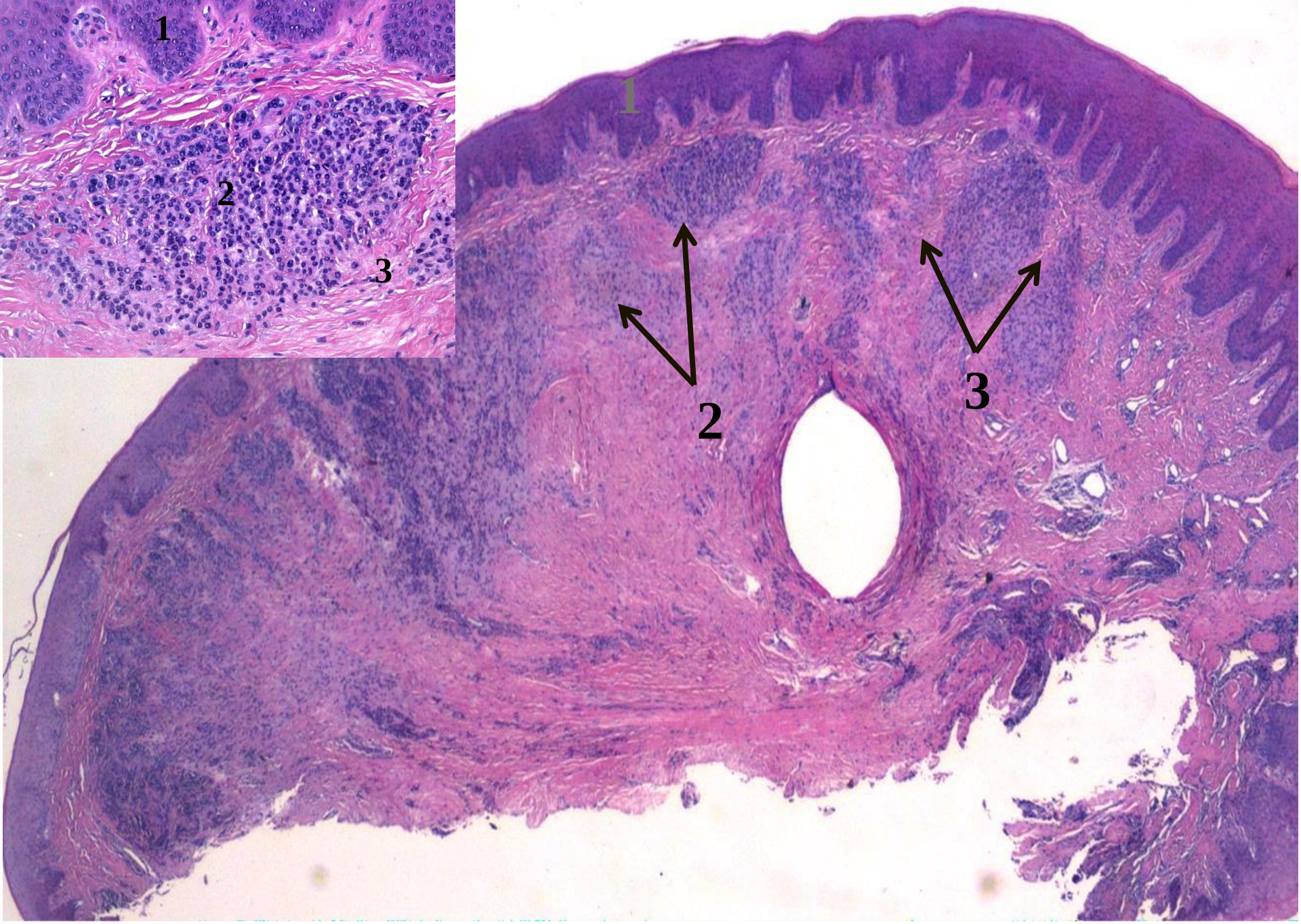
Indications:

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 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 nevus 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).



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

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

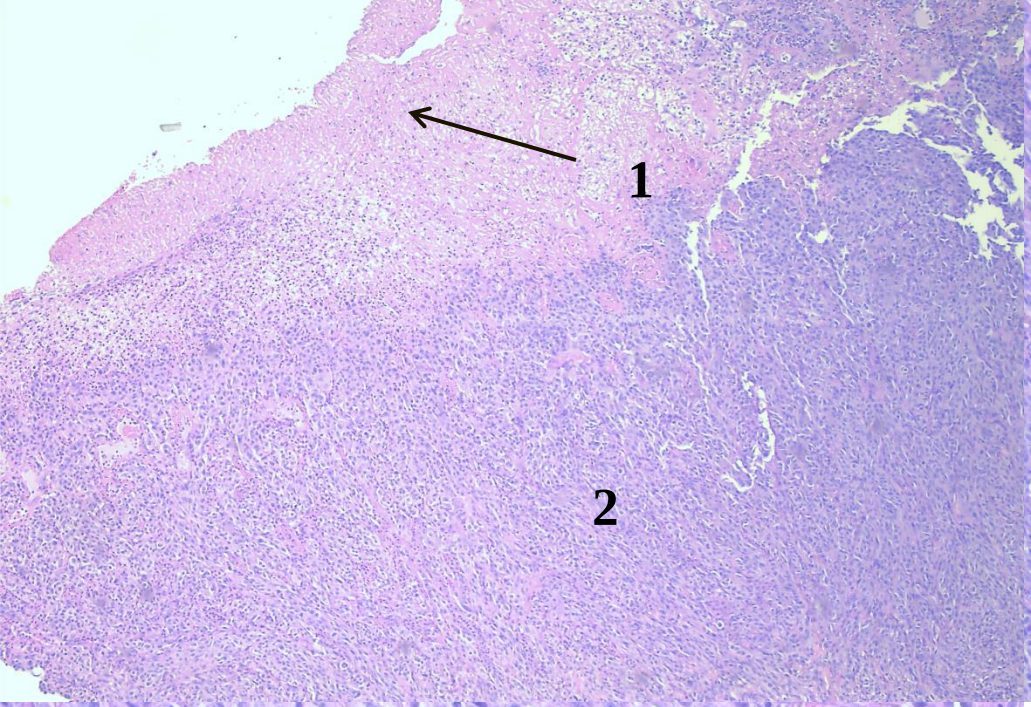
Indications:

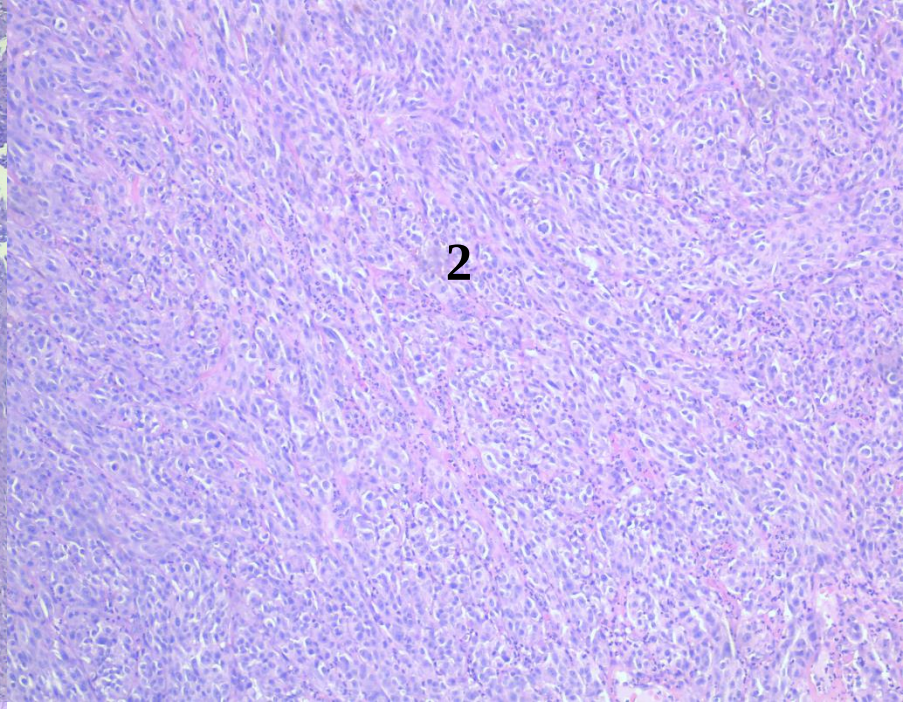
1. Ulcerated superficial epithelium.
2. Nests of malignant melanocytes

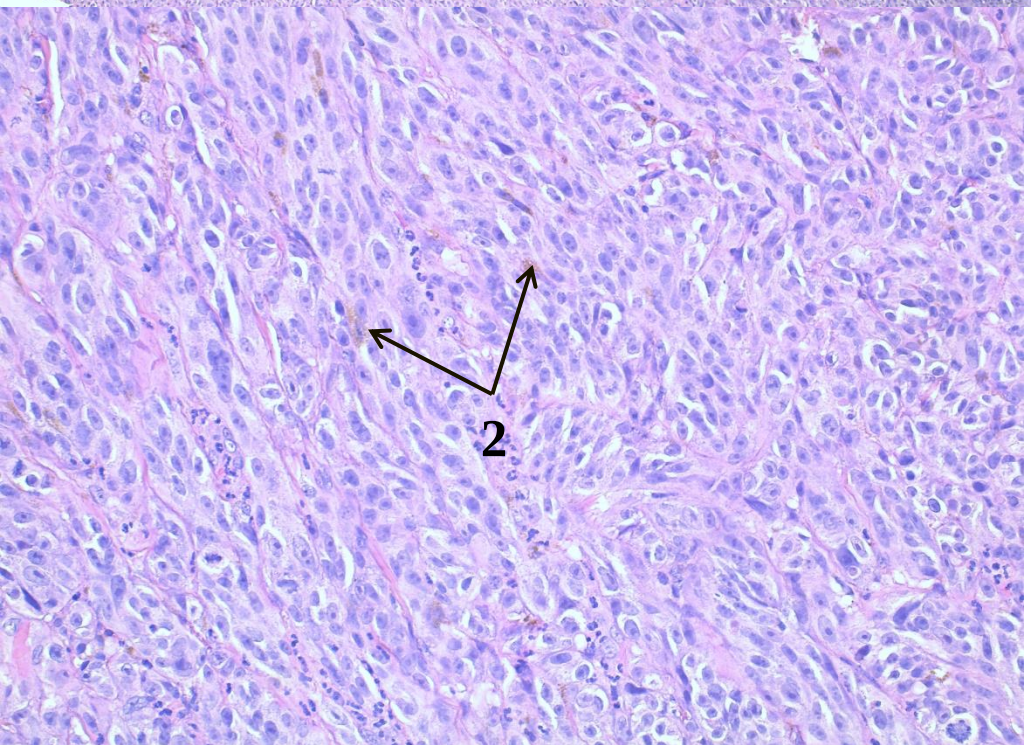
In the microspecimen, multiple nests of malignant melanic cells with vertical development are revealed, which extend both in the surface epithelium and in the underlying connective tissue. Malignant cells have variable shape and size, with pronounced cellular and nuclear polymorphism, hyperchromic nuclei,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







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

II. Macrospecimens:

№ 145. Bone marrow in leukemia.

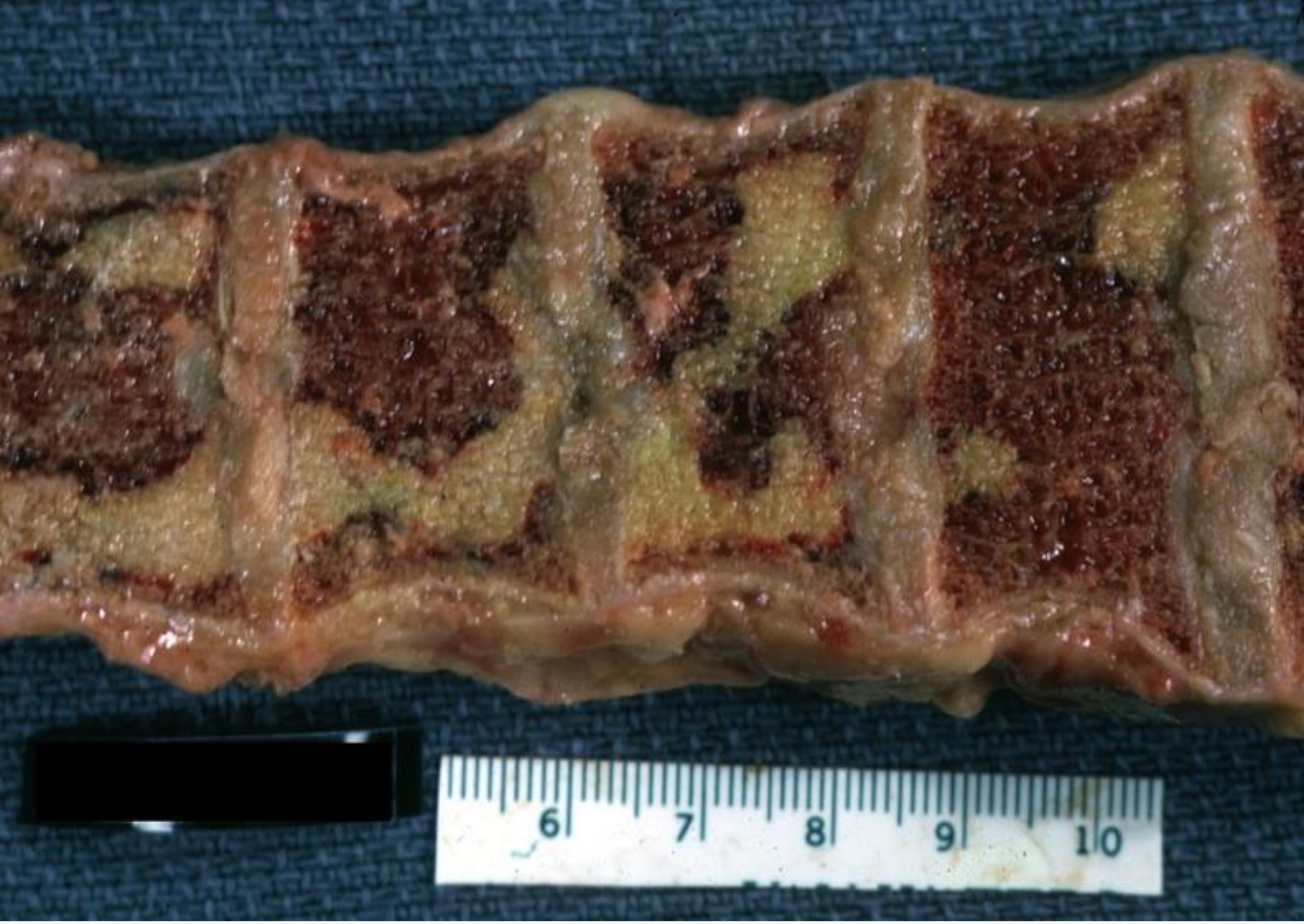
Longitudinal section of the femoral bone, the osteomedullary tissue is homogeneous, juicy, the division into red and yellow marrow is absent, the adipose tissue in the diaphysis region is replaced by active hematopoietic tissue, the color is gray-yellow, has a purulent appearance ("pious bone marrow").

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.

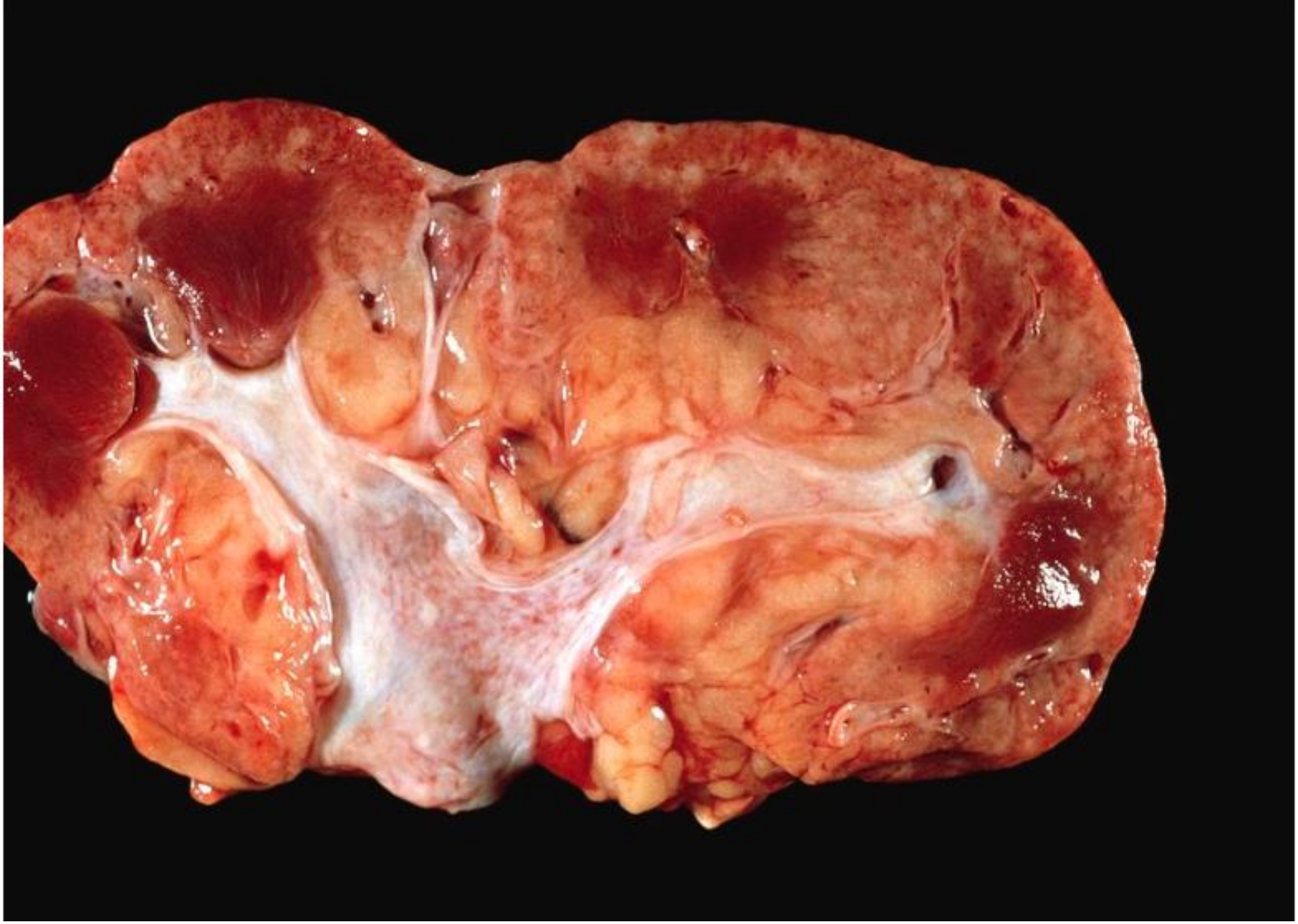
№ 84. Kidney in leukemia.

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.



№ 145. Bone marrow in leukemia.



№ 84. Kidney in leukemia.

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

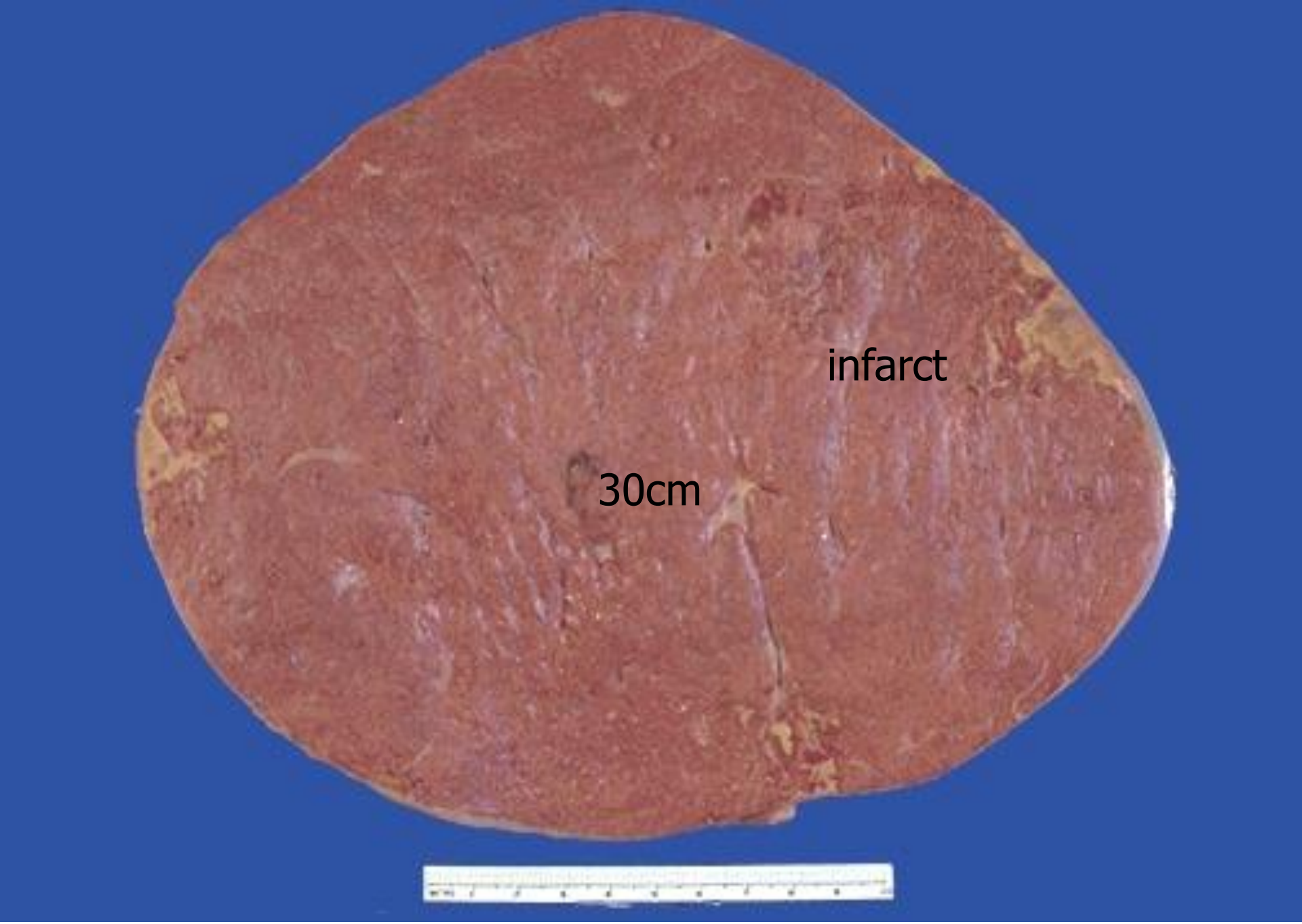
The spleen is considerably enlarged in size, sometimes 20-30 times, the mass reaching a few kg (norm ~ 180 gr), per section reddish-gray color, homogeneous, dense consistency, there may be foci of ischemic infarction and hemorrhage.

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.

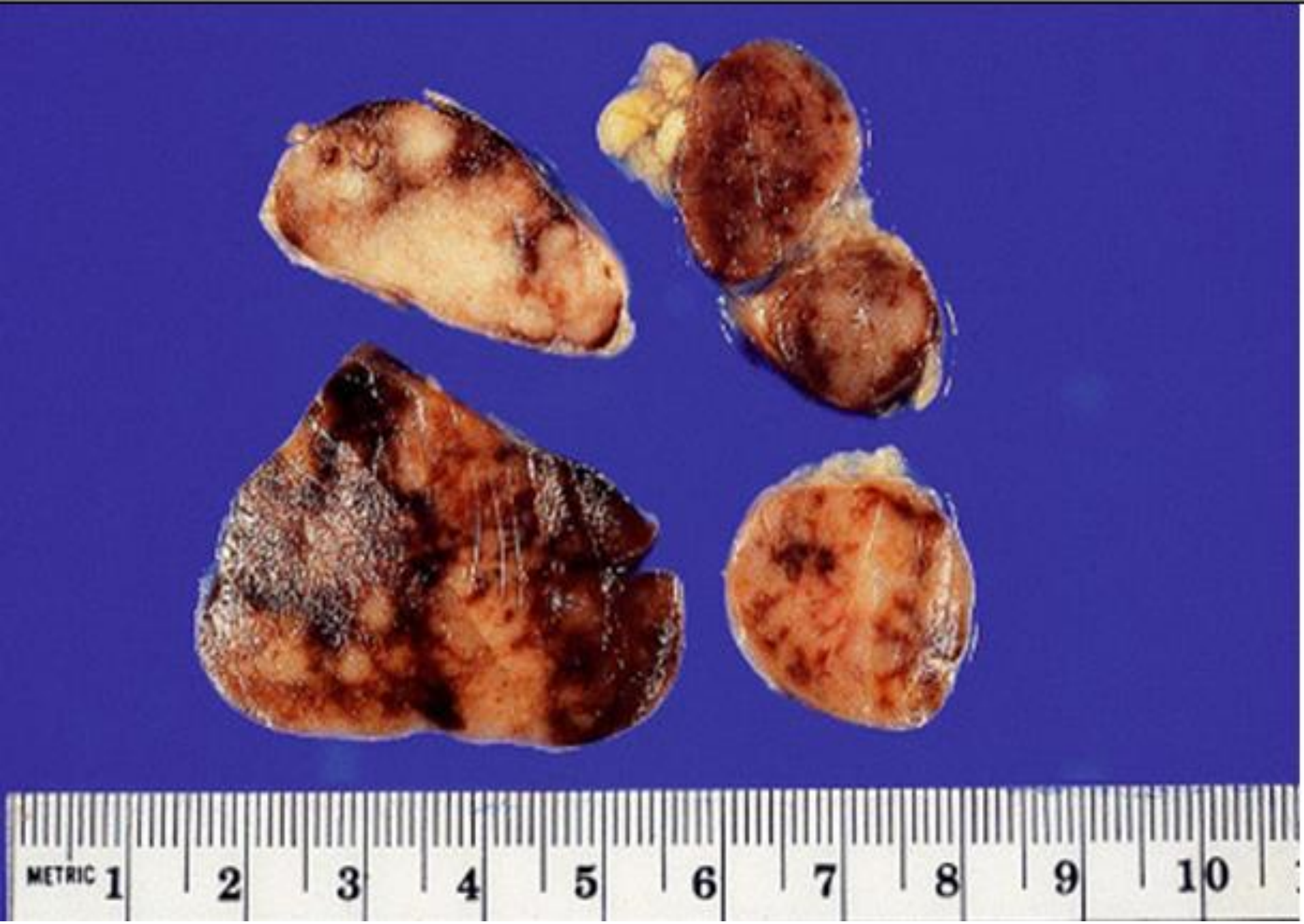
№ 143. Mesenterial lymph node in CLL (chronic lymphoid leukemia).

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 hypogamaglobulinemia, decreased humoral immunity with infectious complications, and autoimmune reactions, primarily hemolytic anemias and autoimmune thrombocytopenias.



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



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

№ 146. Lymph nodes in Hodgkin’s disease.

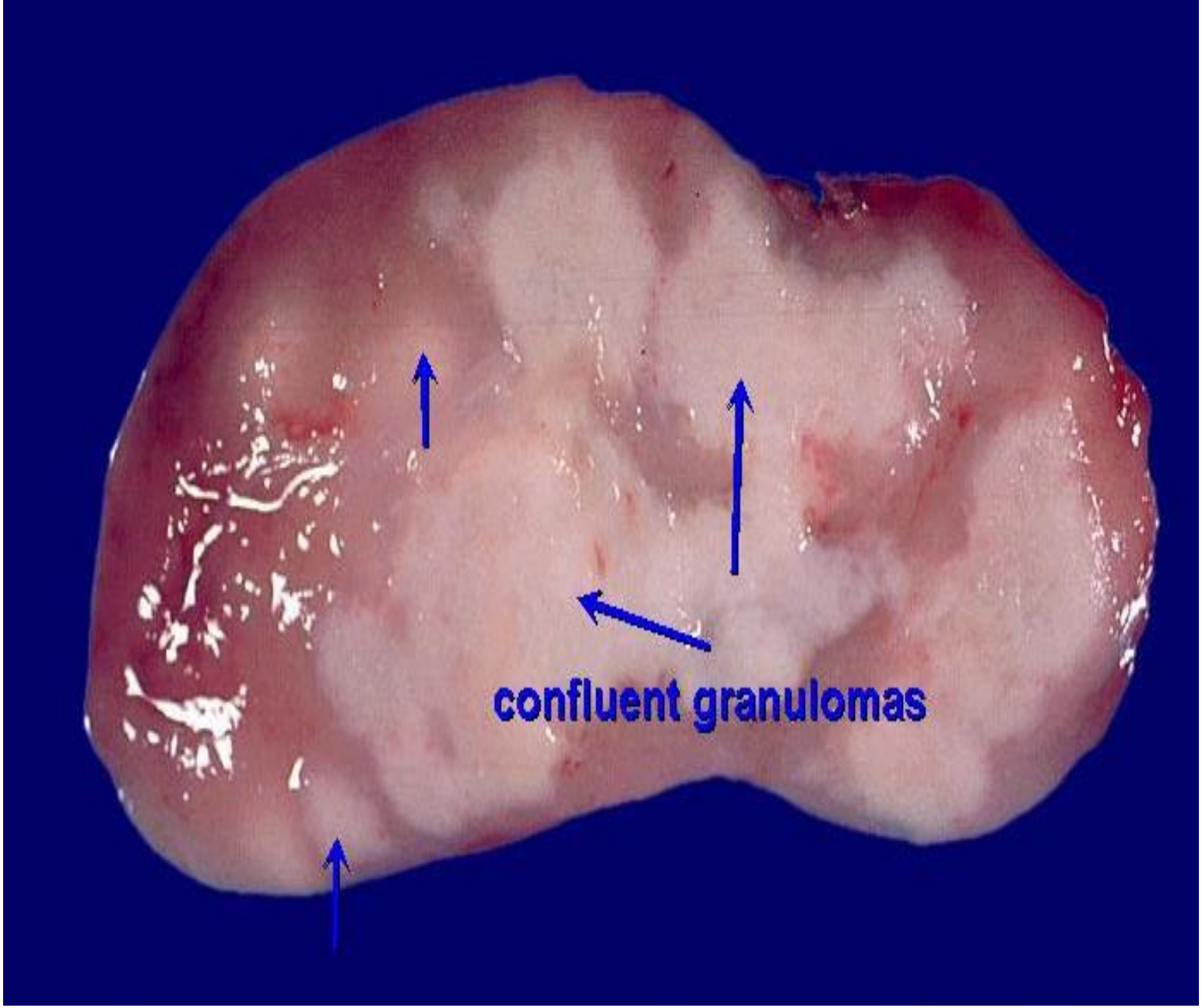
The lymph nodes are unevenly enlarged in size, of dense consistency, light-whitish color, adhere to each other due to infiltration of perinodular connective tissue, on a motley-looking section, white-yellow foci of necrosis and fibrosis.

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.

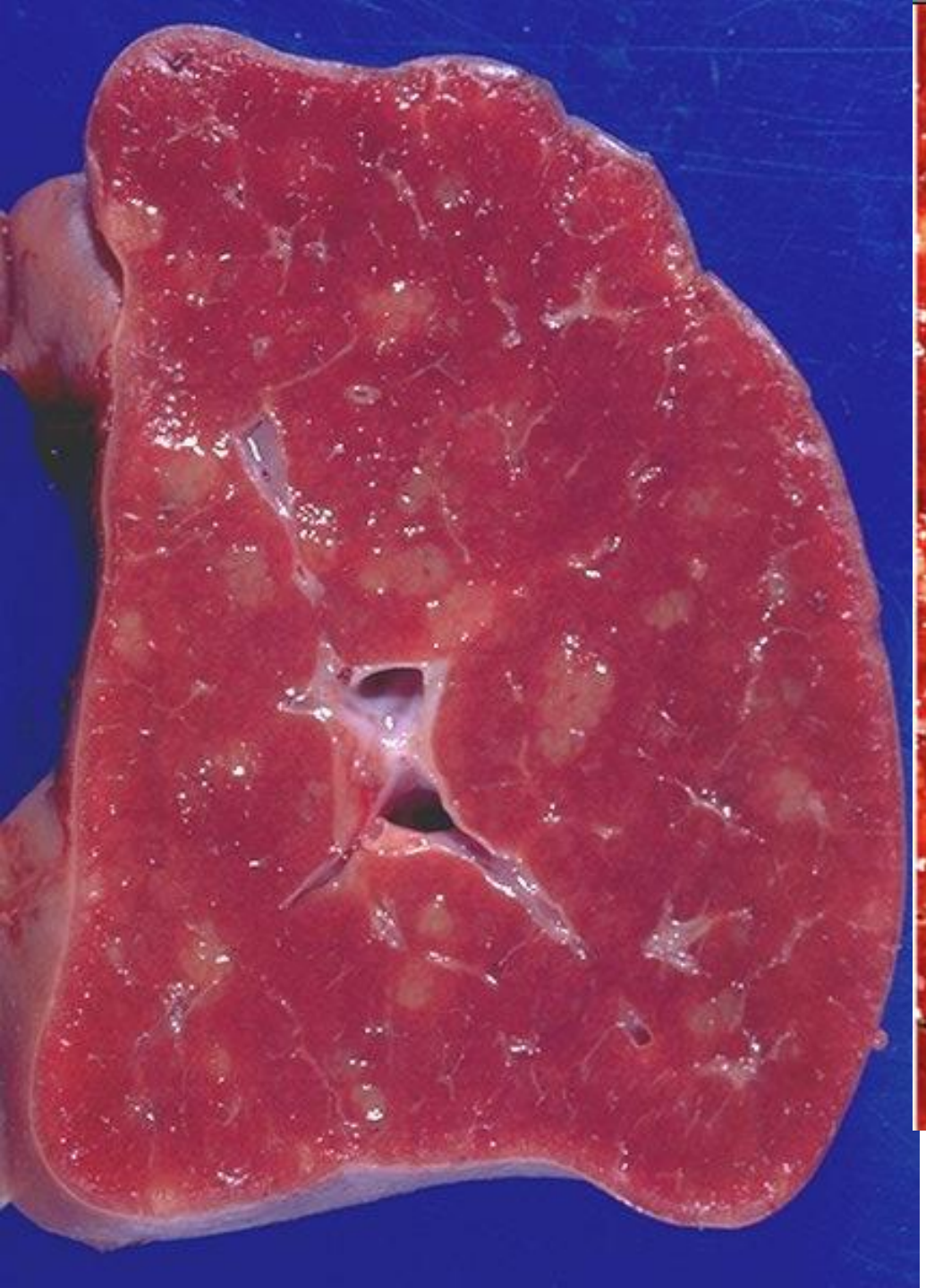
№ 147. Spleen in Hodgkin’s disease.

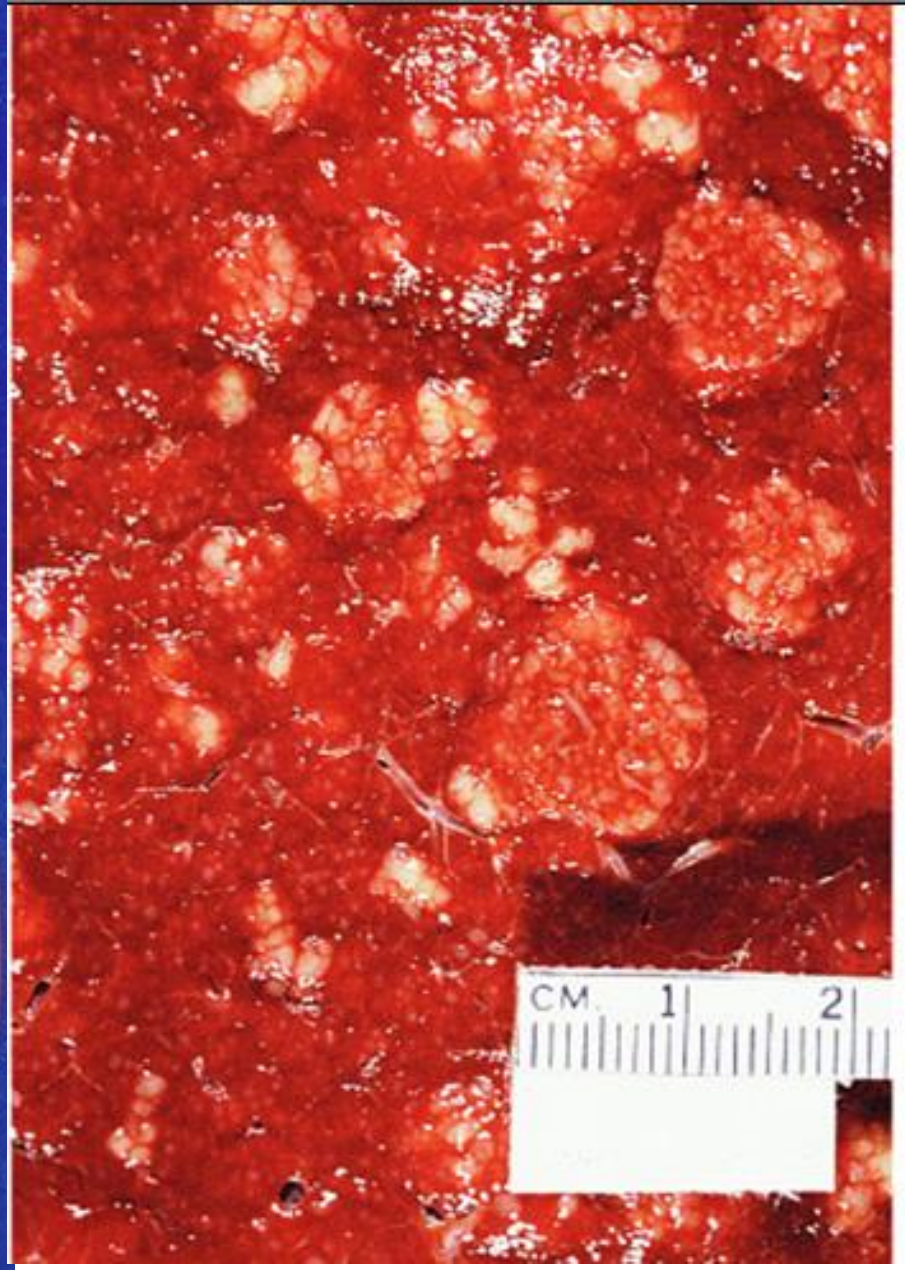
The spleen is enlarged in size 3-5 times, the mass reaching up to 1 kg, dense consistency, on a motley-looking section due to the alternation of white-yellowish proliferative foci and necrosis with whitish sclerosis foci on the background of the red pulp, which gives the spinal tissue an appearance similar 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.

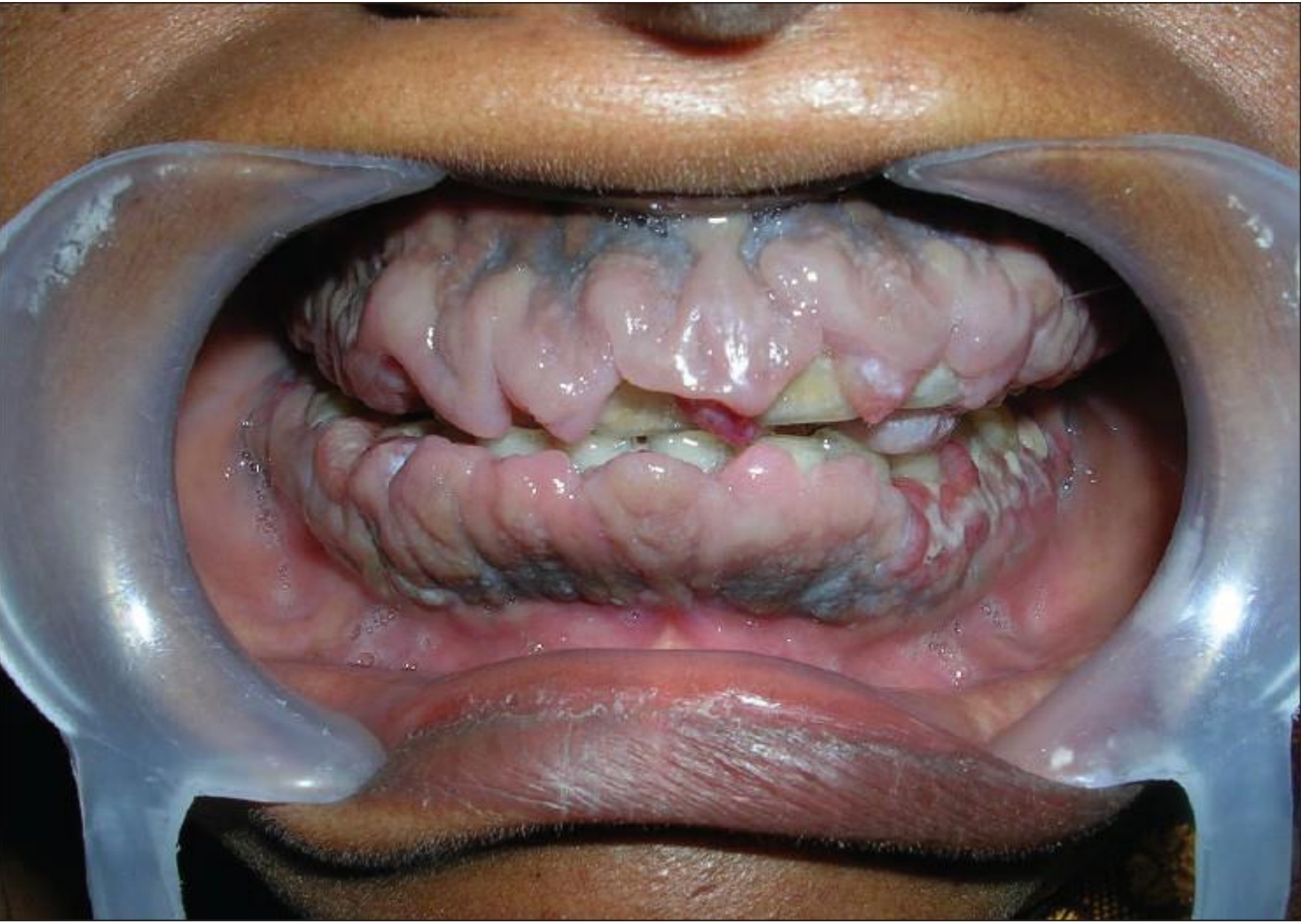


№ 146. Lymph nodes in Hodgkin's disease.

