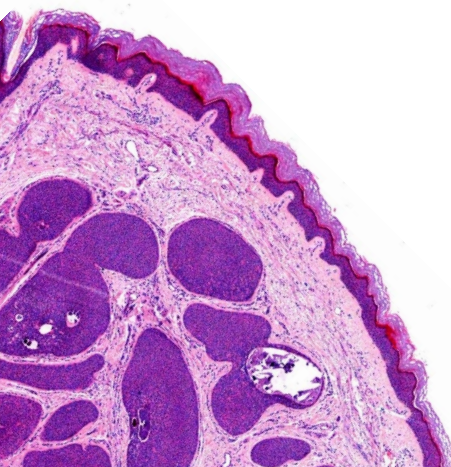
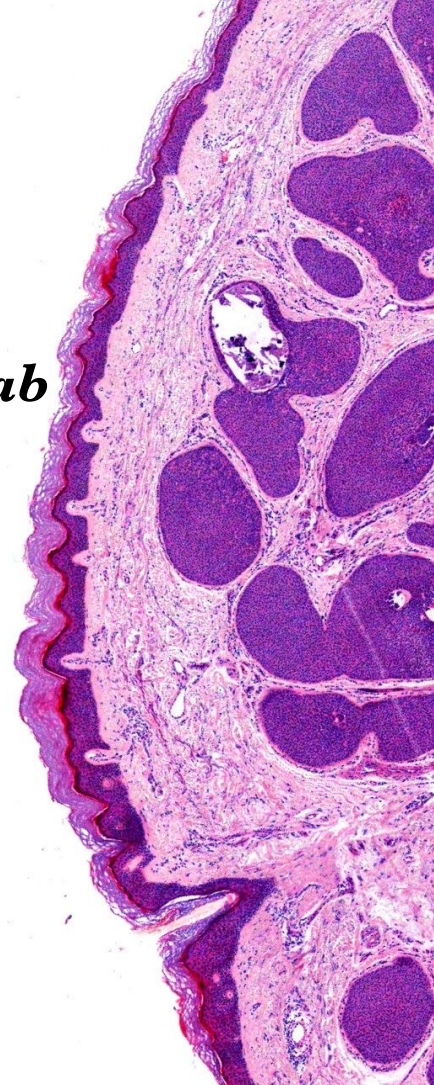
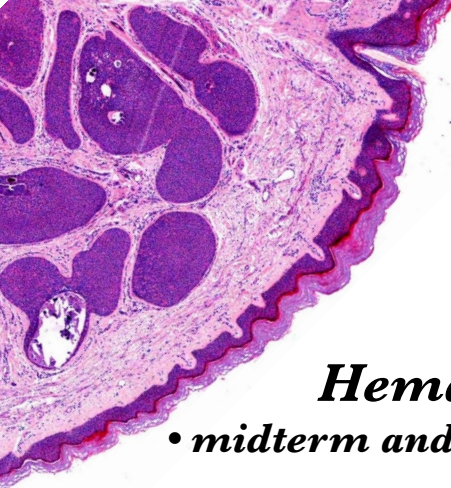


بسم الله الرحمن الرحيم

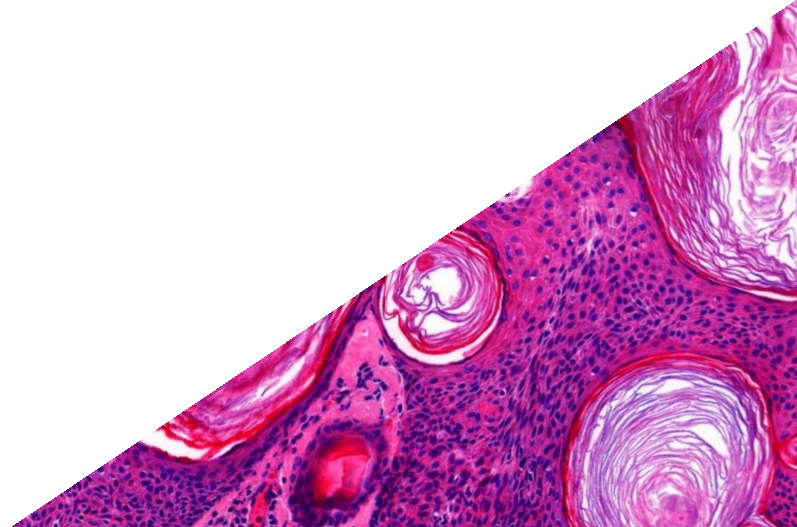
Hematolymphatic System pathology lab

• midterm and final material

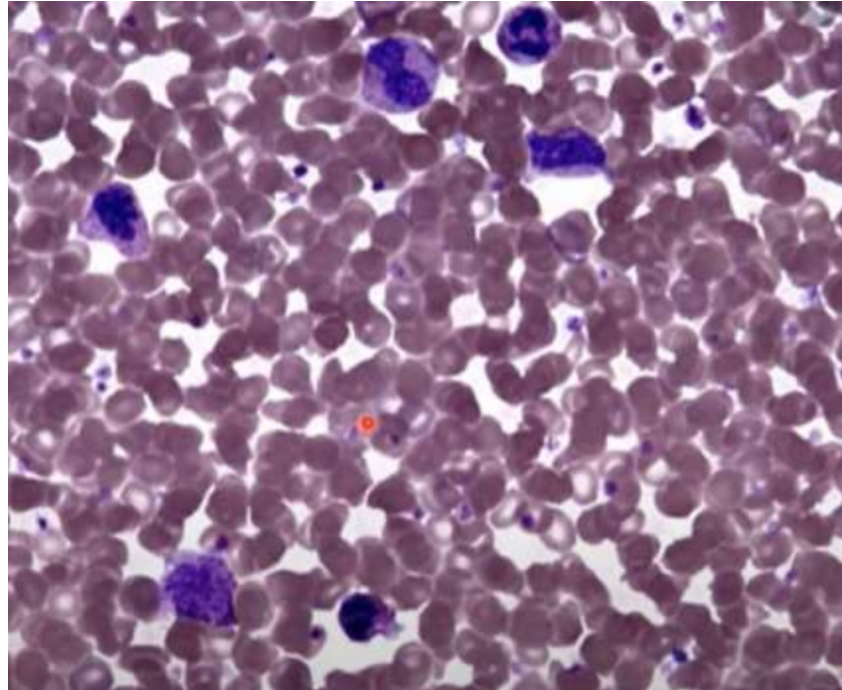
Written By : Reenas Al Khresat



Midterm material



✎ Peripheral blood smear in polycythemia: packed RBCs.
✎ Notice that they're very crowded. Why? Because polycythemia's patients have an increase in RBCs mass . ⬆️



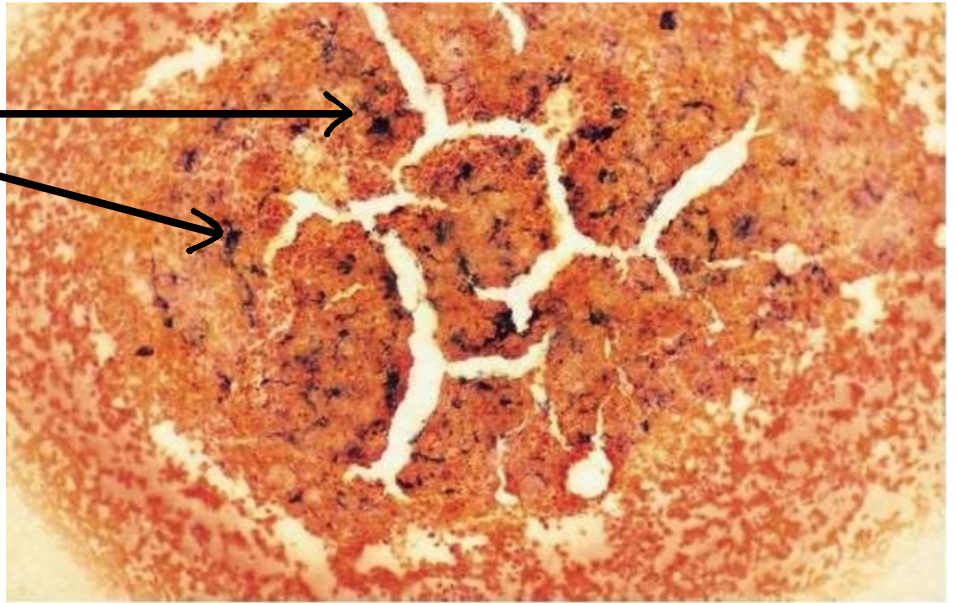
✎ Aspirate of normal bone marrow: bluish-black iron (haem siderin) in macrophages in a fragment .

✎ Hemosiderin stores inside the bone marrow (Aspirate), stained with perl's prussian blue stain.

- Note the granular blue particles which represent hemosiderin (blue circles).

