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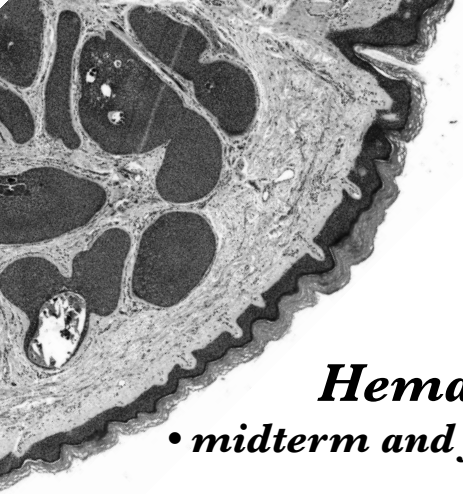
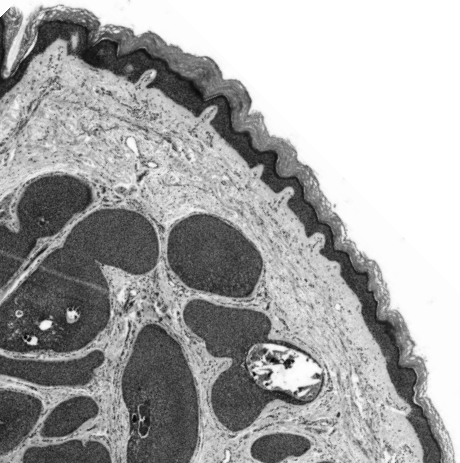
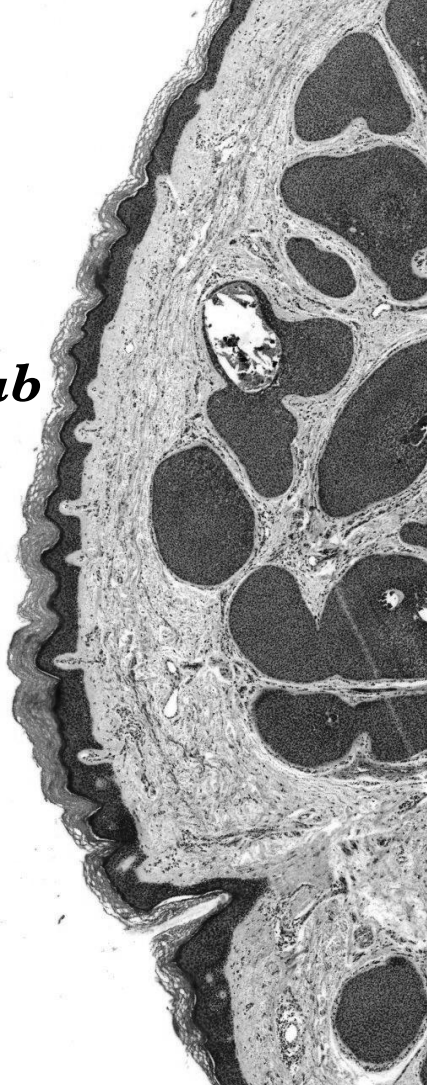