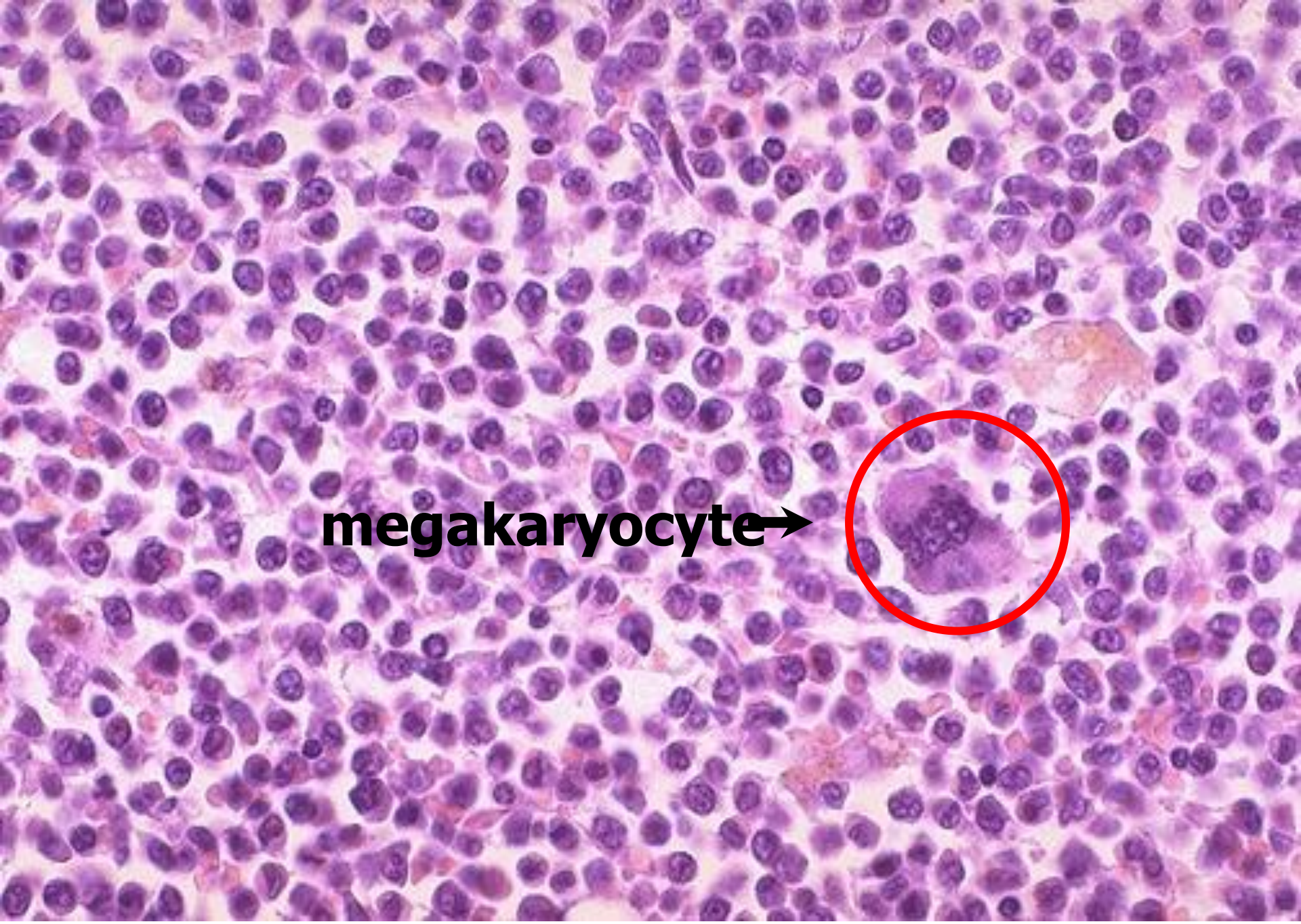




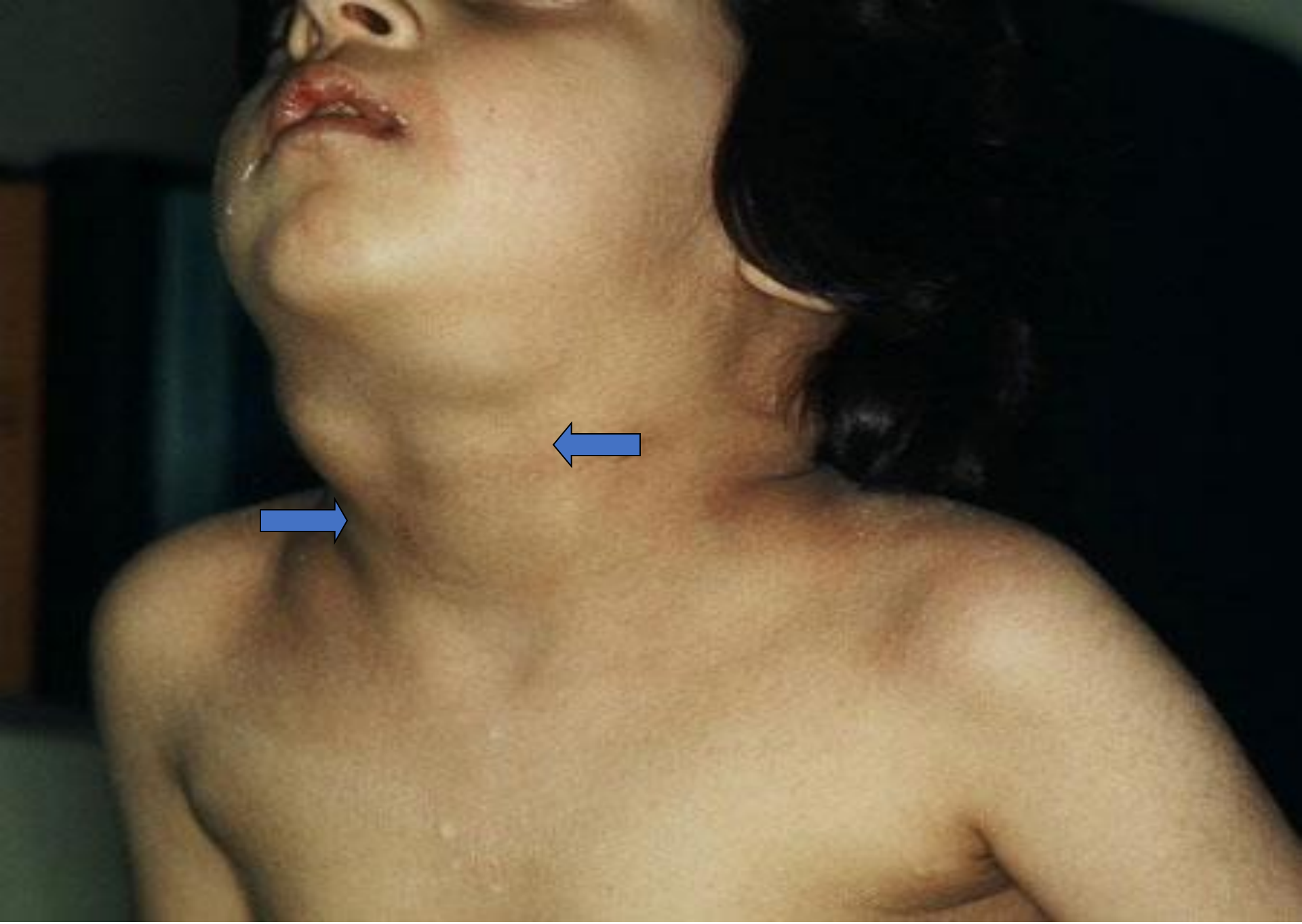
№ 147. Spleen in Hodgkin's disease.



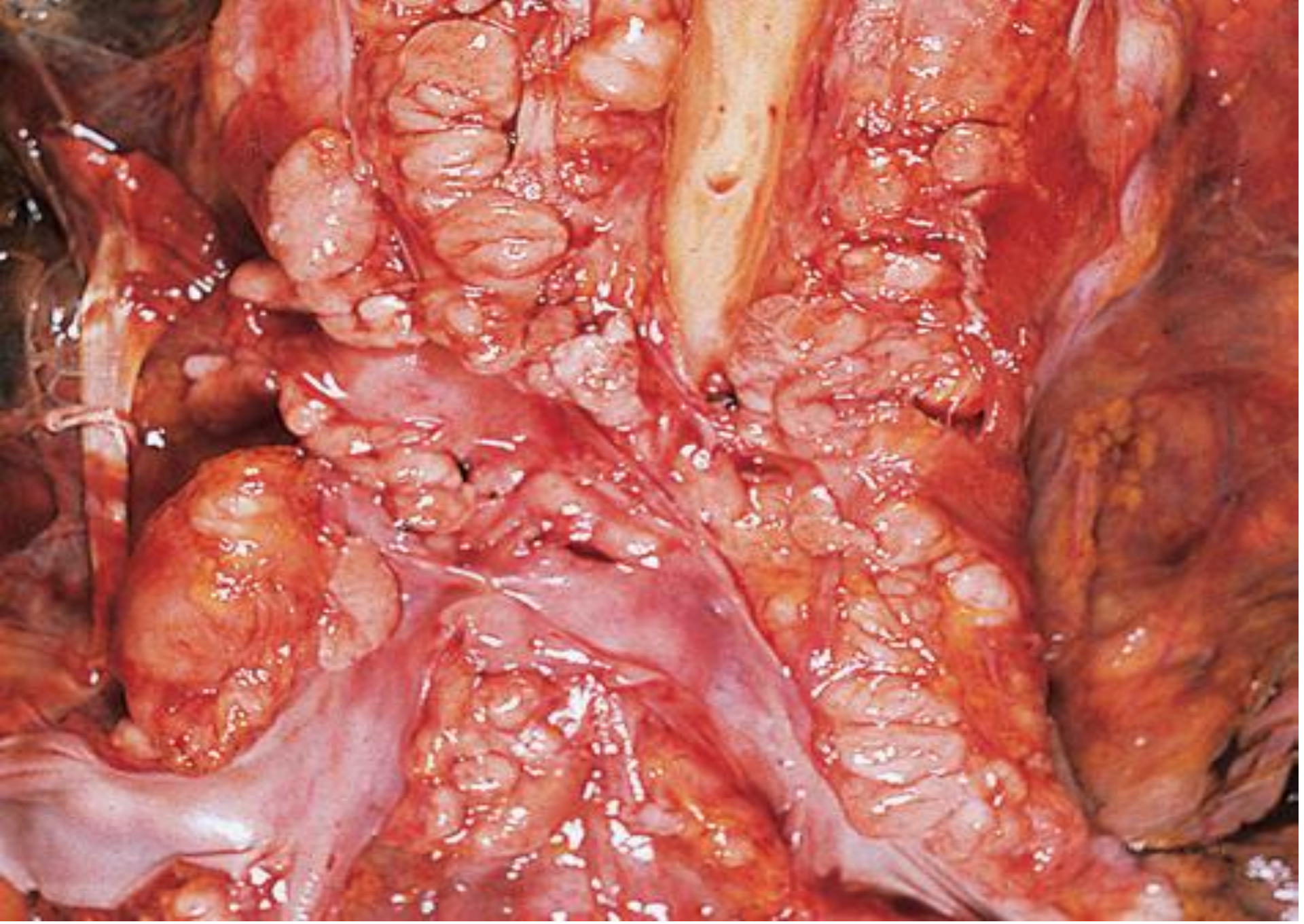
AML - with gingival manifestations.



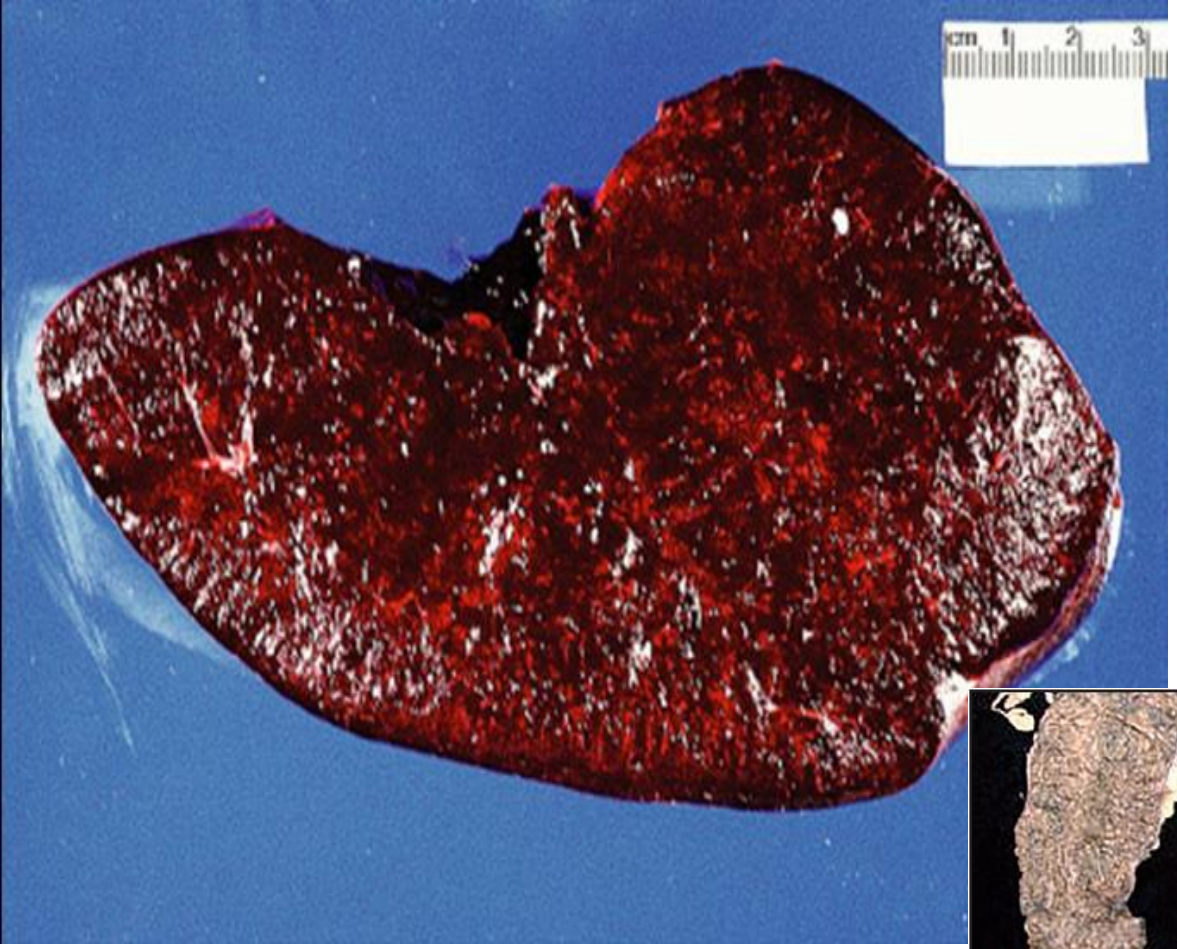
Bone marrow in AML (overloaded with blast cells).



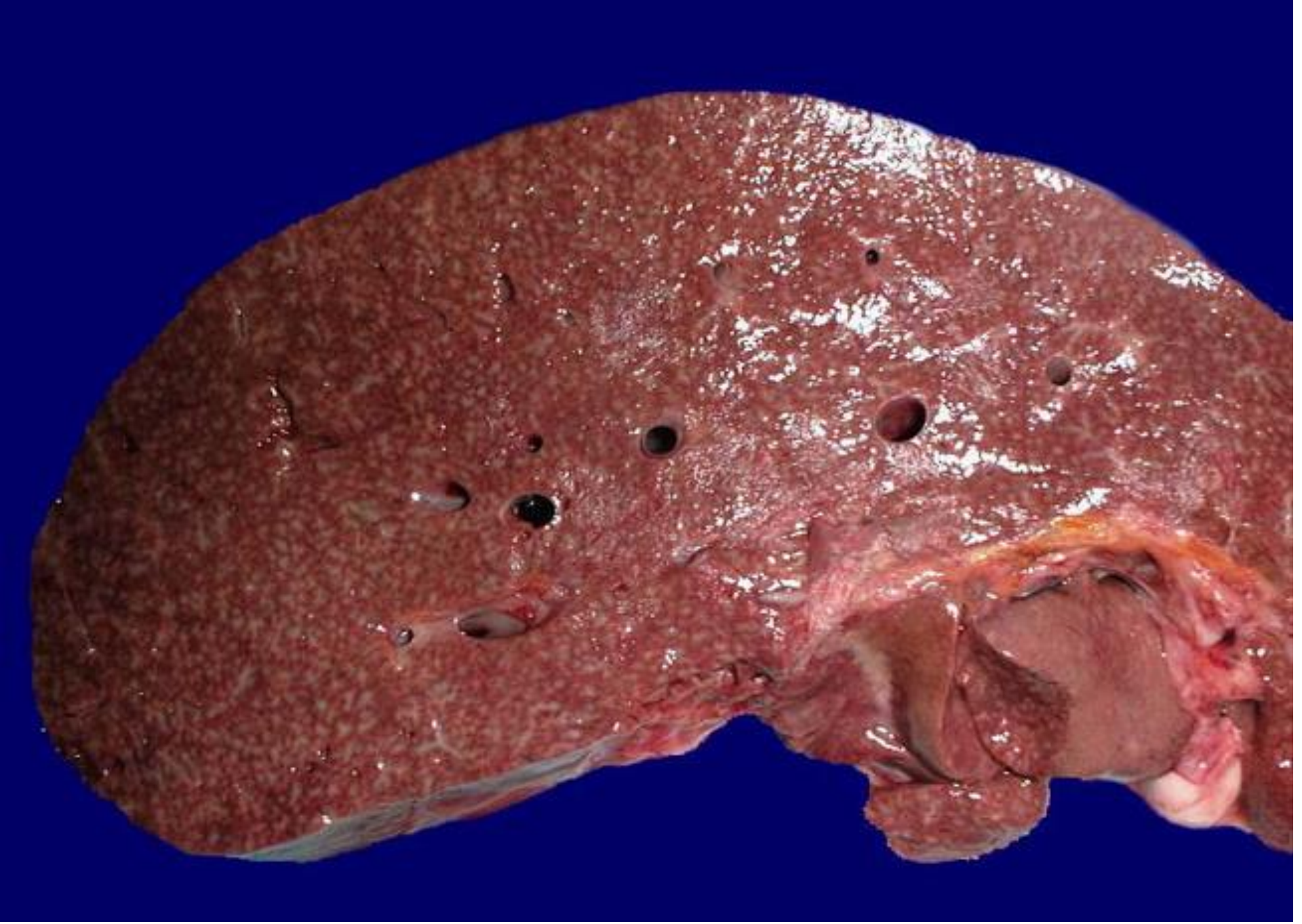
ALL - cervical lymphadenopathy.



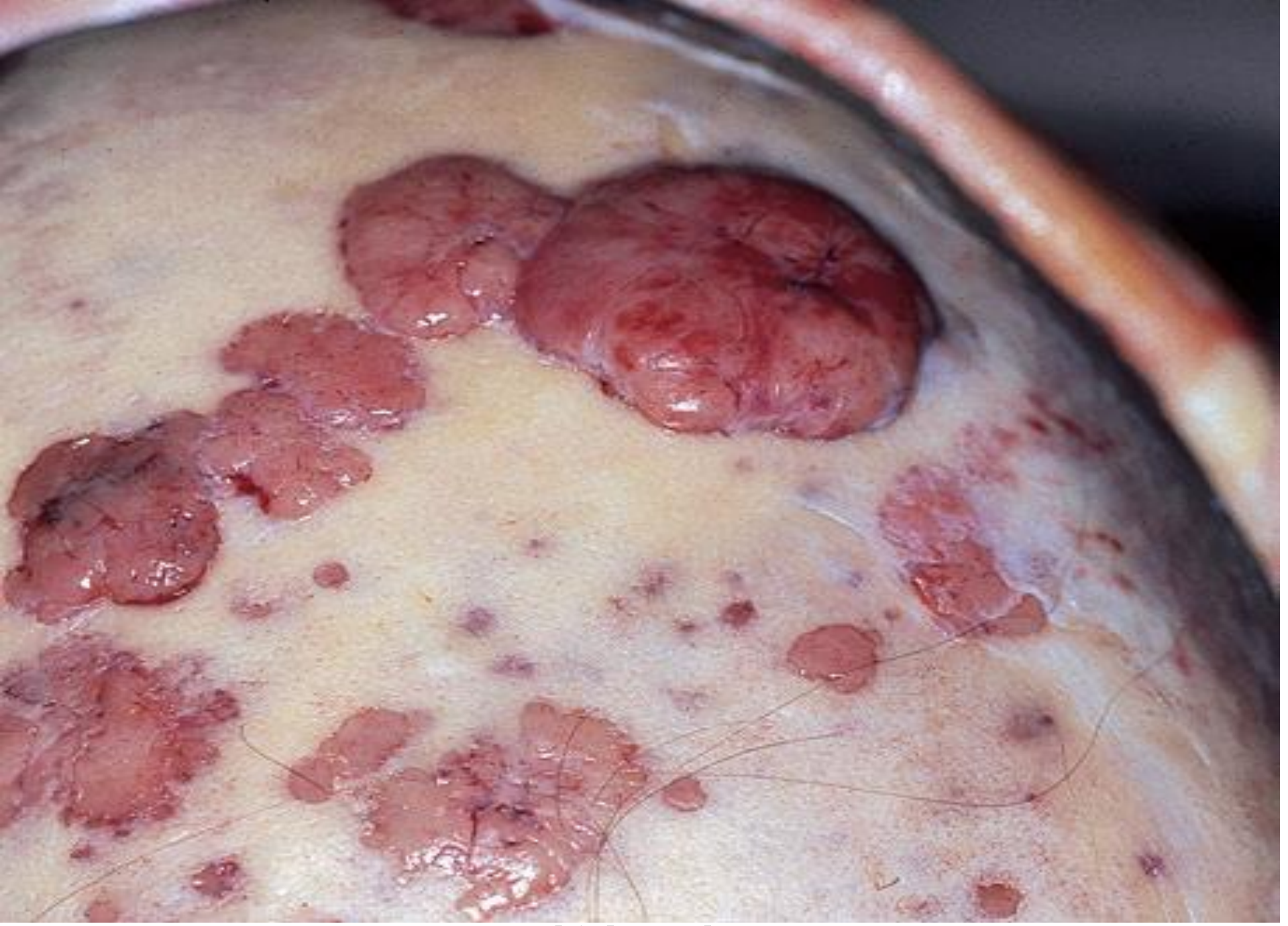
CLL - hyperplasia of periaortic lymph nodes.



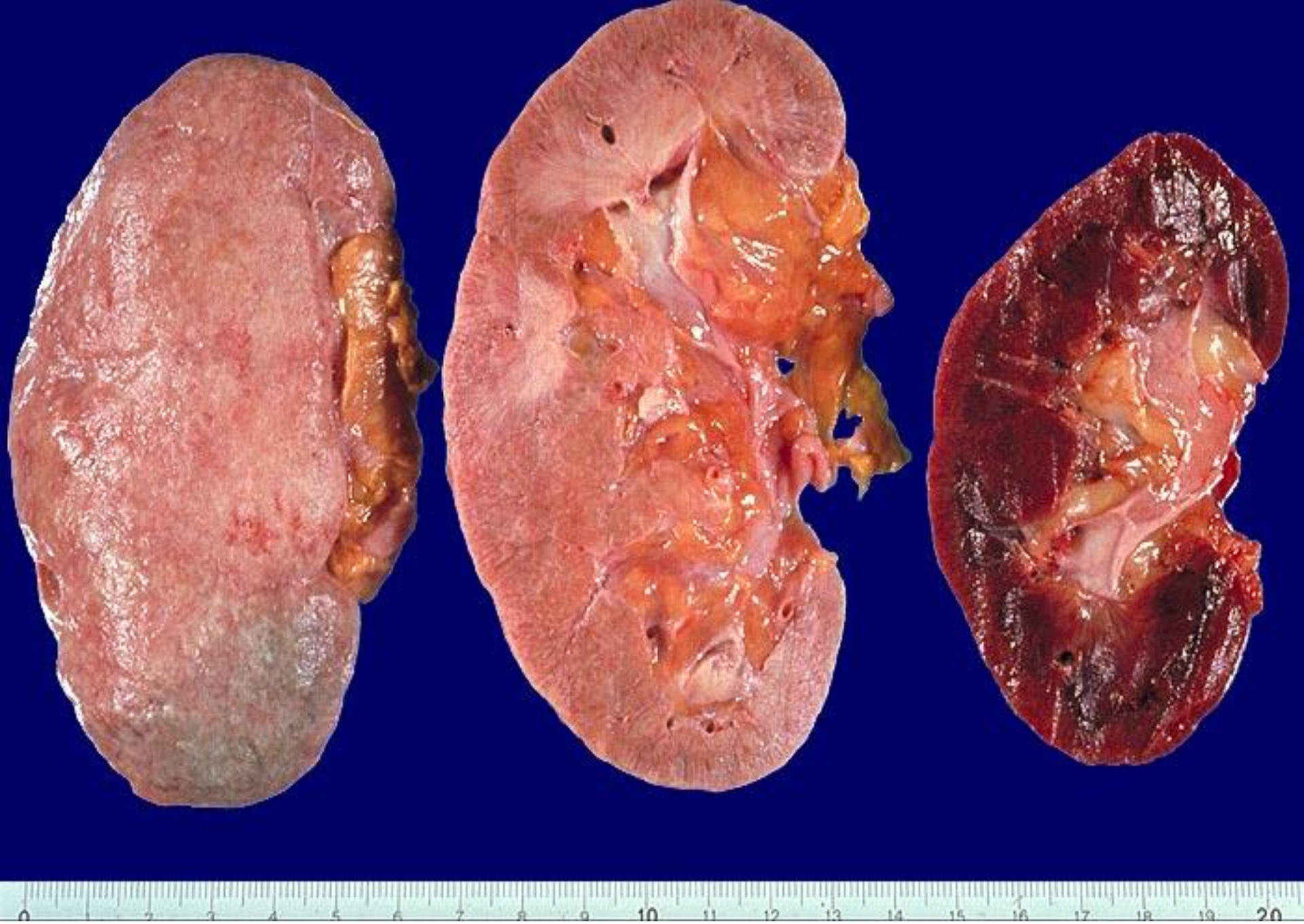
Hyperplasia of the spleen and intestinal lymph follicles in CLL.



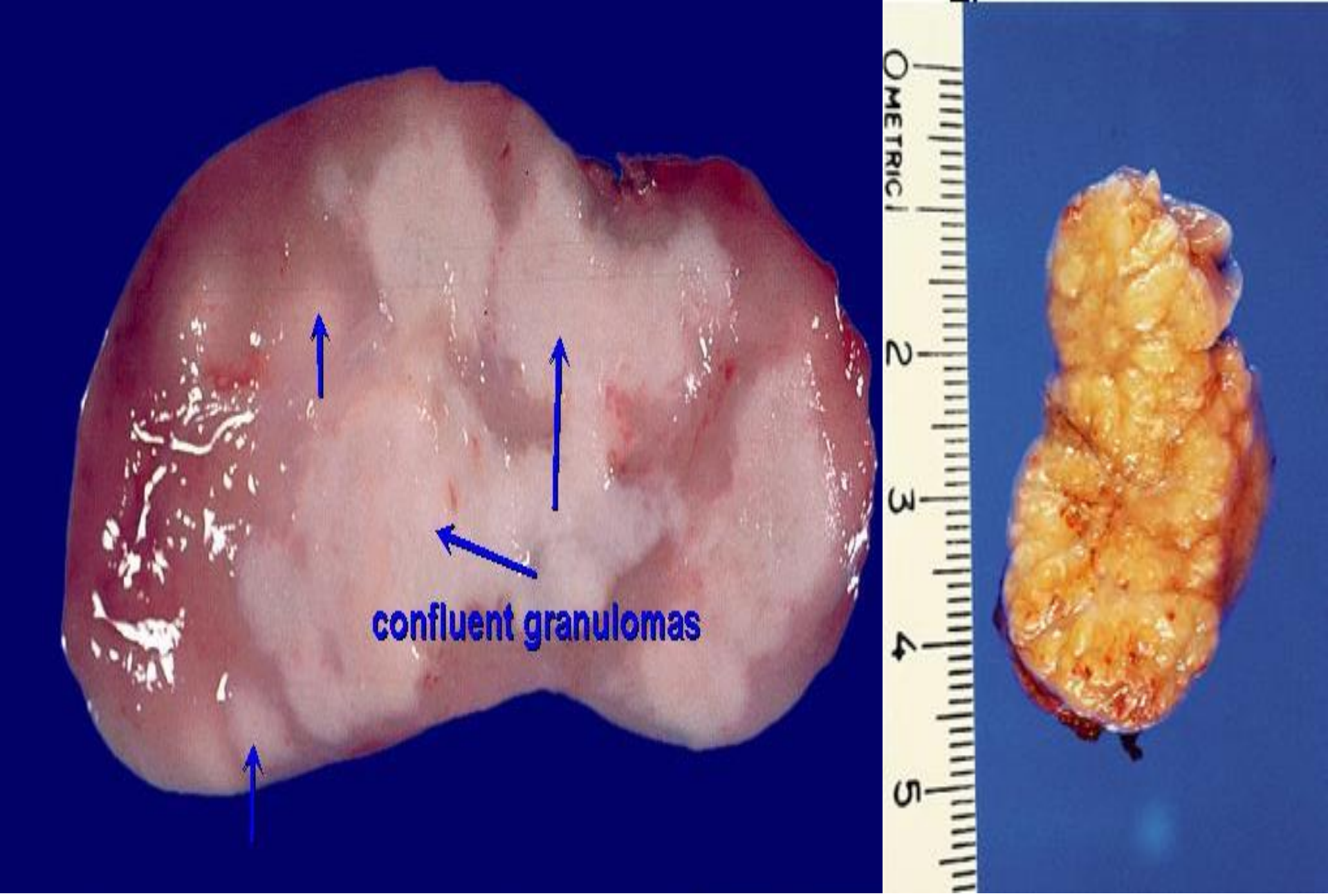
Liver in CLL



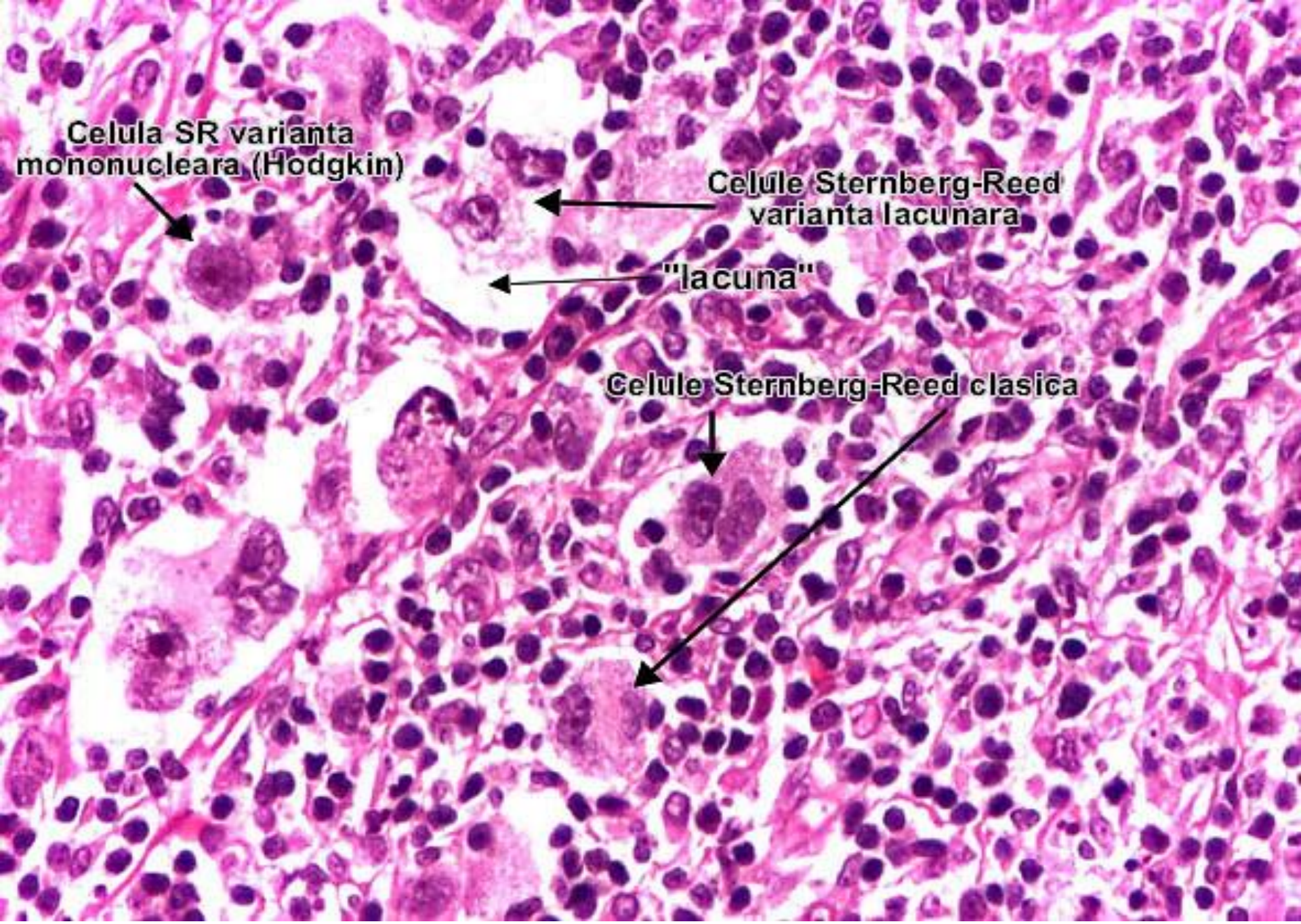
Multiple myeloma.



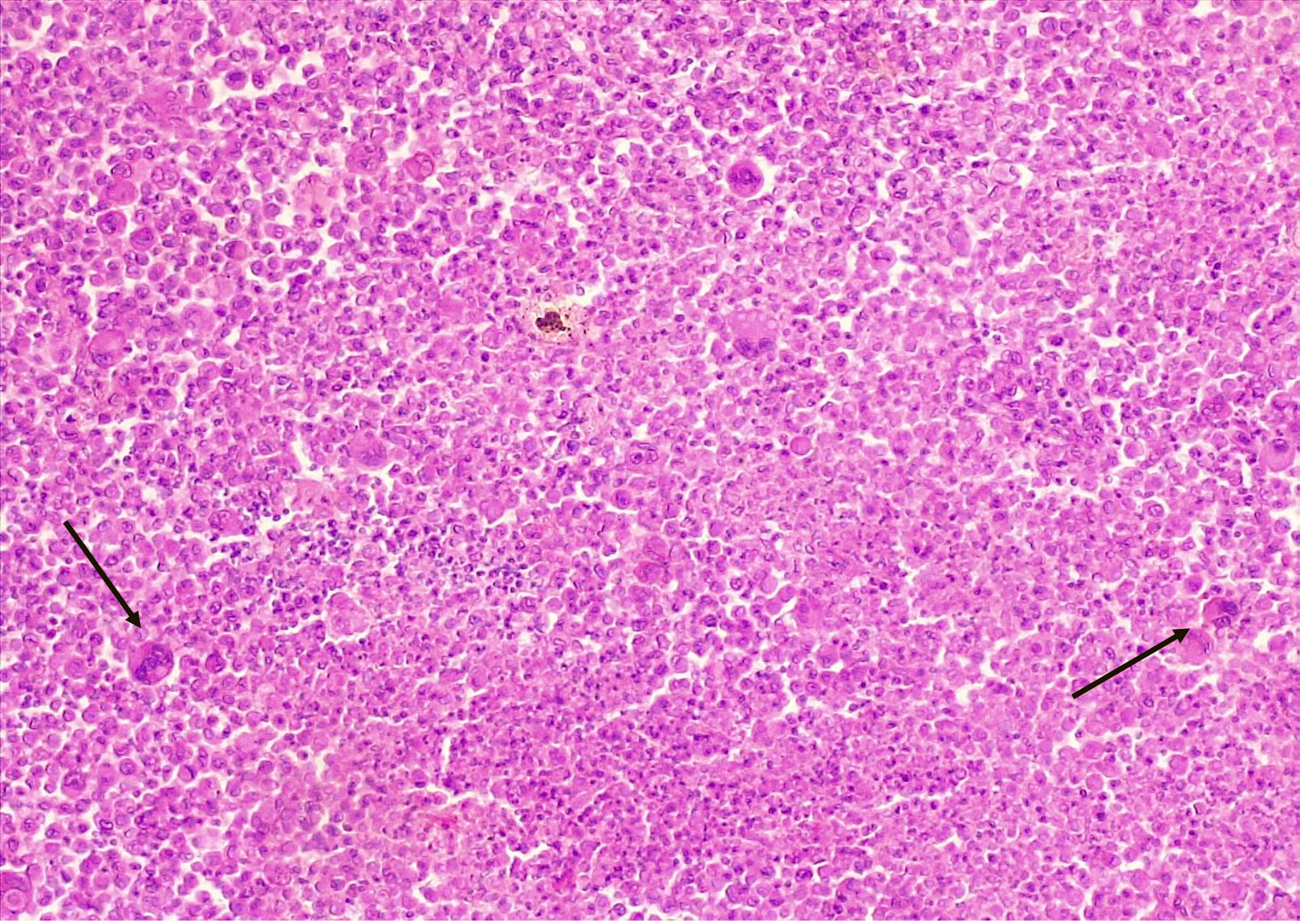
Myeloma kidney and normal kidneys.