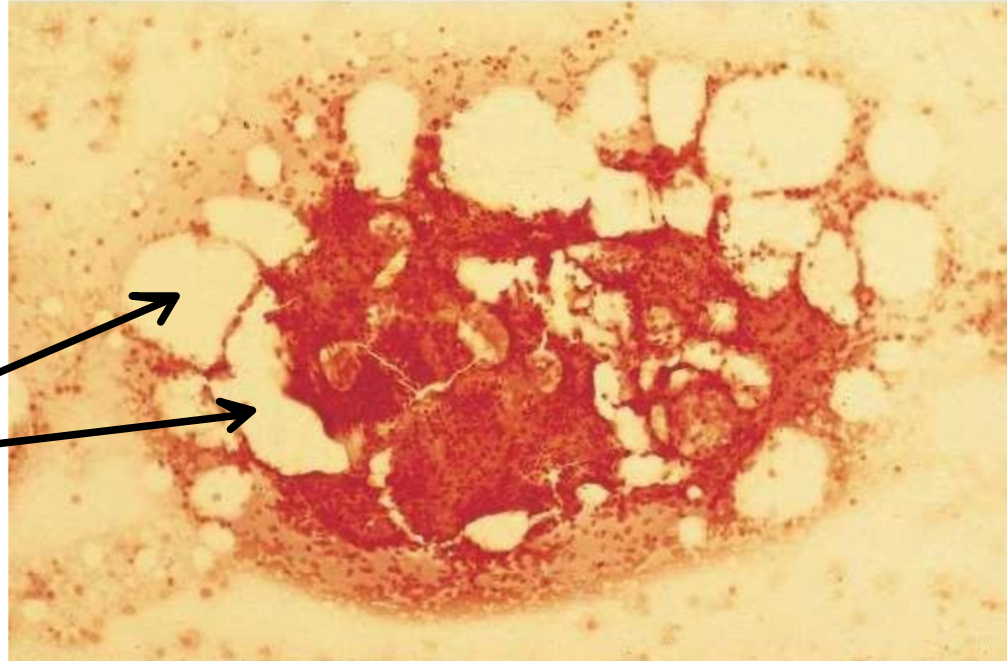
- This patient has normal iron stores.

✎ Any deficiency in the staining amount , patient will have iron deficiency anemia .



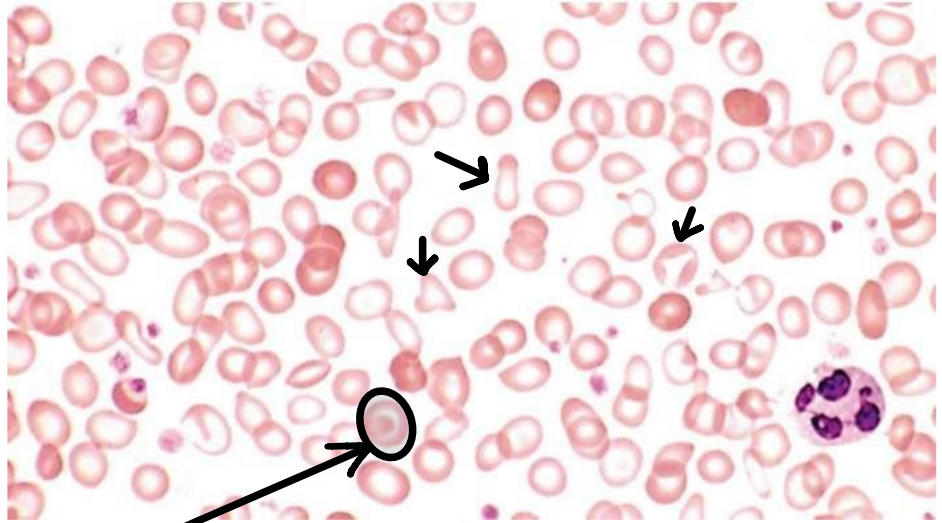
✎ Aspirate of normal bone marrow: a fragment with no stainable iron (Perl's stain)

✎ Iron deficiency anemia, so, no iron is stored in hemosiderin in BM, no blue material.

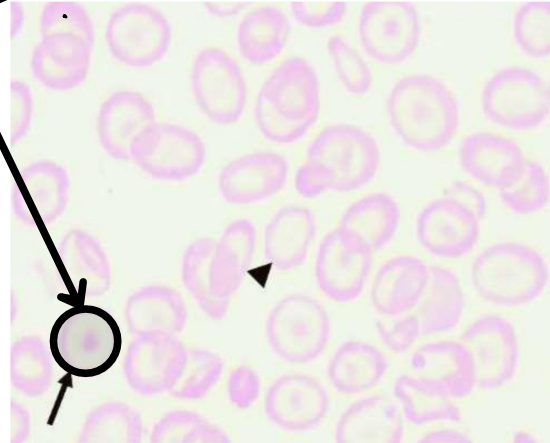


✎ IDA: note the hypochromia and poikilocytosis , RBC is small and pale(large central pale area >1/3)

✎ poikilocytosis Small and elongated



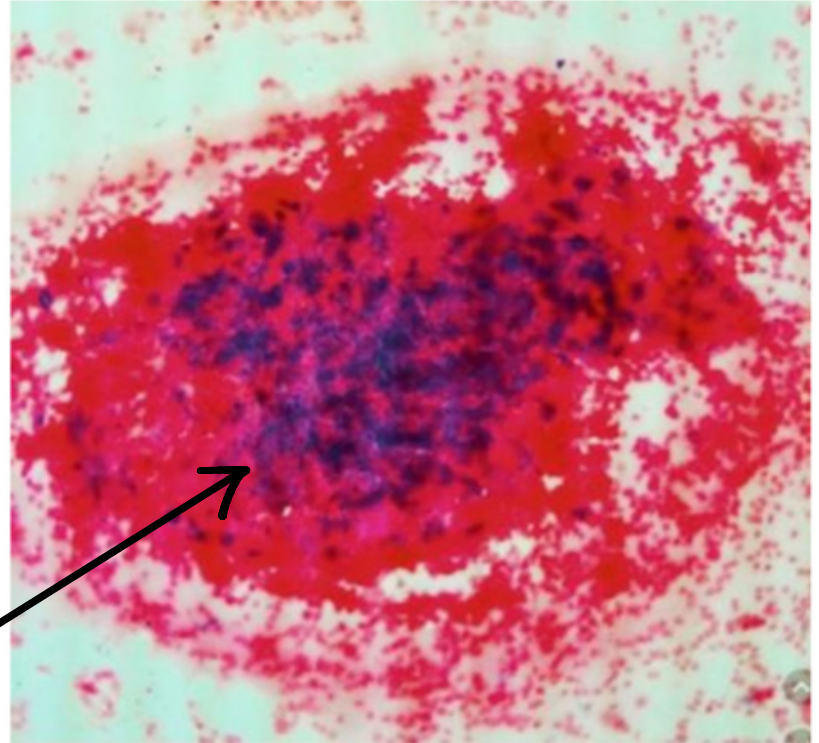
✎ Target cell has red dot inside RBCs




Anemia of chronic inflammation

- ✎ Similar to IDA: serum iron is low, RBCs: normal morphology, then hypochromic microcytic, with decreased Reticulocytes.
- ✎ In contrast to IDA: Bone marrow iron stores are increased, Serum ferritin is also increased.

✎ Note the blue granular material (hemosiderin)



Morphology of megaloblastic anemia:

 **Macroovalocyte** -> big elongated cell with abundant cytoplasm, characteristic of megaloblastic anemia.



- ✎ **Hyper segmented neutrophil with 6 lobes.**
- ✎ **Due to abnormally developed DNA.**
- ✎ **One of the earliest features of B12 and folate deficiency.**

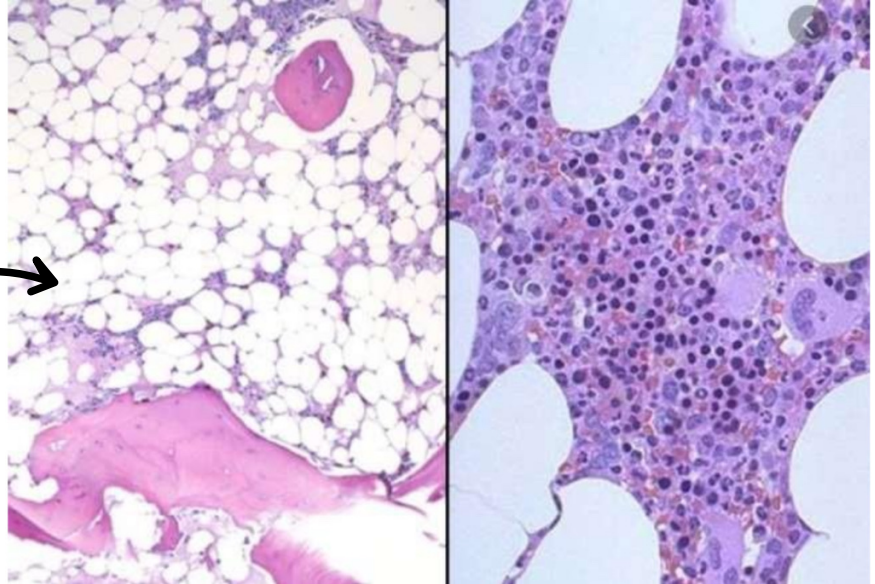


Aplastic Anemia

Normal bonemarrow and stem cells

Damage to multipotent stem cell in bone marrow

- Bone marrow becomes depleted of hematopoietic cells
- Bone marrow: decreased hematopoietic cells and predominance of fat