Hematolymphatic System pathology lab

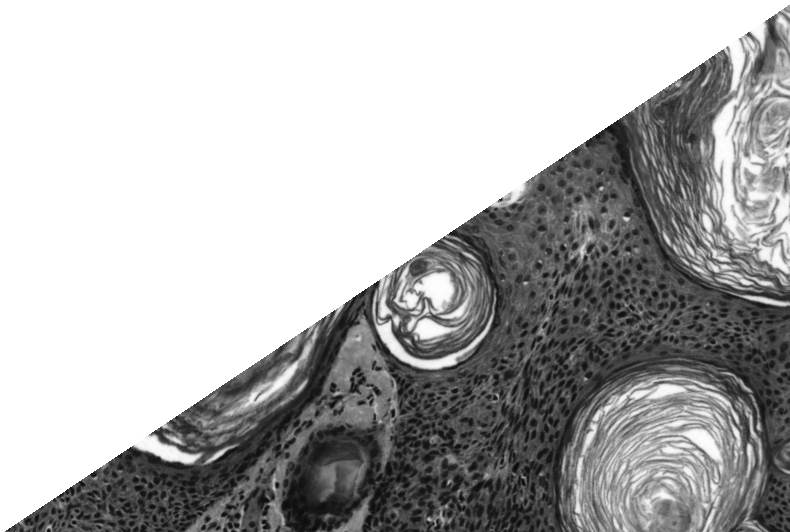
- *midterm and final material*

Written By : Reenas Al Khresat

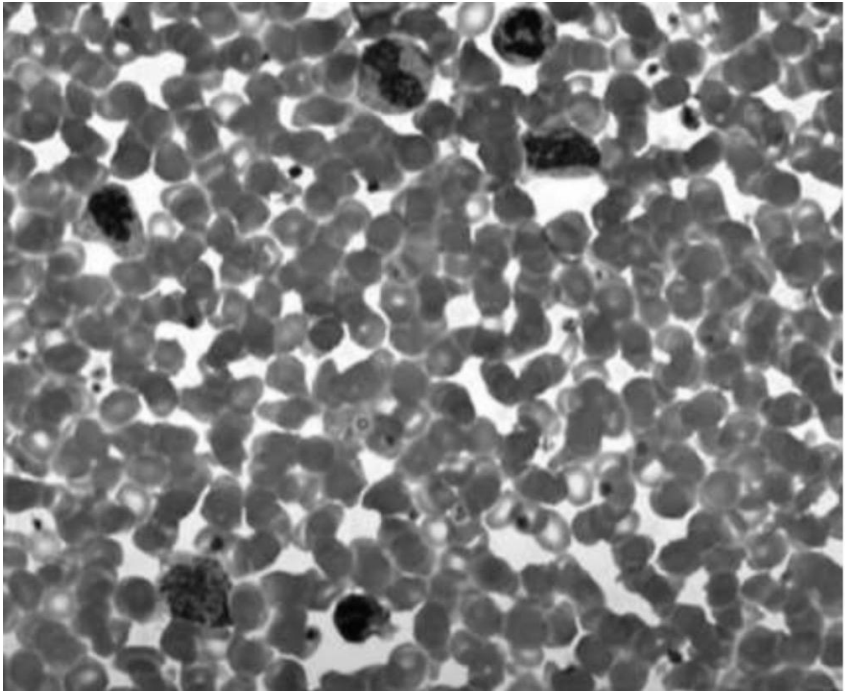




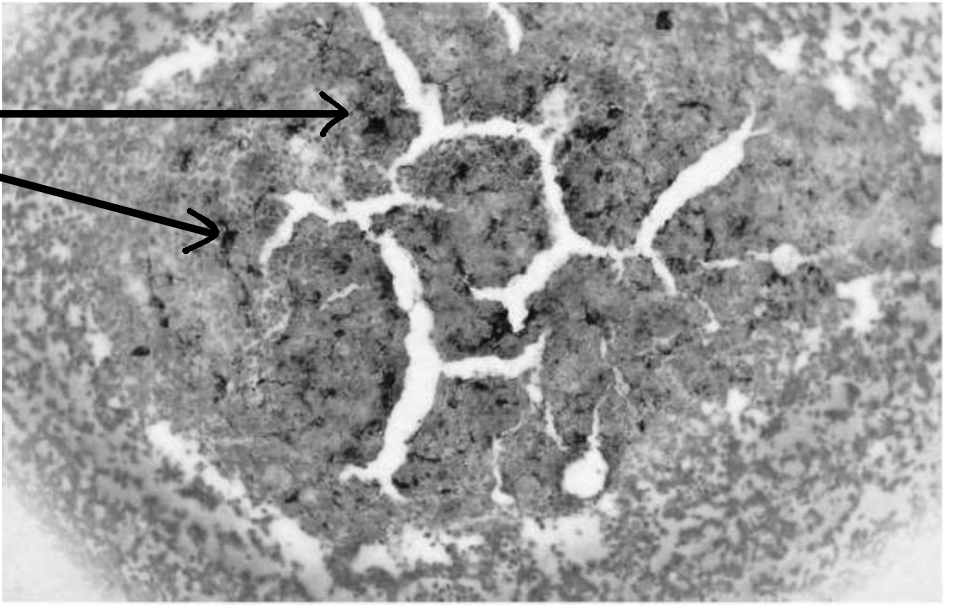
Midterm material



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