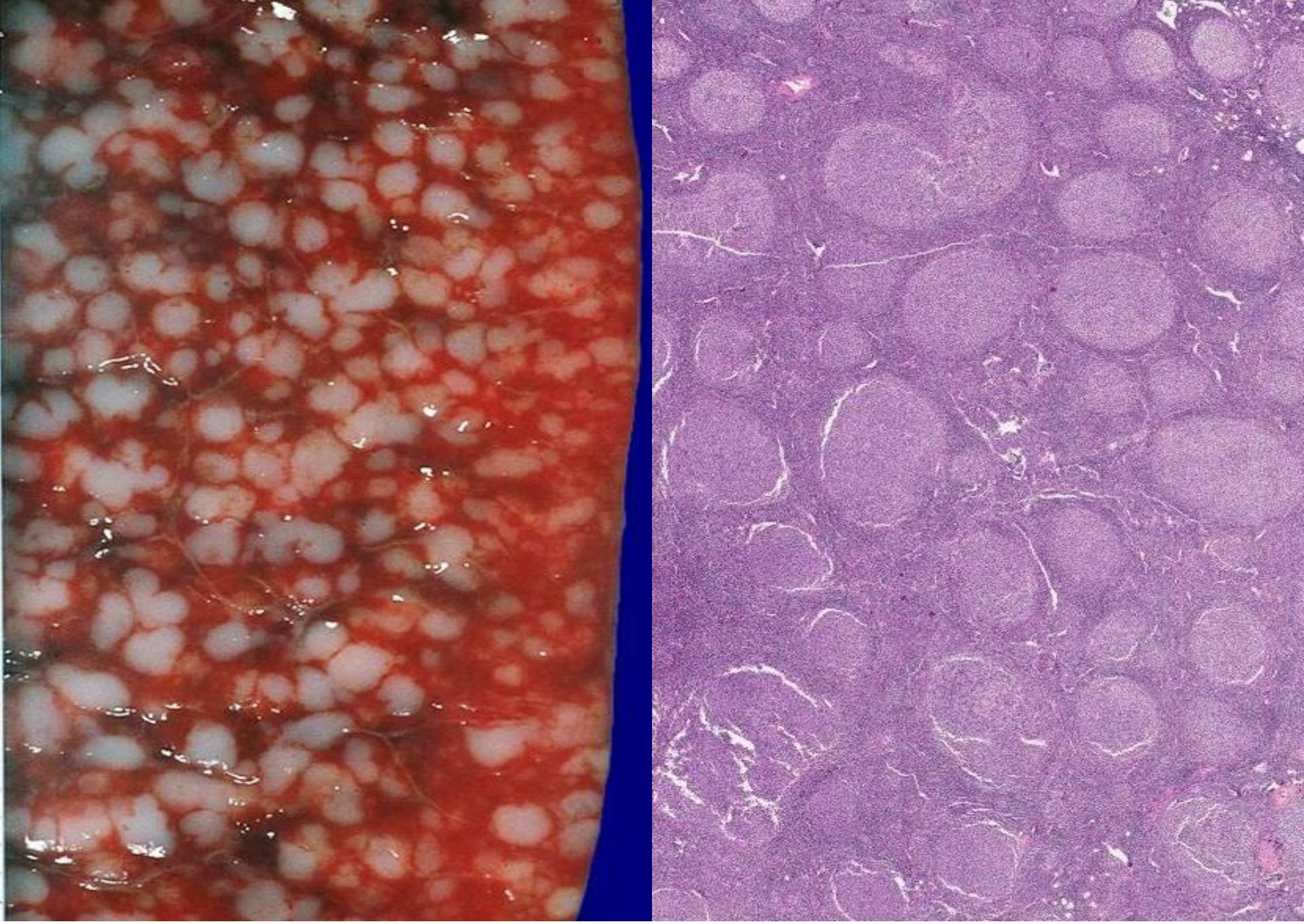
Lymph node in Hodgkin's lymphoma.
***(nodular surface)*.**



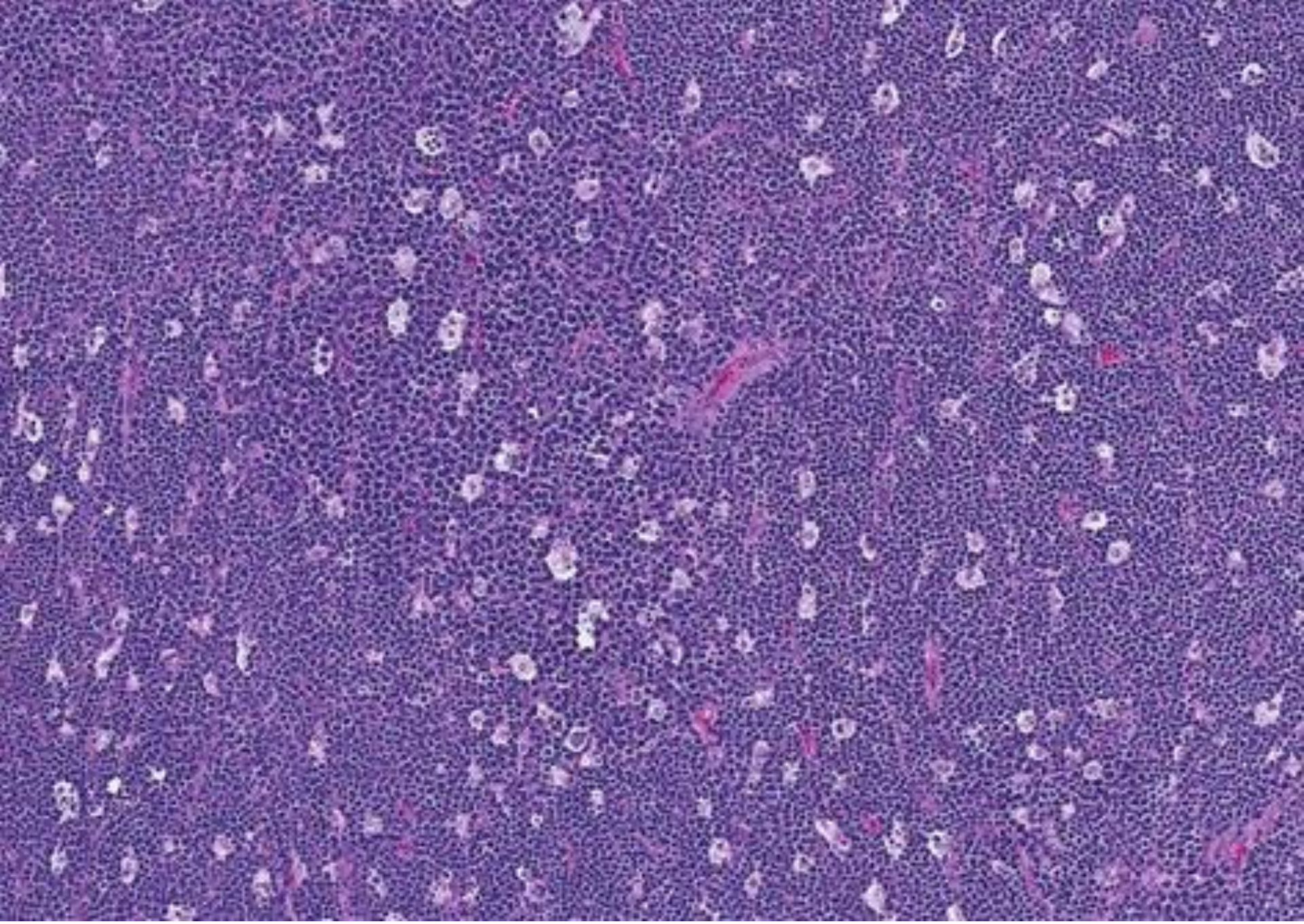
Reed - Sternberg cell.



Lymph node in Hodgkin's disease (mixed-cellularity type). *(H-E stain).*

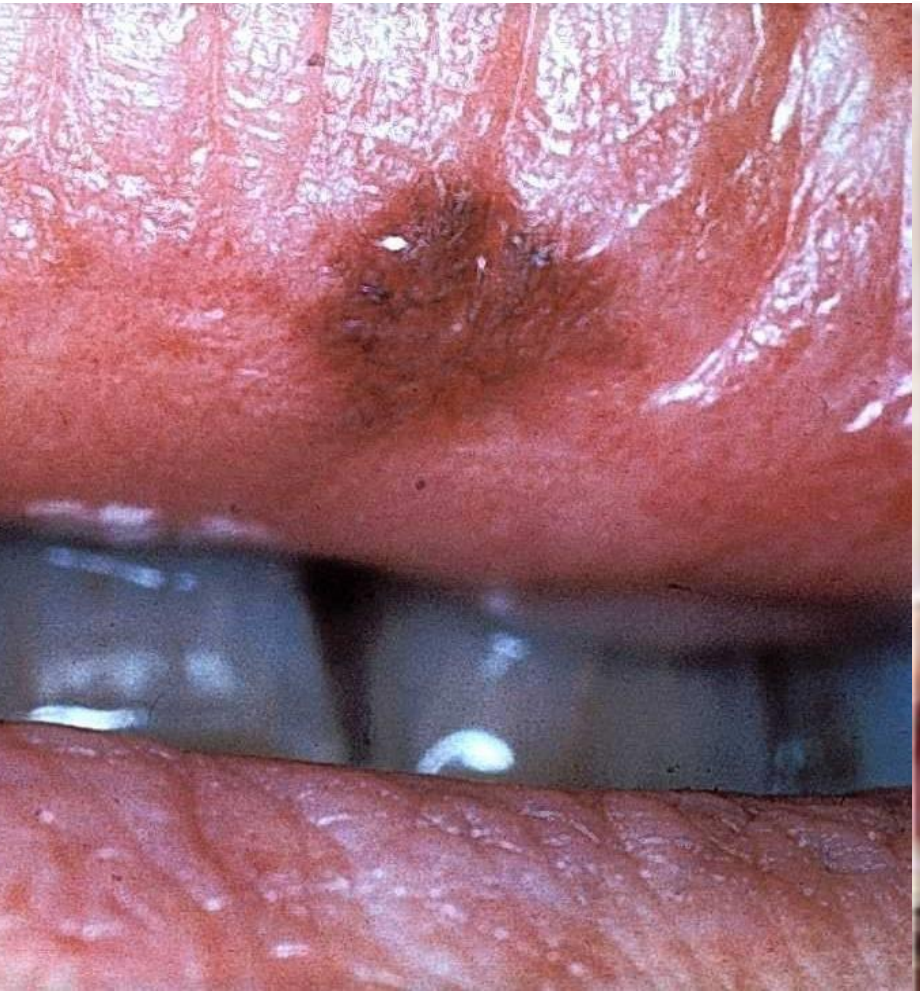


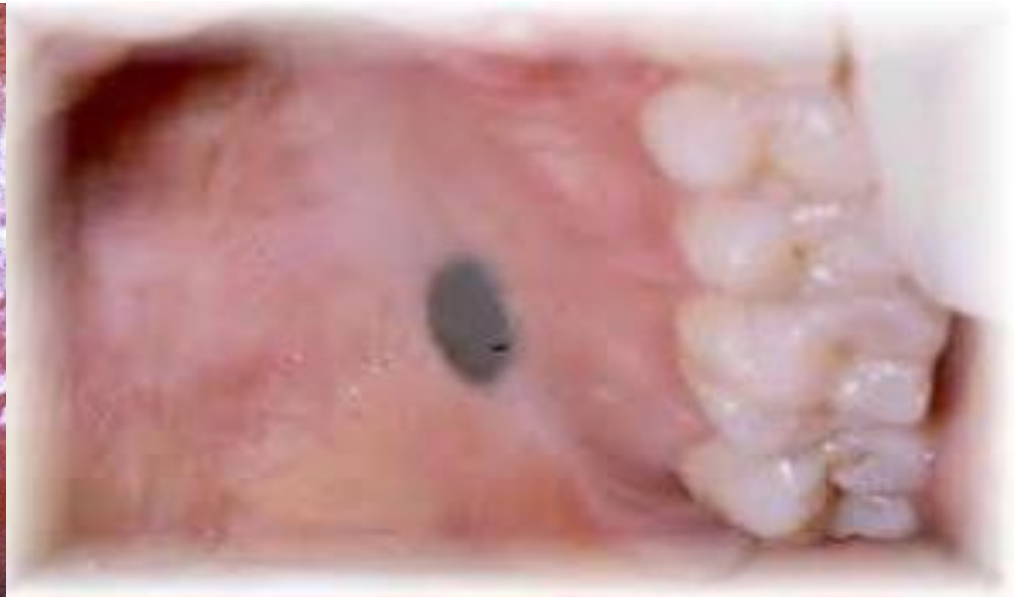
Follicular lymphoma.

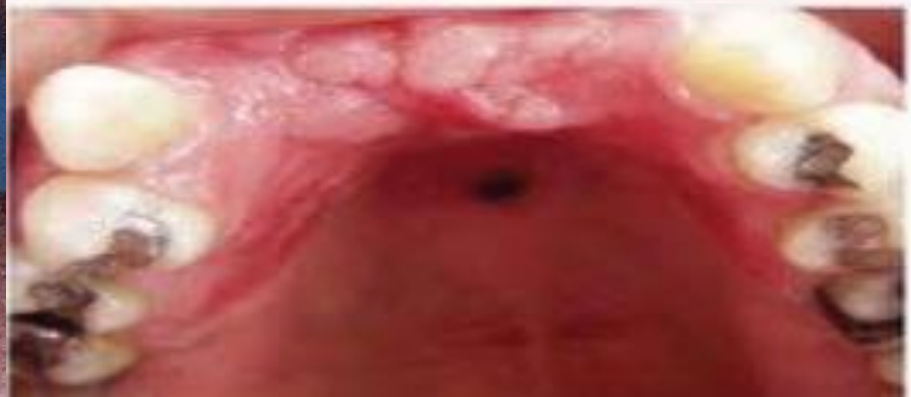


Burkitt's lymphoma *(starry sky appearance)*.

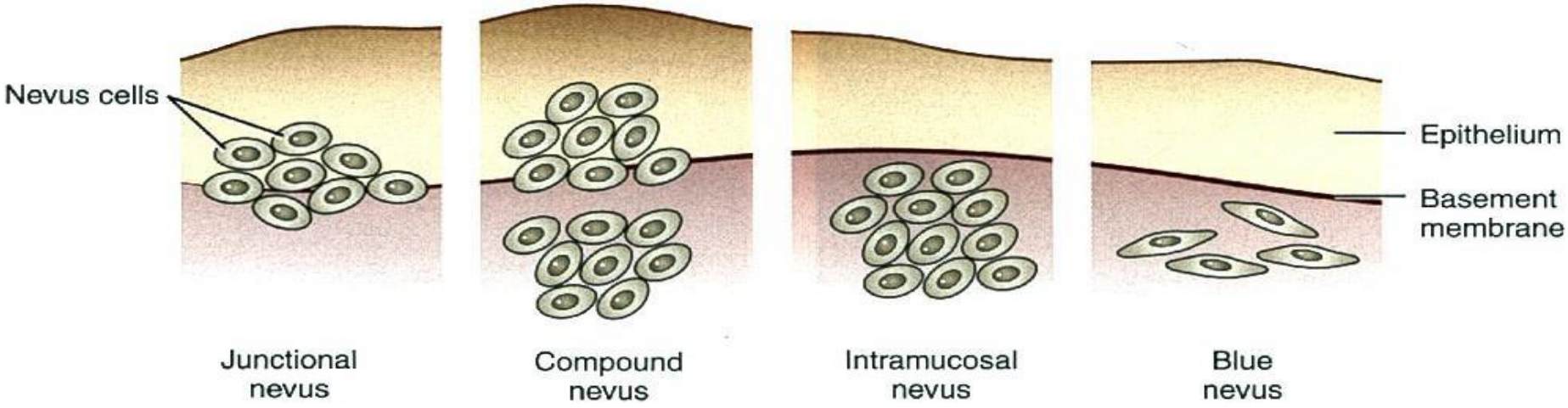
Nevi.





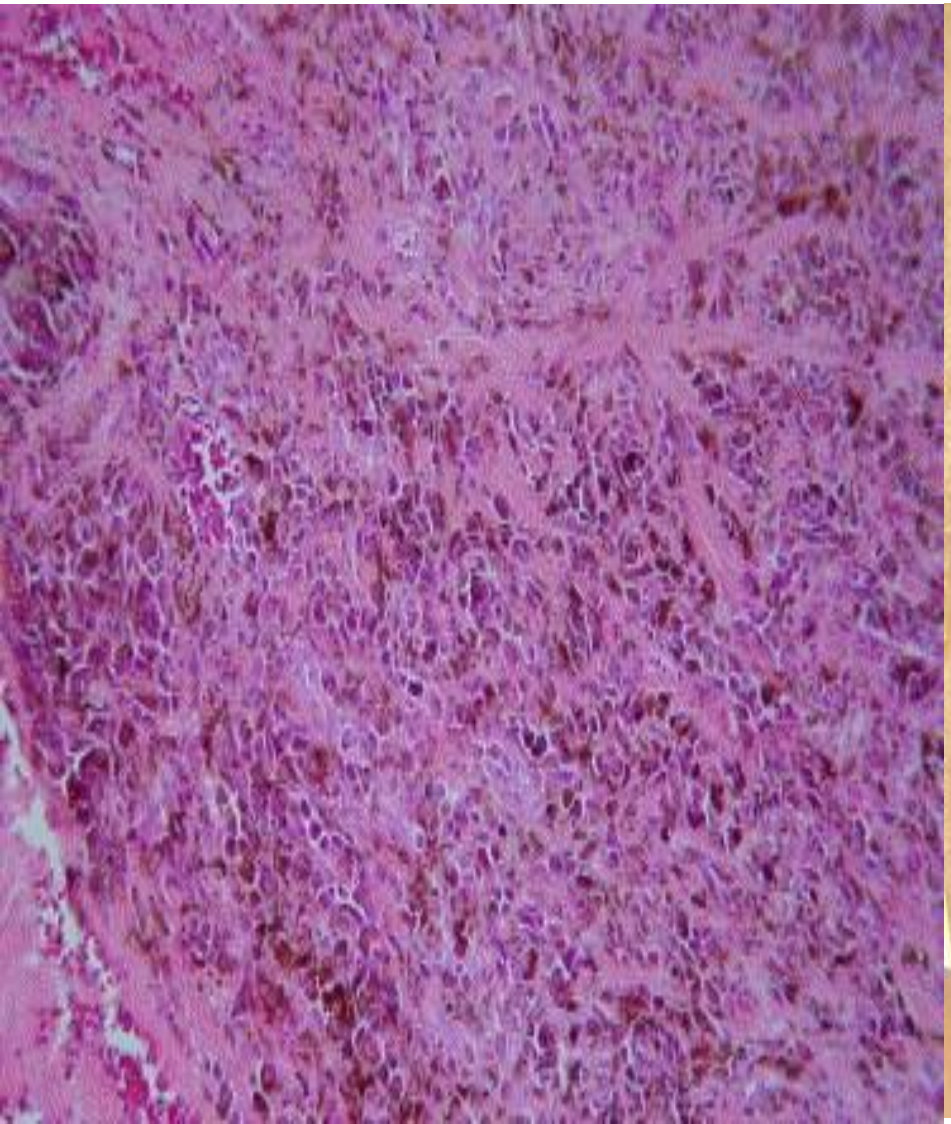


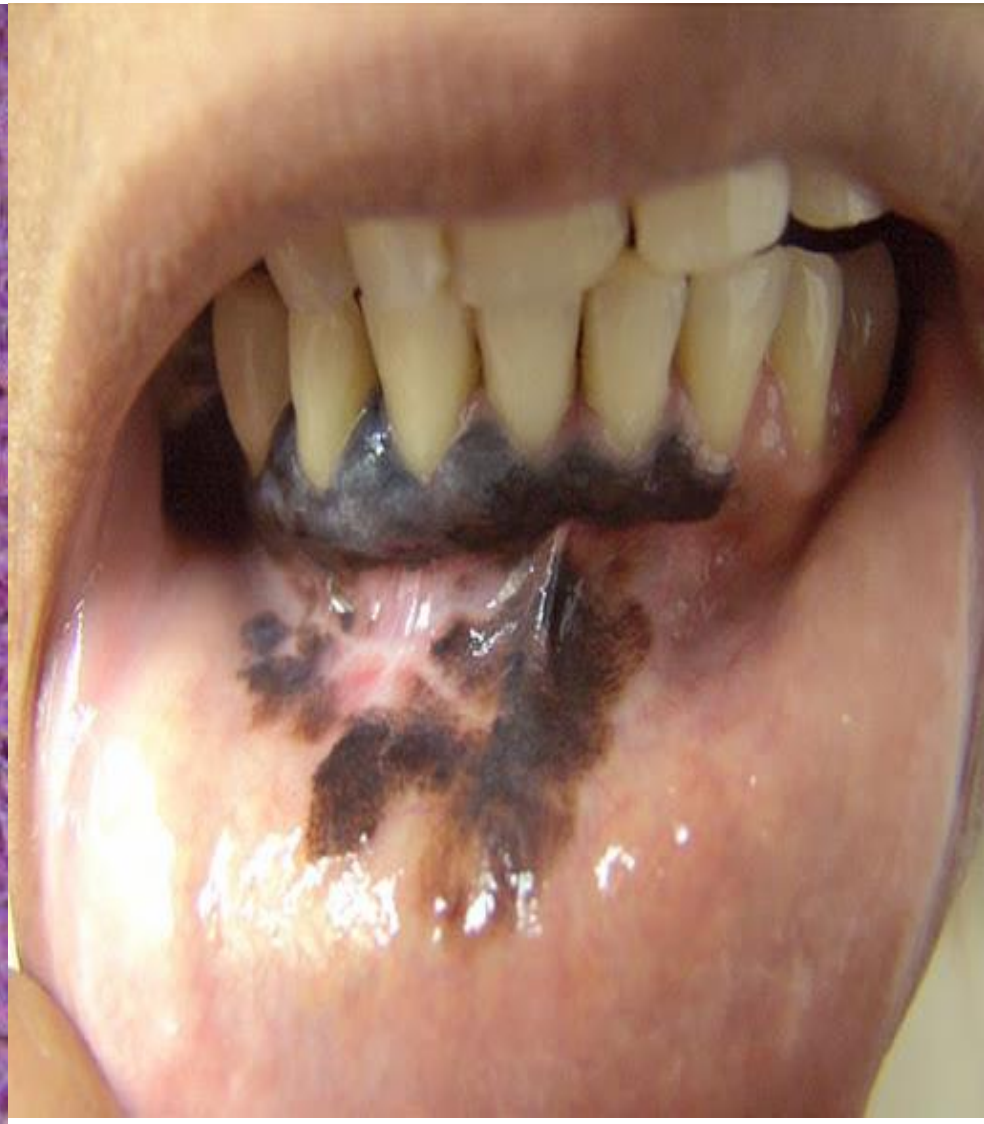
Nevi - types.



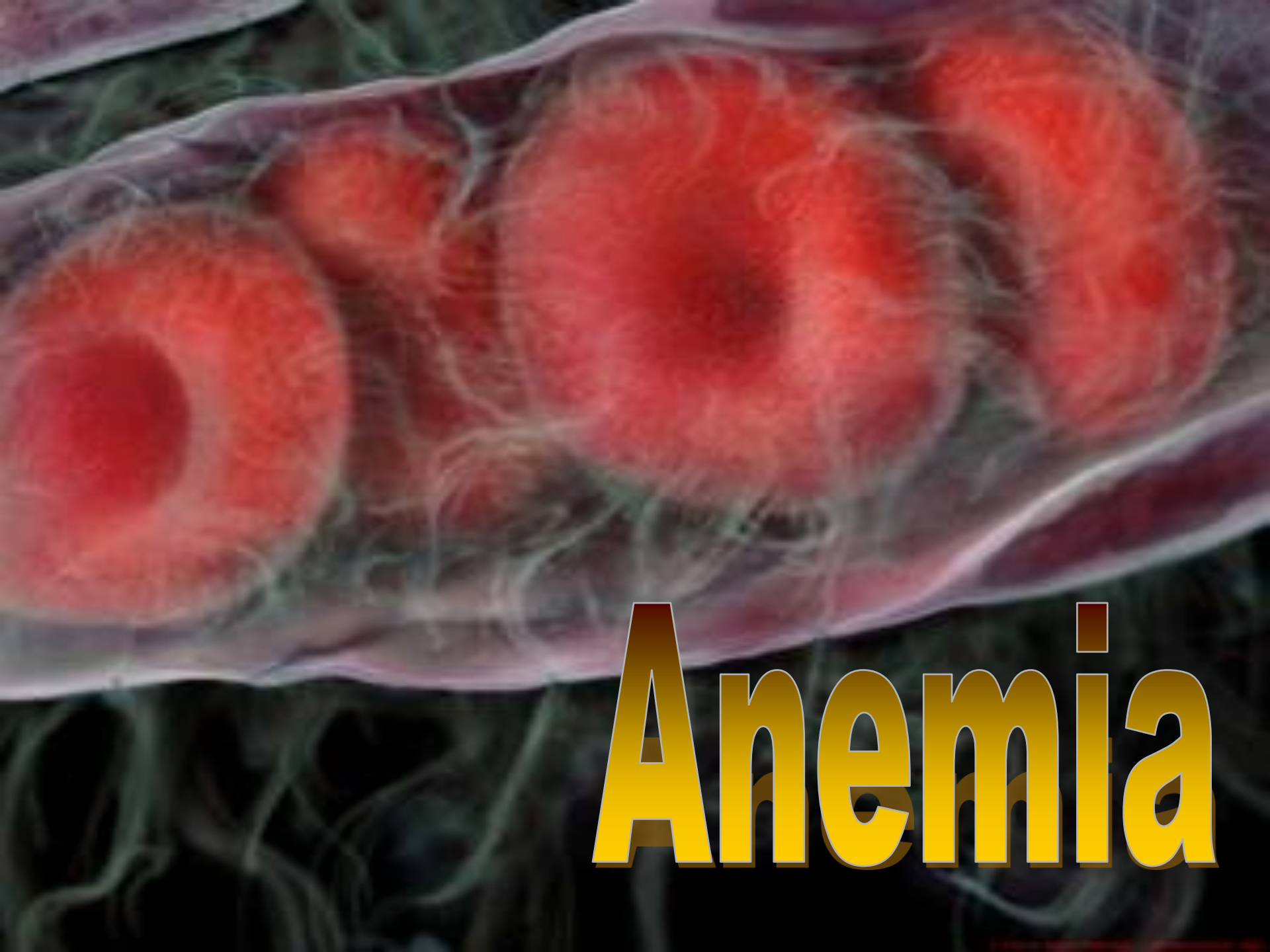
Regezi, Sciuba, Jordan: Oral pathology

Melanoma.





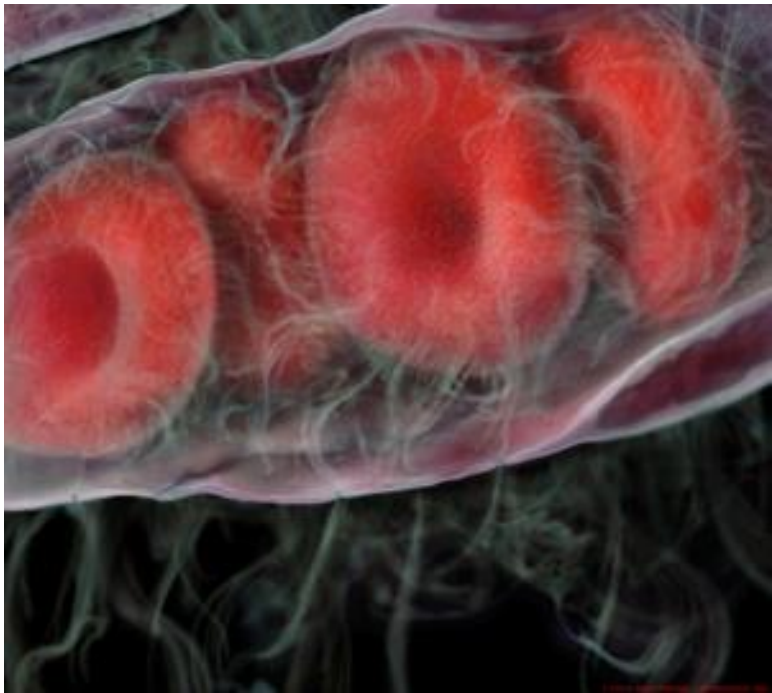
Pathology of the hematopoietic system.


Anemia

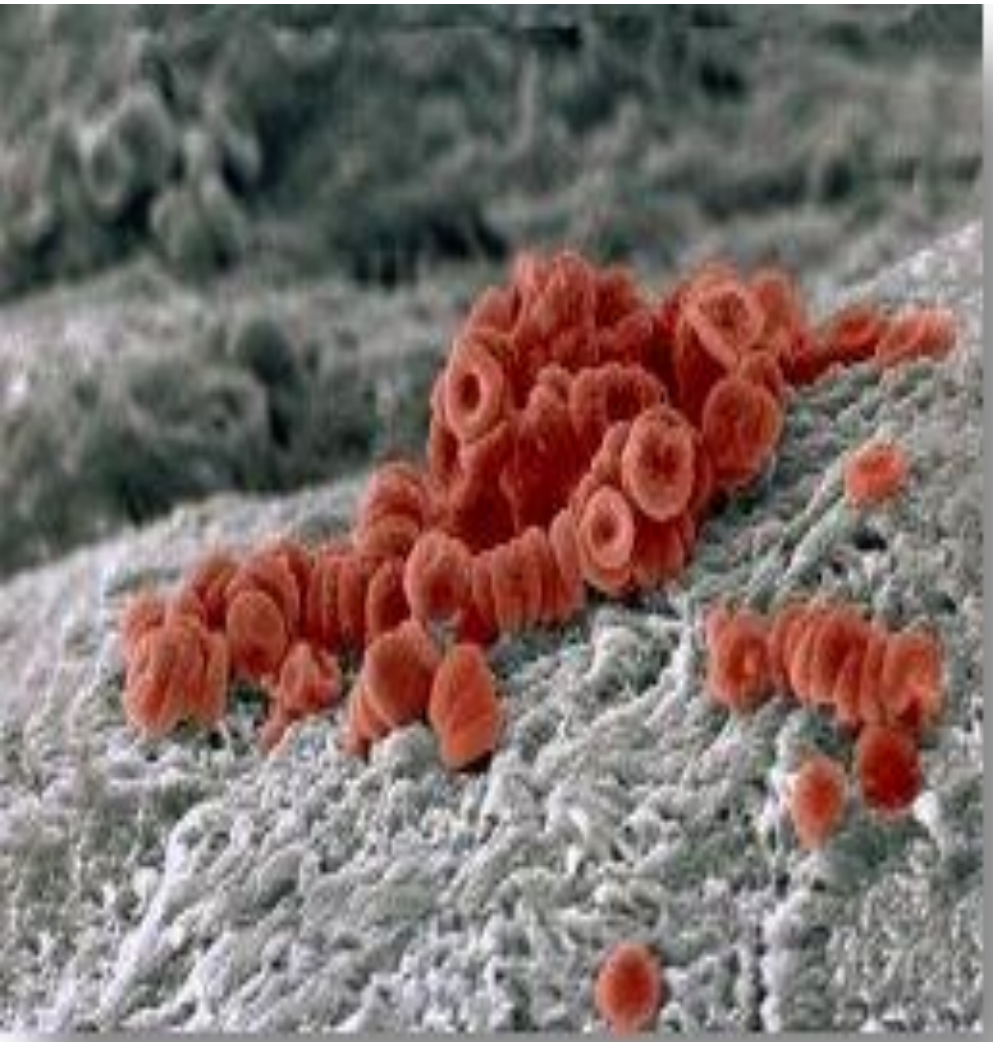
ANEMIAS

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
- **INcreased destruction (HEMOLYTIC)**
- **DEcreased production**



Morphological classification of anemias



Microcytic:

Iron def.
Thalassemia
Anemia of chronic pathologies

Aplastic:

Anemia of chronic pathologies
Acute and chronic bleeding

Macrocytic:

Liver pathologies,
Vitamin B12 and folic acid deficiency

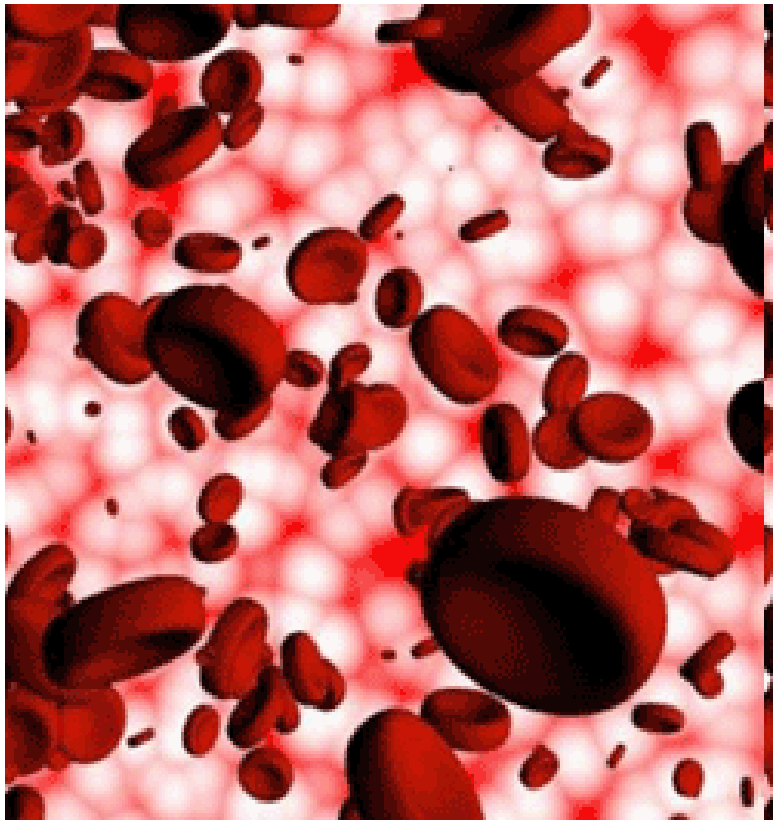
Features of ALL anemias

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

Posthemorrhagic anemias

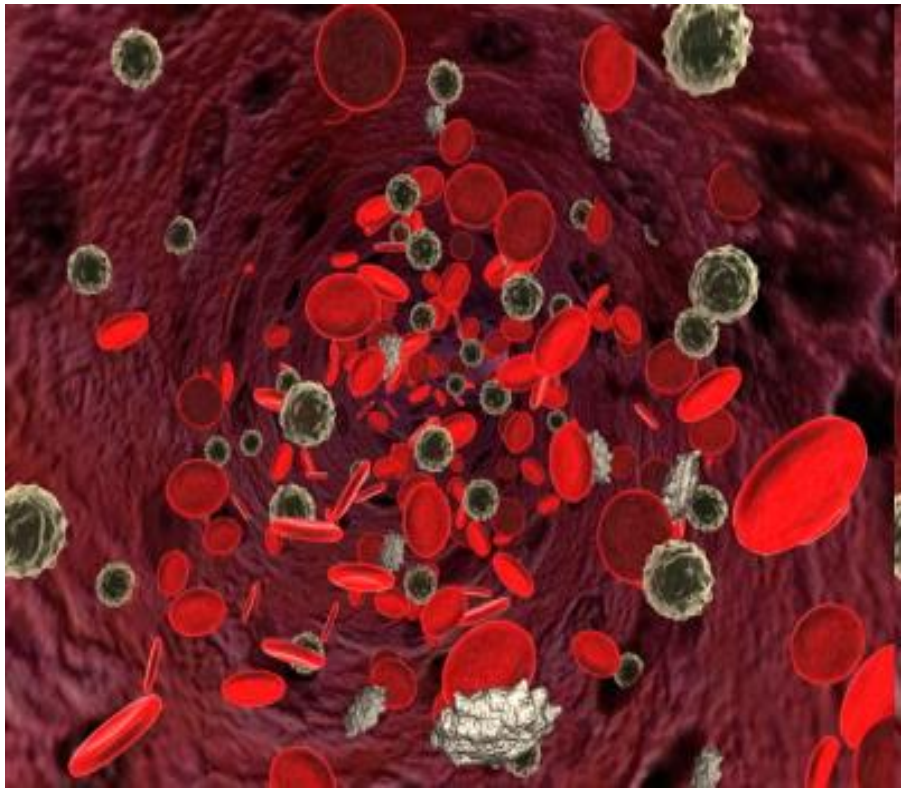
Acute - it is caused by massive hemorrhages in gastric and duodenal ulcers, rupture of the fallopian tube, branch of the pulmonary artery, aortic aneurysm.In the pathogenesis of clinical manifestations of acute blood loss, the basic role is played by the rapid decrease in the general volume of **blood** - plasma and erythrocytes, which lead to acute hypoxia.

Chronic - **develops in prolonged hemorrhages in case of tumors, dilated hemorrhoidal veins, uterine hemorrhages, gastric ulcers, hemophilia.In the pathogenesis of chronic hemorrhagic anemia, the main role belongs to the increase of iron deficiency, for these reasons currently this anemia refers to iron deficiency.**



HEMOLYTIC

- **HEREDITARY**
  - **MEMBRANE disorders: e.g., spherocytosis**
  - **ENZYME disorders: e.g., G6PD deficciency**
  - **HGB disorders (hemoglobinopathies)**
- **ACQUIRED**
  - **ANTIBODY MEDIATED, transfusion or autoantibodies**
  - **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: (Thalassemias)**

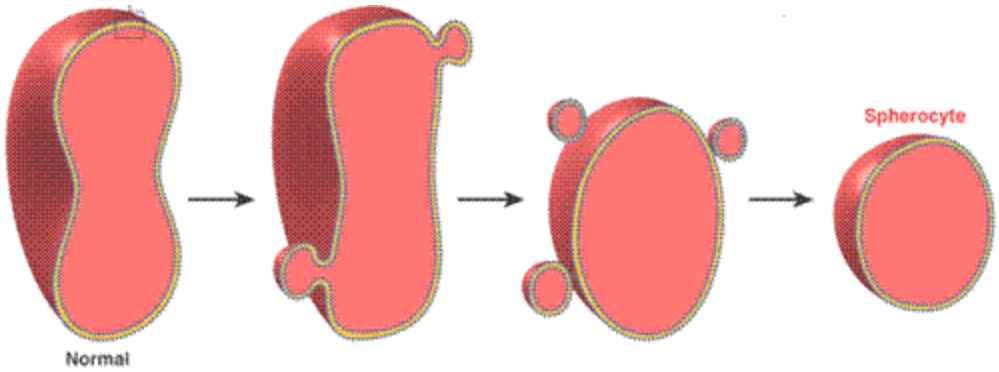
HEMOLYTIC ANEMIAS

- **Life span LESS than 120 days**
- **Marrow hyperplasia**
- **Increased catabolic products, e.g., bilirubin, hemosiderin.**

HEMOLYSIS

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

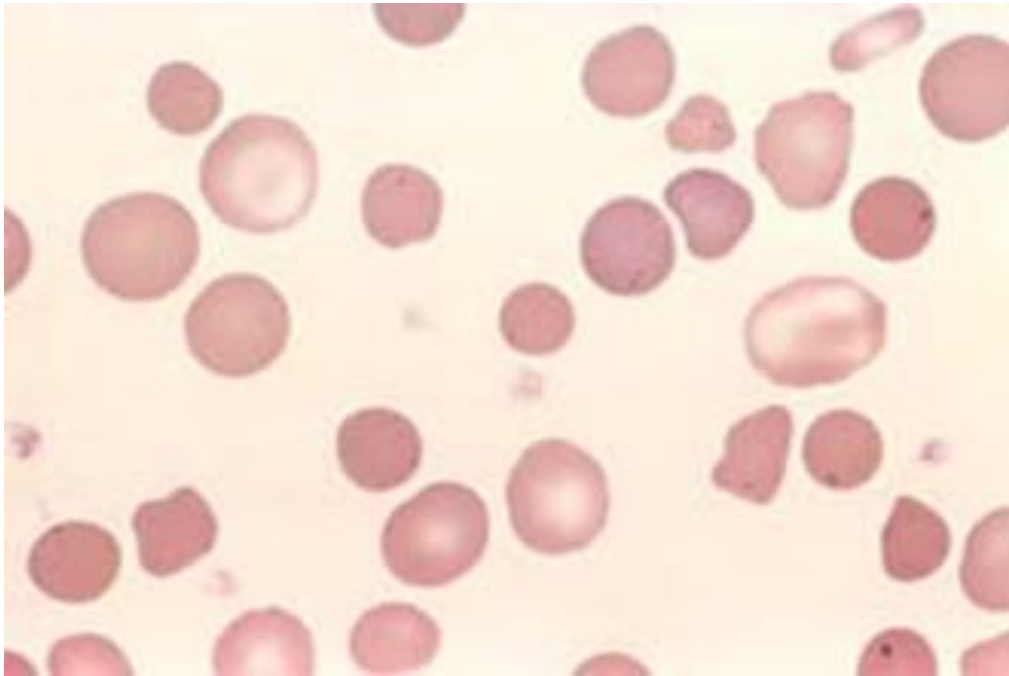
HEREDITARY SPHEROCYTOSIS



Genetic defects affecting ankyrin, spectrin, usually autosomal dominant

Children, adults

Anemia, hemolysis, jaundice, splenomegaly.