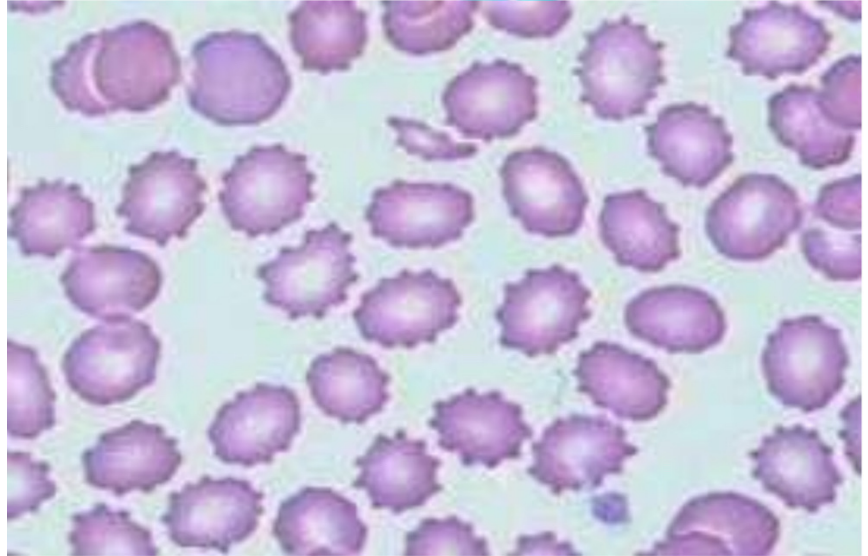


Fat accumulation

Anemia of renal disease

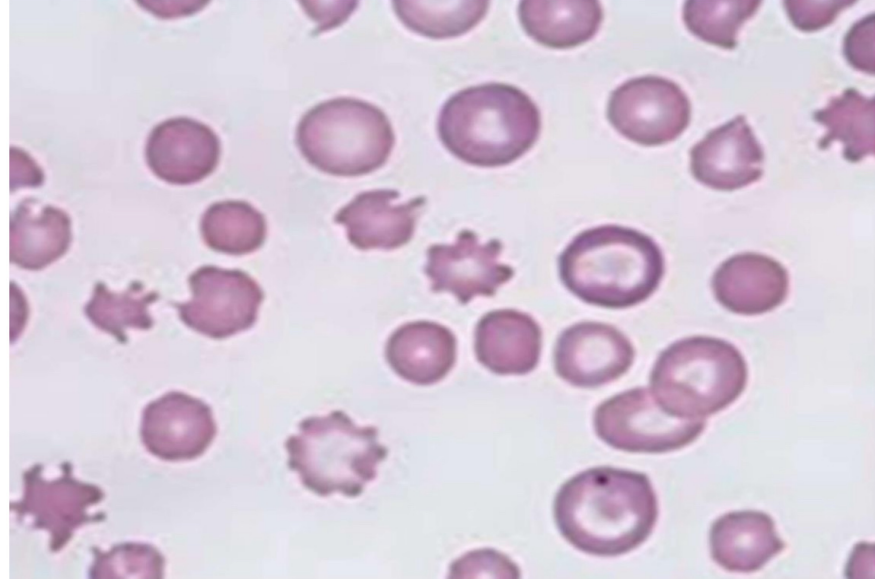
 Decreased erythropoietin production from kidneys

- Does not correlate well with kidney function (serum creatinine)
- Decreased RBC production (low reticulocytes count)
- Patients with uremia develop abnormal platelets function (bleeding), echinocytes (Burr cells) appear



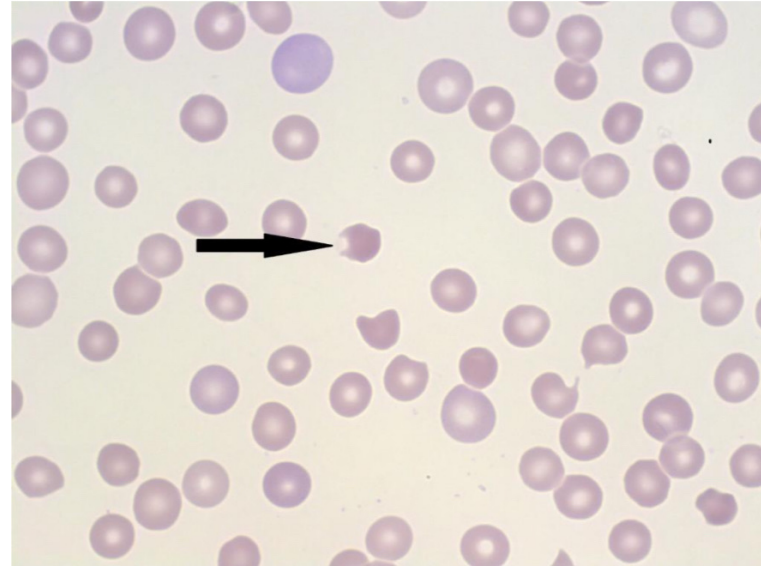
Anemia of liver disease

- ✎ **Multiple factors causing anemia**
 - **Decreased synthesis of clotting factors (bleeding)**
 - **Bleeding from varices**
 - **Decreased synthesis of transferrin**
 - **Acanthocyte (spur cell) appears**




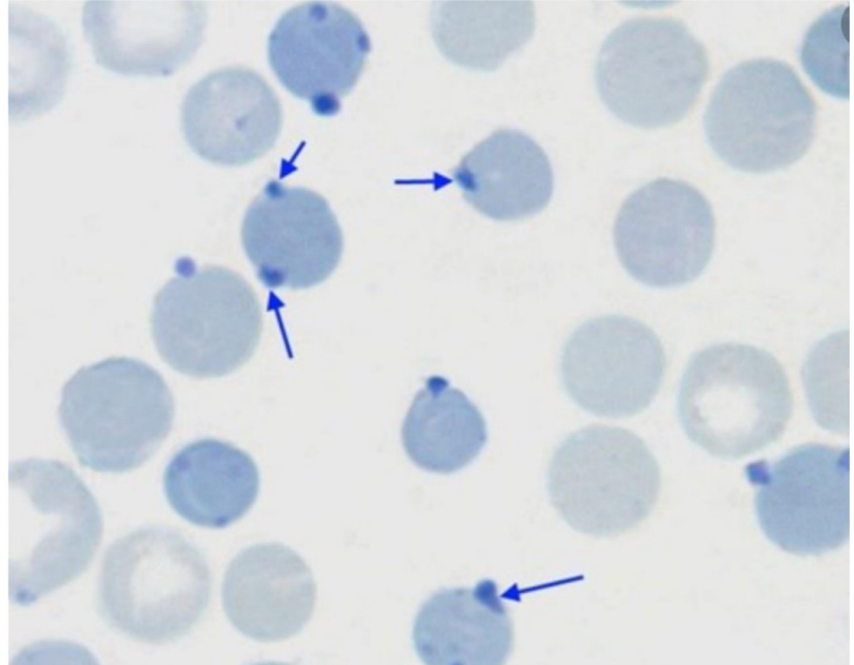
G6PD DEFICIENCY

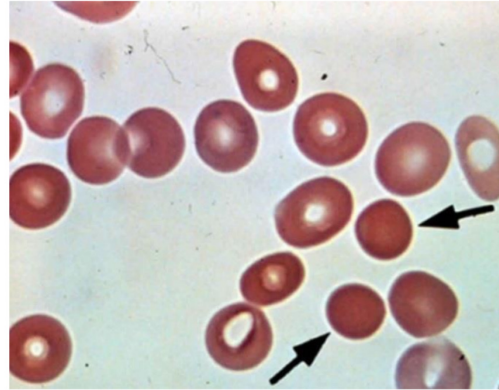
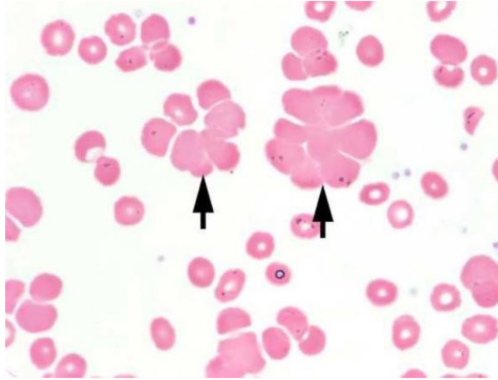
- ✎ In all, large numbers of oxidants are generated, G6PD cannot neutralize them, causing hemoglobin denaturation and precipitate (Heinz bodies), damaging cell membrane and massive hemolysis of RBCs, 2-3 days after trigger
- Other cells lose deformability and partially phagocytosed inside spleen (bite cells)



- ✎ Bite cells: appears are indented defect in part of cell membrane of RBCs

 **Supravital special stain highlights Heinz bodies as membrane-bound, dark spots representing condensed and denatured Hg**



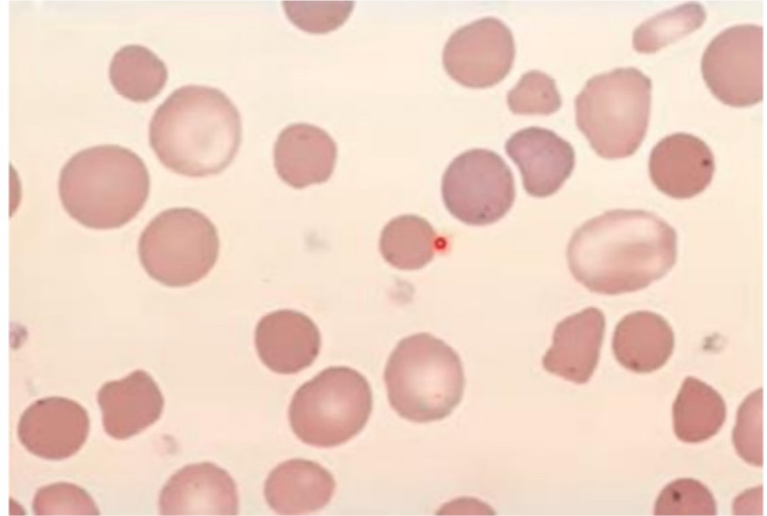


- Left: RBC agglutination: RBC clumps in different directions
- Right: spherocytes appear as small, round hyperchromatic RBC