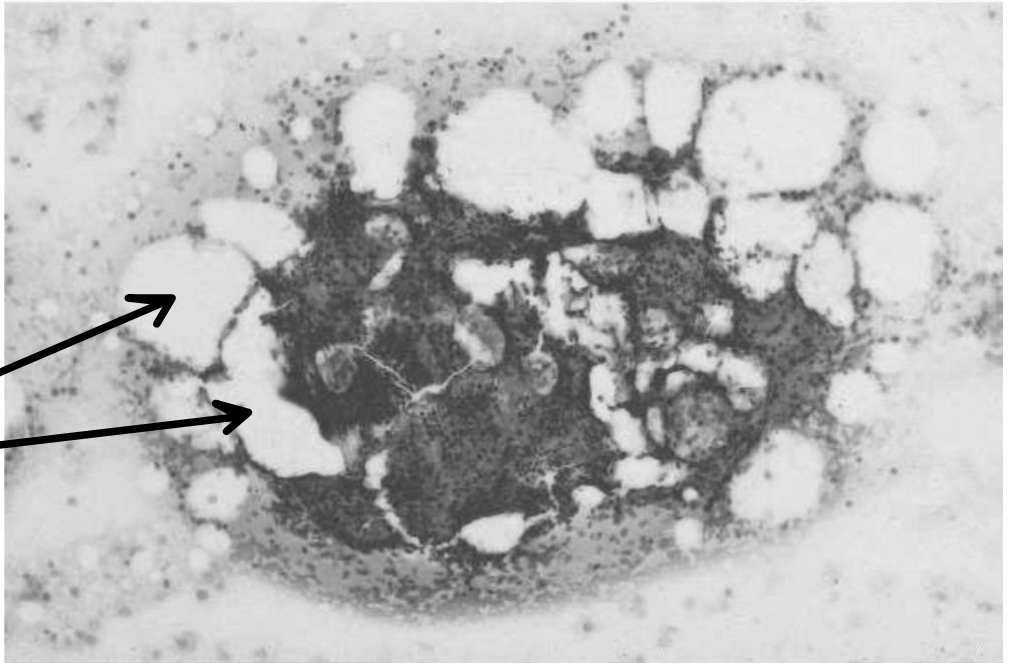
✎ Aspirate of normal bone marrow: bluish-black iron (haemisderin) in macrophages in a fragment .



✎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 .

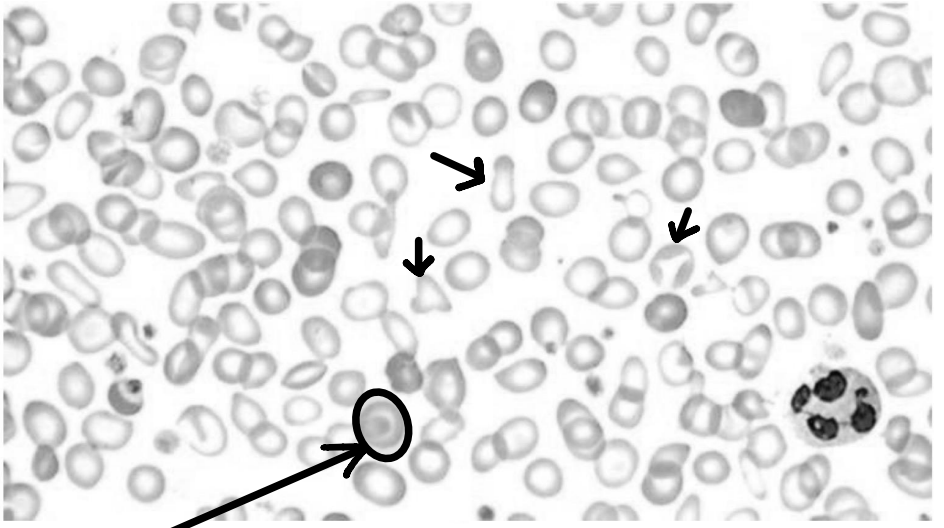
✏️Aspirate of normal bone marrow: a fragment with no stainable iron (Perl's stain)