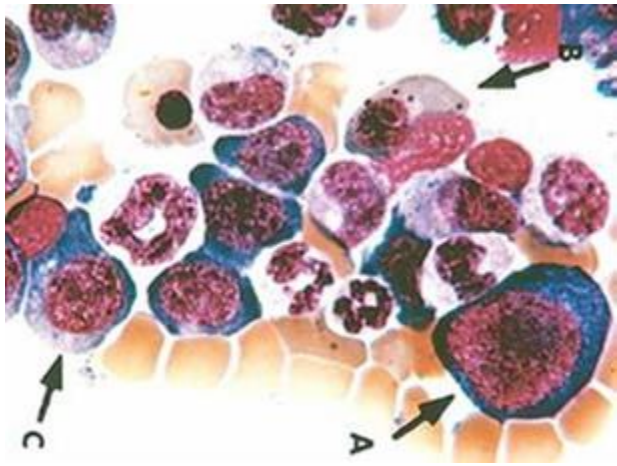


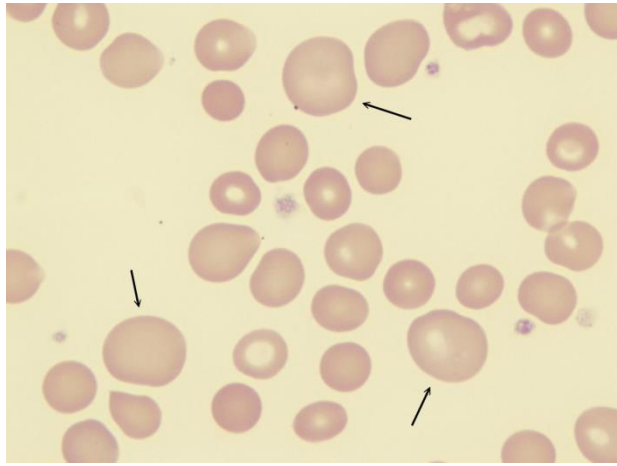
NON-Hemolytic Anemias: i.e., DE-creased Production

- **“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 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**
- **Pregnancy, hyperthyroidism, disseminated cancer**

Vit-B12 Physiology

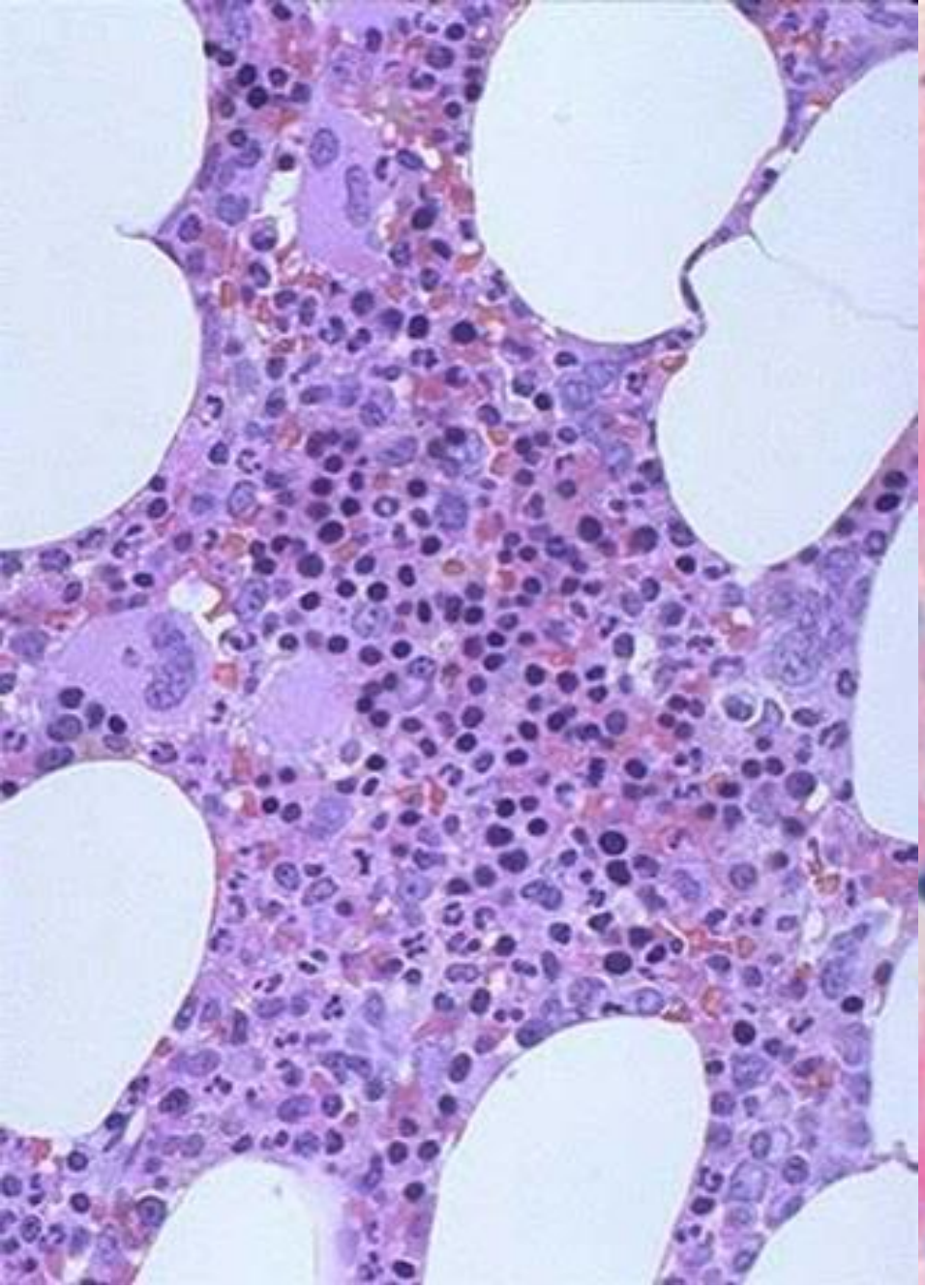
- **Oral ingestion**
- **Combines with INTRINSIC FACTOR in the gastric mucosa**
- **Absorbed in the terminal ileum**
- **DEFECTS at ANY of these sites can produce a MEGALOBLASTIC anemia**

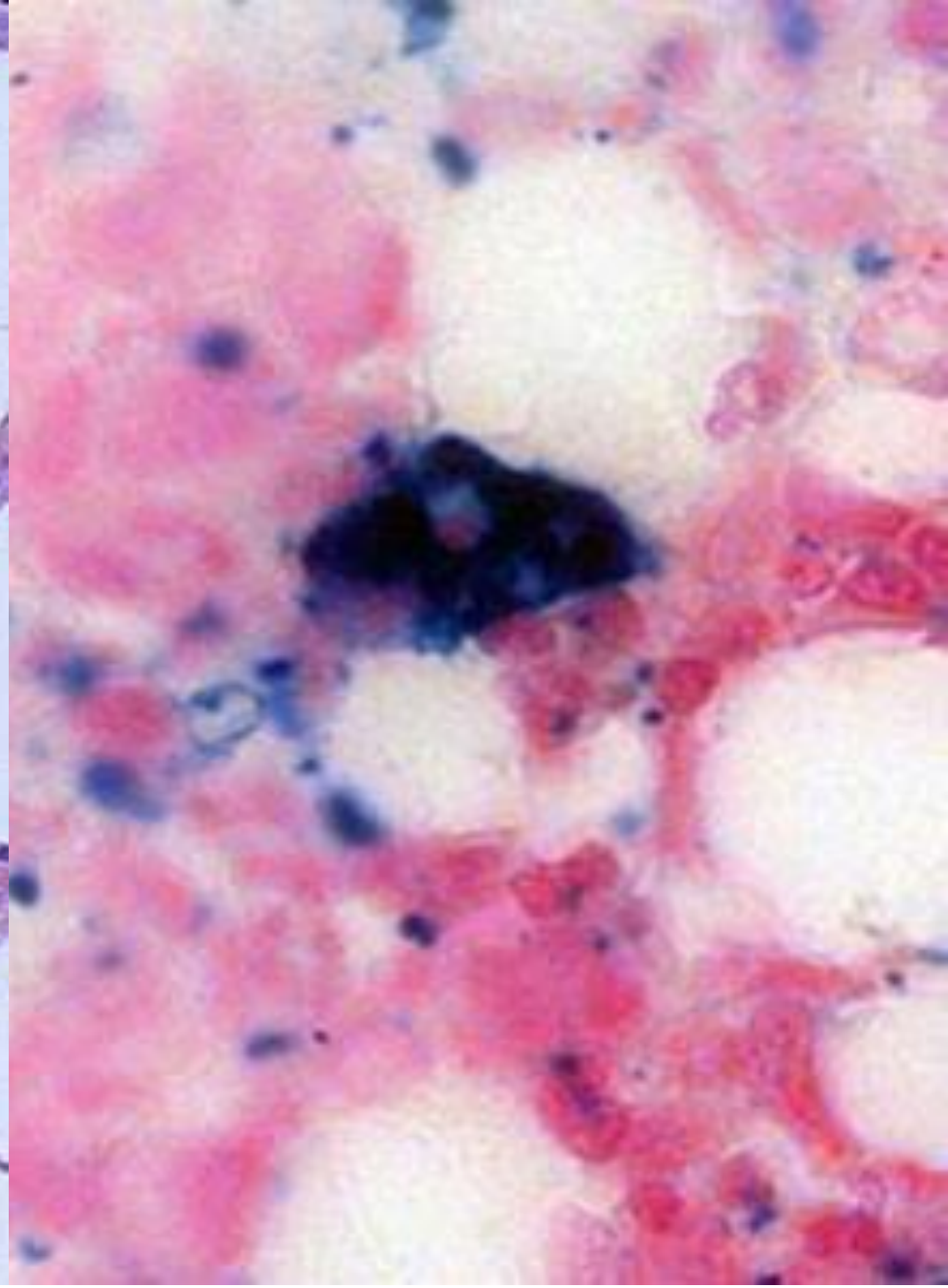
FOLATE DEFICIENCY MEGALOBLASTIC AMEMIAS

- **Decreased Intake: diet, infancy**
- **Impaired Absorption: intestinal disease**
- **DRUGS: anticonvulsants, 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**





Golden brown refractile pigment on H&E is HEMOSIDERIN when it stains BLUE by the Prussian Blue method! Any marrow that has stuff staining with Prussian Blue, is NOT an iron deficiency!

Anemia of Chronic Disease*

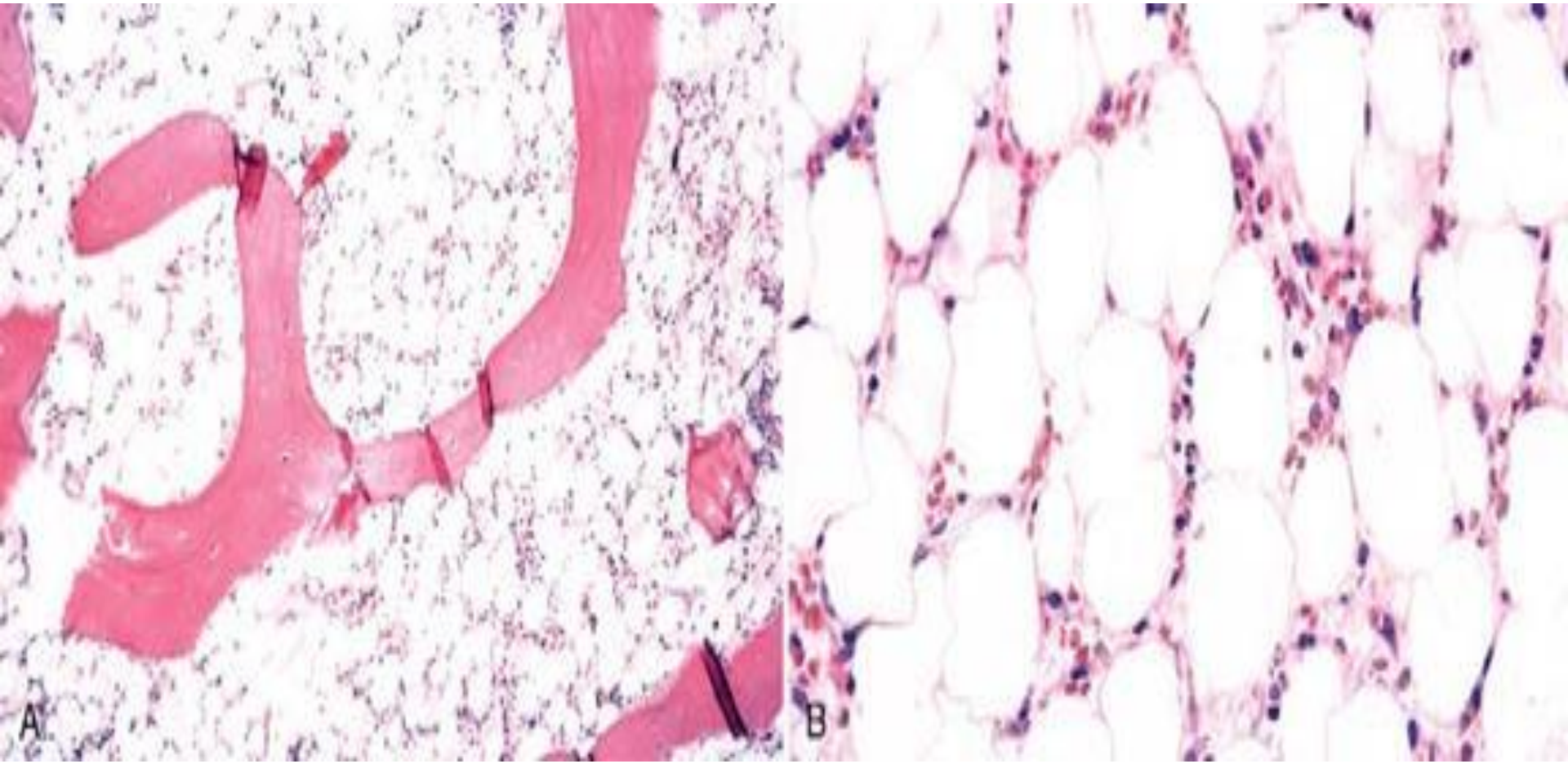
- **CHRONIC INFECTIONS**
- **CHRONIC IMMUNE DISORDERS**
- **NEOPLASMS**
- **LIVER, KIDNEY failure**

*** Patients may 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

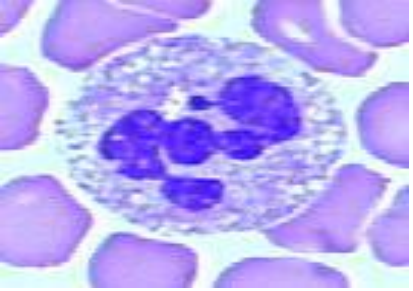
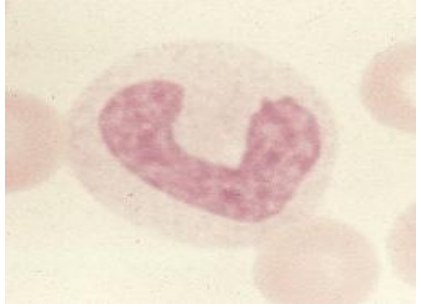
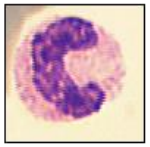
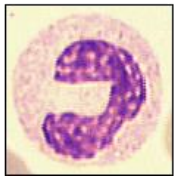
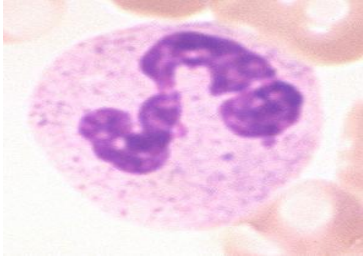


APLASTIC ANEMIAS

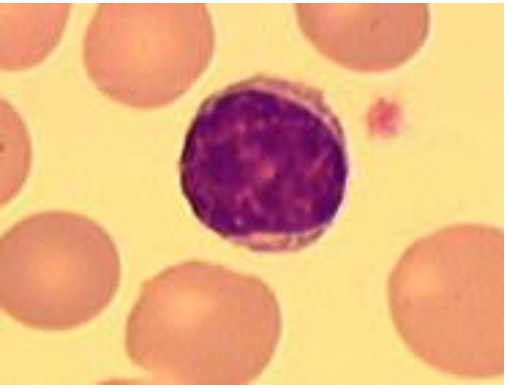
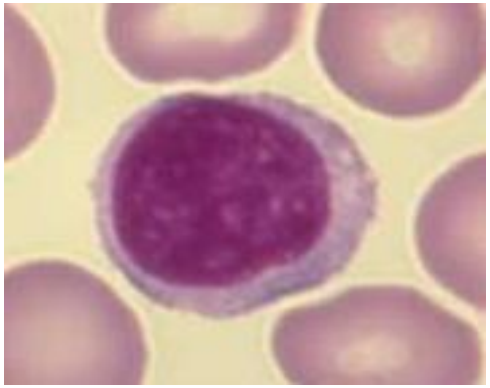
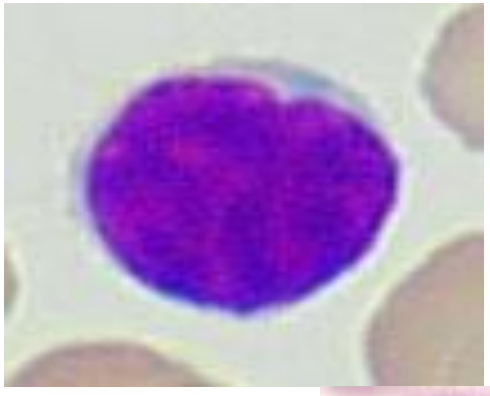
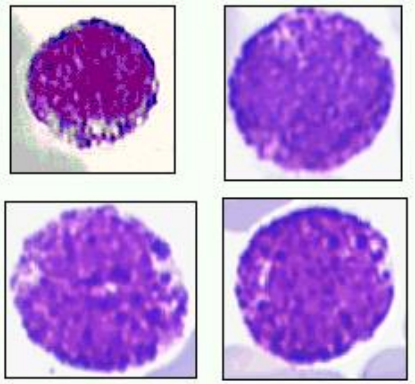
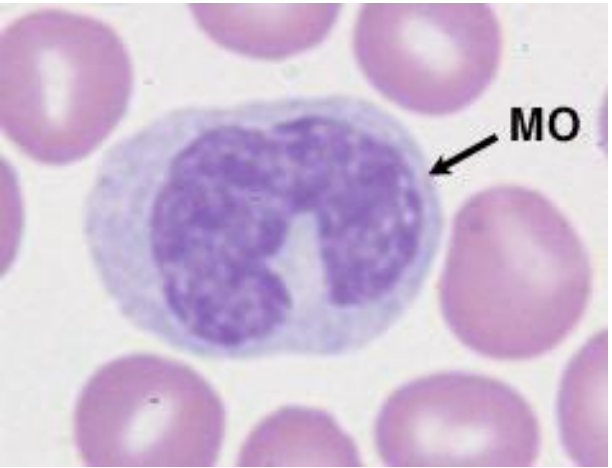
- **CHLORAMPHENICOL**
- **OTHER ANTIBIOTICS**
- **CHEMO**
- **INSECTICIDES**
- **VIRUSES**
  - **EBV**
  - **HEPATITIS**

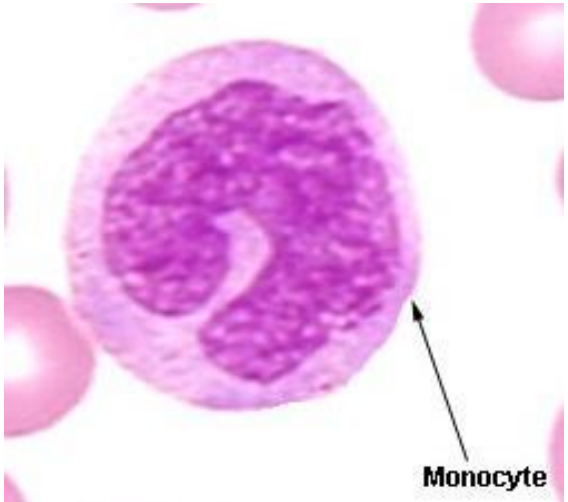
MYELOPHTHISIC ANEMIAS

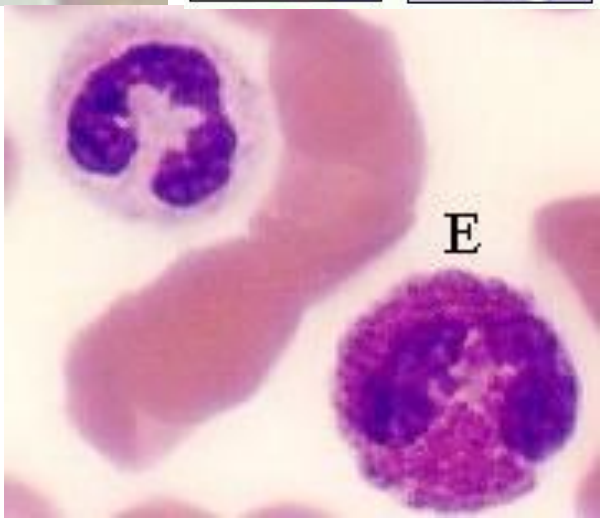
- **Are anemias caused by metastatic tumor cells replacing the bone marrow extensively**

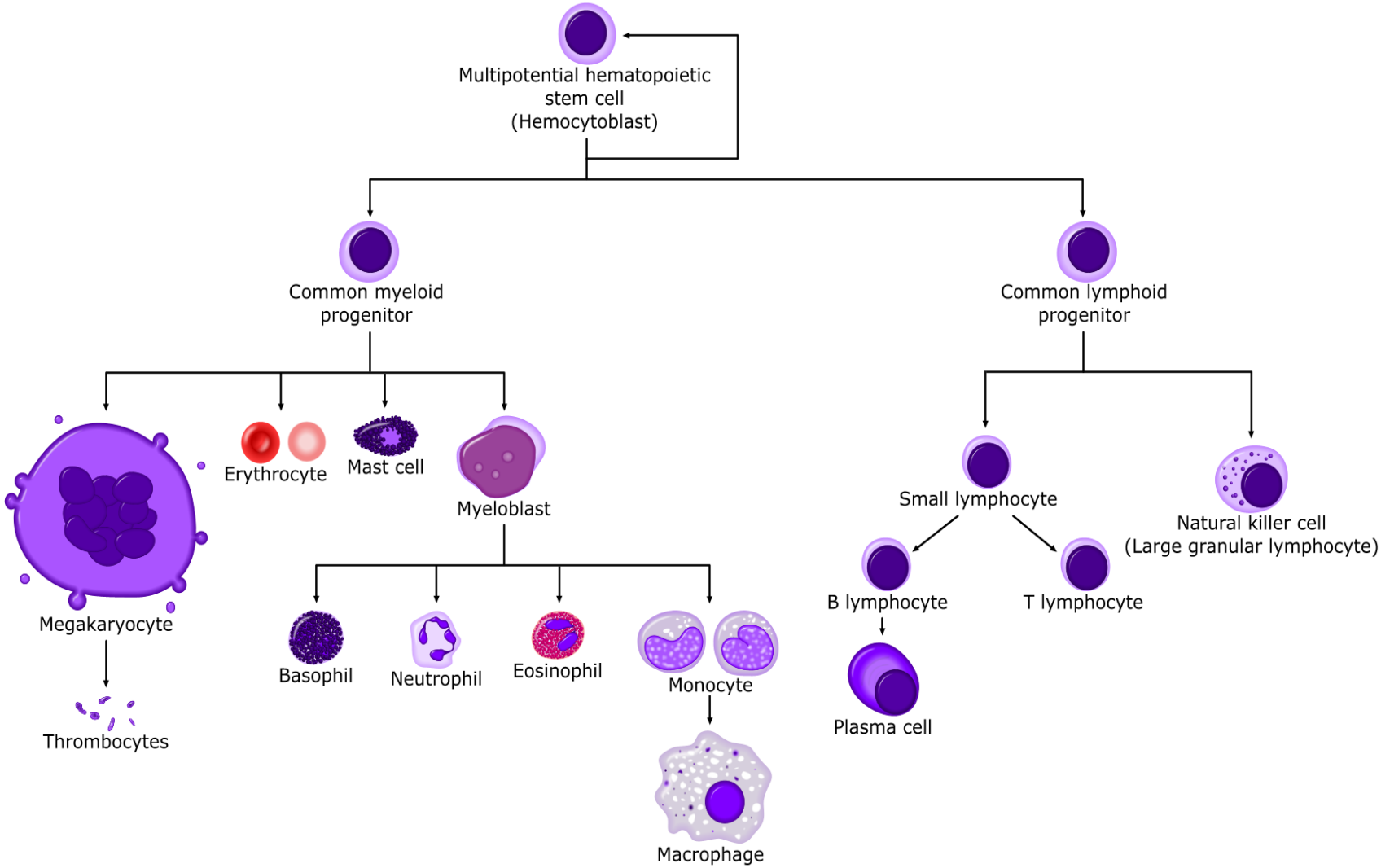






DISEASES OF WHITE CELLS AND LYMPHOID TISSUE







Myeloid

Lymphoid

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

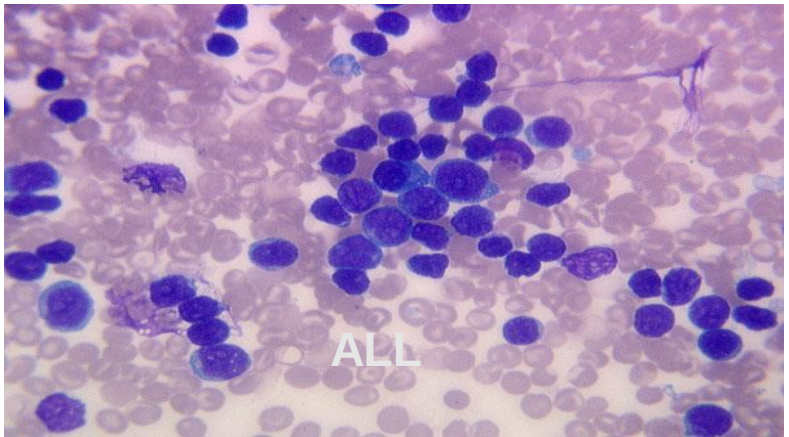
- **NODAL or EXTRANODAL**
- **T or B**
- **SMALL or LARGE CELLS**
- **FOLLICULAR or DIFFUSE**
- **Hodgkins or NON-Hodgkins**
- **"F.A.B. classification" is currently popular this week (FrenchAmericaBritish), for the NON-Hodgkins lymphomas**

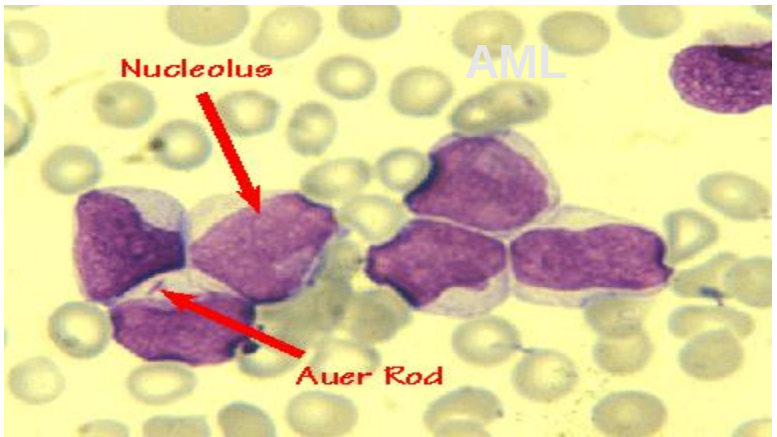
LEUKEMIAS

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

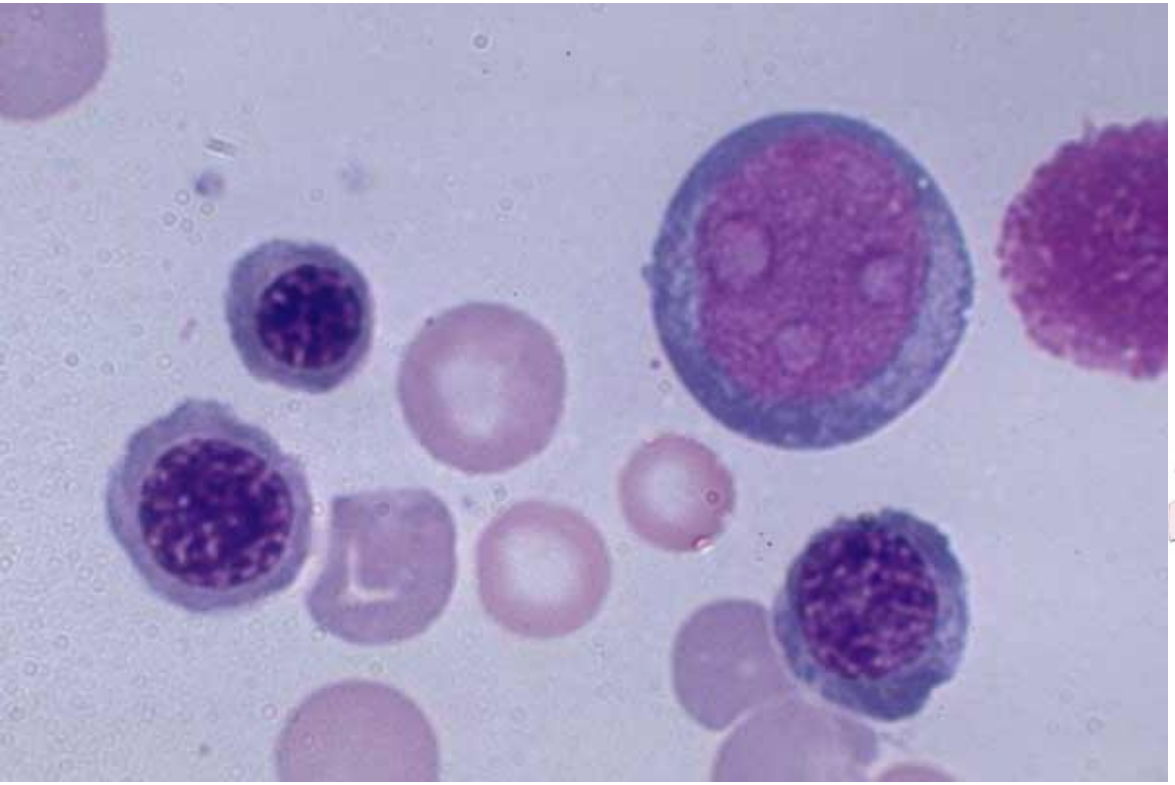
Types of Leukemias

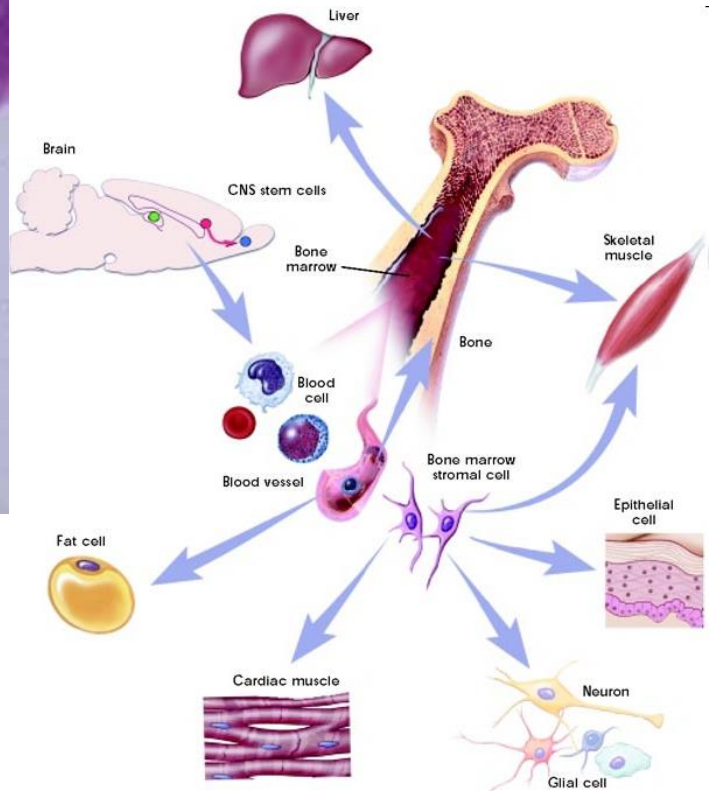
1. **Acute Lymphoblastic leukemia** (ALL) ~30% of all leukemias, the most common among children under 5 years old a second peak occurs after age 60. The marrow contains more than 30% lymphoblasts. The prognosis is inversely proportional to age, responds remarkably well to chemotherapy & marrow transplant, 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



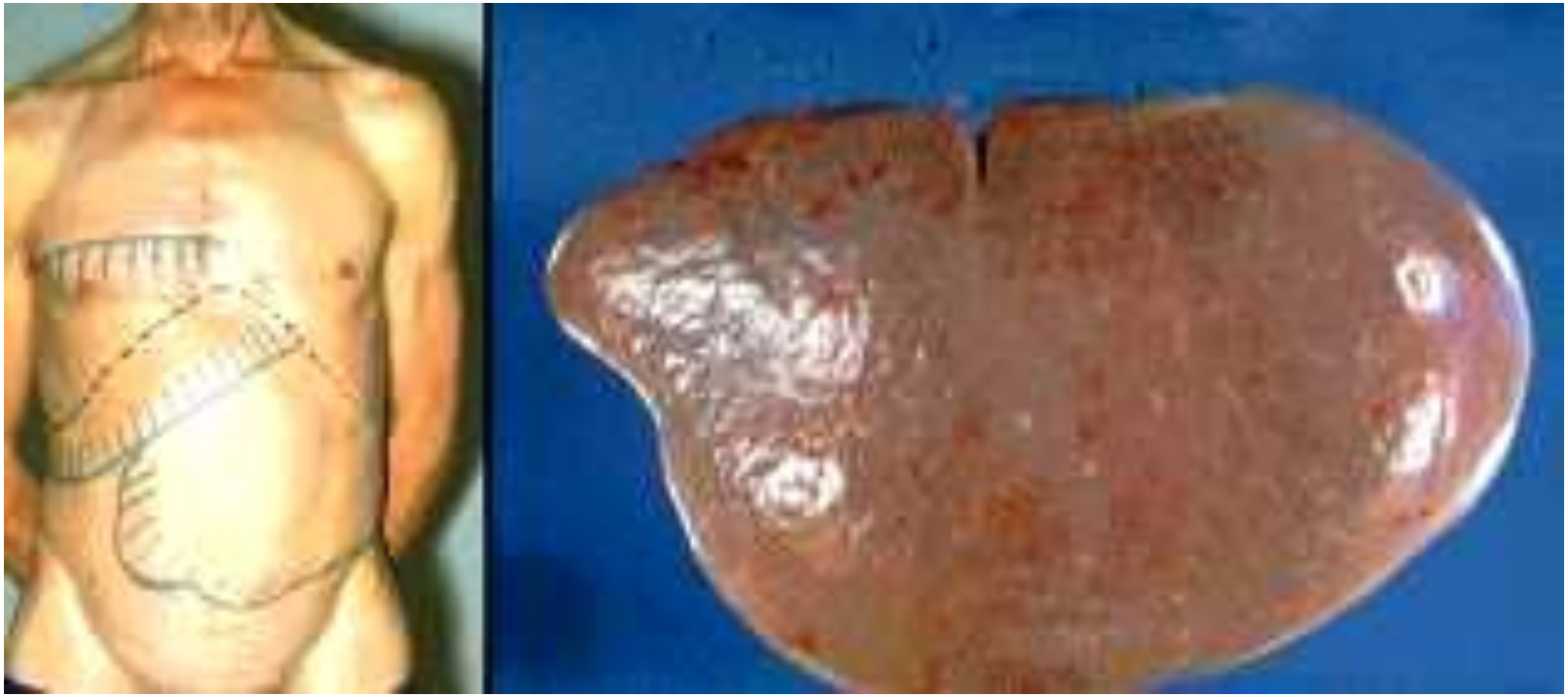

Liver
Brain
CNS stem cells
Bone marrow
Skeletal muscle
Bone
Blood cell
Blood vessel
Bone marrow stromal cell
Epithelial cell
Fat cell
Cardiac muscle
Neuron
Glial cell

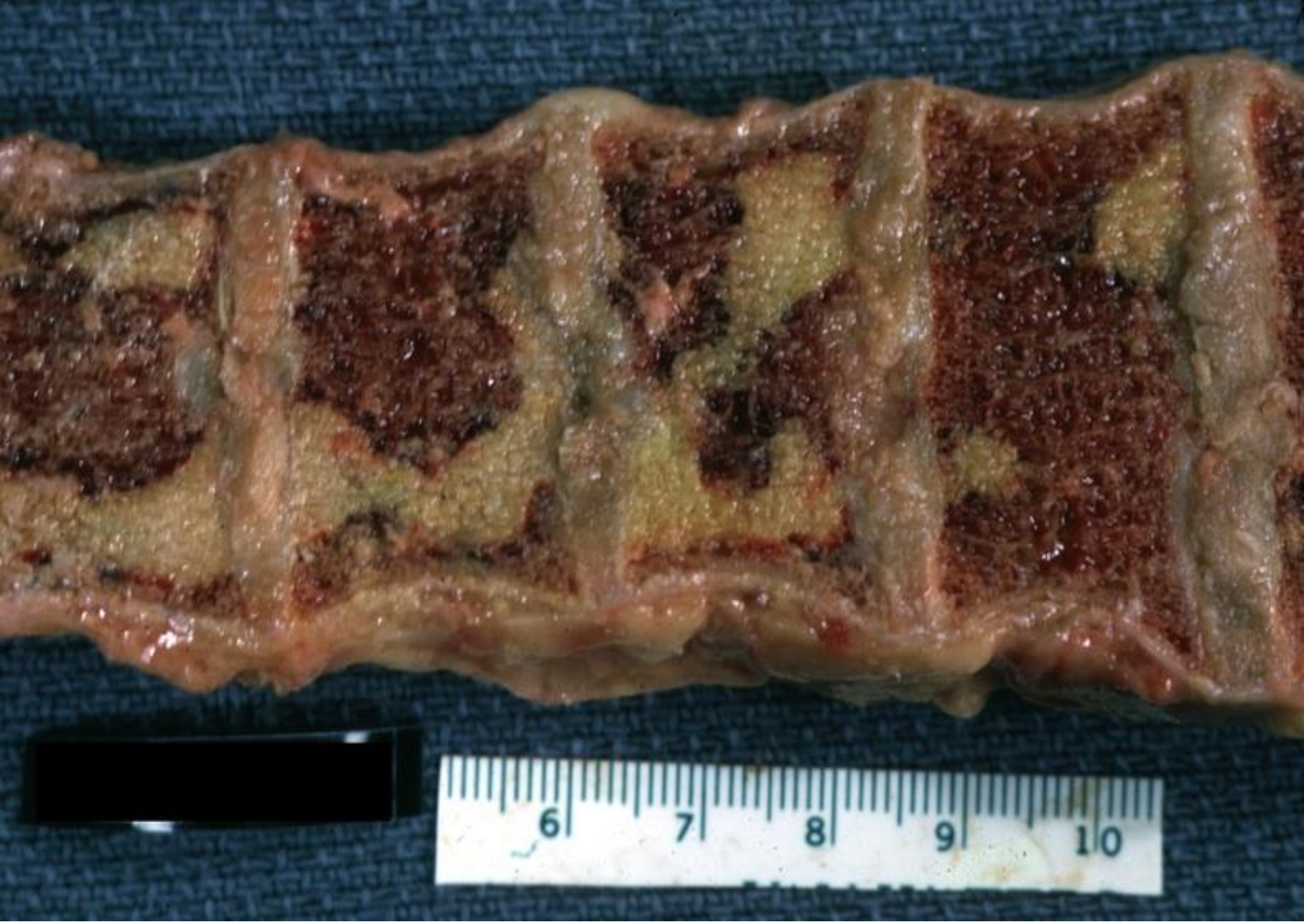
Types of Leukemias

3. **Chronic lymphocytic leukemia** (CLL) Peak incidence is in elderly males >60years 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.