HEREDITARY SPHEROCYTOSIS

 Autosomal Dominant, sometimes recessive

- Mutation is RBC cell membrane skeleton
- Most commonly affects ankyrin, band 3 or spectrin
- Cell membrane becomes unstable, keeps losing parts of it as the RBC age
- Little amount of cytoplasm is lost
- With decreasing surface area, the RBC loses its normal biconcave morphology and becomes a smaller sphere

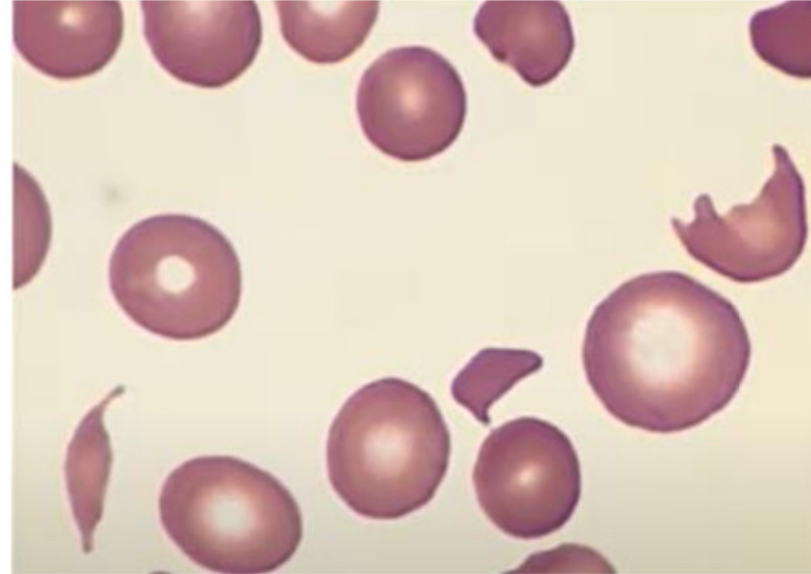


 Appearance of spherocytes in peripheral blood



- Spherocytes have a smaller size (low MCV)
- Little cytoplasm is lost, normal amount of Hg (normal MCH)
- MCHC is increased 
- Spherocytes show increased fragility  when put in hypotonic solution (increased  osmotic fragility)

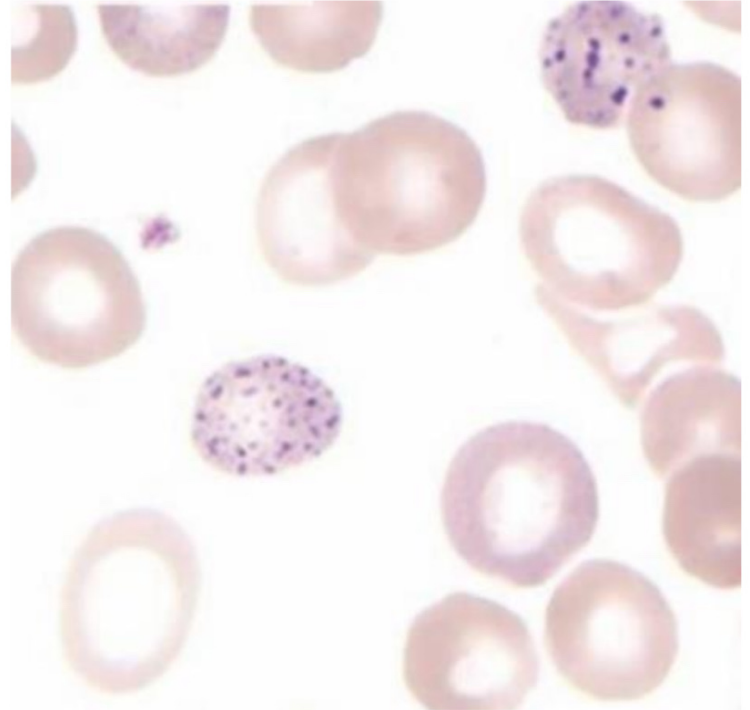
TRAUMATIC HEMOLYSIS

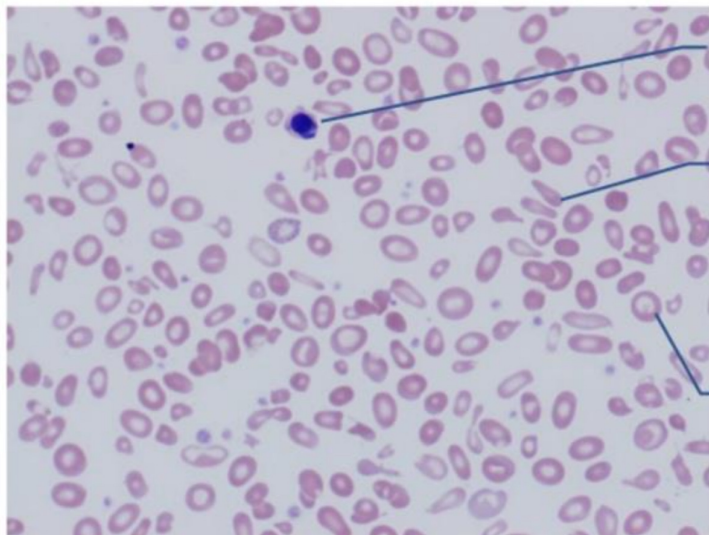
- Direct physical force, or turbulence causing lysis of RBCs
- Prosthetic heart valves
- Repetitive physical pounding (marathon, boxing, marching)
- Disseminated thrombi (microangiopathic hemolytic anemia)
- Hallmark of traumatic hemolysis: schistocytes



BASOPHILIC STIPPLING OF RBCS

 Blue dots  are residual ribosomes that appear in the thalassemia





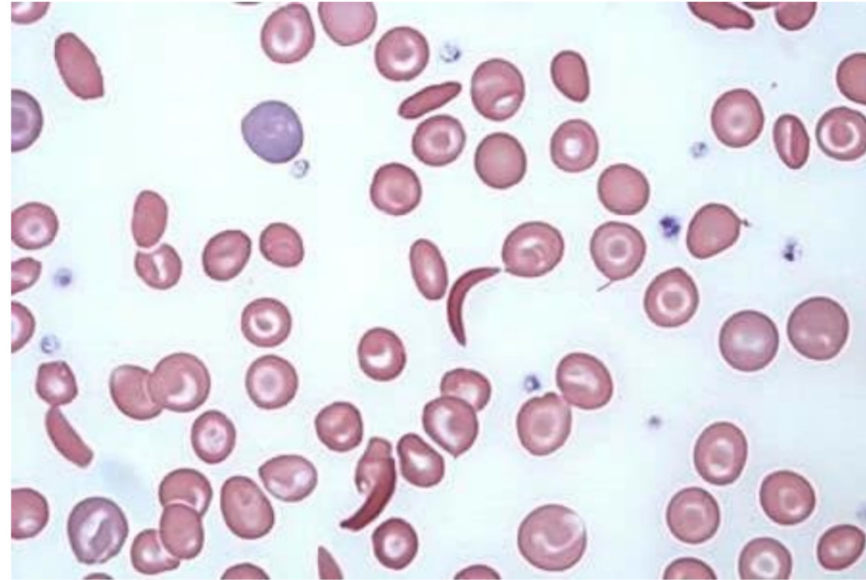
Nucleated RBC

Poikilocytosis

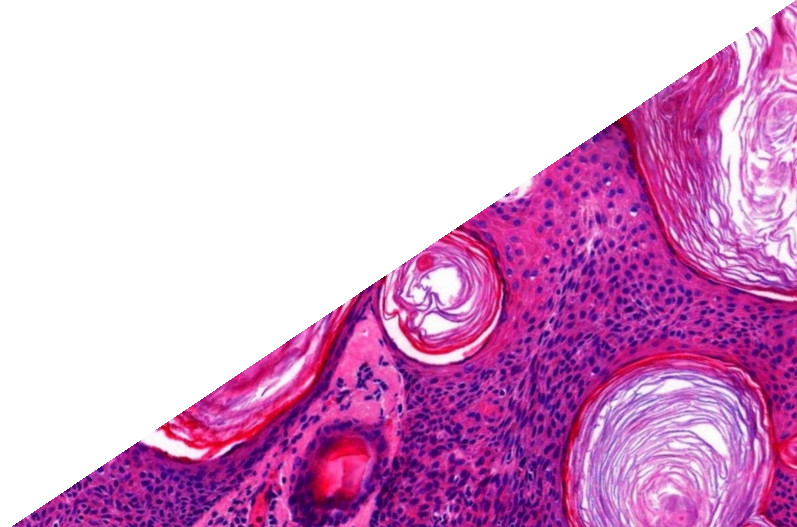
Hypochromia

SICKLE CELL ANEMIA

- ✎ Routine blood smear: presence of sickle cells, target cells
 - Sickling test: adding hypoxic agent to RBCs promote sickling
 - Hemoglobin electrophoresis
 - In sickle cell trait, Blood smear is normal