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

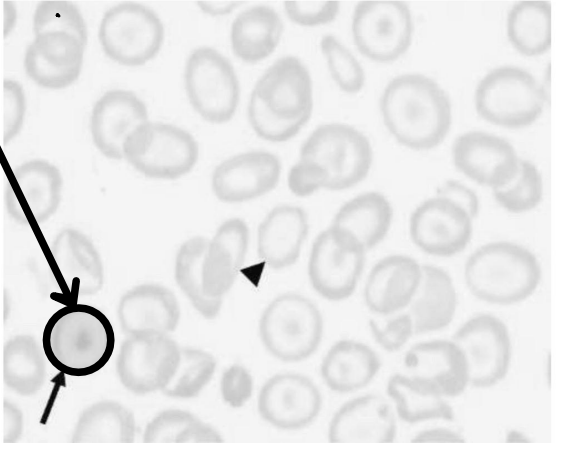


✎IDA: note the hypochromia and poikelocytosis , RBC is small and pale(large central pale area >1/3)

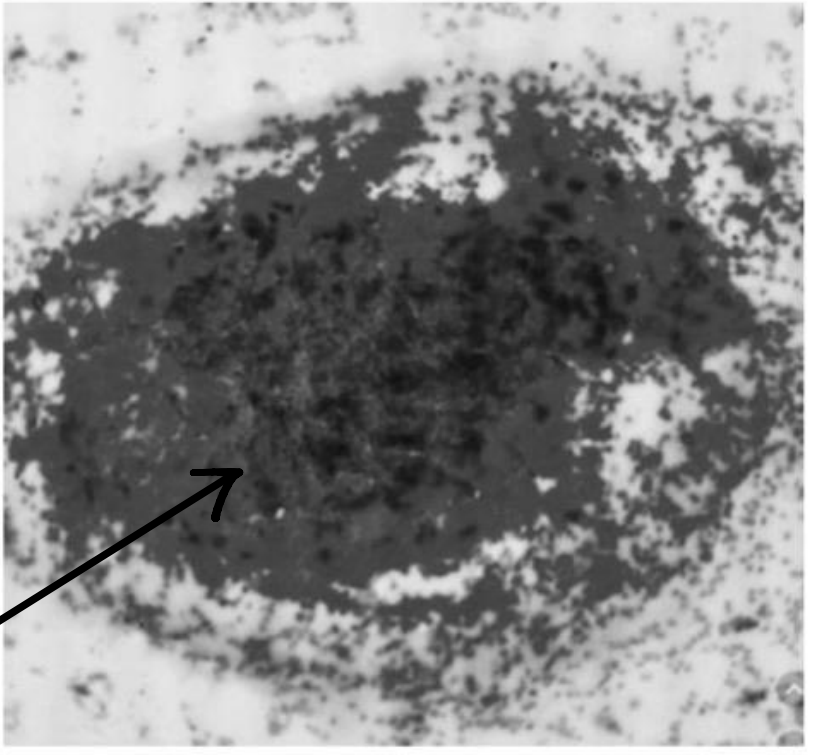
✎poikelocytosis Small and elongated