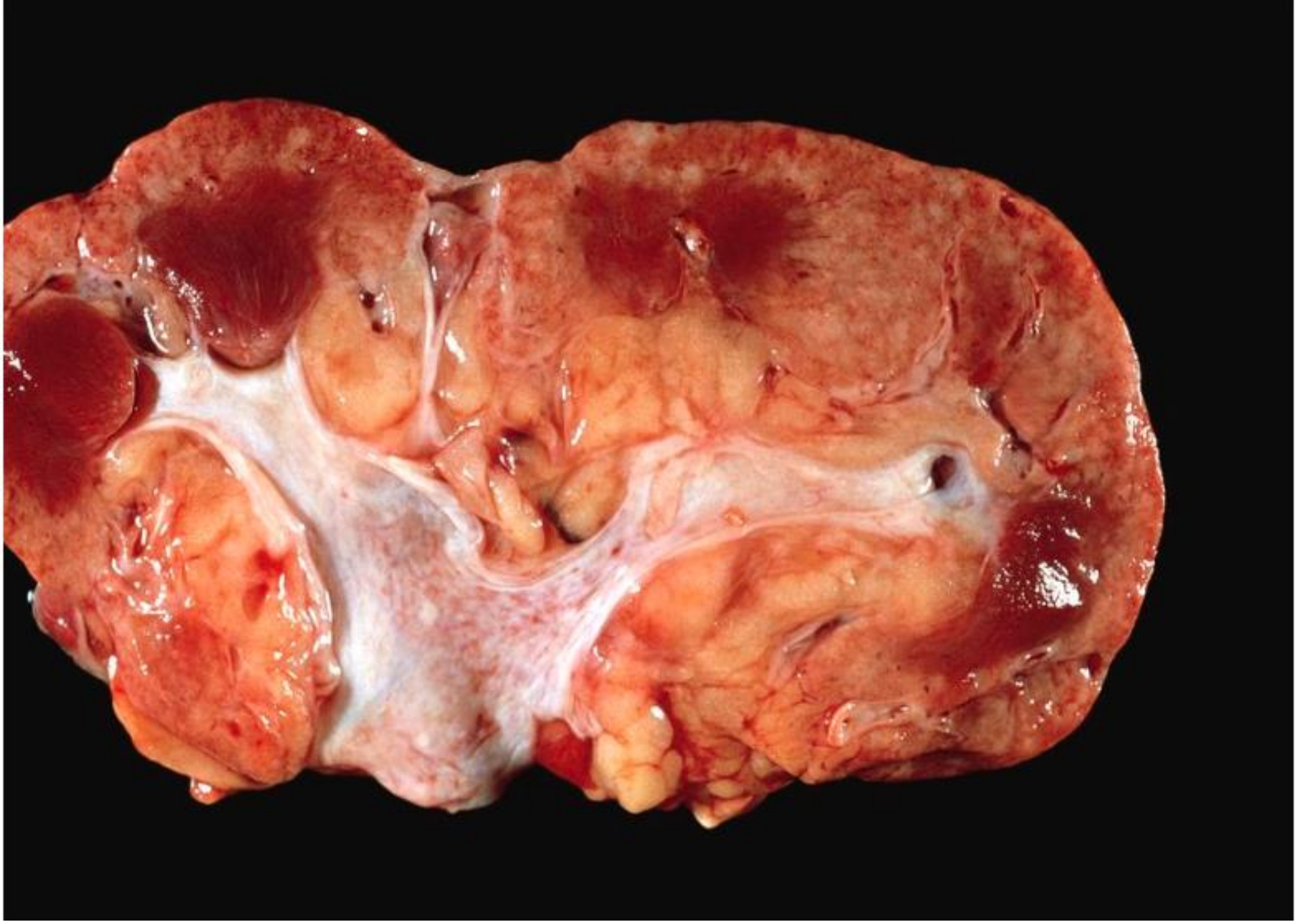
4. **Chronic myelogenous leukemias** (CML) Peak incidence is 35-50 years old. Symptoms are related to loss of normal marrow functioning; anemia, bleeding & infection. Associated wit hthe presence of the Philadelphia chromosome. Peripheral WBC counts in the 20-50,000 range with large component of "more 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



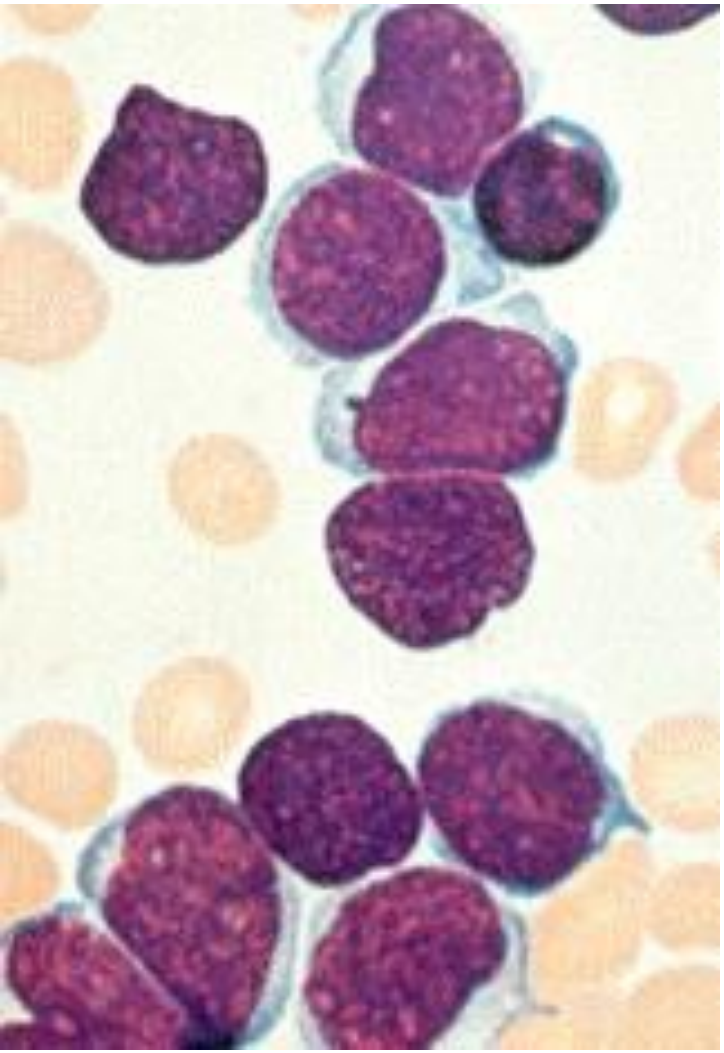


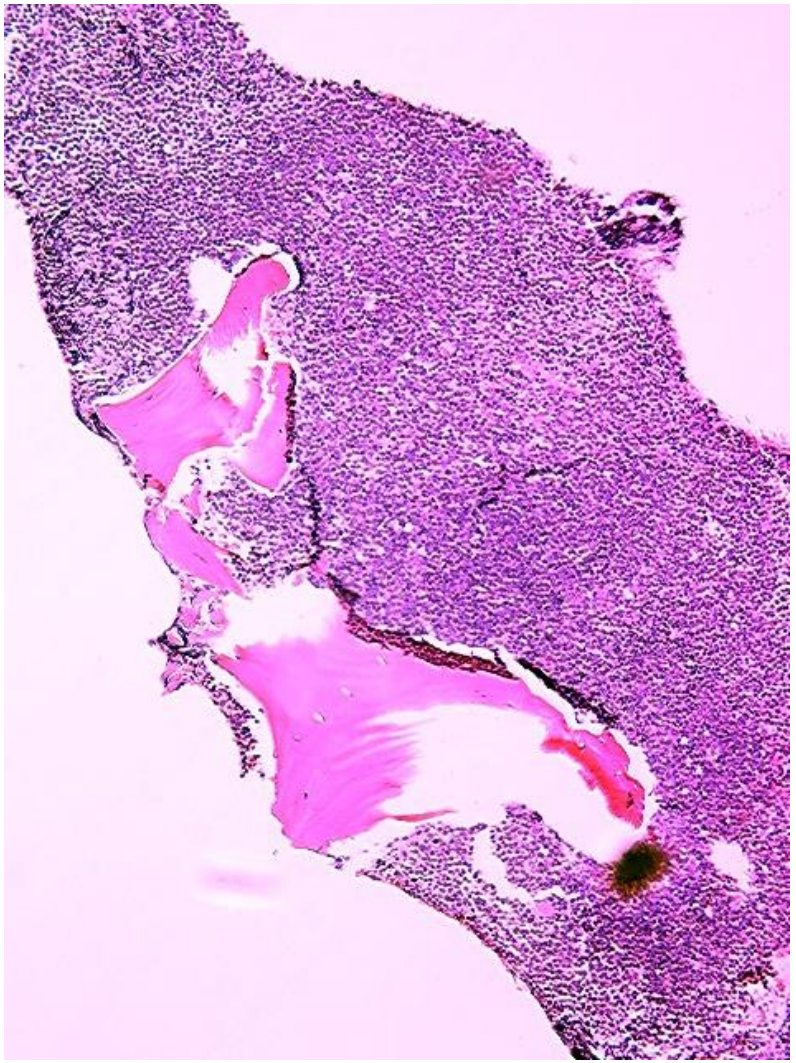
Bone marrow in leukemia.



Kidney in leukemia.

A.L.L.

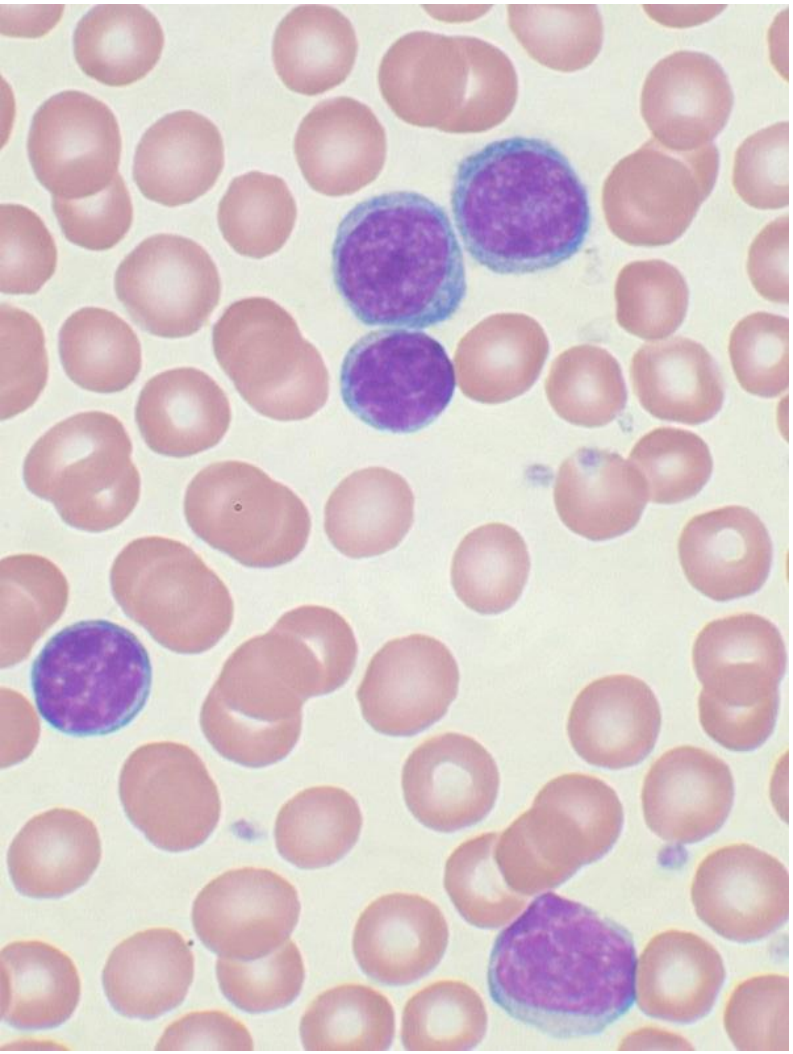


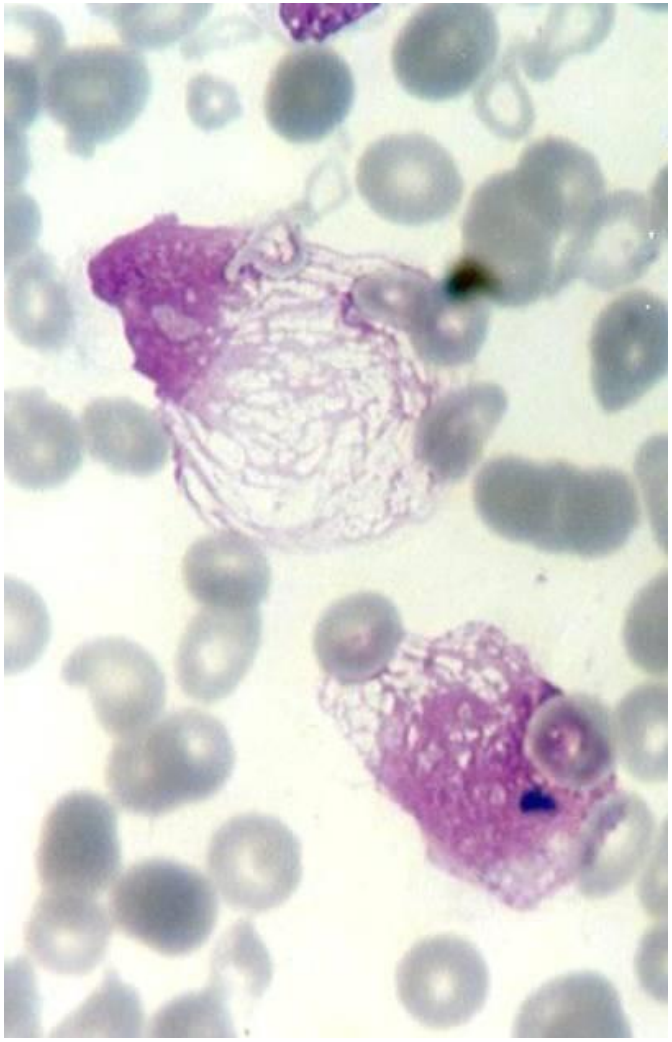


C.L.L.

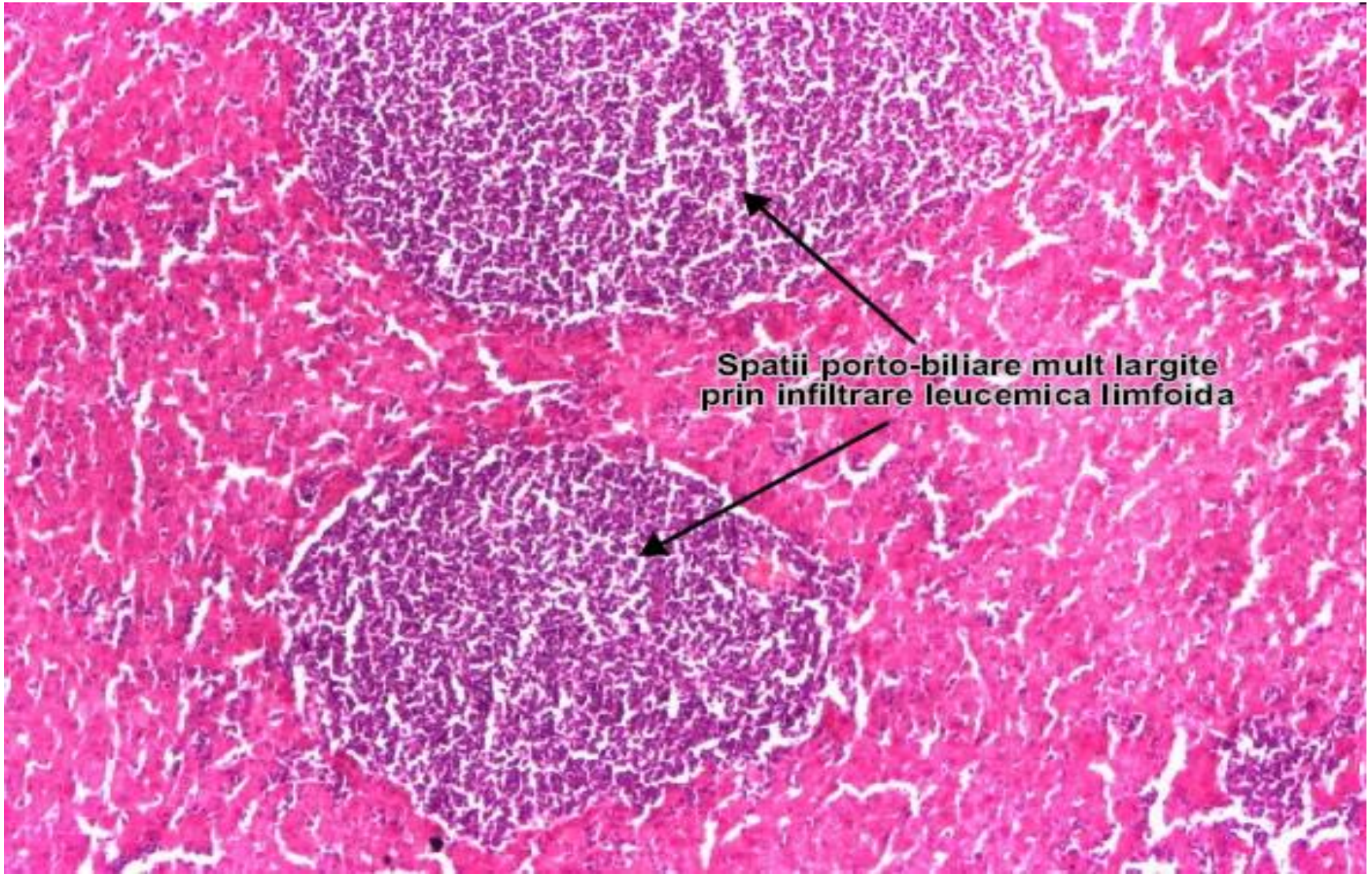
- **Unexplained sustained (months) lymph count of > 4000/mm3 is CLL, usually picked up on CBC**
- **M>F**
- **Lymphs look normal and are NOT blasts**
- **No need for marrow exam for dx, but progressive involvement of marrow, nodes, and other organs is the usual biologic behavior**
- **Liver can be involved portally or sinusoidally**
- **Translocations RARE, but trisomies and deletions common**

C.L.L.





CLL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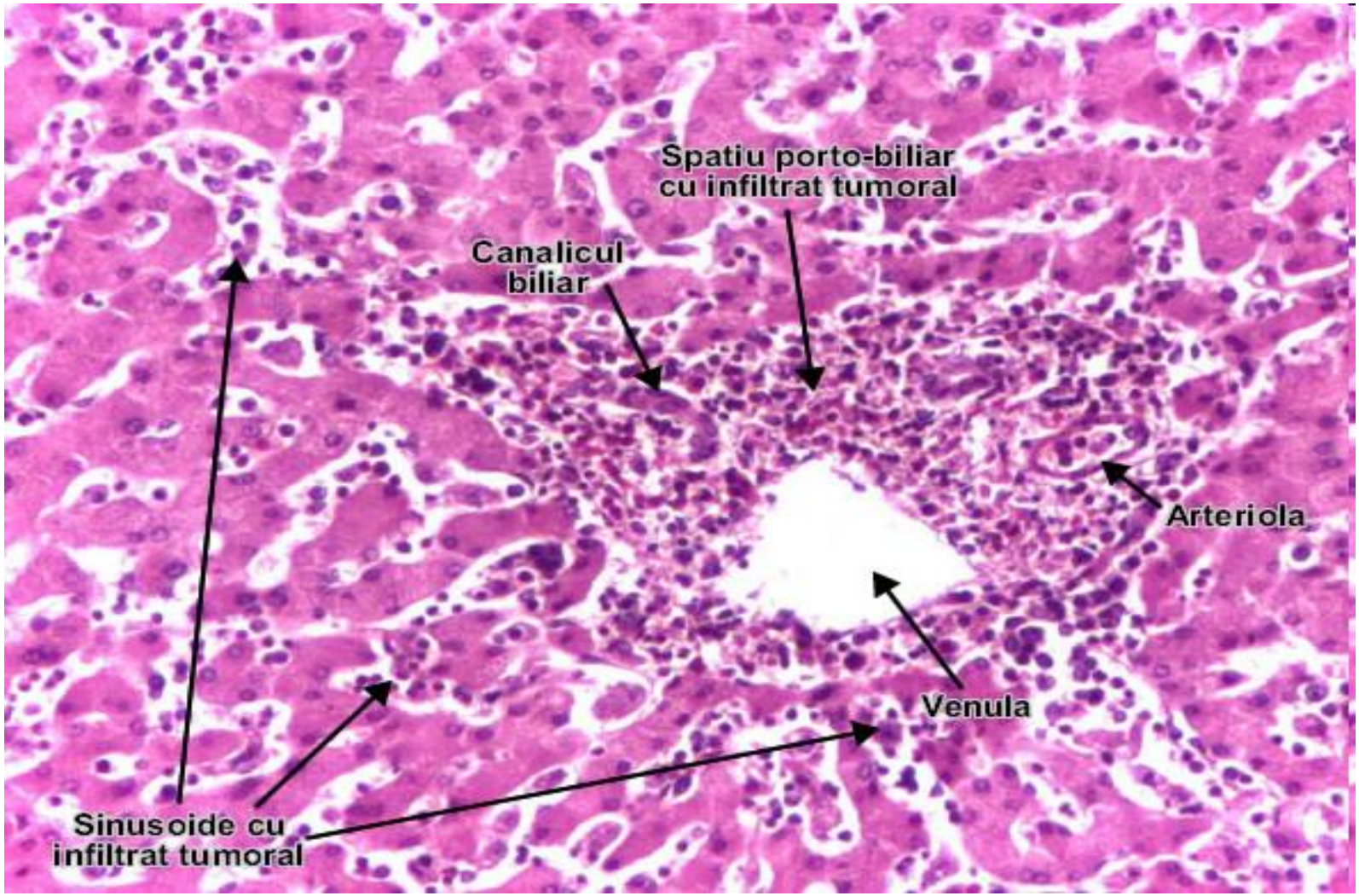
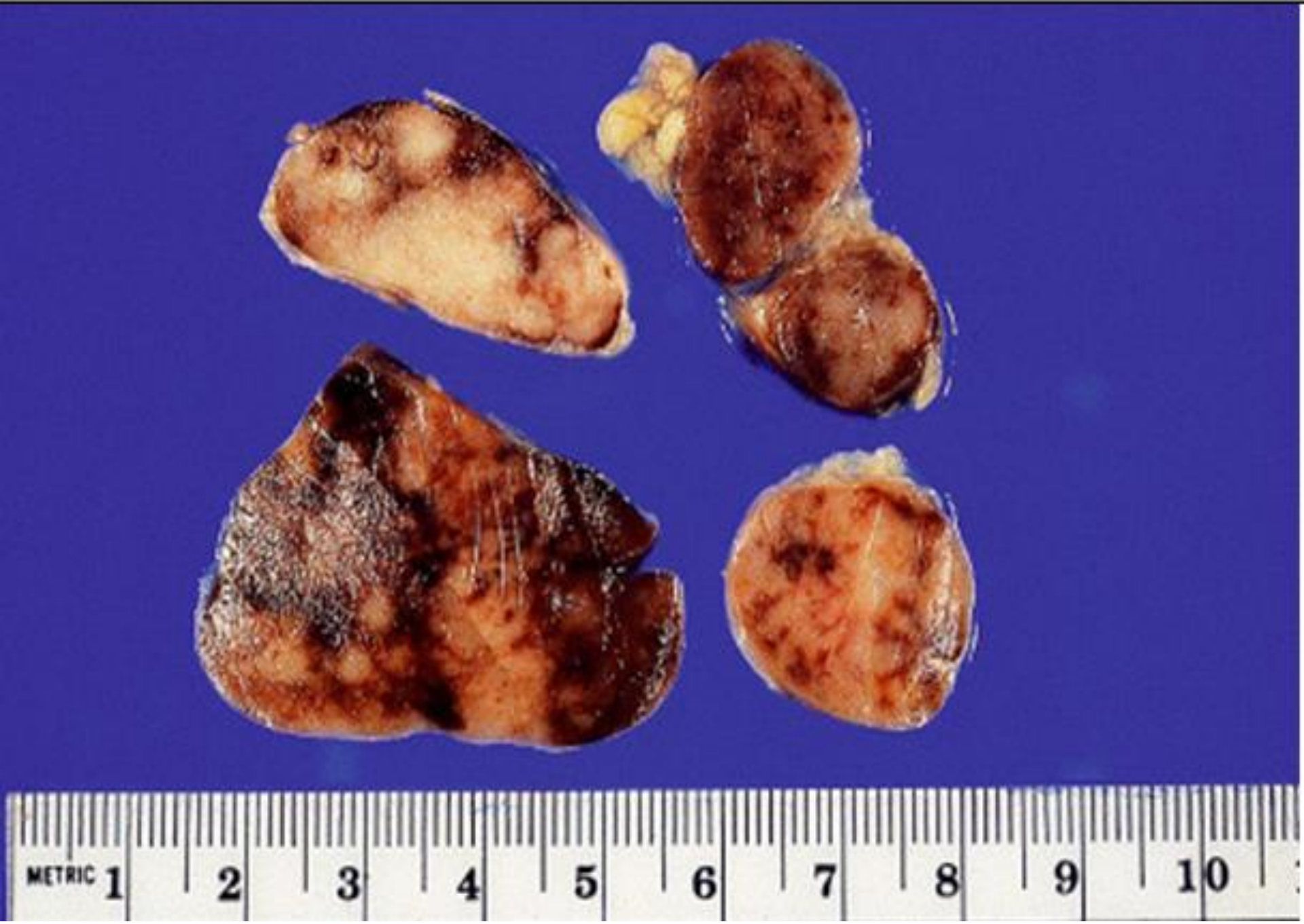
prin infiltrare leucemica limfoida

CLL


Spatiu porto-biliar
cu infiltrat tumoral
Canalicul
biliar
Arteriola
Venula
Sinusoide cu
infiltrat tumoral



_(chronic lymphoid leukemia).

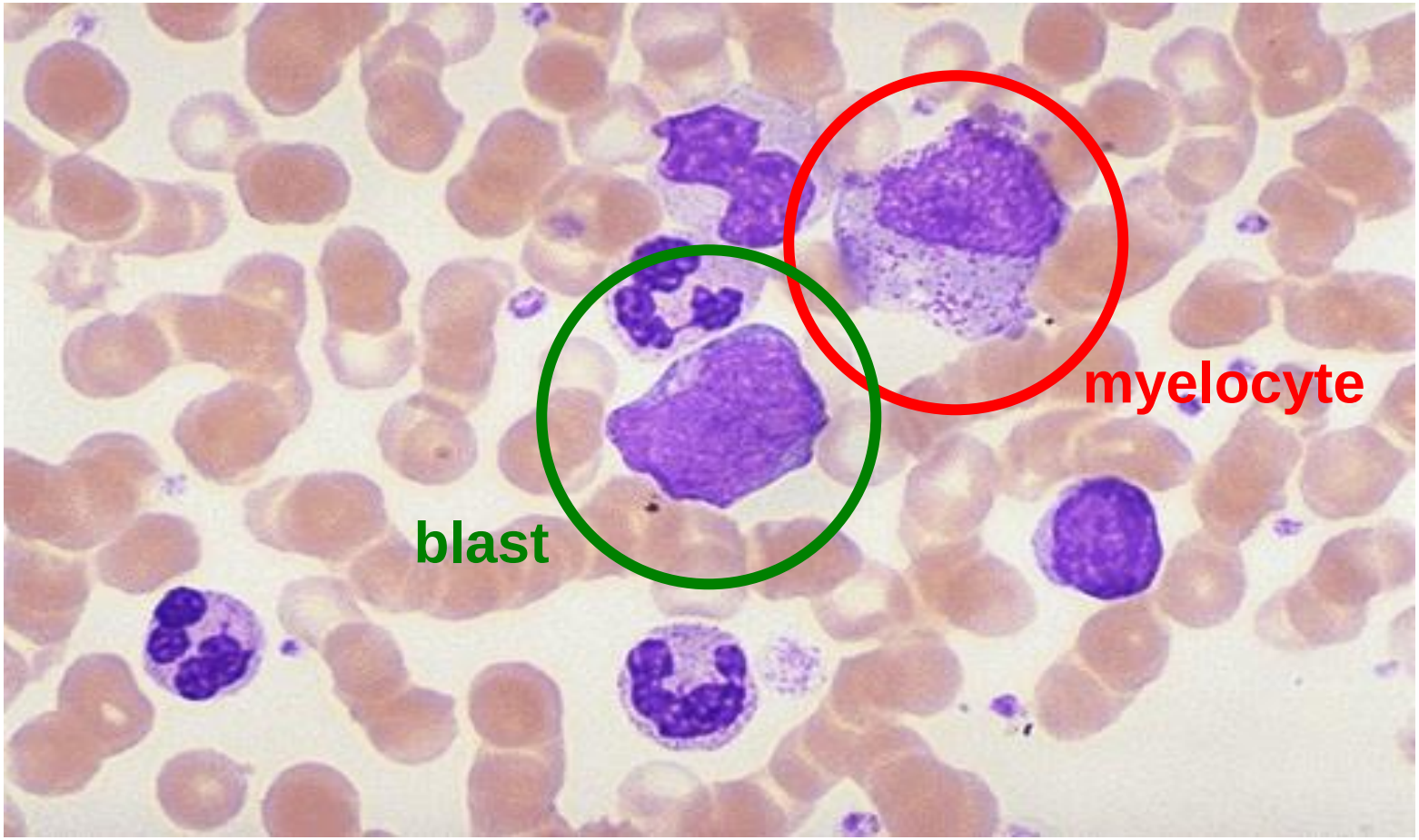
A.M.L.

- **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**

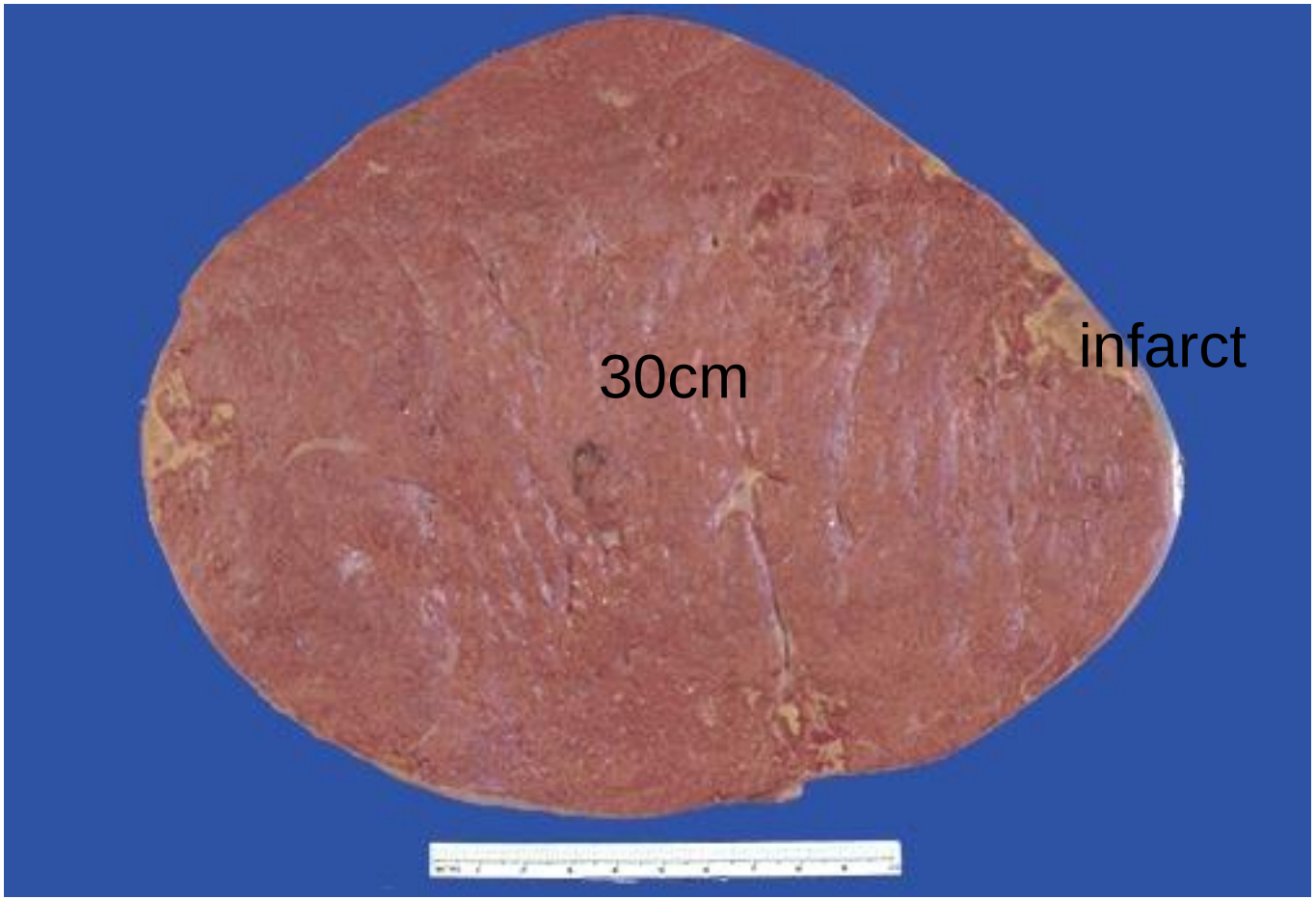
A.M.L.

- **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.**

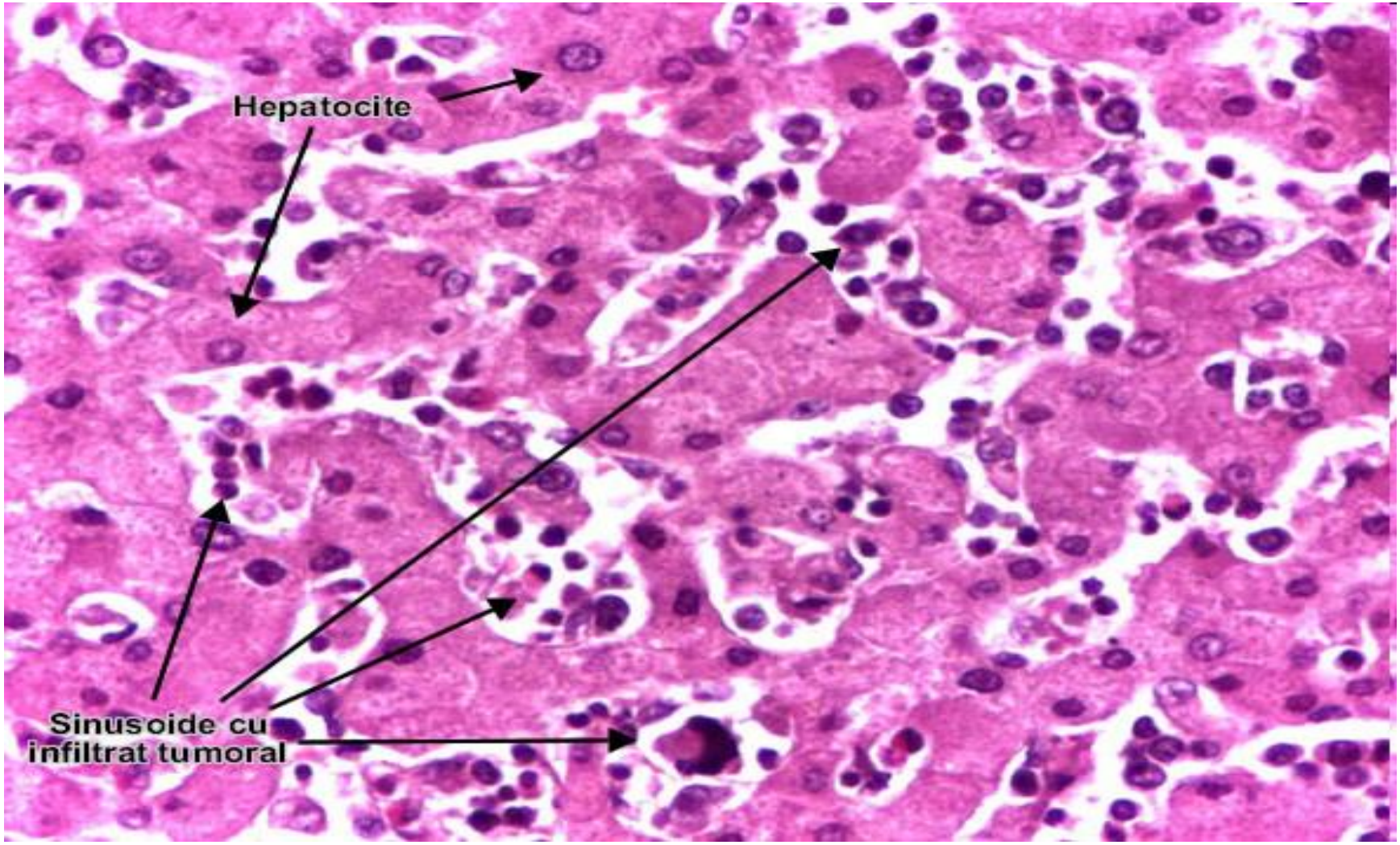
CML high-power



Massive splenomegaly in CML



CML



PLASMA CELL DISORDERS

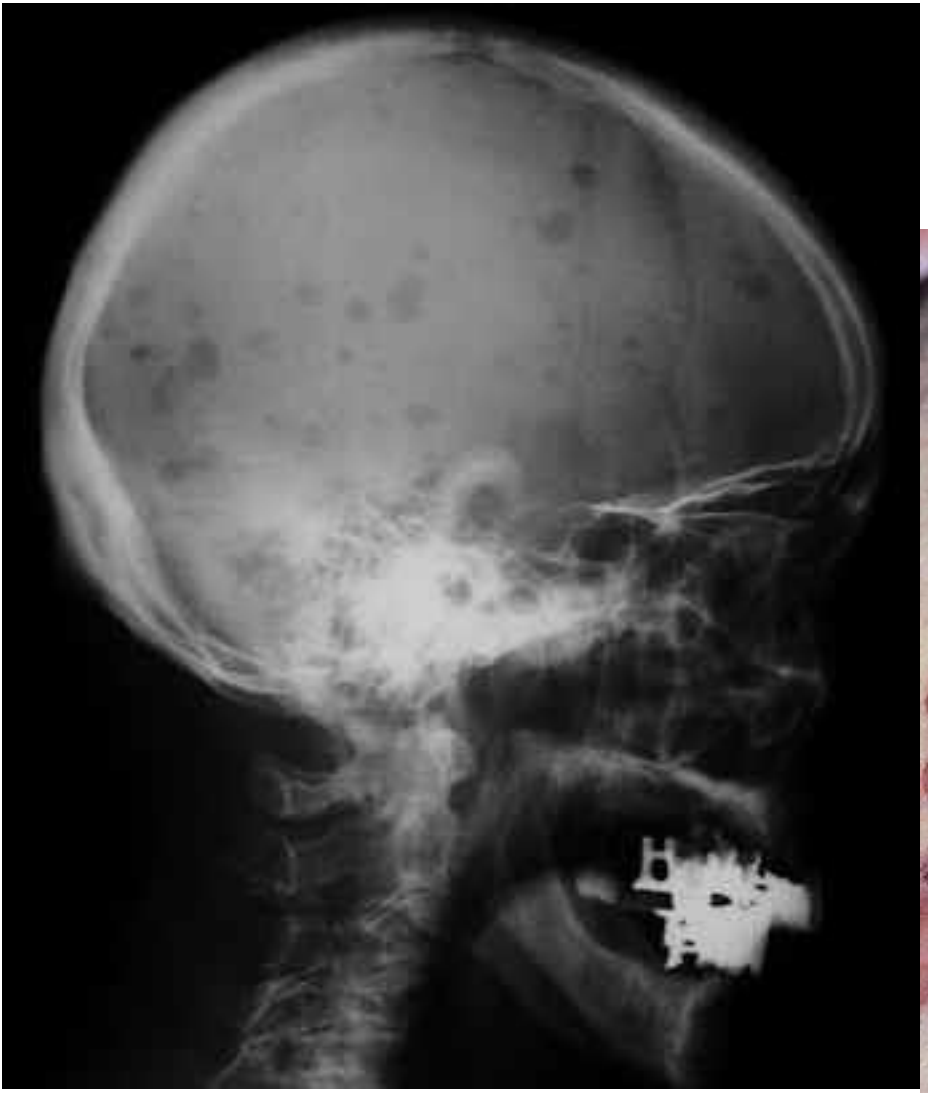
Main types

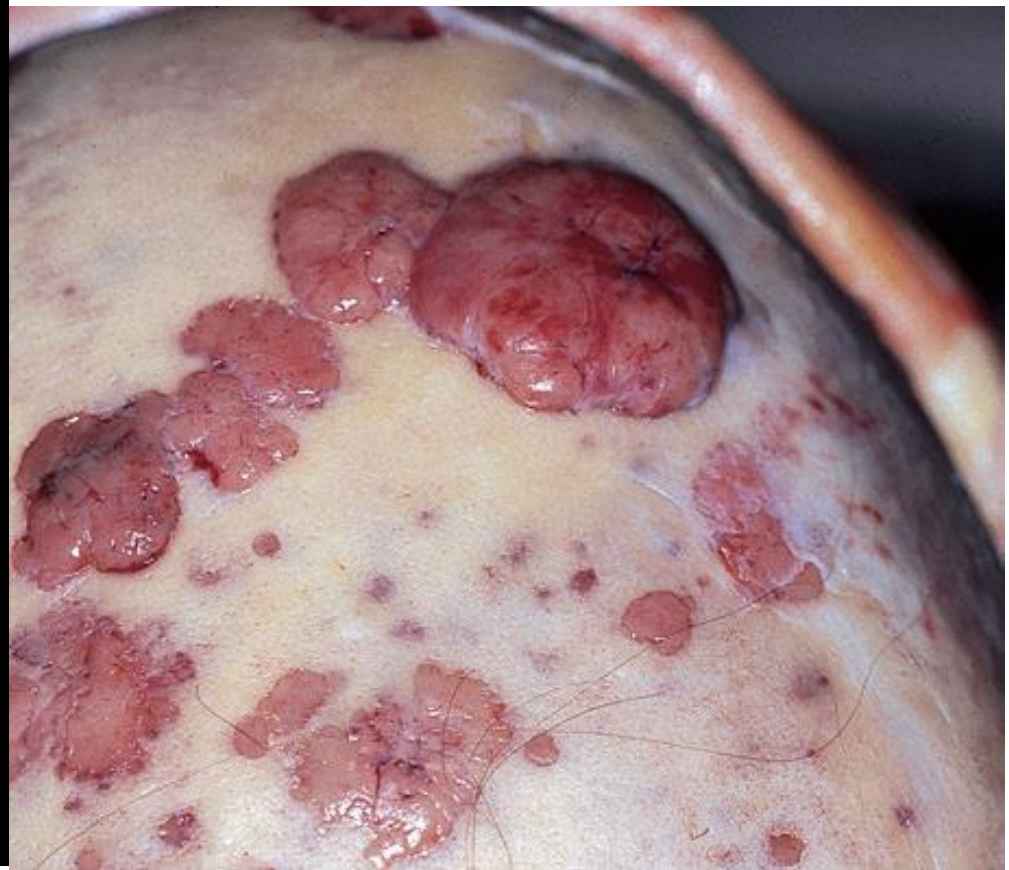
- **Multiple myeloma**
- **Waldenstrom macroglobulinemia**: A malignancy of plasmacytoid lymphocytes that secrete IgM resulting in a hyperviscosity syndrome with renal, retinal and cerebral ischemia as a result of microvascular occlusion. Infiltration of plasmacytoid cells in the marrow, spleen and nodes.
- **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.