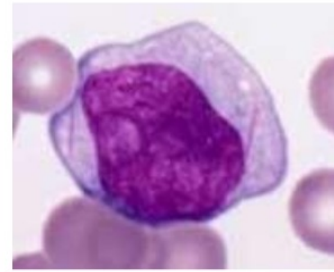
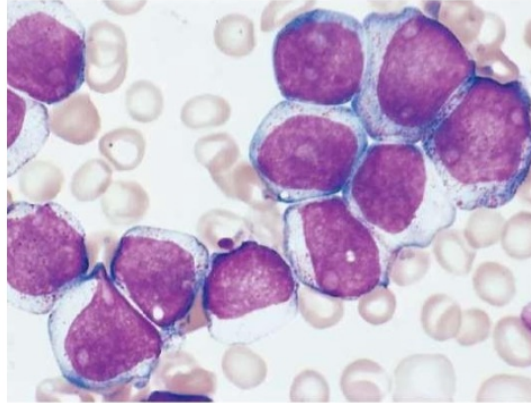


Final material



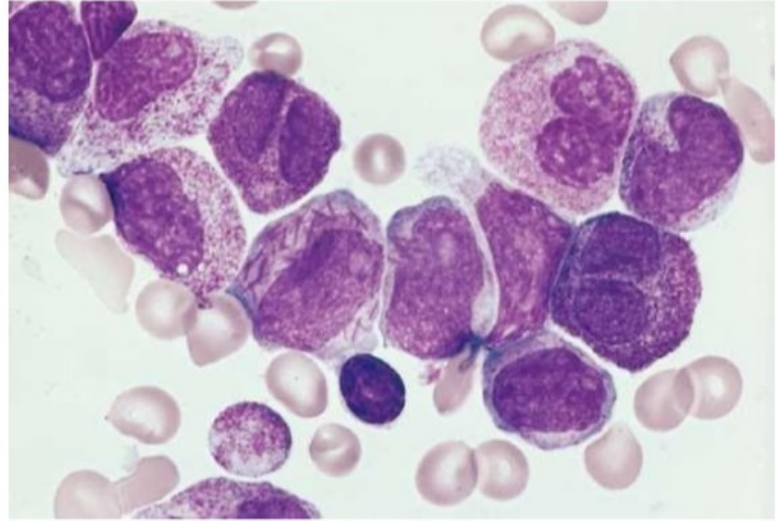
Acute myeloid leukaemia

- **Morphology:** large cells, high N/C ratio, fine granules in cytoplasm, fine chromatin, prominent nucleoli
- **Auer rods:** small pink rods present in cytoplasm, represent peroxidase enzyme
- **Myeloblasts express** CD34, myeloperoxidase (MPO), CD13, CD33
- **Sometimes:** monoblast, erythroblast, megakaryoblast



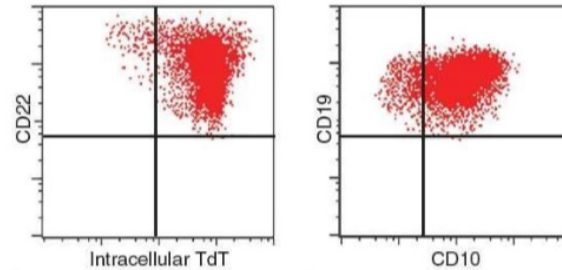
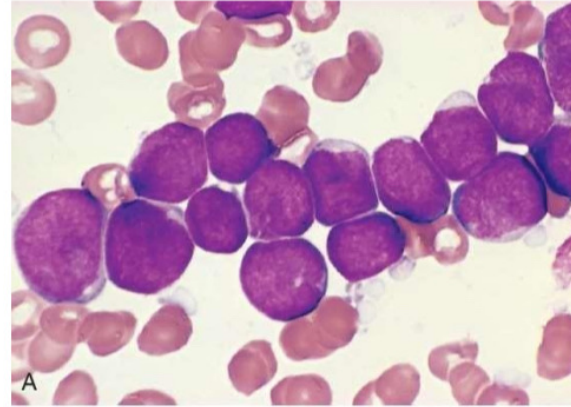
Acute ProMyelocytic Leukemia (APL)

- ✎ APL: malignant promyelocytes show numerous cytoplasmic granules and Auer rods.
- ✎ The nuclei are commonly cleaved.



Precursor B and T cell neoplasm

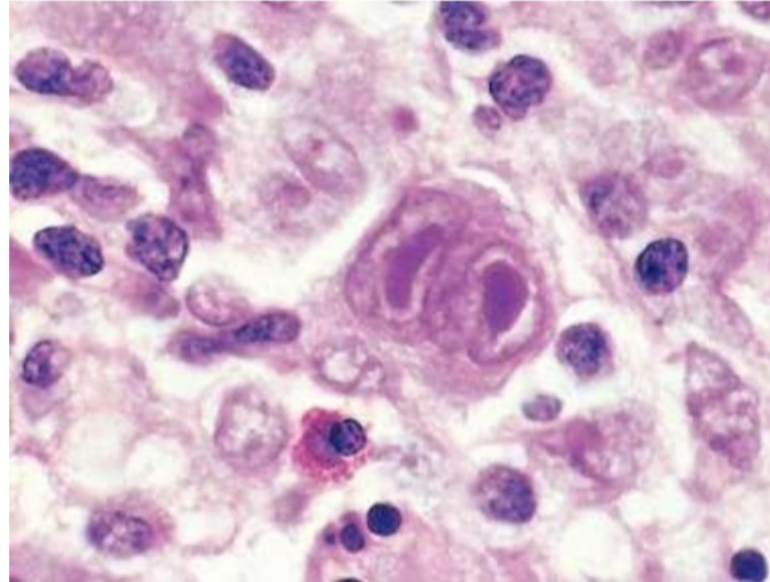
- ✎ Blasts are large, high N/C ratio
- Chromatin is open (pale)
- Nucleolus sometimes present
- Cytoplasm is not granular



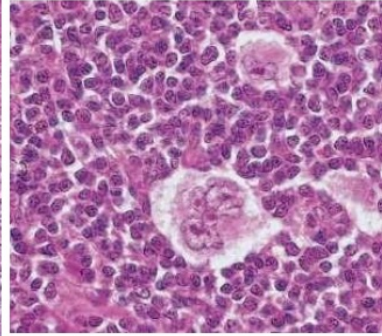
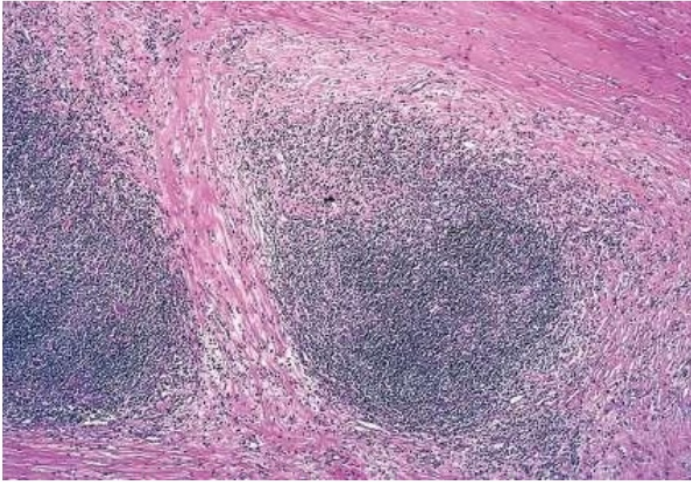
Hodgkin lymphoma

✎ Reed-Sternberg cells: bi or multi-nucleated giant cell, prominent nucleoli, abundant cytoplasm

✎ Hodgkin cells: mononuclear giant cell
Both express CD30 and CD15, and negative for CD20, CD3 and CD45



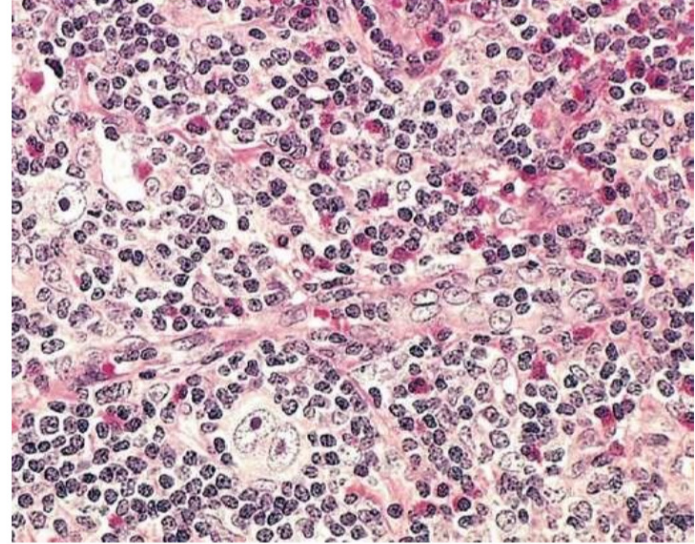
Nodular Sclerosis HL



- ✎ Common in children and young adults
- ✎ Thick fibrous bands separating nodules of lymphocytes
- ✎ RS cells show clear cytoplasm, as a retraction artifact from formalin, called Lacunar cells