✎Target cell has red dot inside RBCs



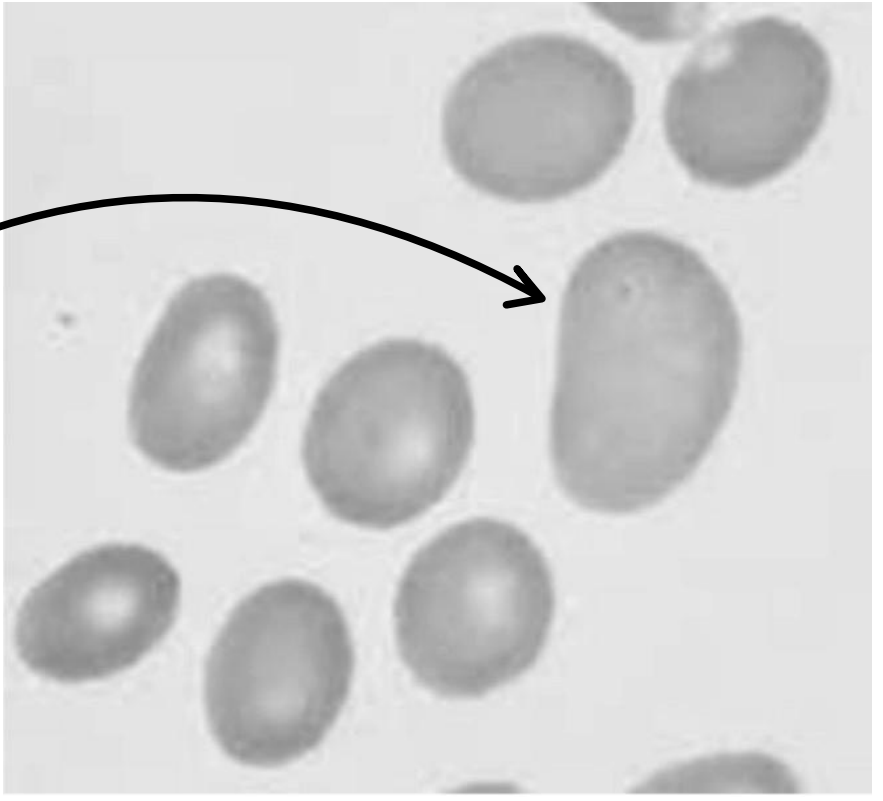
Anemia of chronic inflammation



- 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.

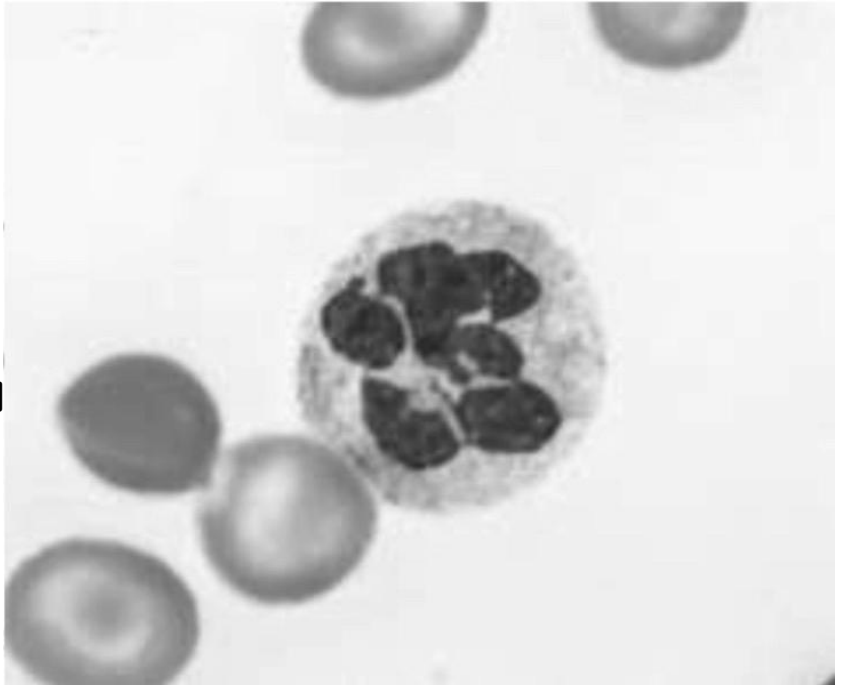
- Note the blue granular material (hemosiderin)

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.