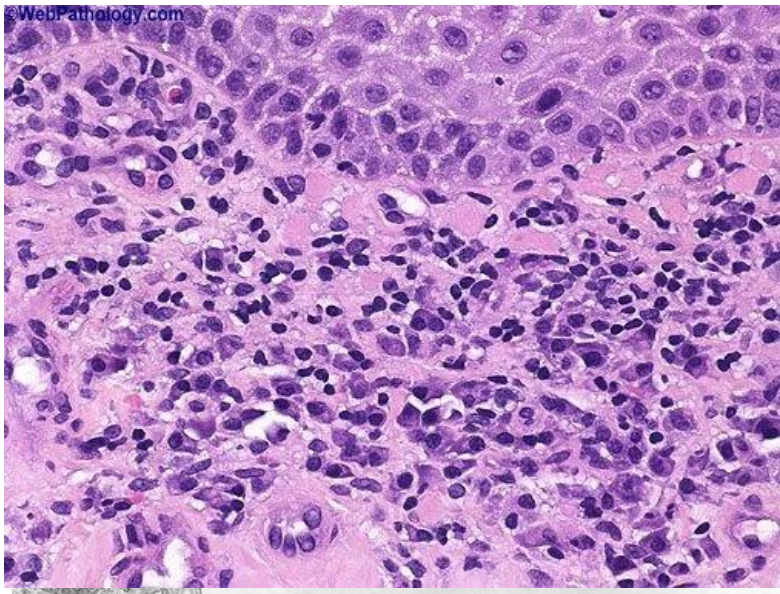
Multiple Myeloma: Skull X-ray

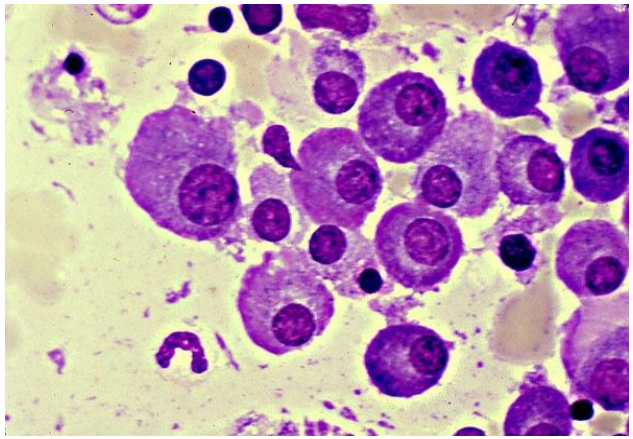


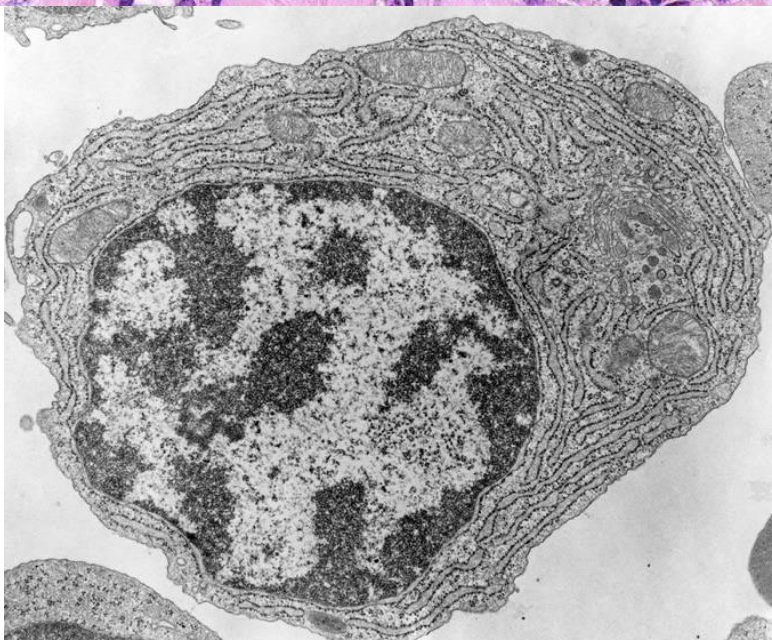


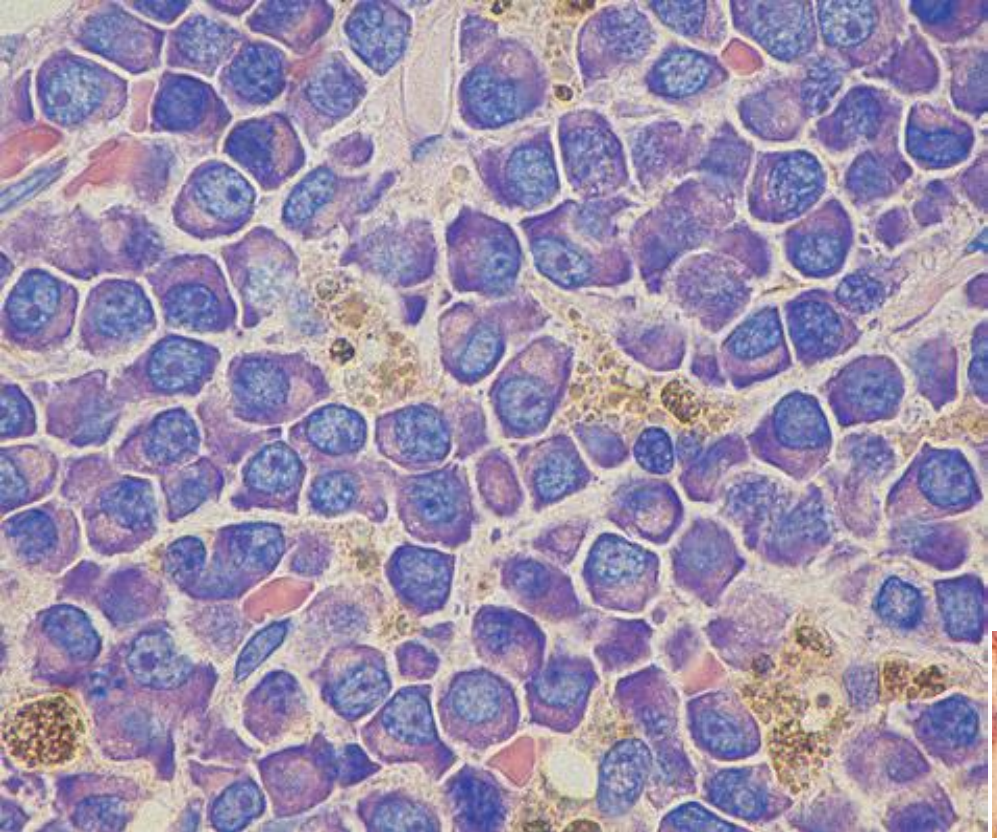
PLASMA CELL classic features

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









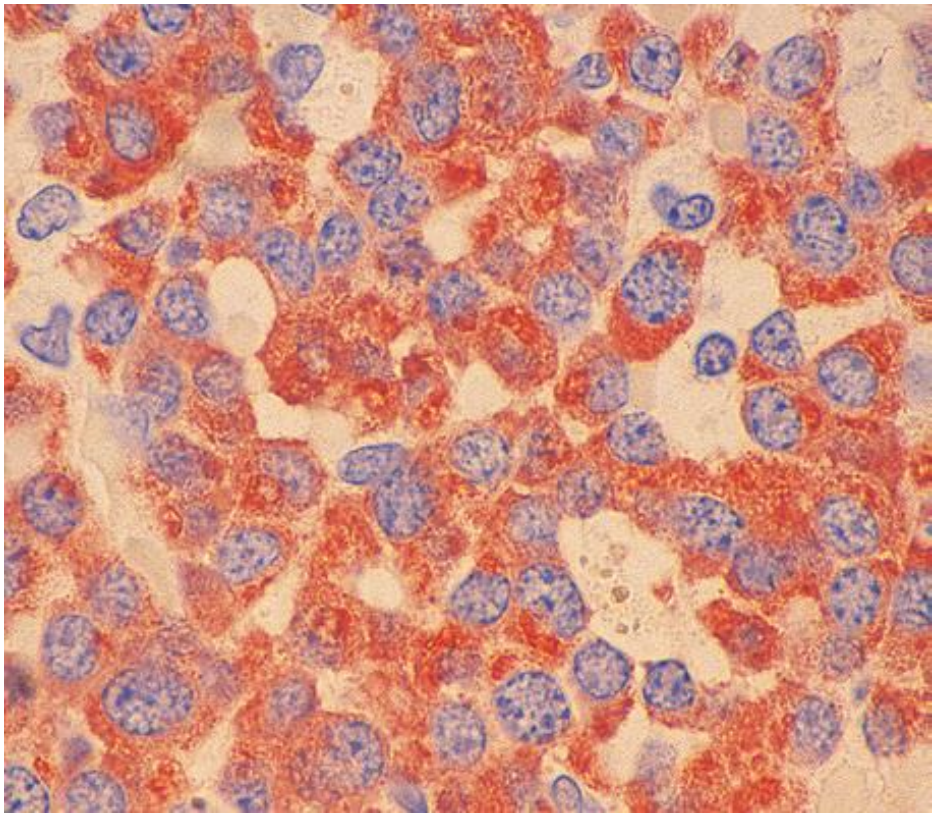
↑

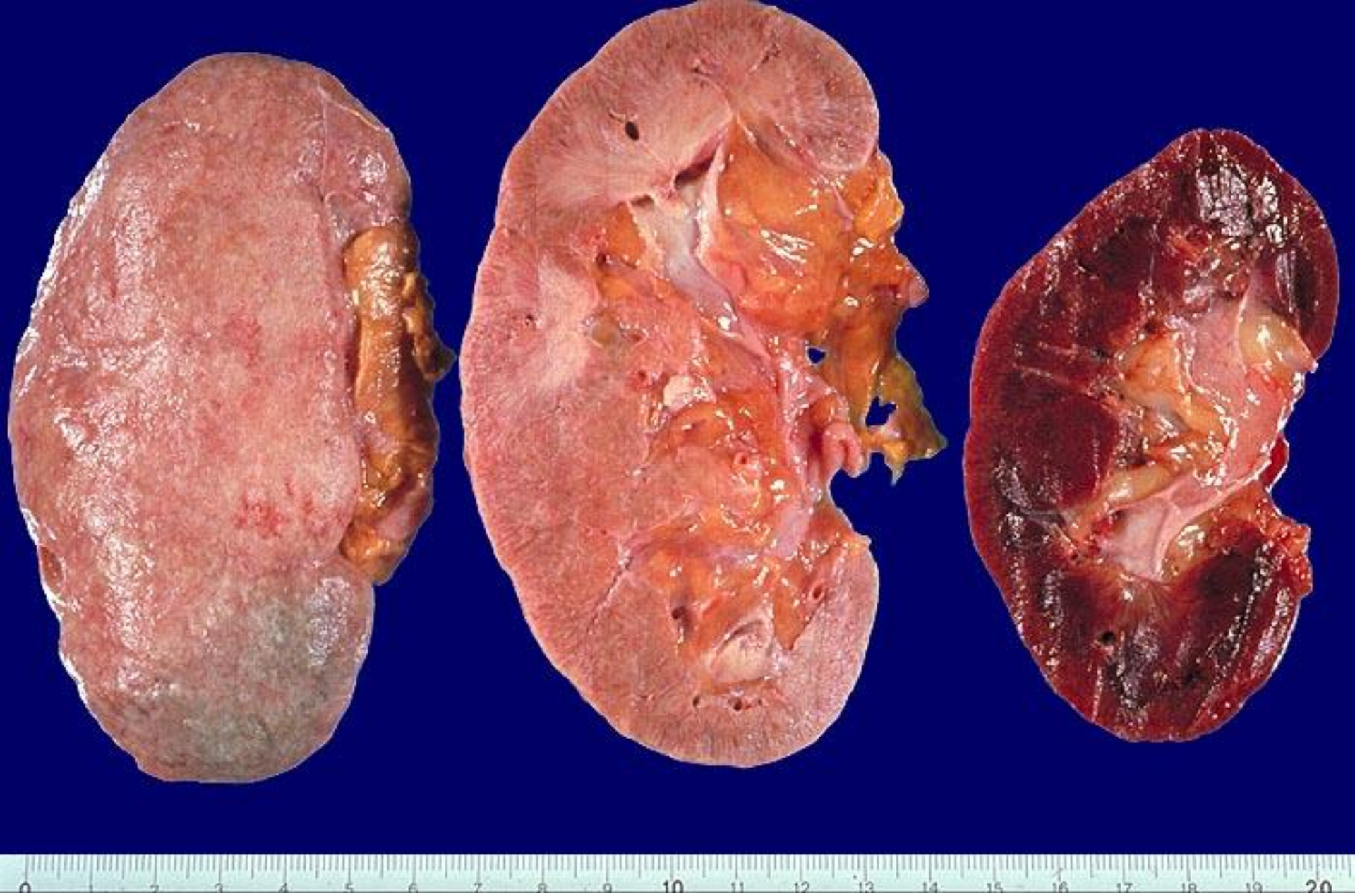
Plasmacytoma (plasma cell origin, tumor cells)

Plasmacytoma

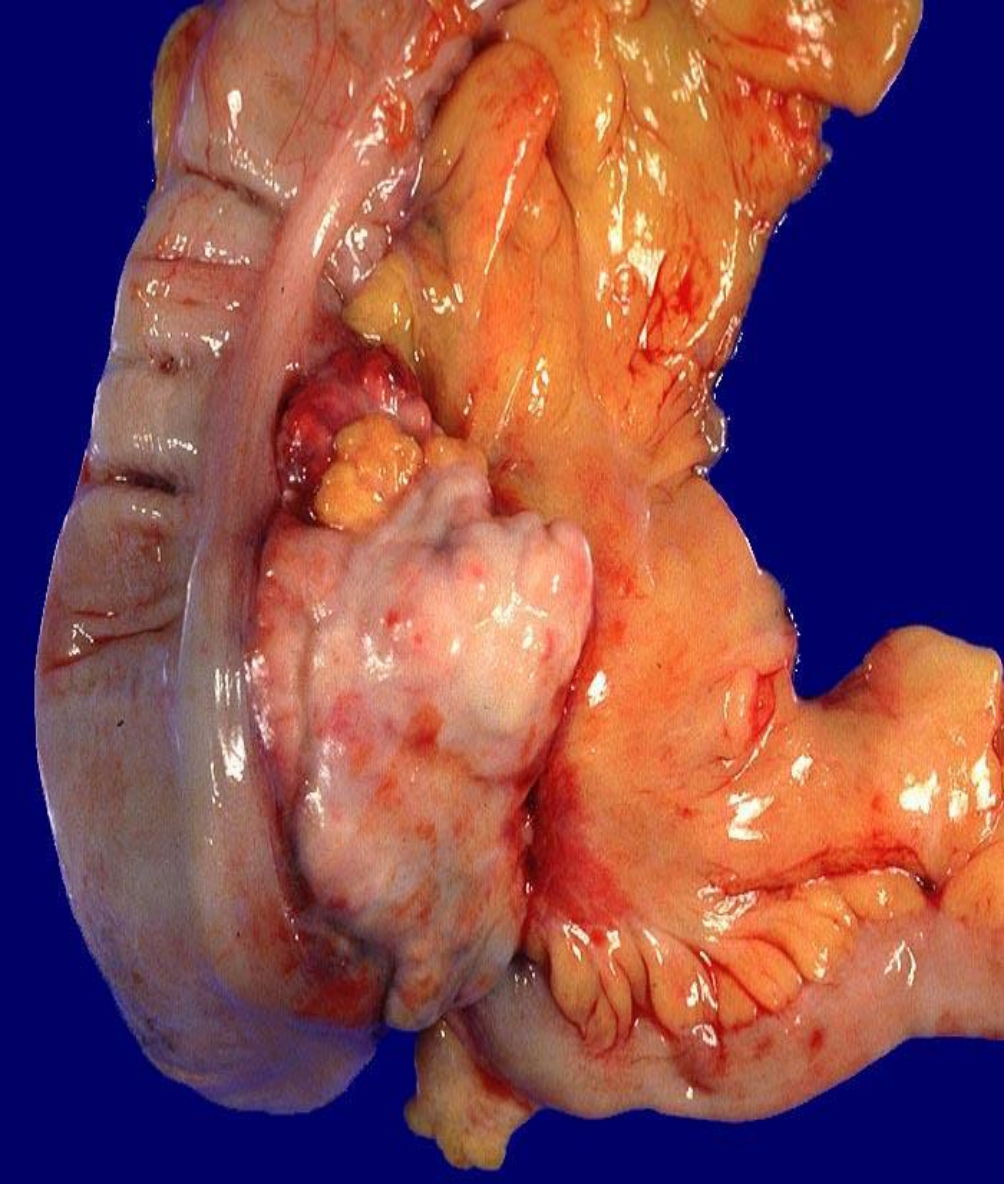
(immunohistochemical reaction for IgG light chains)

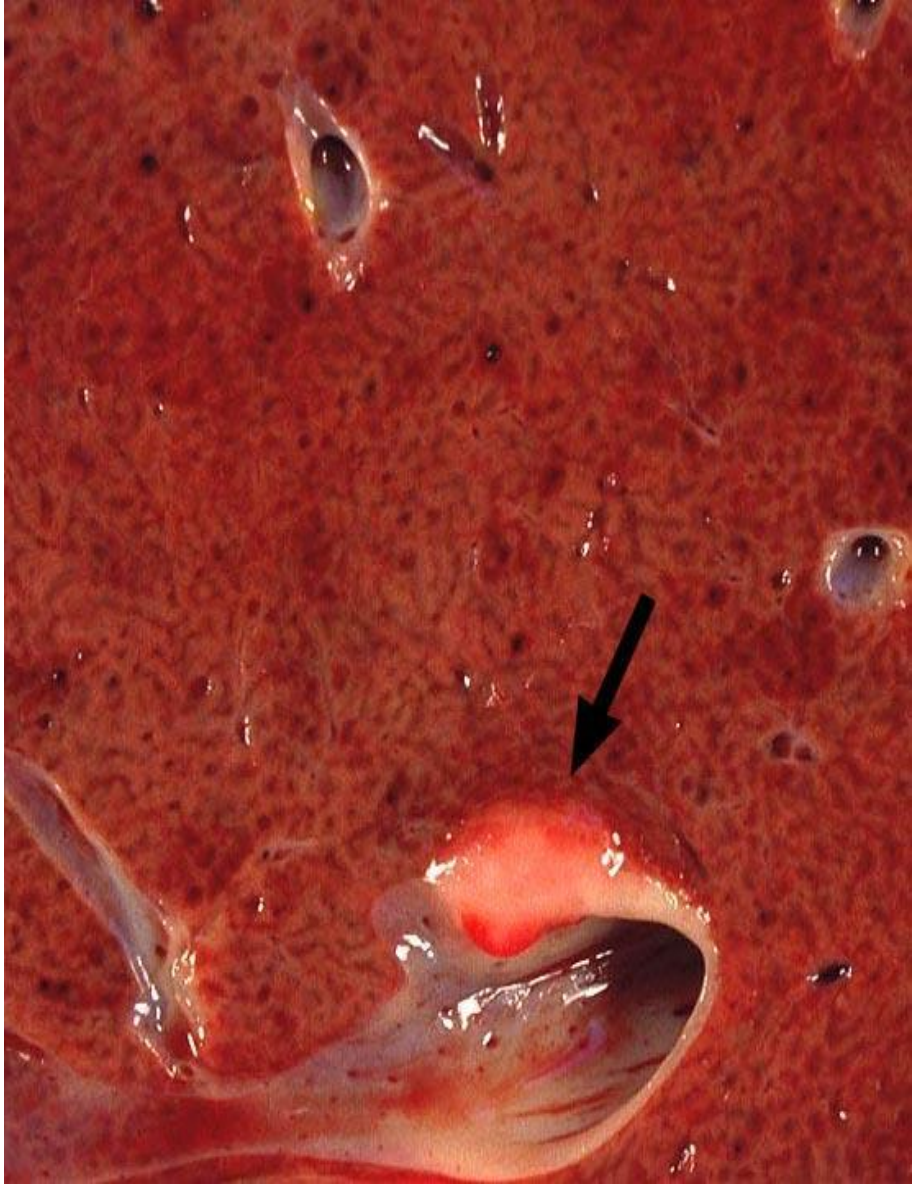
↓





Myeloma kidney and normal kidney.





Extramedullary myeloma (ileocecal angle and liver)

LYMPH NODES

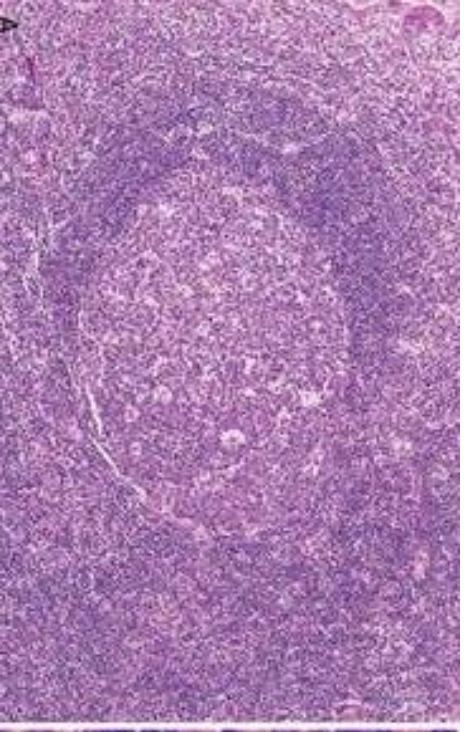
- **Normal Structure, Function**
- **Benign enlargement/Benign disease**
  - **Acute**
  - **Chronic (follicular vs. “sinus histiocytosis”)**
- **Lymphomas/Malignant Lymphomas**
  - **Adjectives of various classifications**
  - **Features**
  - **STAGING**
- **Metastatic disease TO lymph nodes**

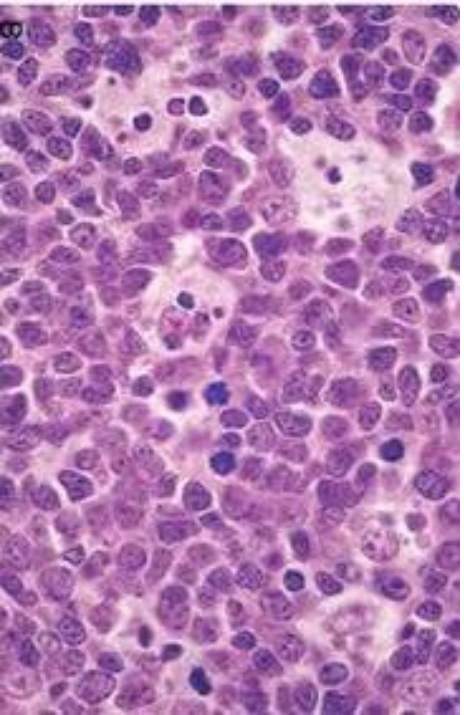
Definition of TERMS

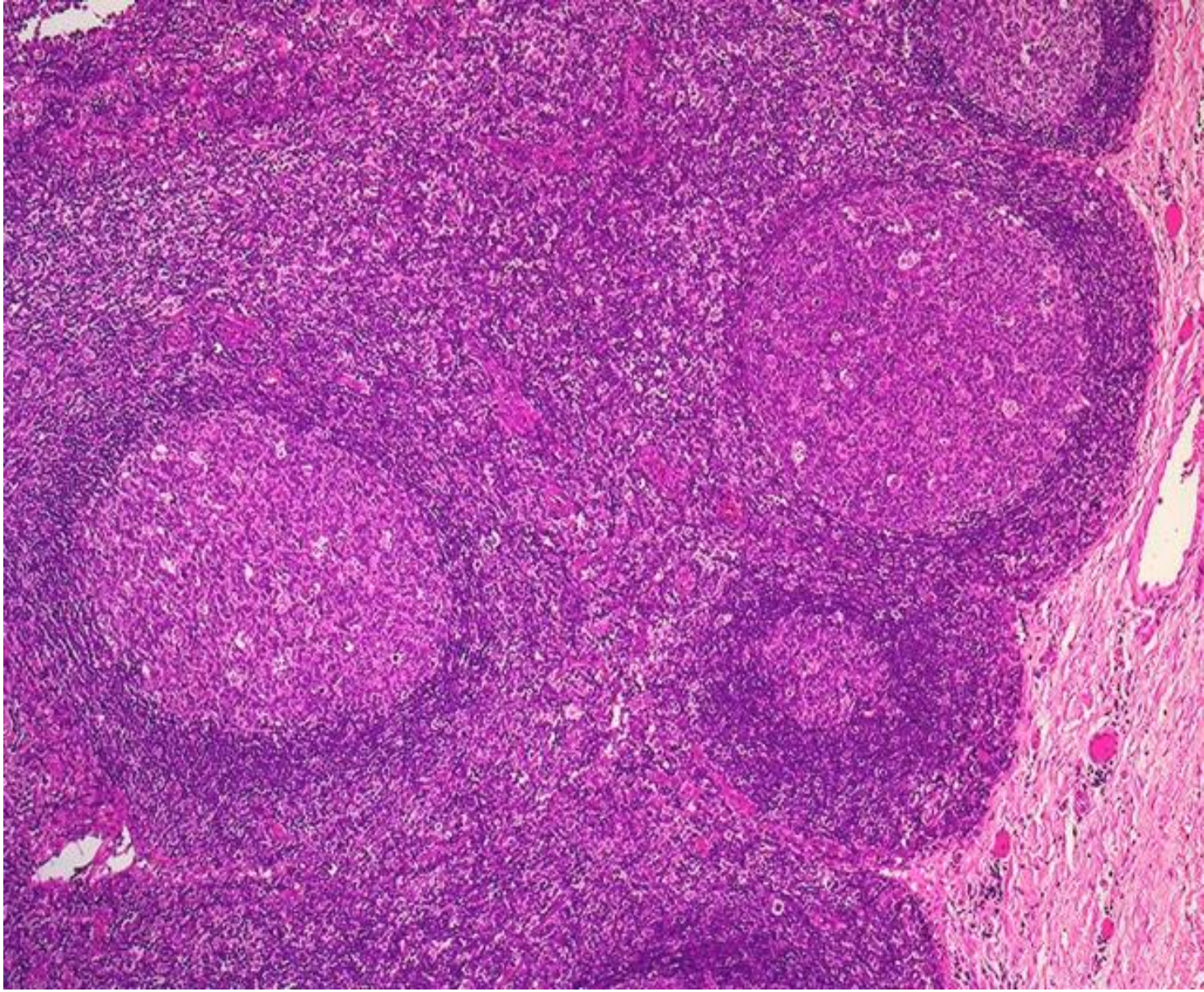
- **Lymphadenopathy**
- **Lymphadenitis**
- **What to do if a lymph node is enlarged?**
- **Diffuse/Follicular**
- **T/B/NK, Small/Large, Cleaved/Non-cleaved**
- **Precursor/Peripheral**
- **HD/Non-HD**

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)**







BENIGN FOLLICULAR HYPERPLASIA. Larger and more numerous than normal follicles. MEDULLA may be compromised.

LYMPHOMAS (MALIGNANT)

- **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)**

Hodgkin's lymphoma	*nonHodgkin lymphoma*
more frequently a single group of cervical, mediastinal or paraaortal lymph nodes	more frequently several groups of peripheral lymph nodes
mesenteric and pharyngeal ring lymph nodes are rarely affected	mesenteric and pharyngeal ring lymph nodes are usually involved
the process extends through continuity	it does not extend through continuity
extranodal localization is not characteristic.	extranodal localization is characteristic.

Hodgkin's lymphoma

More common in young people over ~ 30 years old, clinically - fever and intoxication.

In all cases, cervical, supraclavicular, axillary,mediastinal, inguinal lymph nodes,and later - the spleen (65-80%), the liver, the bone marrow.

Clinical-anatomical forms:

- **isolated form– a single group of lymph nodes;**
- **generalized form– several groups of lymph nodes and spleen.**

Lymph nodes adhere to each other, forming packages, conglomerates.

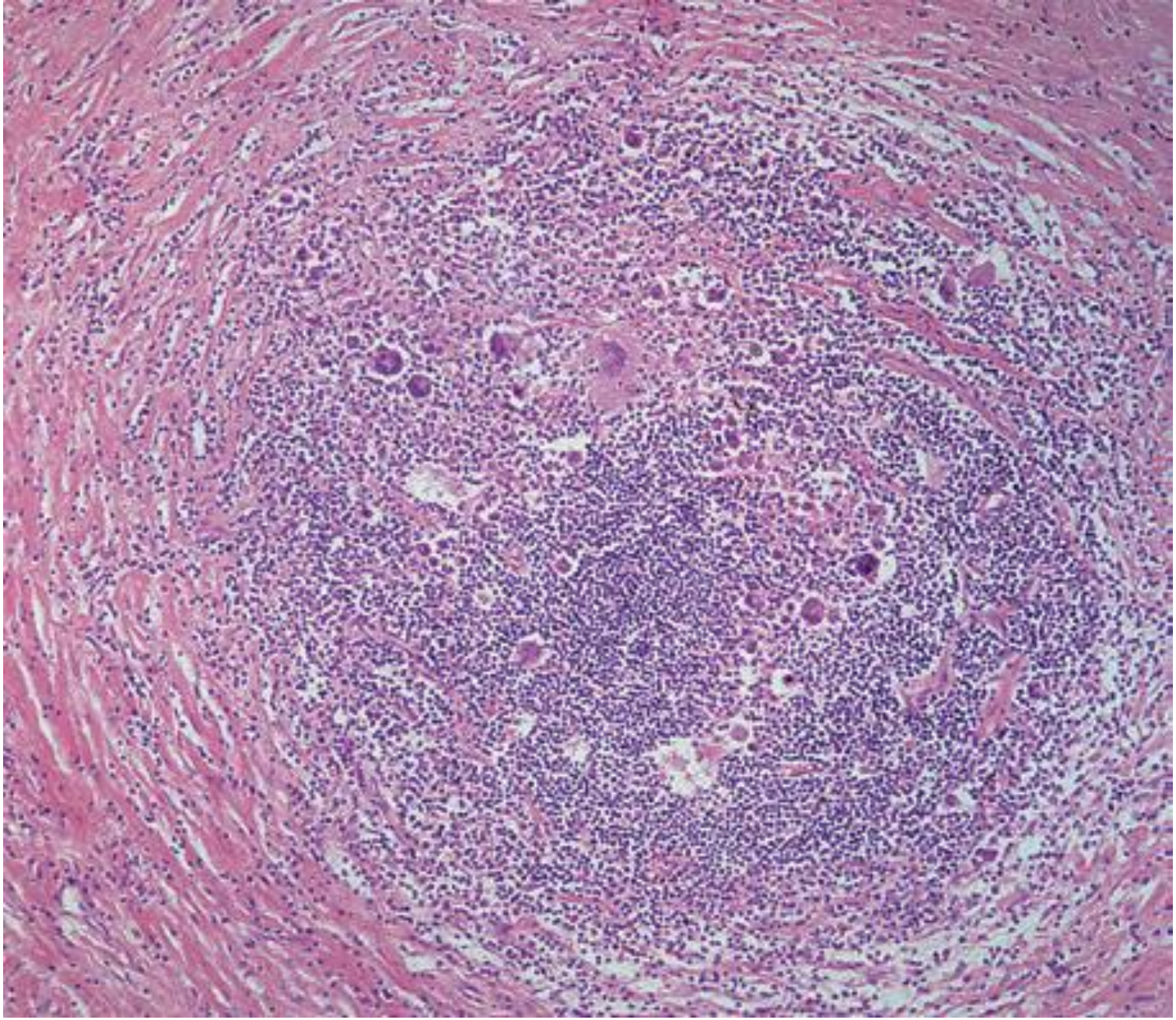
Spleen enlarged up to 1 kg, with motley appearance - due to the association of foci of tumor proliferation, inflammation, caseous necrosis and sclerosis.

Hodgkin's lymphoma

Clinical-morphological classification

- Nodular sclerosis (60 - 80%)

It is characterized by a relatively benign evolution, the initial process being located in the mediastinum. Microscopically, the proliferation of fibrous tissue that surrounds the foci of cell agglomerations can be noticed, among which are R-S cells and at the periphery lymphocytes and other cells.



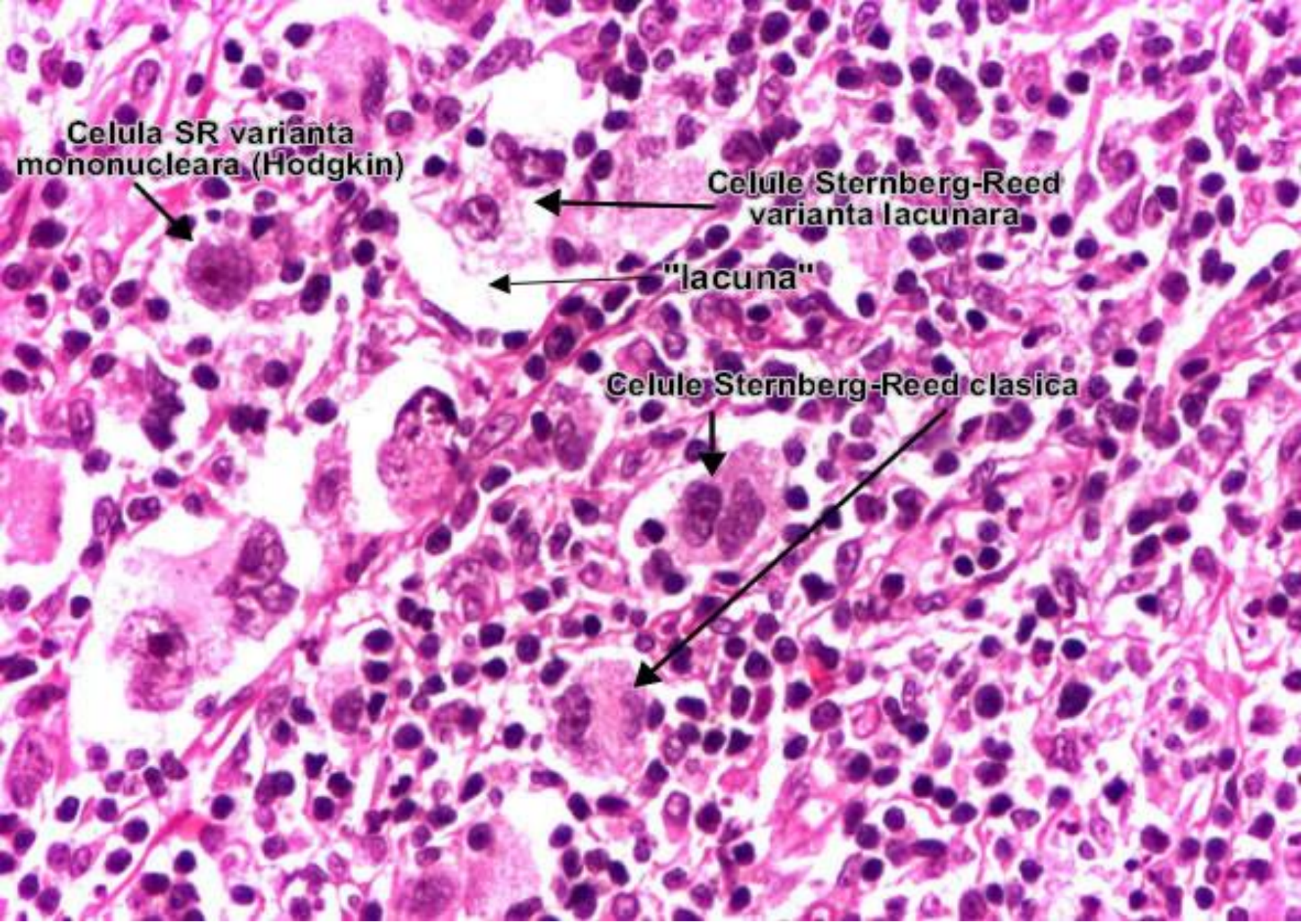
Hodgkin's lymphoma - Nodular sclerosis form

- **Lymphocyte rich or with lymphocyte predominance (5%)**

It is characteristic for the early phase of the disease and for its localized forms, it corresponds to stage I-II of the disease. Microscopically, only the proliferation of mature lymphocytes and partially of histiocytes can be noticed, which leads to the fading of the lymph nodes pattern. In the evolution of the disease, the **Lymphocyte rich** variant changes to the with mixed cellularity

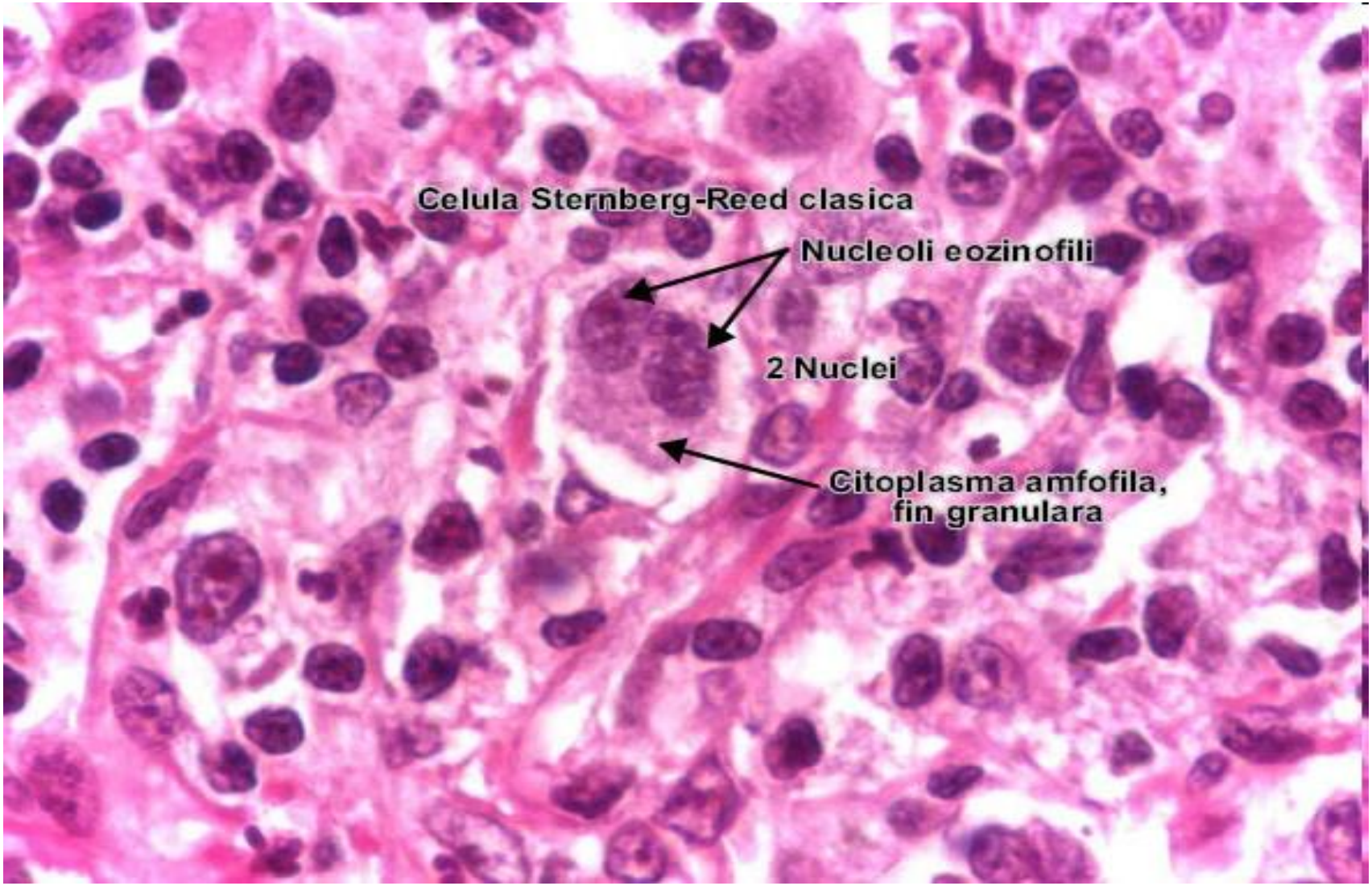
- **Mixed cellularity (15 - 30 %)**

It reflects the generalization of the process and corresponds to stages II-III of the disease. Microscopically it is detected; proliferation of lymphoid elements with varying degrees of maturity; classical and lacunar R-S cells; agglomerations of lymphocytes, eosinophils, plasma cells; foci of necrosis and fibrosis.