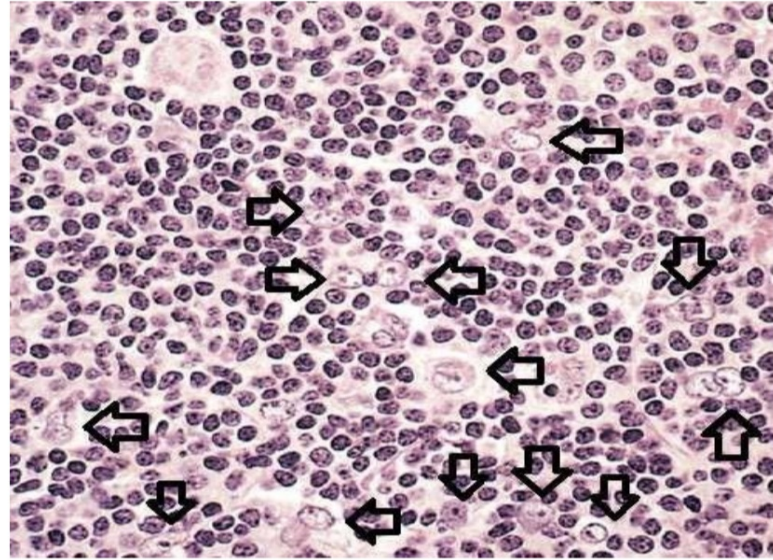
Mixed cellularity HL

- ✎ Common in old people
- ✎ Numerous RS cells
- ✎ Lacks fibrous bands
- ✎ Associated with EBV
- ✎ Background: mixed neutrophils, eosinophils, lymphocytes, plasma cells and histiocytes



Lymphocytic- predominant HL

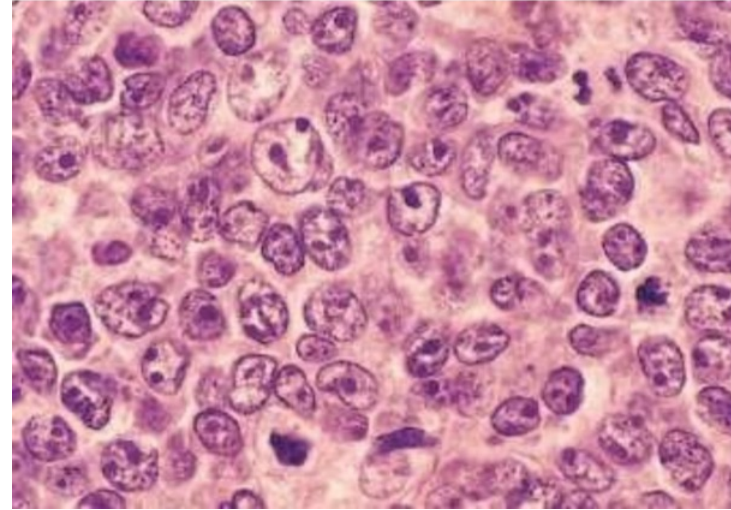
- ✎ Malignant cells are called lymphohistiocyte (L&H) variant RS cell, or simply LP cells
 - ✎ Resemble popcorn (popcorn cells)
 - ✎ Giant cell with multilobated vesicular nuclear lobes and small blue nucleoli
 - ✎ Express normal B-cell markers (CD45, CD20), negative for CD30 and CD15
 - ✎ Background of lymphocytes, arranged in nodules
- ! Excellent prognosis



Popcorn cells 🍿

Diffuse Large B cell Lymphoma

- ✎ Most common NHL
- ✎ Predominantly in adults
- ✎ High-grade (rapidly growing mass)
- ✎ Most common non-cutaneous extranodal lymphoma (GI most common)
- ✎ 2/3 have activating mutation of Bcl6 promotor gene, which is an important regulator of gene expression in germinal center B-cells
- ✎ 30% have t(14;18) (Bcl2 IgH) which results in overexpression of Bcl2 protein (anti-apoptotic)
- !! Few has mutation in MYC gene



- ✎ DLBCL: cells are large (3x normal lymphocytes), irregular nuclei, small nucleoli, frequent mitosis. Positive for CD20

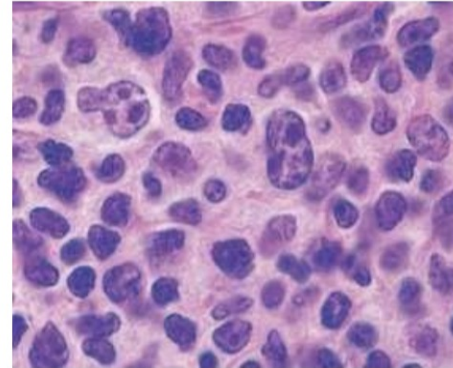
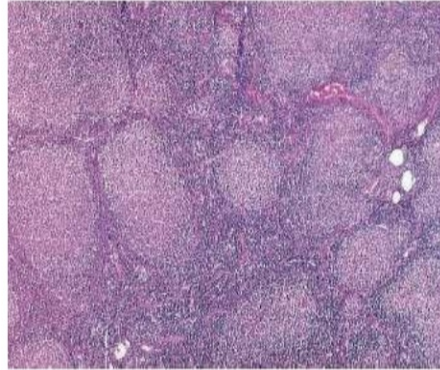
Follicular Lymphoma

- The normal architecture of lymph node is effaced by nodular proliferation (follicles)

- The follicles are composed of small irregular “cleaved” lymphocytes “centrocytes” and large lymphocytes with vesicular nuclei and small nucleoli (centroblasts)

- In most cases, the centrocytes predominate (low-grade). With time, centroblasts increase and the disease becomes high- grade

- Cells express CD20, Bcl2, Bcl6

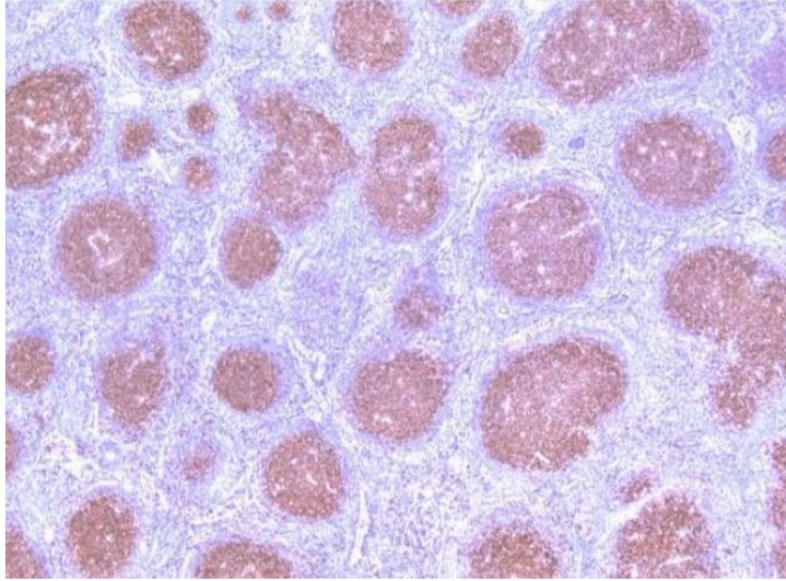


Morphology of FL,

=> **left:** nodular (follicular growth of neoplastic cells effacing the entire lymph node architecture.

=> **Right:** most cells in this field are centrocytes, appear as small dark cells with cleaved nuclei.

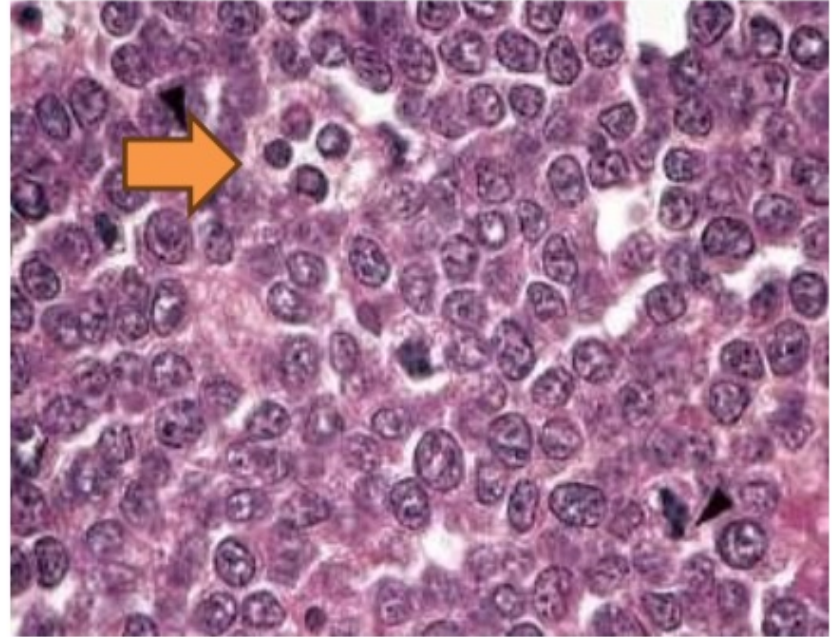
- There are few large cells with multiple nucleoli, corresponding to centroblasts



Bcl2 immunohistochemical stain is positive in follicles in follicular lymphoma

Burkitt lymphoma

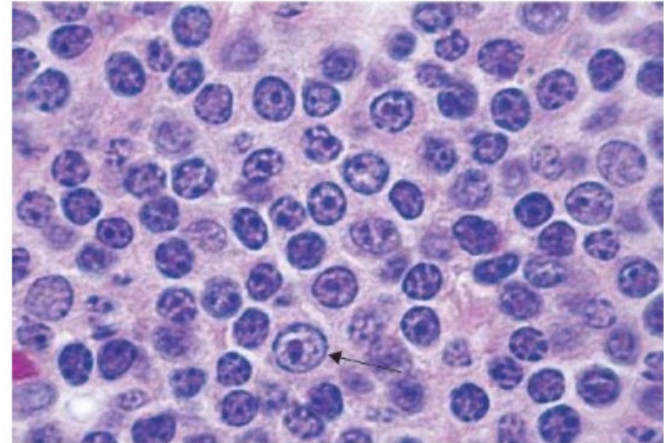
- ✎ Intermediate size cells
- ✎ Monomorphic
- ✎ Round or oval, multiple small nucleoli
- ✎ Lipid vacuoles in cytoplasm
- ✎ Very high mitosis, tingible body macrophages engulfing nuclear debris