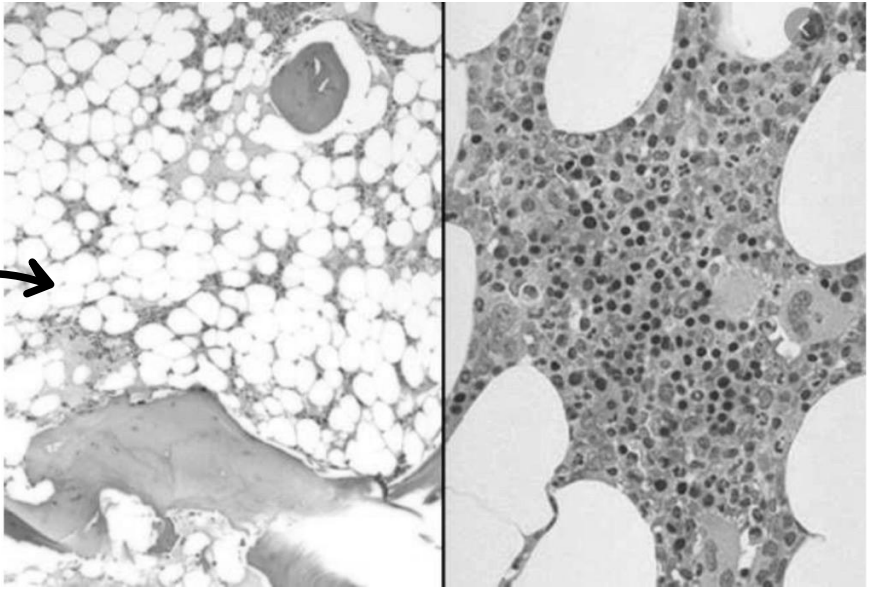


Aplastic Anemia

Damage to multipotent stem cell in bone marrow

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

Normal bonemarrow and stem cells

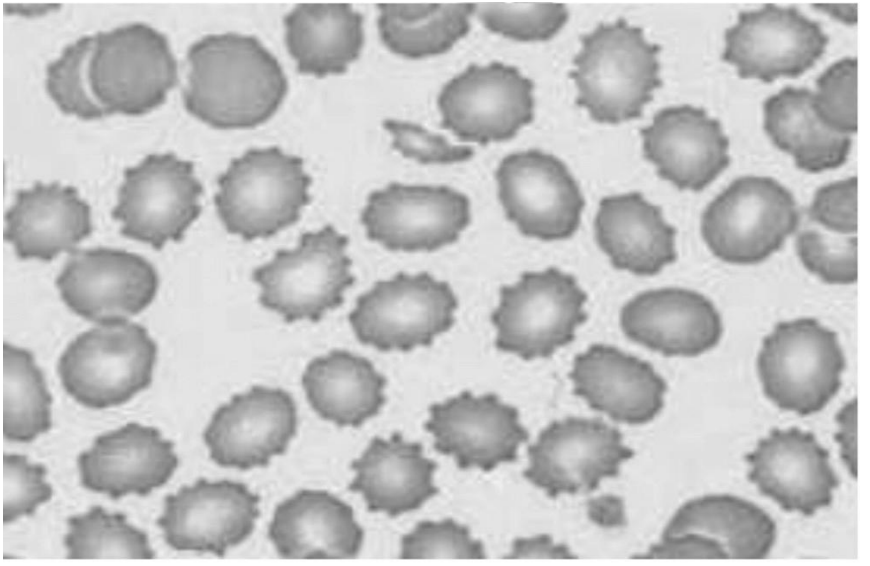


Fat accumulation

Anemia of renal disease

🔪Decreased erythropoietin production from kidneys

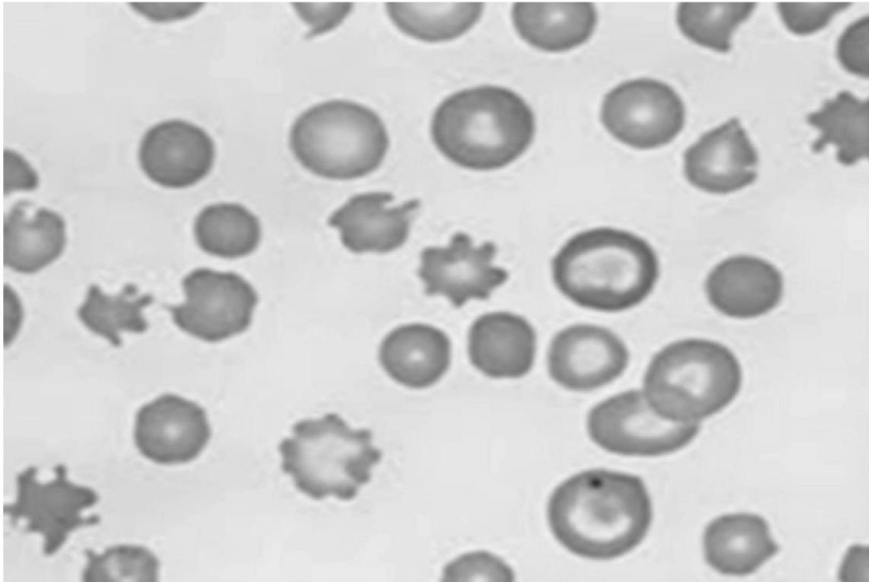
- Does not correlate well with kidney function (serum creatinine)
- Decreased RBC production (low reticulocytes count)
- Patients with uremia develop abnormal platelets function (bleeding), echinocytes (Burr cells) appear