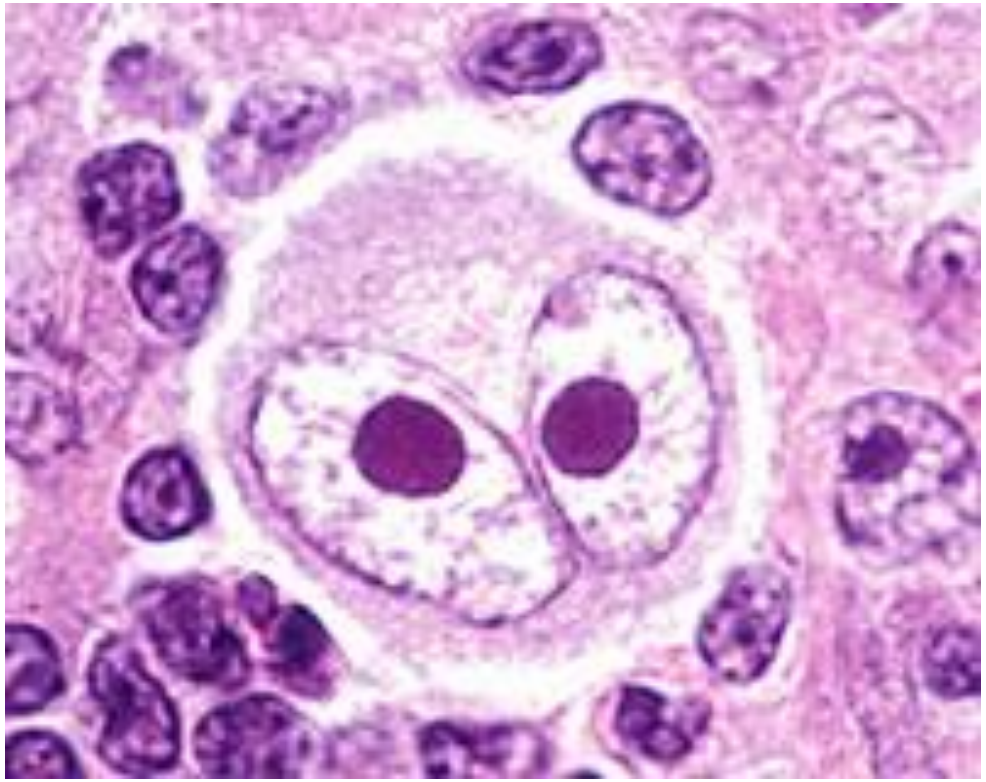
Hodgkin's lymphoma - Mixed cellularity

Hodgkin's lymphoma



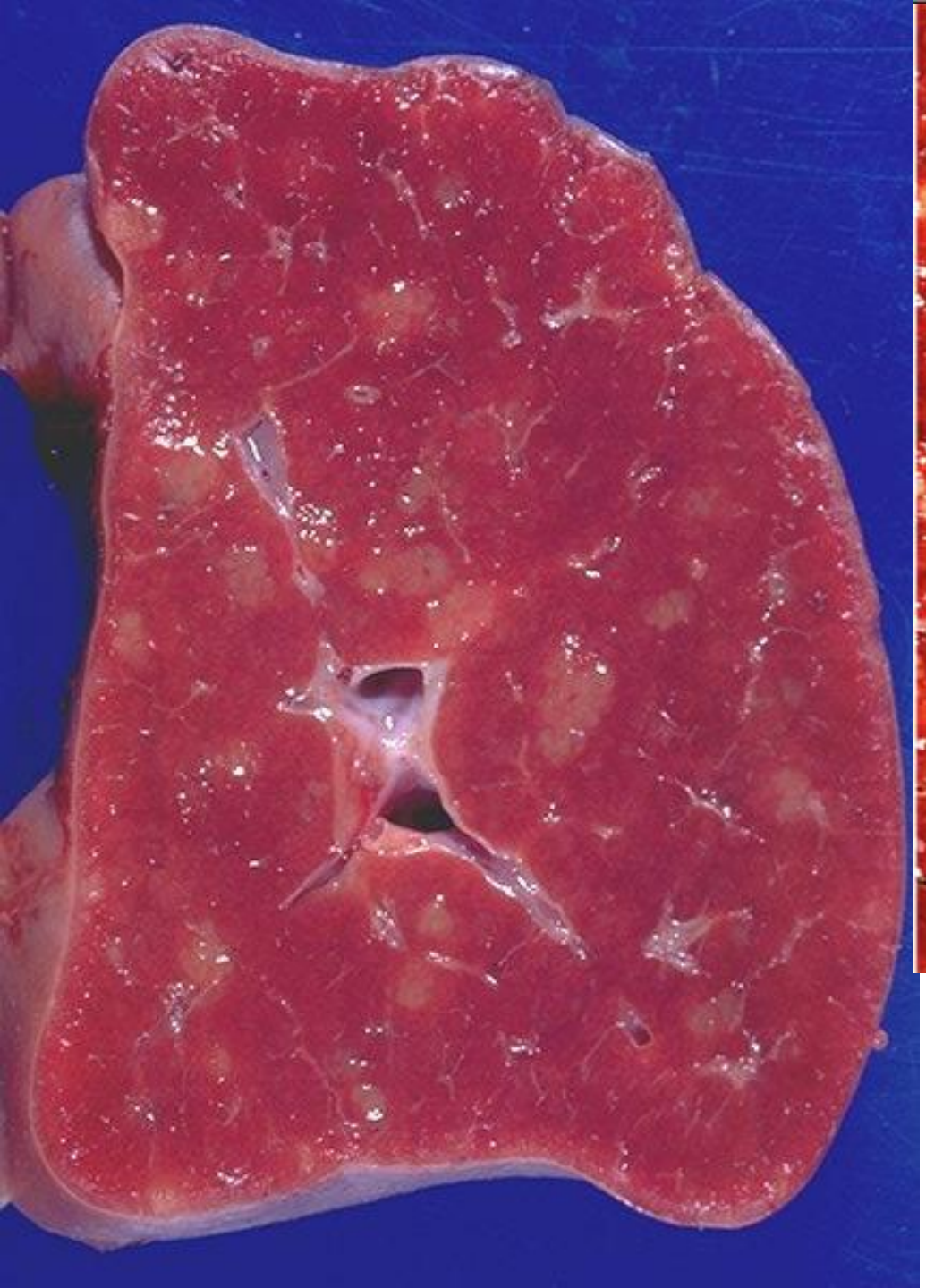
STERNBERG-REED CELL

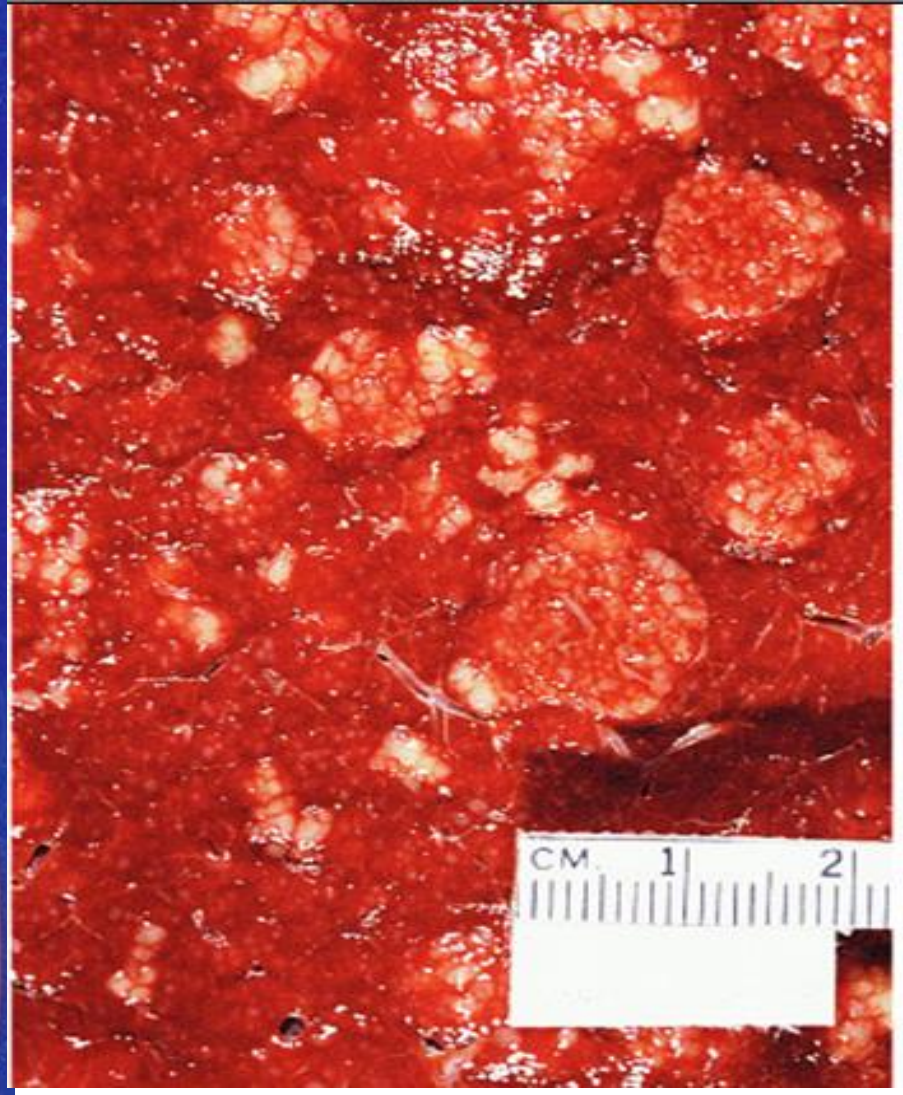
STERNBERG-REED CELL



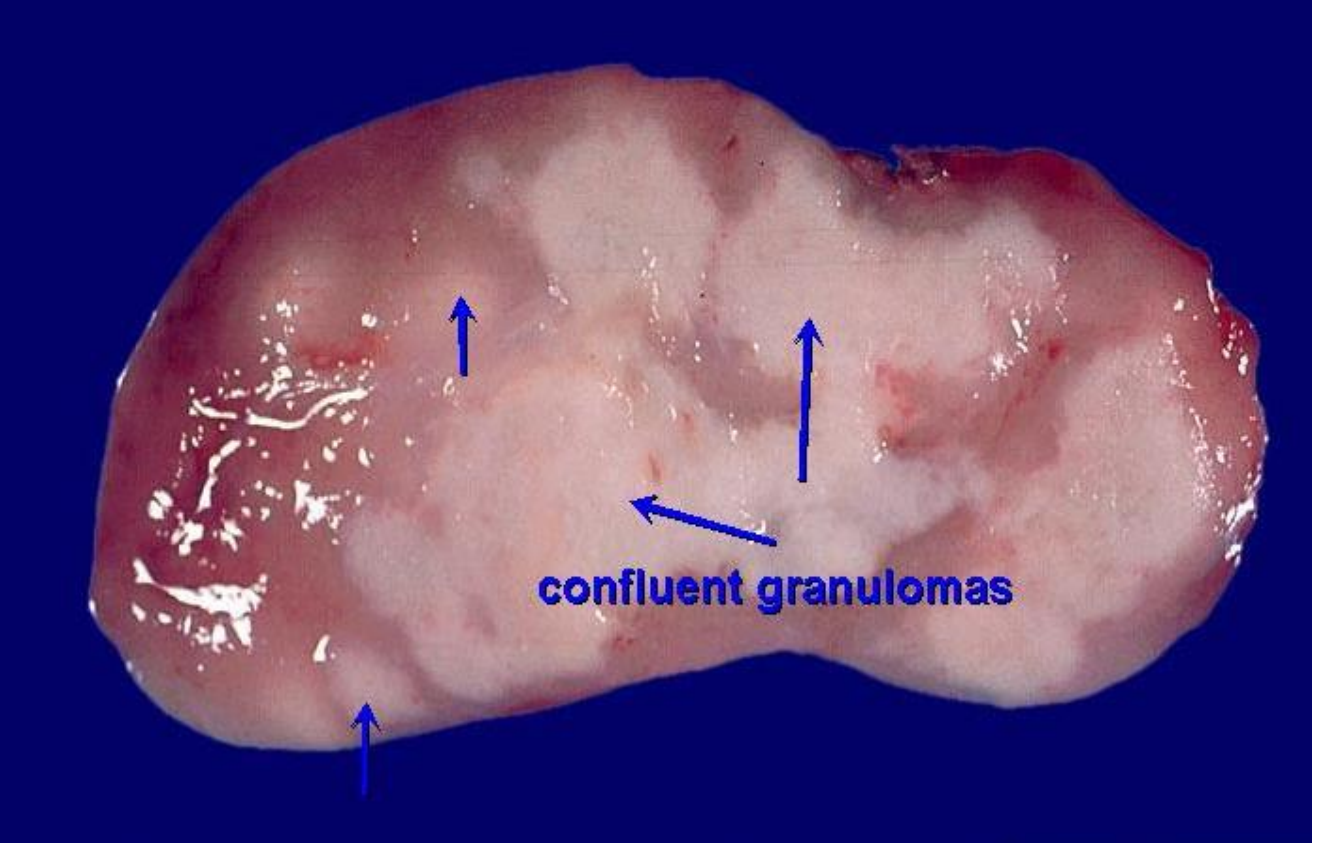
- **Lymphocyte depletion (less than 1%)**

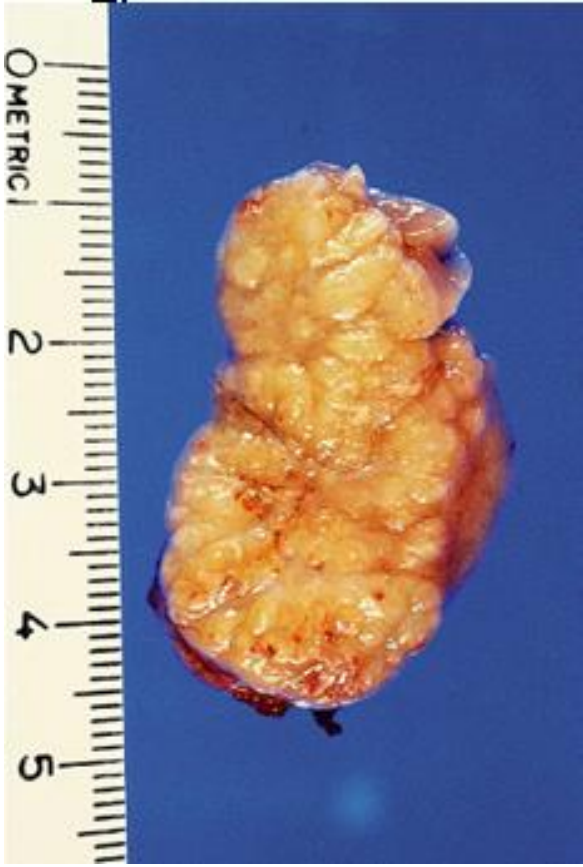
It is found in the unfavorable evolution of the disease, it reflects the generalization of Hodgkin's disease. Sometimes the diffuse proliferation of the connective tissue is observed, among the fibrillar structures whose atypical cells are found, in others the lymphoid tissue is replaced by atypical cells among which H and R-S cells predominate; sclerosis is missing.





Mottled spleen in Hodgkin's lymphoma





Lymph node in Hodgkin's lymphoma(nodular surface)

Non-Hodgkin's lymphomas:

a) nodular;
b) diffuse.

According to the degree of malignancy :

a) with low malignancy (lymphocytes proliferate);
b) with high malignancy (lymphoblasts proliferate).

65% - lymph node involvement,
35% - extranodal lesions (digestive tract, liver, lungs, pharynx).

The tumor process begins in different areas of the lymph nodes, eg:
follicular lymphoma – in B areas,
lymphocytic - in the marginal and medullary areas,
lymfoblastic - in the paracortical areas.

65% come from B lymphocytes,
15% - from lymphocytes T.

The most common form of NH lymphoma is follicular lymphoma

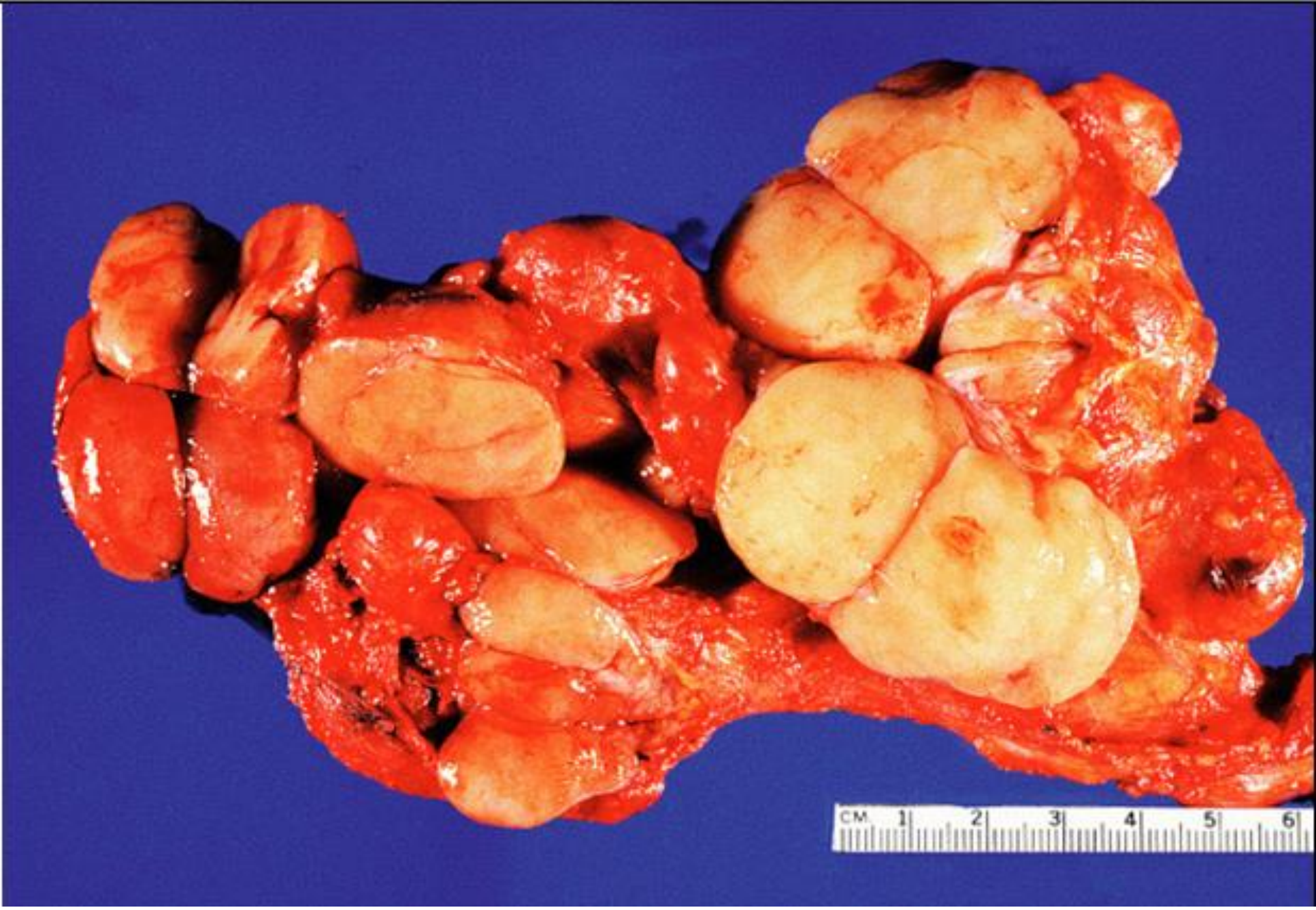
Stages of non-Hodgkin's lymphomas:

I - affecting one group of lymph nodes in a single area;

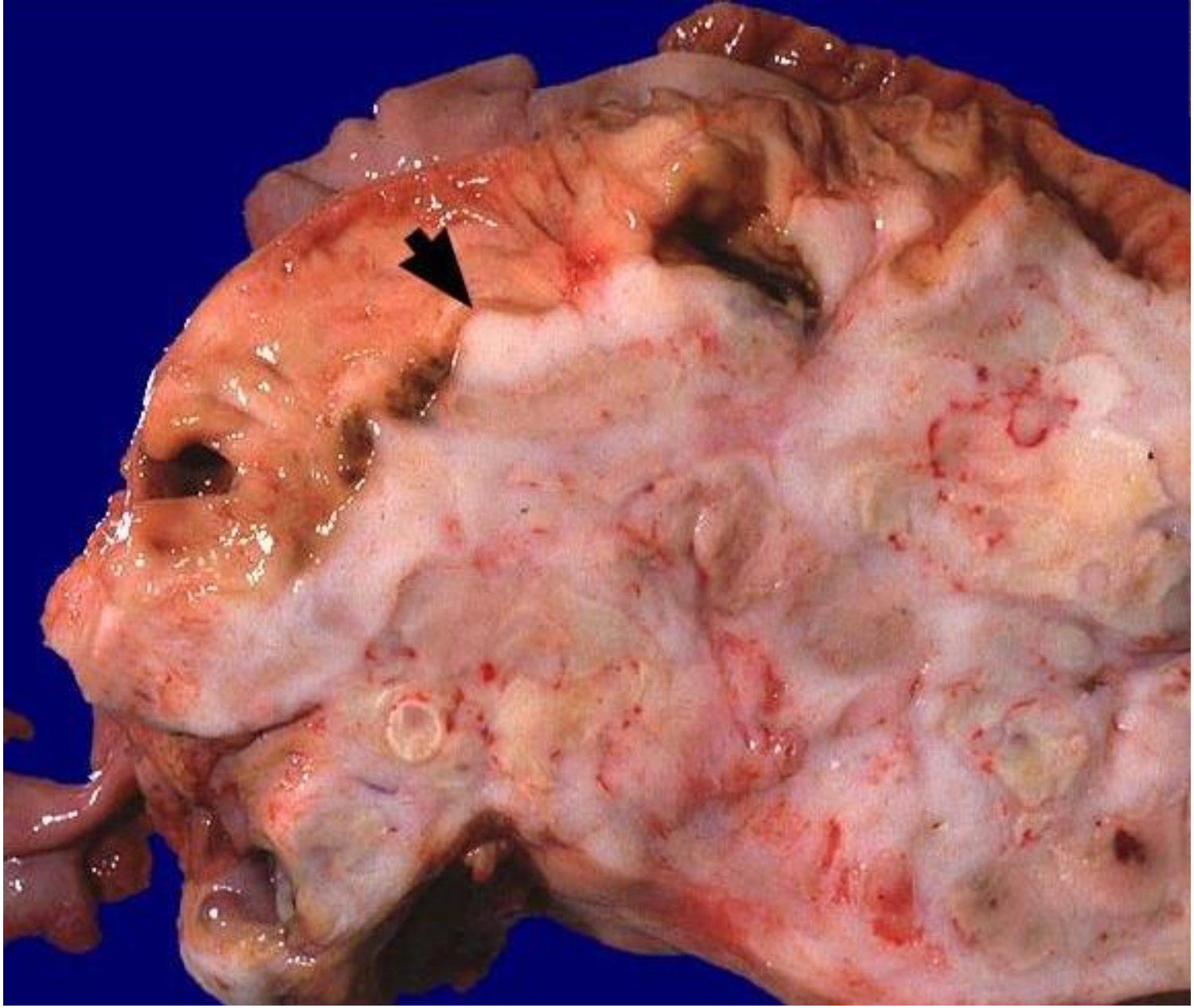
II - affecting 2 or more groups of lymph nodes but on the same side of the diaphragm;

III – affecting 2 or more groups of lymph nodes on both sides of the diaphragm;

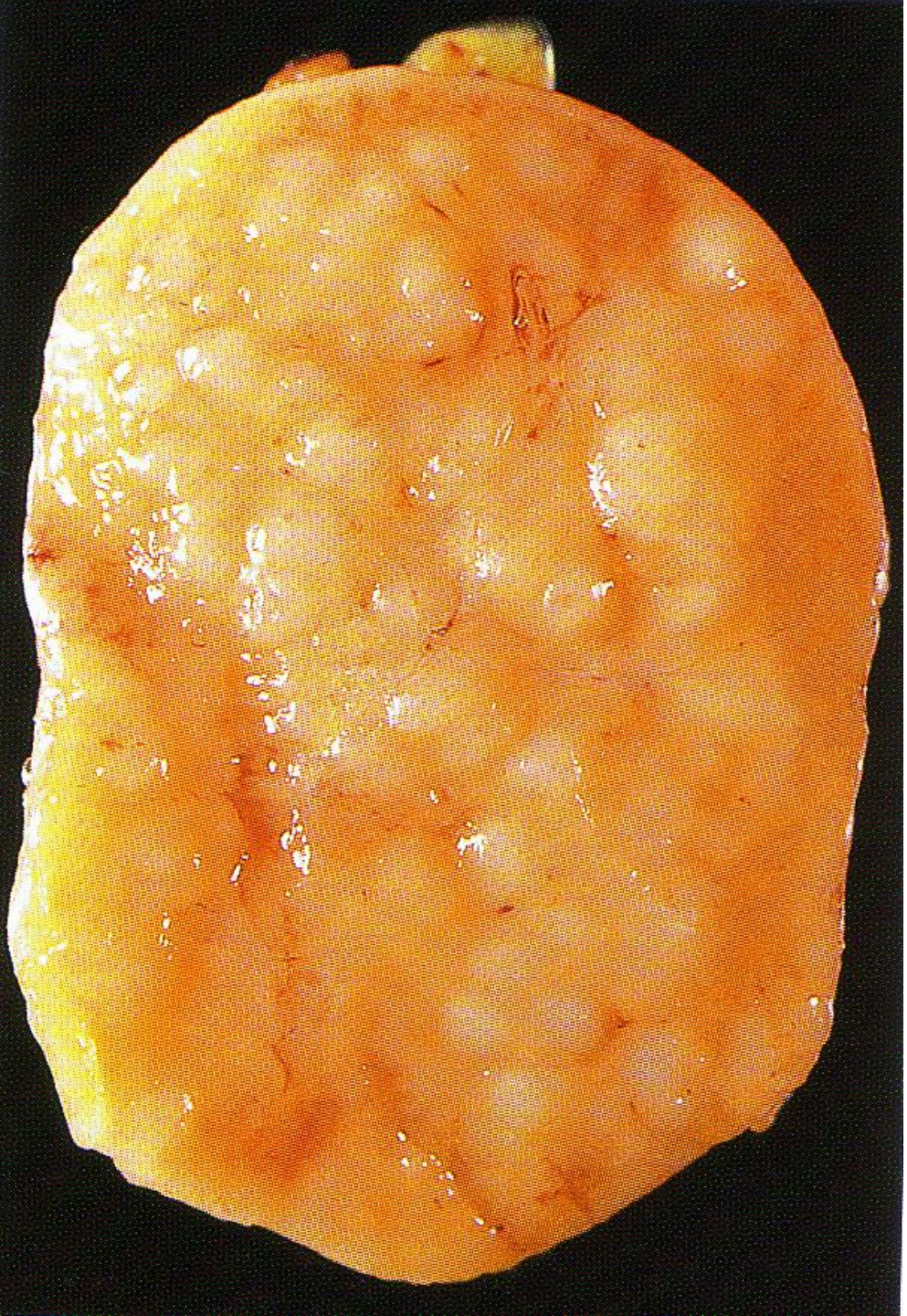
IV – multiple extranodal foci.



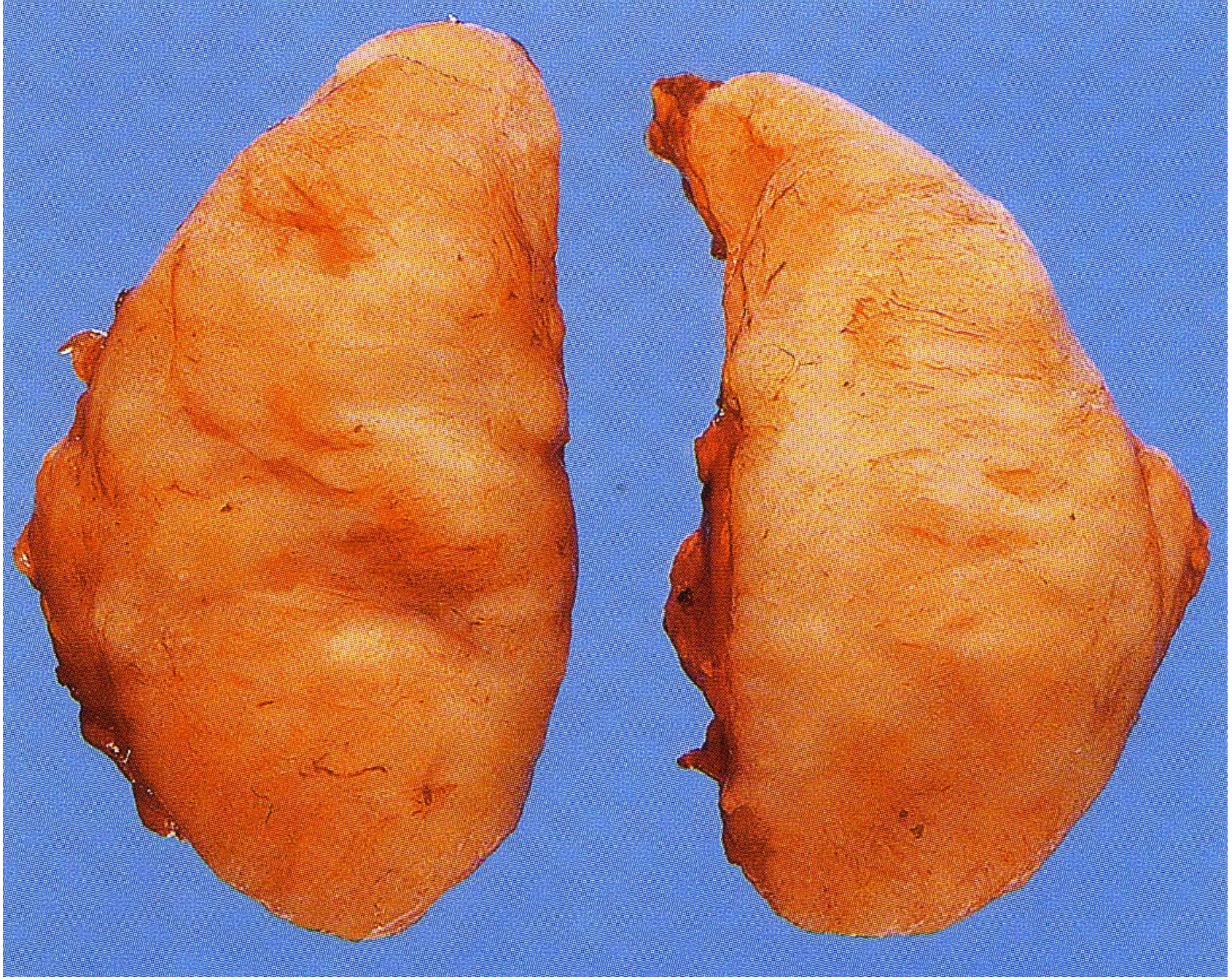
Non-Hodgkin's lymphoma (from B lymphocytes)