Small lymphocytic lymphoma / chronic lymphocytic leukemia

LN shows effacement of architecture

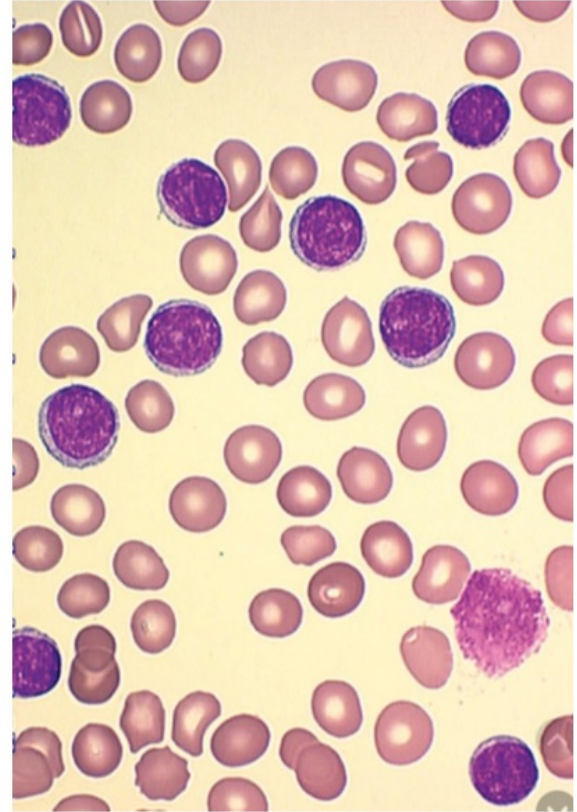
- Most of neoplastic cells are small in size, round, dark chromatin, along with few large cells with central prominent nucleolus (prolymphocyte)
- Proliferation centers: focal areas containing large number of prolymphocytes and increased mitosis



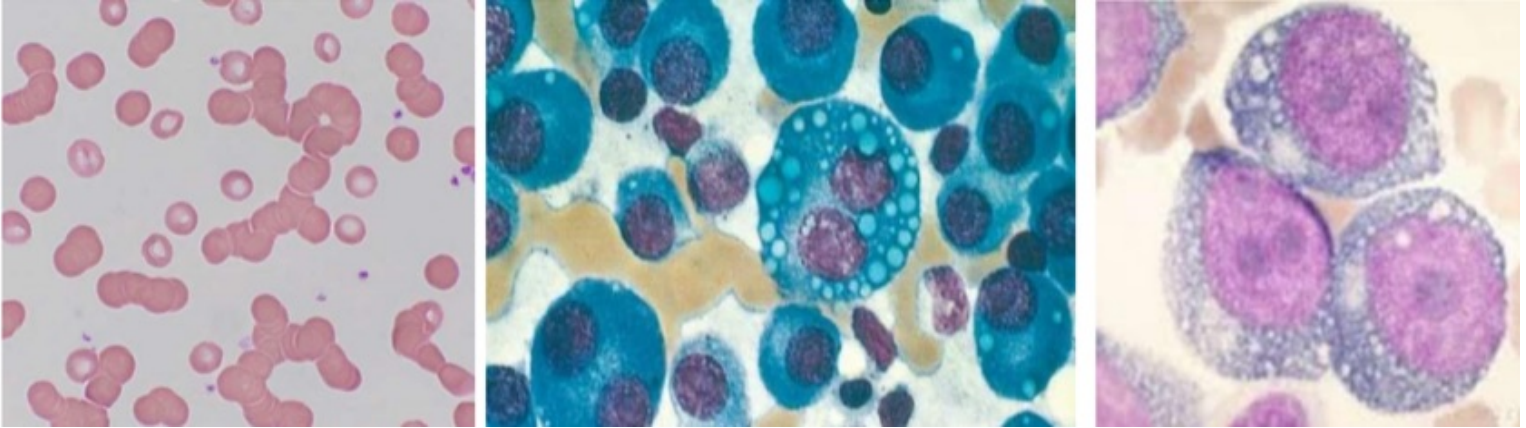
chronic lymphocytic leukemia (CLL) morphology

Leukemic cells appear similar to lymphocytes

- Occasional prolymphocytes
- Smudge cells



Plasma cell Myeloma



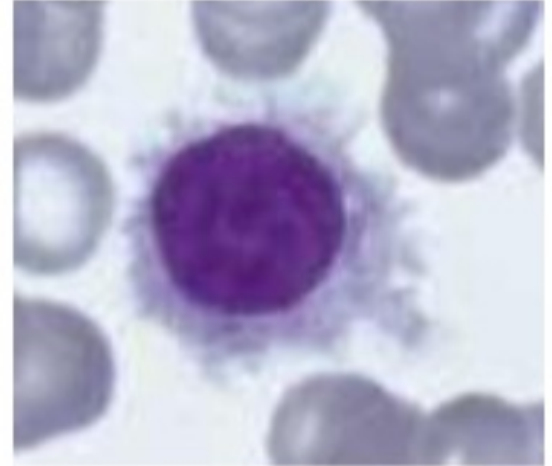
Peripheral blood: RBCs show rouleaux formation

- **BM: increased number of plasma cells (>10% of bone marrow cells)**
- **Morphologically might resemble normal plasma cells, or become abnormal (prominent nucleoli, multinucleation, cytoplasmic vacuoles)**

Hairy cell leukemia

Uncommon low-grade B-cell leukemia

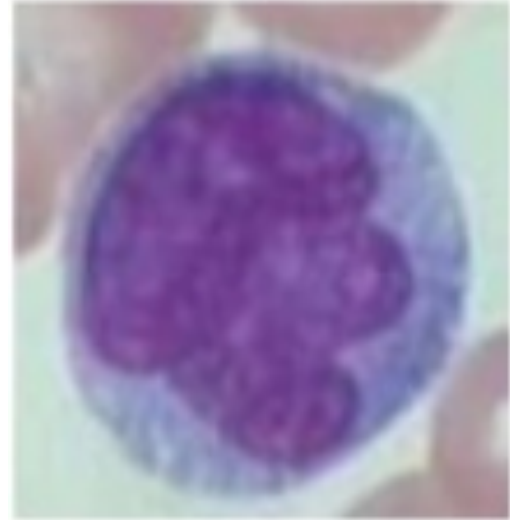
- Affects older patients, more common in men, smokers
- Leukemic cells are few in number, have prominent cytoplasmic projections
- Splenomegaly, pancytopenia (Leukemic cells heavily infiltrate BM and spleen)
- Leukemic cells are biologically active, inhibit hematopoiesis and cause bone marrow fibrosis
- LN involvement is very rare
- Mutation in serine/threonine kinase BRAF gene
- Very sensitive to chemotherapy



Mycosis Fungoides and Sezary Syndrome

Neoplastic CD4+ T-cells, that home to skin

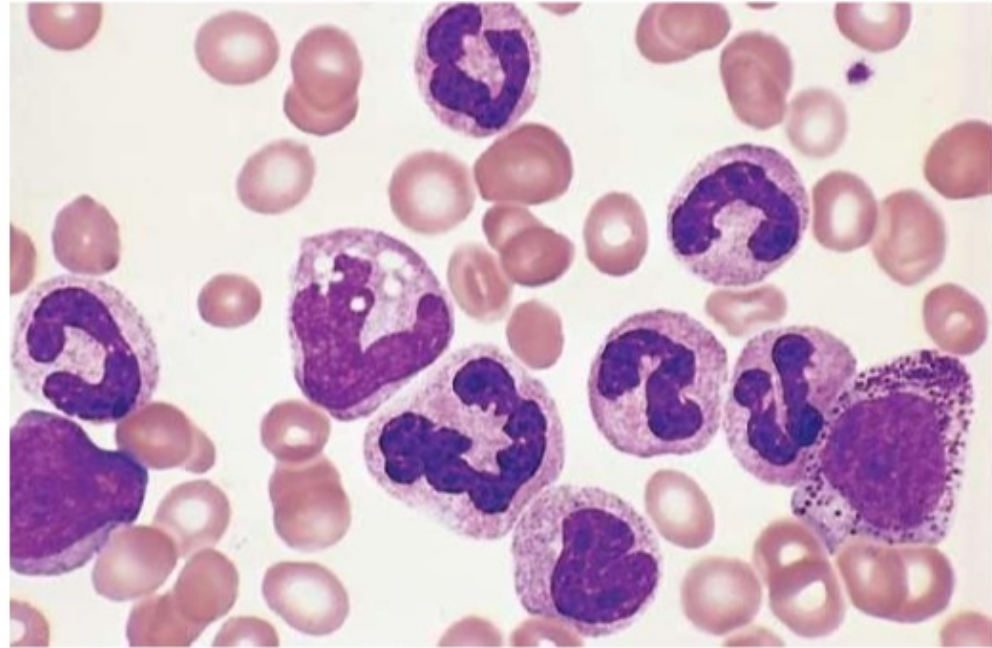
- Patients present with erythema, progressive to plaque then tumor
- Neoplastic lymphocytes have irregular nuclear membrane (cerebriform), affecting epidermis and dermis.
- With disease progression, lymphoma disseminates to LNs and viscera
- Sezary syndrome: a variant of MF, patients present initially with widespread erythema and blood leukemia of neoplastic cells (Sezary cells)