Anemia of liver disease

🔪Multiple factors causing anemia

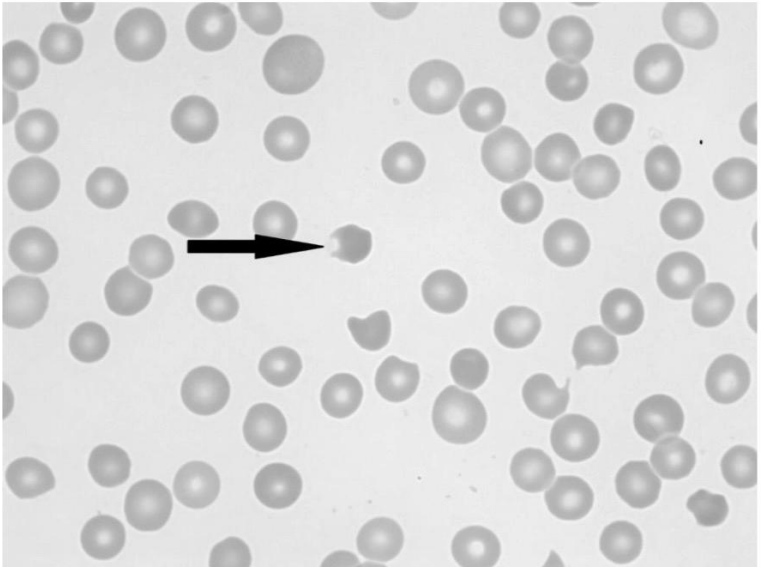
- Decreased synthesis of clotting factors (bleeding)
- Bleeding from varices
- Decreased synthesis of transferrin
- Acanthocyte (spur cell) appears



G6PD DEFICIENCY

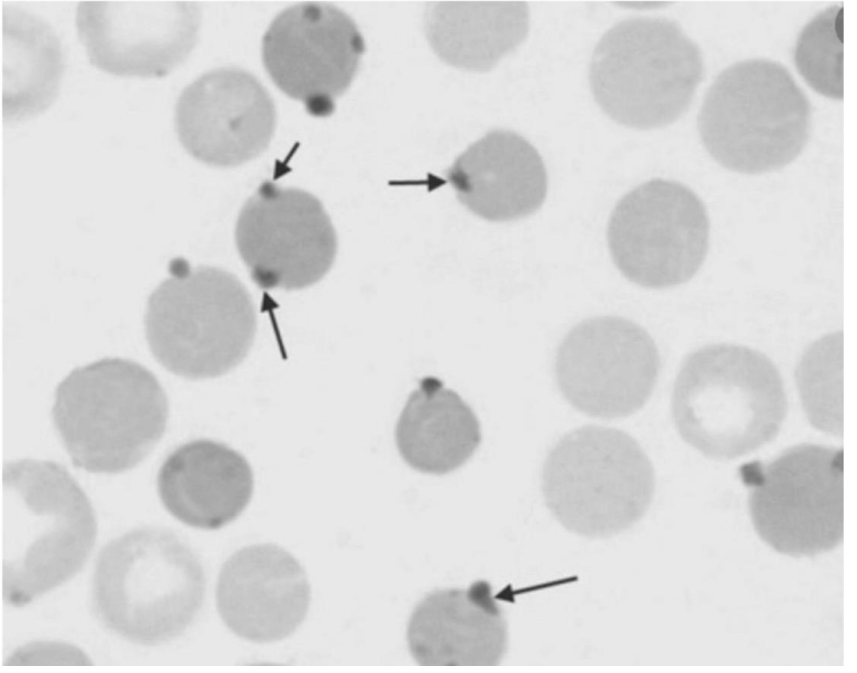
✏️In all, large numbers of oxidants are generated, G6PD cannot neutralize them, causing hemoglobin denaturation and precipitate (Heinz bodies), damaging cell membrane and massive hemolysis of RBCs, 2-3 days after trigger