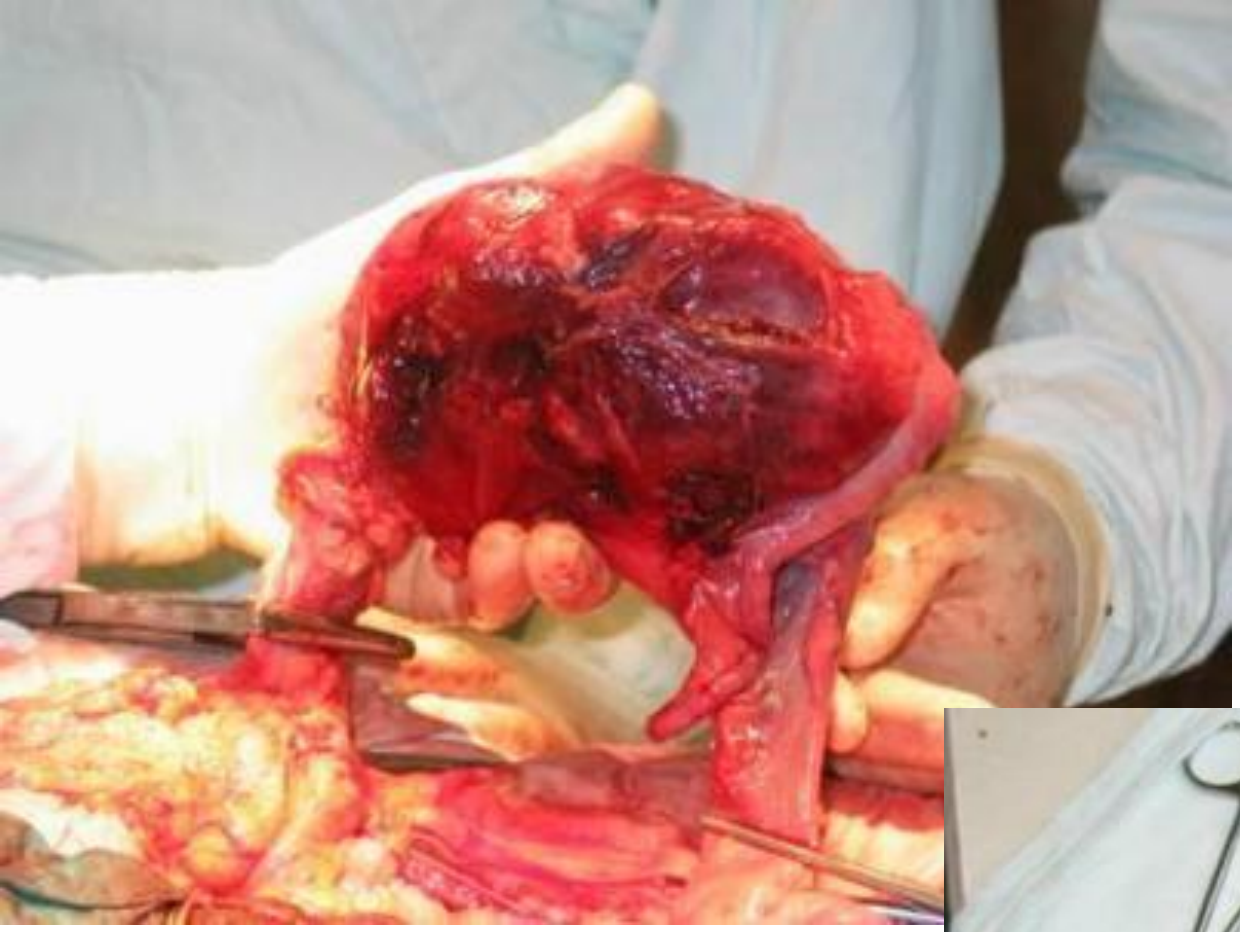
Non-Hodgkin's lymphoma

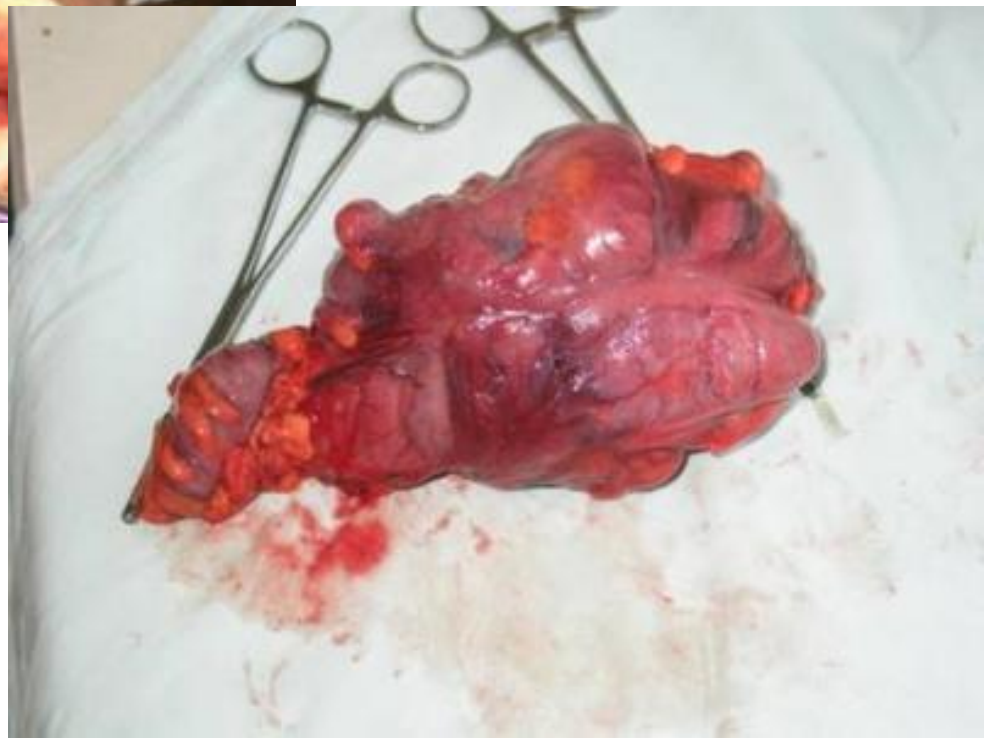


Lymph node in nodular lymphoma

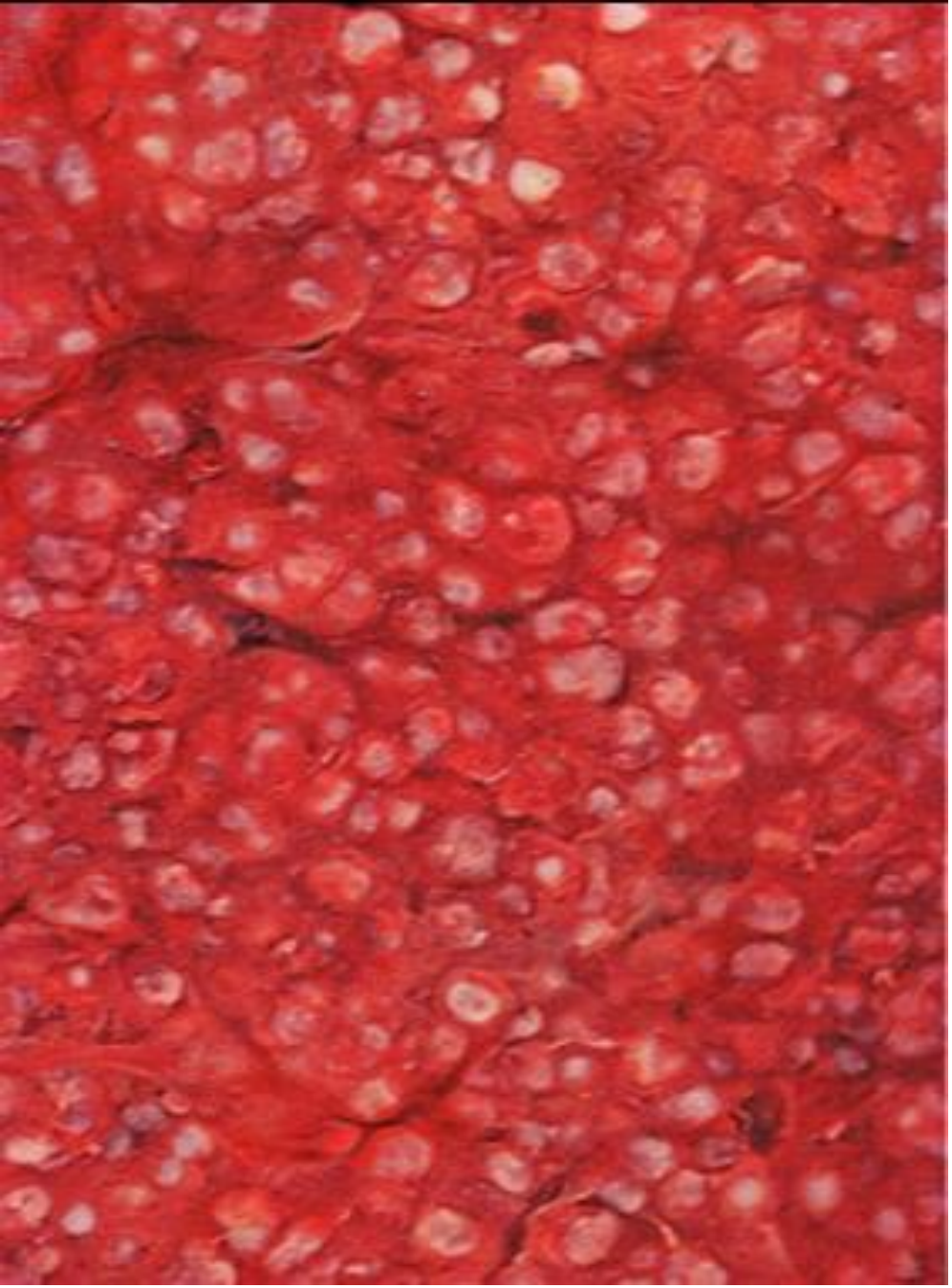


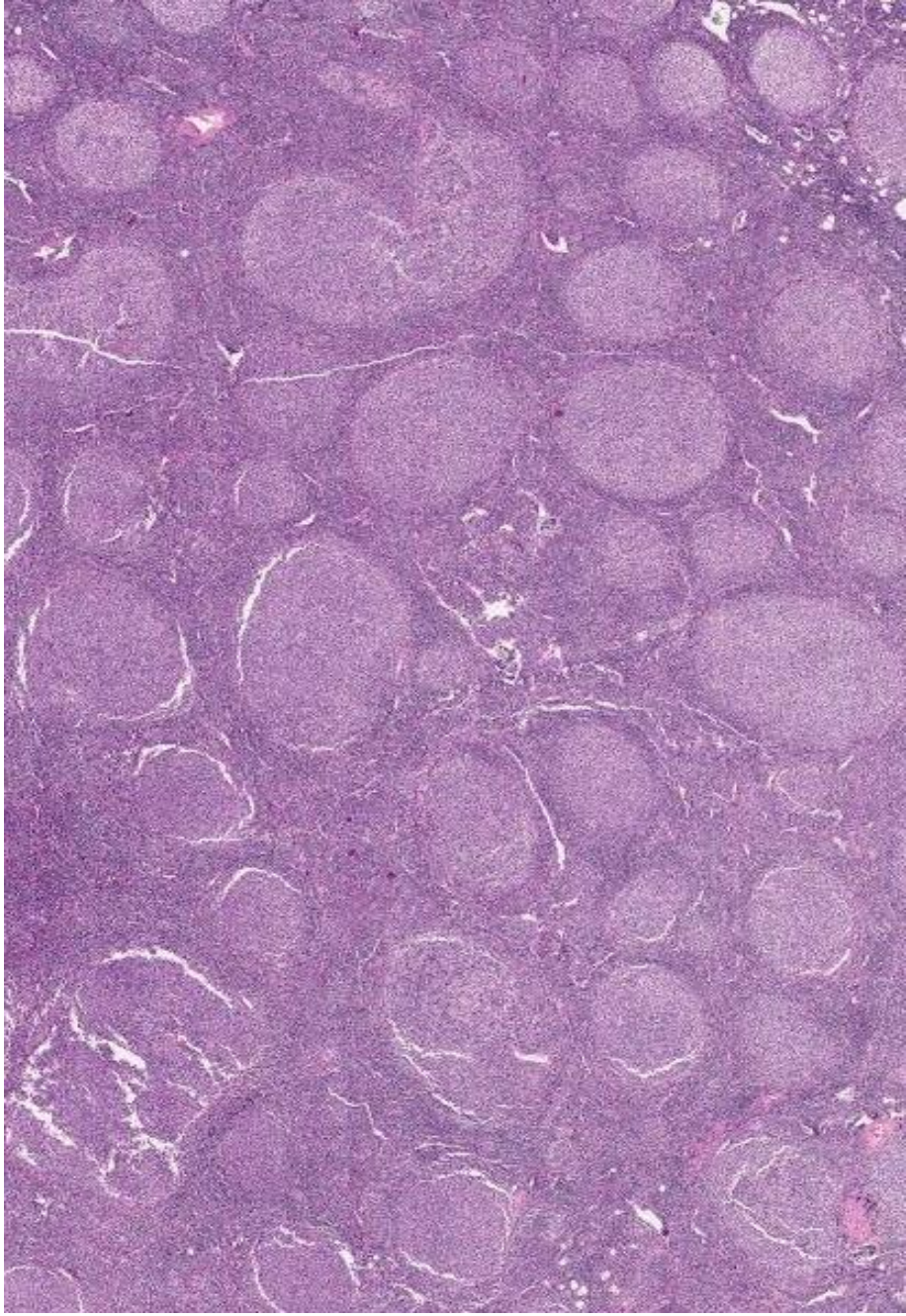
Lymph nodes in diffuse lymphoma



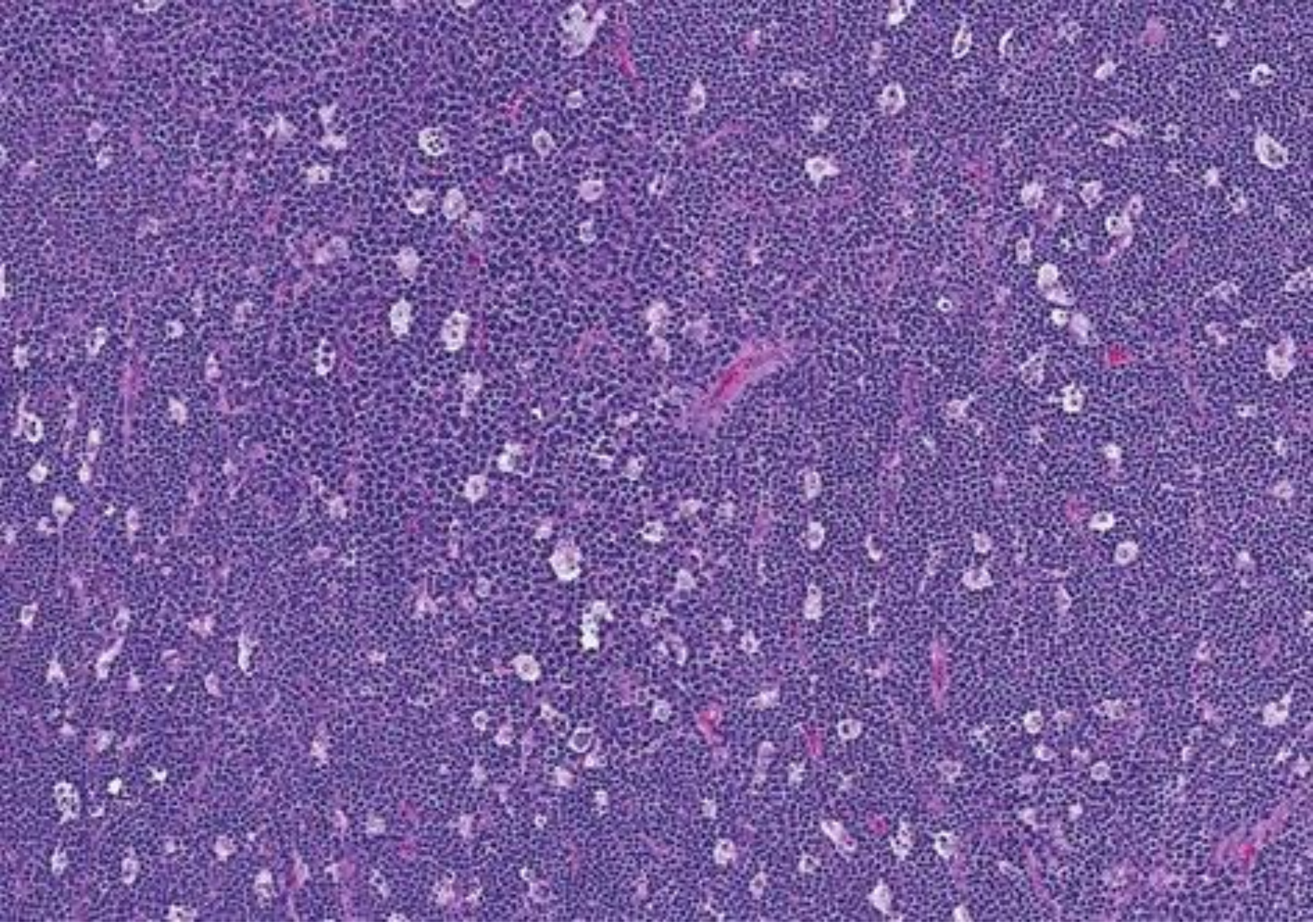


B-lymphoma (ileocecal area)





Follicular lymphoma



Burkitt's lymphoma (starry sky).

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”**

Nevus

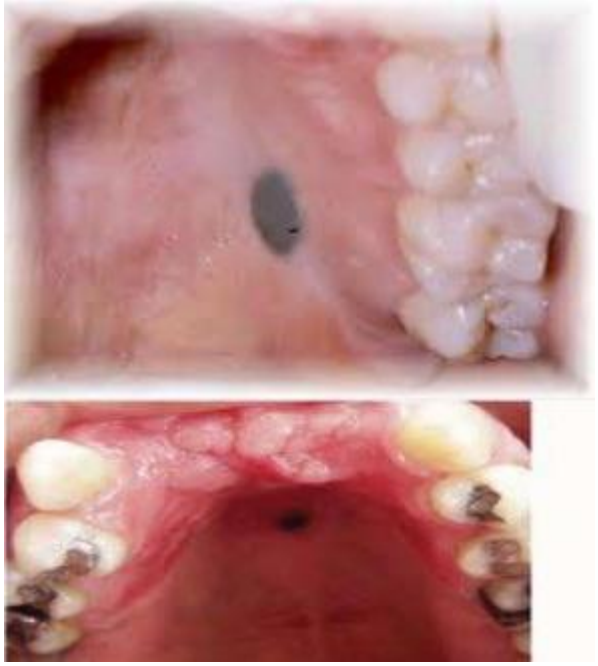
- They may be present at birth or may appear shortly after birth.

- About 15% of intramucosal nevi are not pigmented.

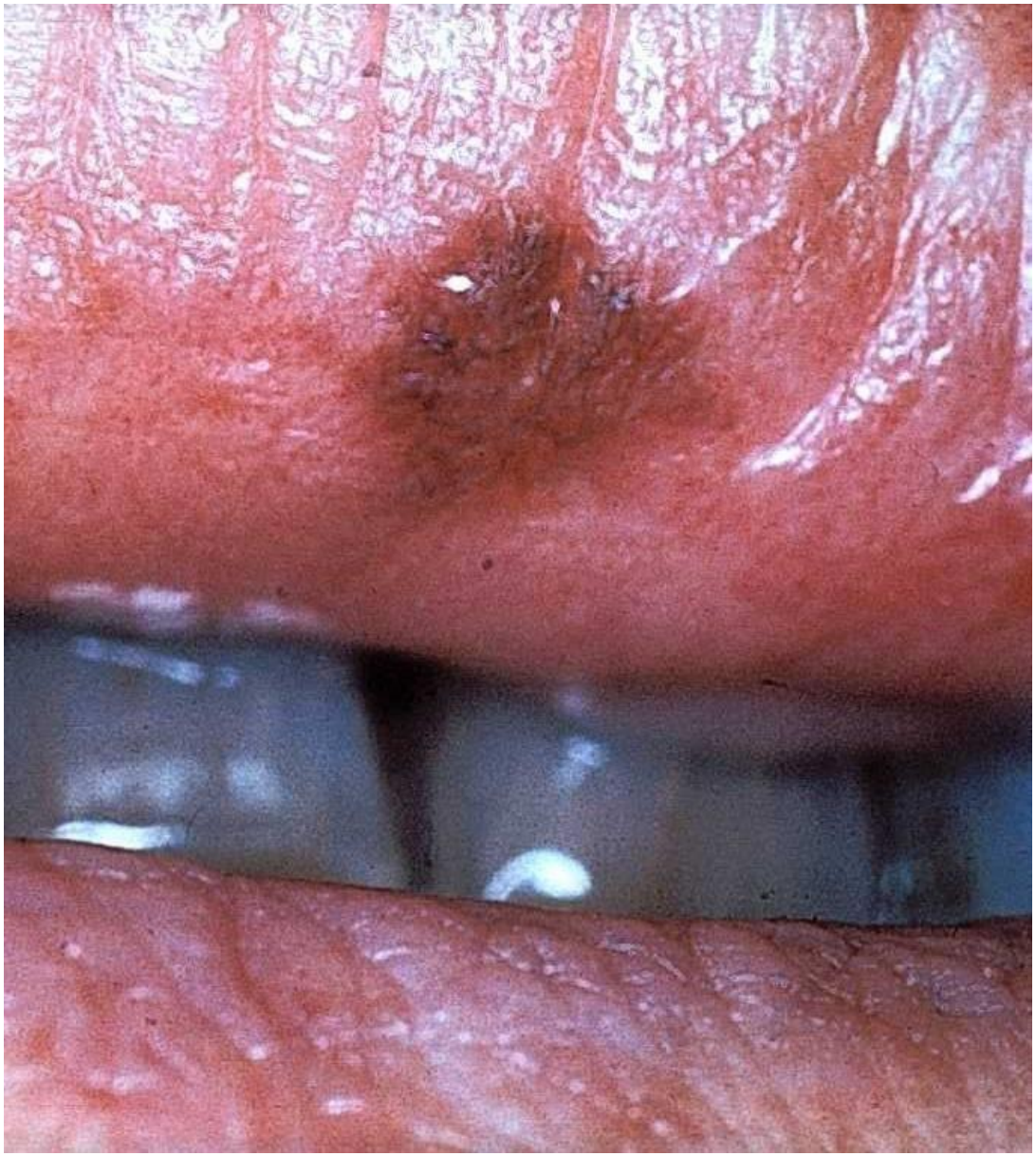
- Most frequently they appear on the hard palate (40%). The second most common location is the oral mucosa (20%), 10% of all types of oral nevi are found on the gums.

- About 75% of nephews are smaller than 0.6 cm.

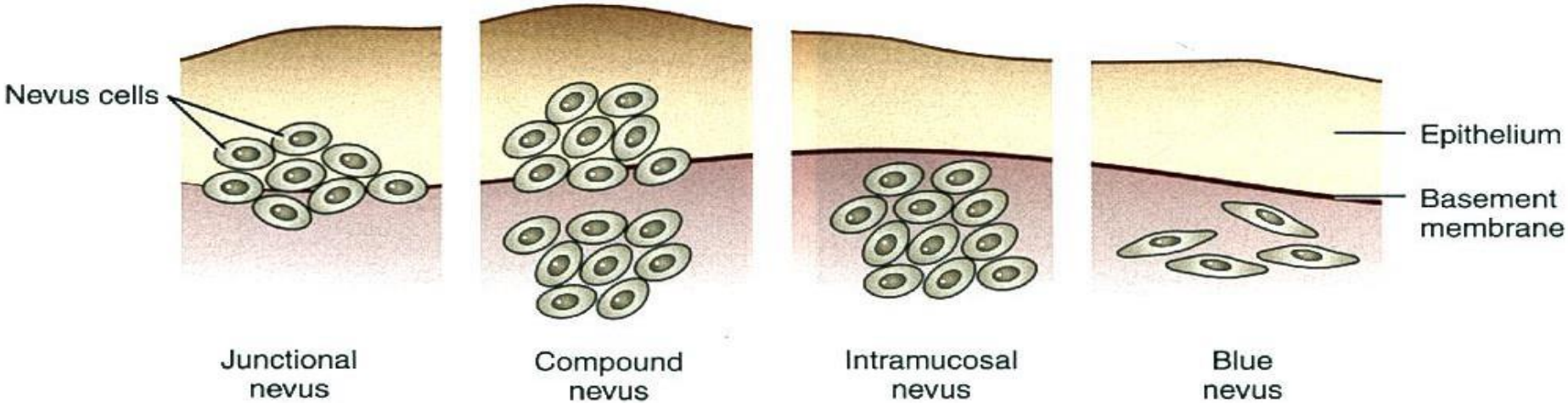
- Slightly elevated papule or flat macula



Nevus

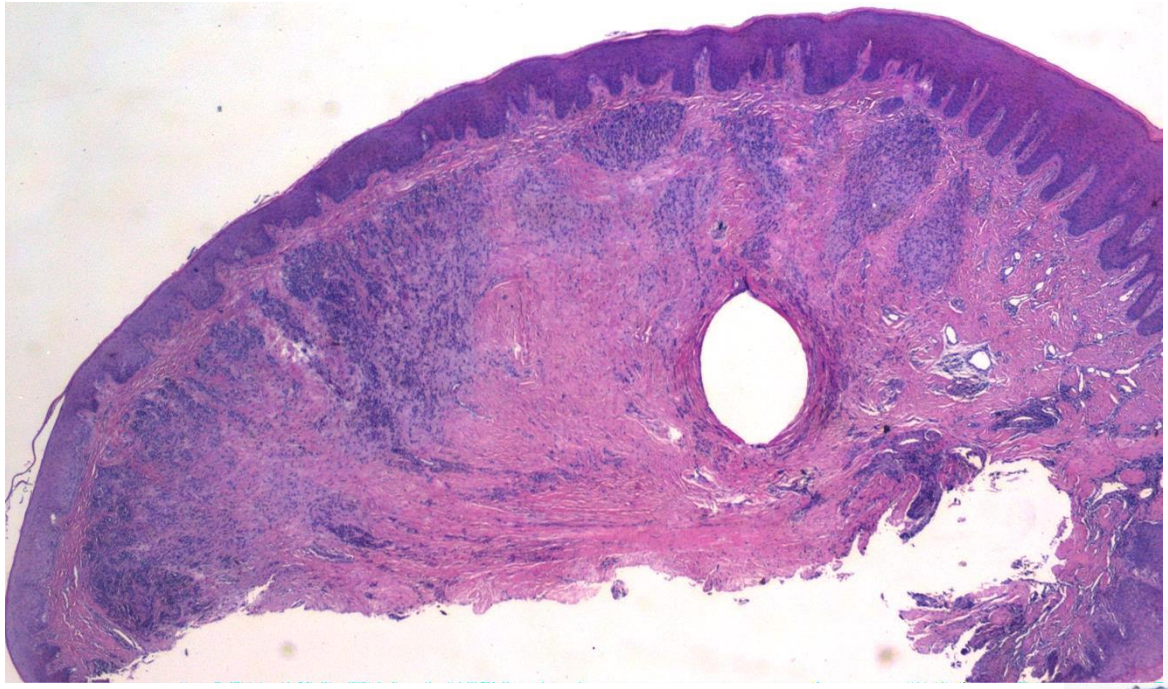


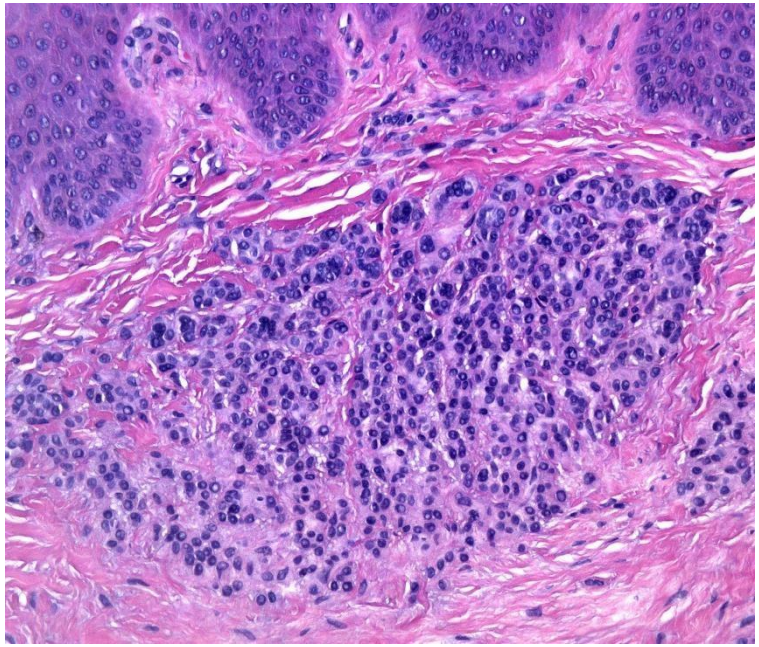
Nevi - types

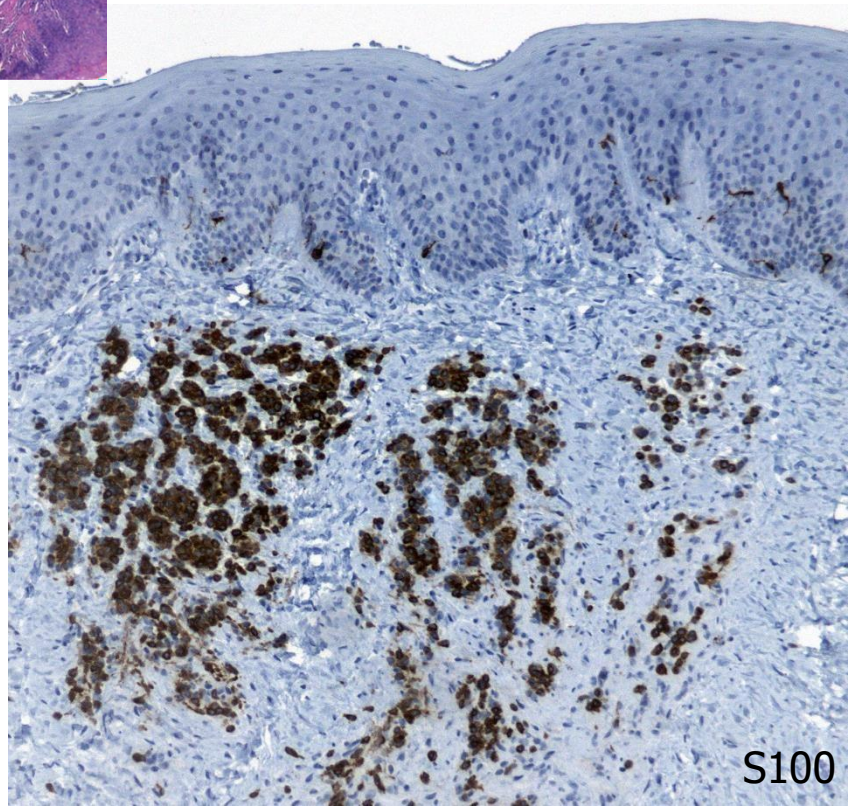


Regezi, Sciuba, Jordan: Oral pathology

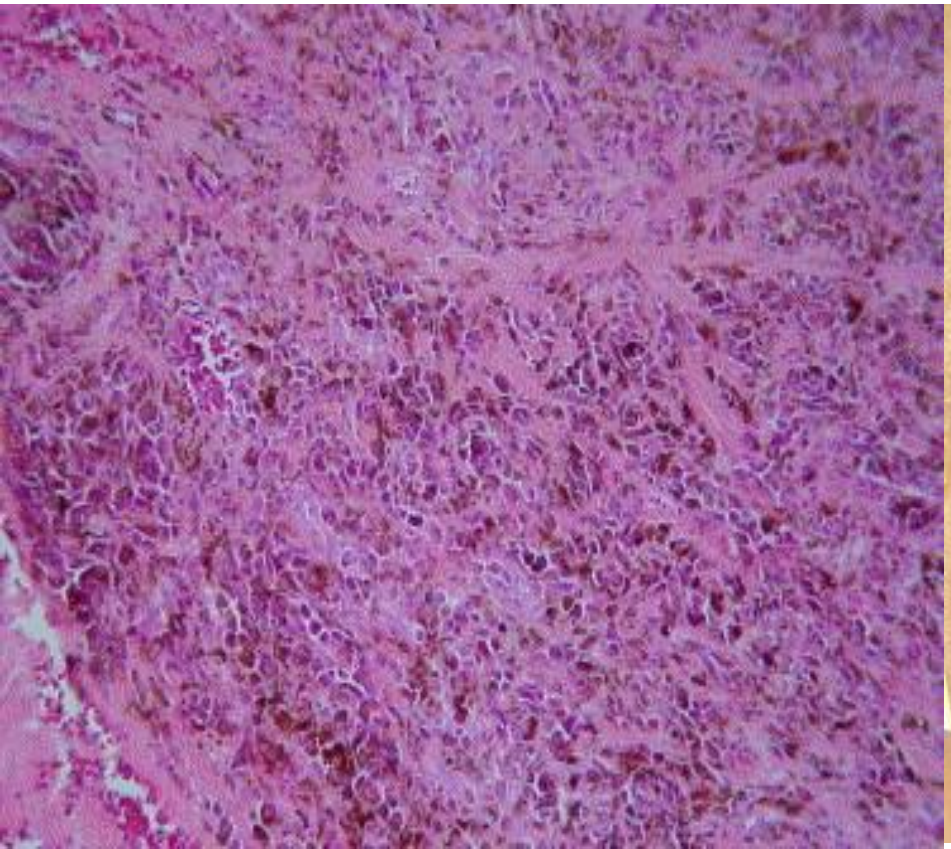
Intramucosal nevus

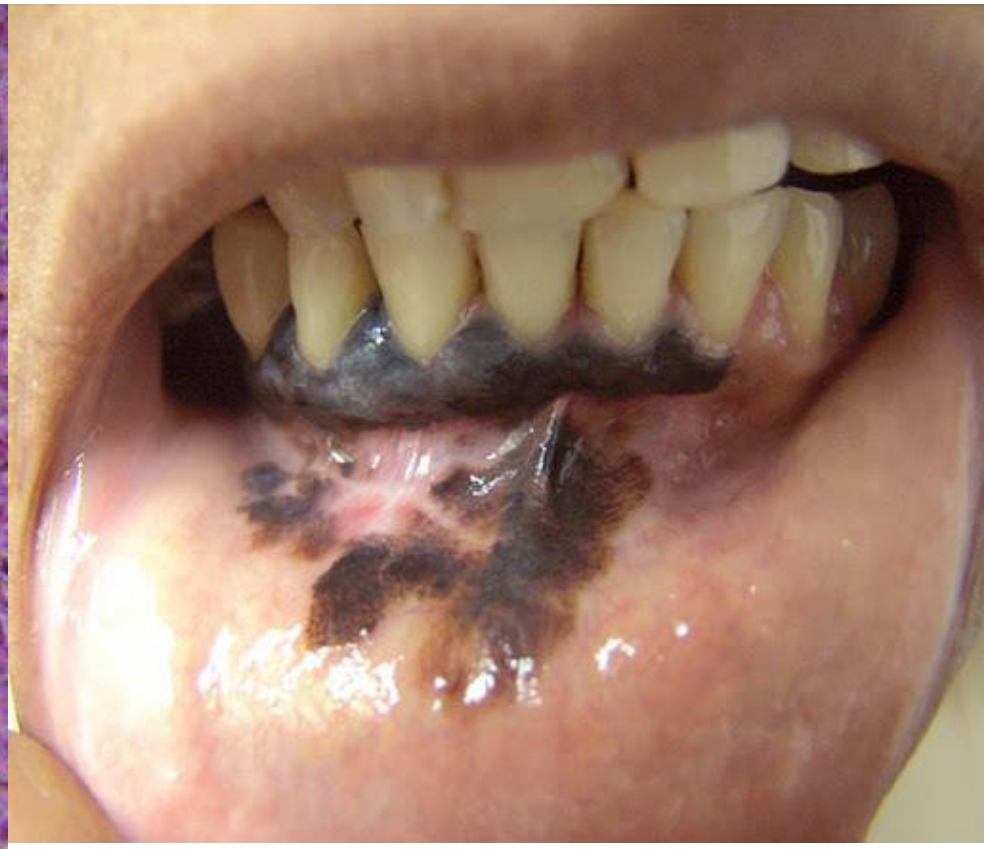






Melanoma is a malignant tumor of melanocytic origin, which is found on the skin, in the oral mucosa, anorectal, esophagus, meninges, eyeball. It is extremely aggressive, a tumor with a thickness of only a few mm can produce multiple metastases. Lymphogenous metastases in regional lymph nodes, and more 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.





Oral Manifestation

- Uncommon neoplasm of the oral mucosa
- 0.2–8%
- melanoma of the oral mucosa - one of the most common sites for the neoplasm in Japanese
- Melanomas in Blacks are seldom found in the skin yet occur on mucous membranes and on the plantar skin

Oral Manifestation

- Primary oral melanoma is nearly twice as common in men as in women
- 55 years (40 and 70 years)
- definite predilection for the palate and maxillary gingiva/alveolar ridge
- also recorded on the buccal mucosa, mandibular gingiva, tongue, lips and floor of the mouth
- deeply pigmented area
- At times ulcerated and hemorrhagic
- tends to increase progressively in size
- Amelanotic melanoma accounts for 5–35% of oral melanomas which appear as a white, mucosa-colored, or red mass

Oral Manifestation

- focal pigmentation precedes before the development of the actual neoplasm
- the appearance of melanin pigmentation in the mouth and its increase in size and in depth of color should be viewed seriously
- melanomas of the oral mucosa - can exist in radial- and vertical-growth phases

Oral Manifestation

types of oral melanomas are

1. Superficial spreading
2. nodular

H/P

- malignant cells - nest or cluster in groups in an organoid fashion
- however, single cells can predominate
- Cells are round or polygonal
- melanoma cells have large nuclei, often with prominent nucleoli, and show nuclear pseudoinclusions due to nuclear membrane irregularity
- The abundant cytoplasm may be uniformly eosinophilic or optically clear
- Occasionally, the cells become spindled or neurotized in areas (interpreted as a more aggressive feature)

H/P

SUPERFICIAL SPREADING MELANOMA

- The intraepithelial component (radial-growth phase) is characterized by the presence of large, epithelioid melanocytes distributed in a so-called ‘pagetoid’ manner (‘buckshot scatter’)

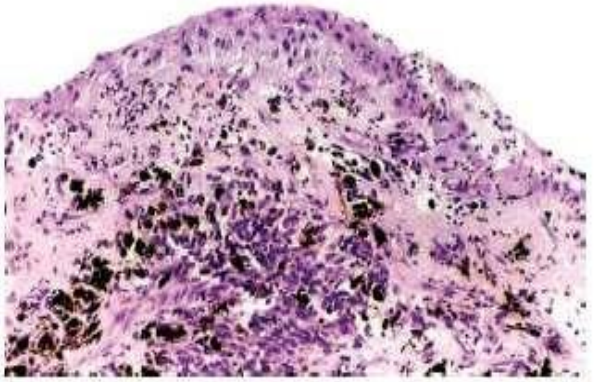
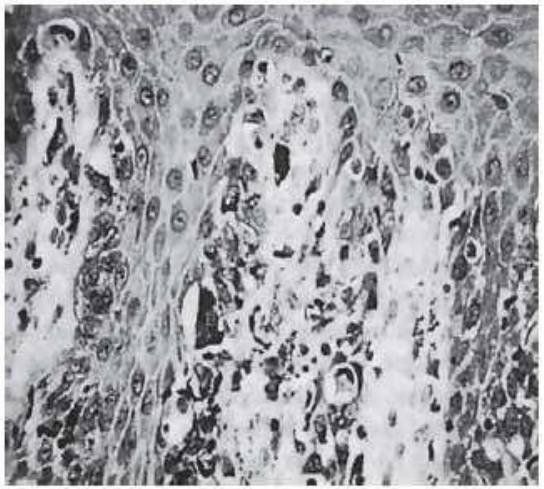


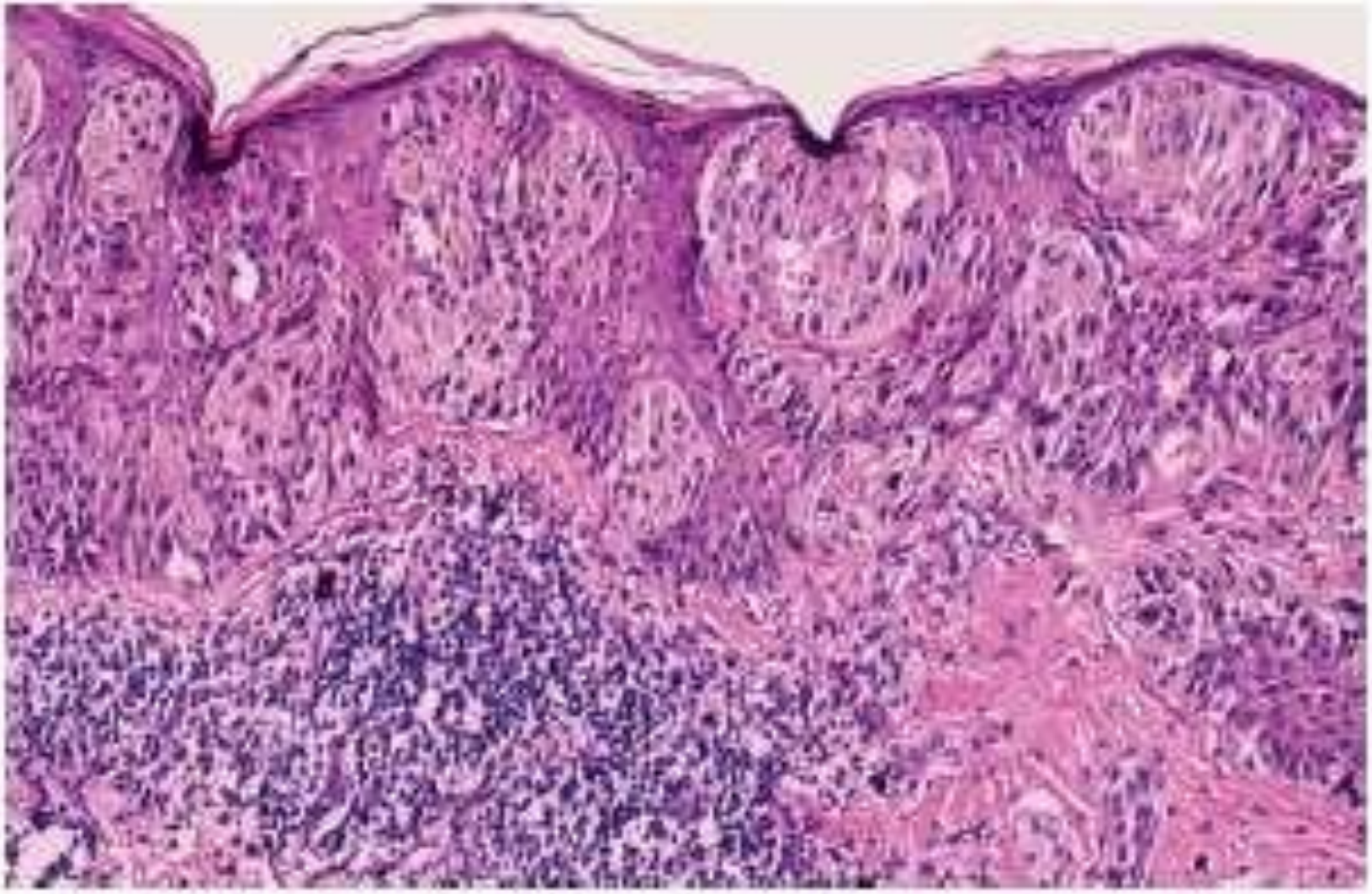
Figure 2-36. Vertical growth phase characterized by malignant melanocytes invading the underlying connective tissue



H/P

SUPERFICIAL SPREADING MELANOMA

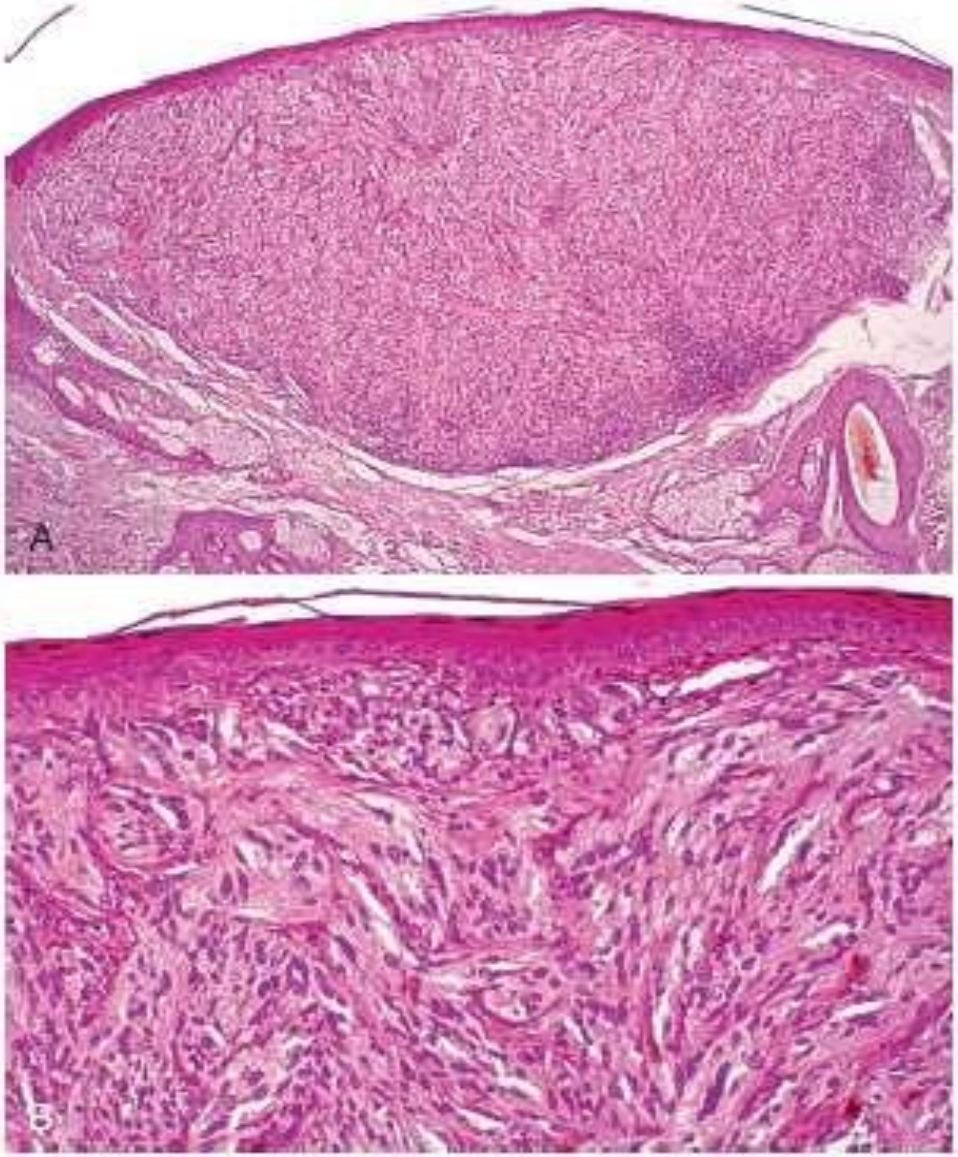
- Malignant cells - confined to the epithelium - no host cell response in the underlying connective tissue
- If Melanocytes penetrate basement membrane, a florid host cell response of lymphocytes develops
- Macrophages and melanophages may be present
- The tumor cells are often destroyed by this cellular response
- The vertical-growth phase is characterized by the proliferation of malignant epithelioid melanocytes in the underlying connective tissues
- The cells may be arranged singly or in clusters
- Melanin pigment is usually scanty



• **Fig. 10-142 Superficial Spreading Melanoma.** The radial growth phase is characterized by the spread of atypical melanocytes along the basilar portion of the epidermis. Also note the presence of individual melanocytes invading the higher levels of the epithelium.

H/P

- Nodular melanoma also is characterized by large, epithelioid
- melanocytes within the connective tissue. However, small
- ovoid and spindle-shaped cells may be present. Melanin
- pigment is usually but not invariably present. The tumor
- cells may invade and ulcerate the overlying epithelium and
- penetrate the deep soft tissues



• **Fig. 10-144 Nodular Melanoma. A,** Low-power photomicrograph showing a nodular mass of malignant melanocytes invading into the dermis. Note the lack of radial growth in the adjacent overlying epidermis. **B,** Higher-power photomicrograph showing atypical spindle-shaped melanocytes.

Treatment and Prognosis

- The treatment of cutaneous malignant melanoma is surgical excision
- regional lymph node dissection is indicated when nodes are involved
- tumors greater than 0.75 millimeters in thickness and located in the so-called BANS (back, arm, neck and scalp) sites have a greater tendency to metastasize
- On the other hand, melanomas of the skin of the face have a much more favorable prognosis
- Chemotherapy, immunotherapy and radiation therapy have been used in the treatment of cutaneous melanoma

Treatment and Prognosis

- Unfortunately, oral mucosal melanomas have a far worse prognosis than cutaneous melanomas
- the five-year survival rate for such tumors is approximately 7%

Treatment and Prognosis

- The level of tumor invasion is another important indicator of the prognosis of MM
- The **Clark system is generally** used to grade tumor invasion based on the deepest histologic cutaneous structure the tumor infiltrates