Chronic Myeloid Leukemia (CML)

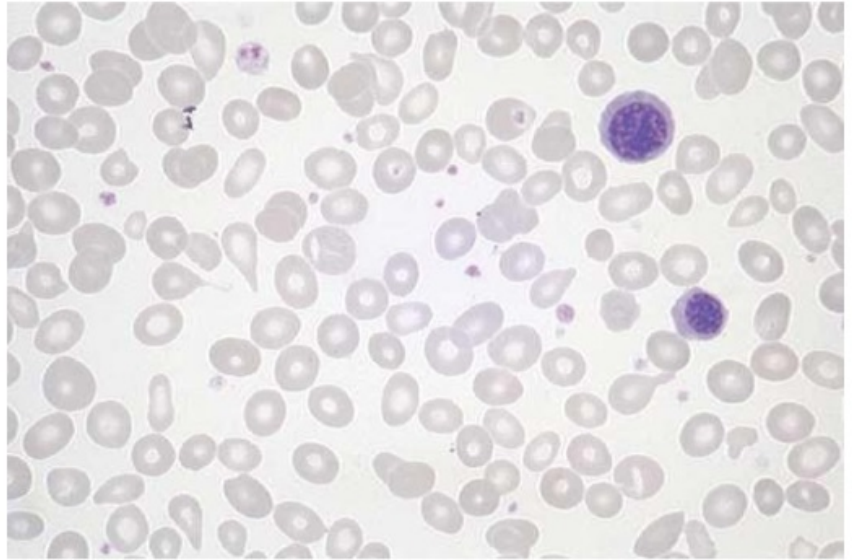
Leukocytosis, can be >100K

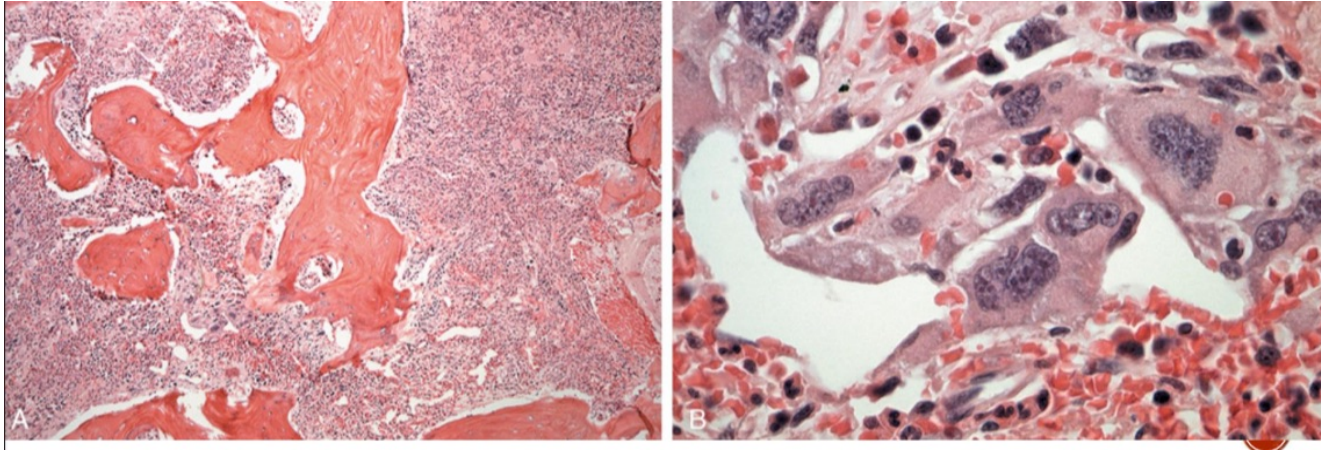
- Shift to left
- Basophilia, eosinophilia
- Thrombocytosis
- Anemia
- BM: increased myeloid and megs
- Spleen: EMH
- Blasts: low
- Leukemoid reaction: high WBC and shift to left, occurs in severe inflammation



Primary Myelofibrosis (PMF)

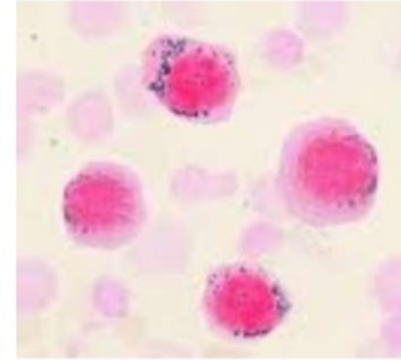
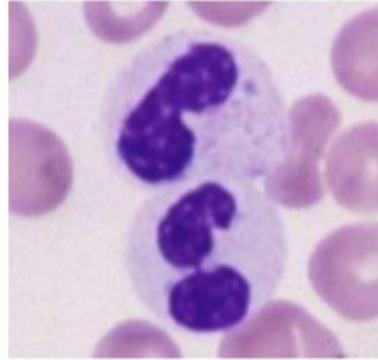
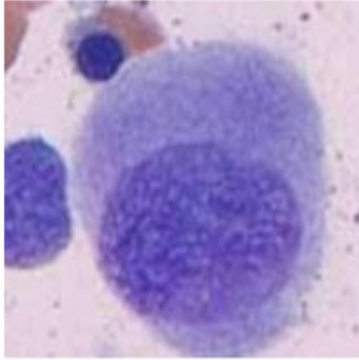
- ✎ Peripheral blood: tear-drop cells, nucleated RBCs, shift to left (leukoerythroblastic anemia)
- WBC: can be normal or increase
 - Plt: high, then low





PMF: left: hypercellular and thick bone trabeculae, right: clusters of abnormal megakaryocytes with large and hyperchromatic “cloud-like” nuclei.
Note the dilated sinusoid !

MyeloDysplastic Syndrome



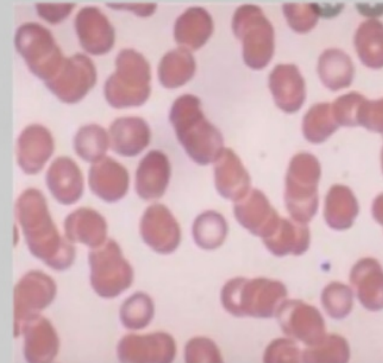
- ✎ Erythroid: macrocytic anemia, megaloblastoid nuclei, ring sideroblasts (iron accumulation inside mitochondria)
- Myeloid: decreased granulation, hyposegmented nuclei of neutrophils
- Megkaryocytes: small, hypolobated nuclei
- Myeloblasts: can be increased, but <20% of nucleated cells

Past paper questions



198. All of the following are seen in the disease that causes this feature in blood sample except?

- A. Hypercalcemia
- B. Amyloidosis
- C. Renal failure
- D. Bone fractures
- E. Plasma cells are less than 5% of bone marrow cells.

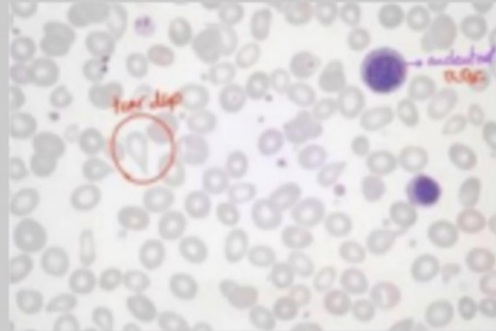


ANSWER : E

199. all of these seen in a disease that causes the morphology in the picture, expect:

- A. JAK2 mutation
- B. Shift to the left Neutrophils
- C. Mild splenomegaly
- D. Thrombocytopenia
- E. Anemia

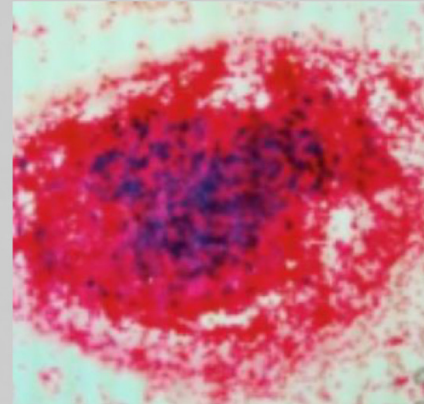
ANSWER : C



197. All of the following are helpful, but which one is not effective in diagnosing?

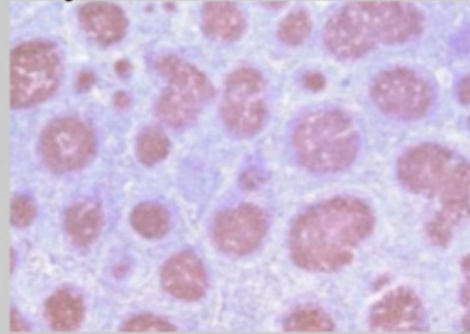
- A. Elevated HgA2
- B. Decrease in ferroportin
- C. Increase hepcidin level
- D. High TIBC (total iron binding capacity)
- E. Long history of cancer

ANSWER : A



200. This morphology indicates disease that is known by:

- A. The presence of follicular proliferation
- B. The presence of centroblasts and centrocytes
- C. CD34
- D. The presence of jak2 Mutation
- E. In early stages it is high grade



ANSWER : B