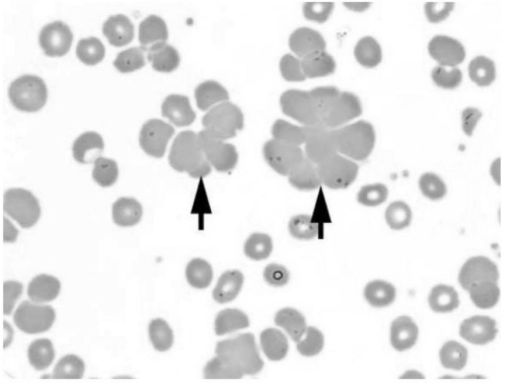
- Other cells lose demorfmability and partially phagocytosed inside spleen (bite cells)

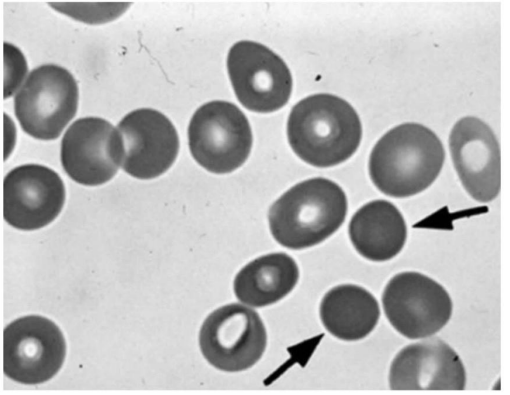


✏️Bite cells: appears are indented defect in part of cell membrane of RBCs

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



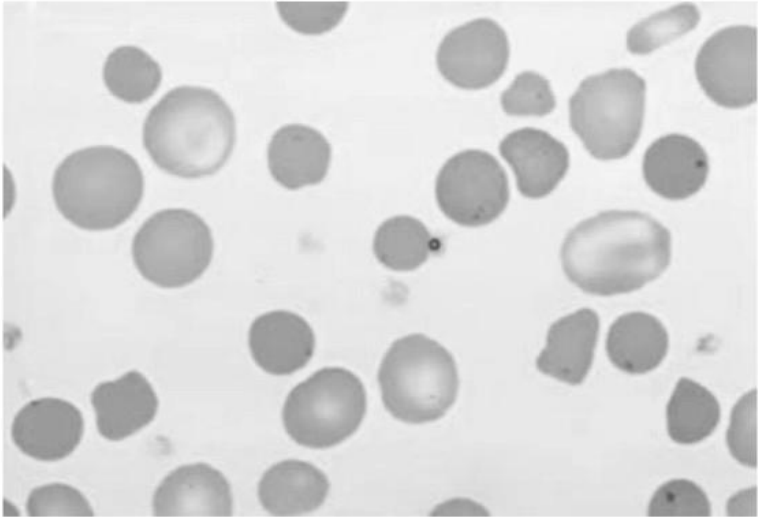




- Left: RBC agglutination: RBC clumps in different directions
- Right: spherocytes appear as small, round hyperchromatic RBC

HEREDITARY SPHEROCYTOSIS

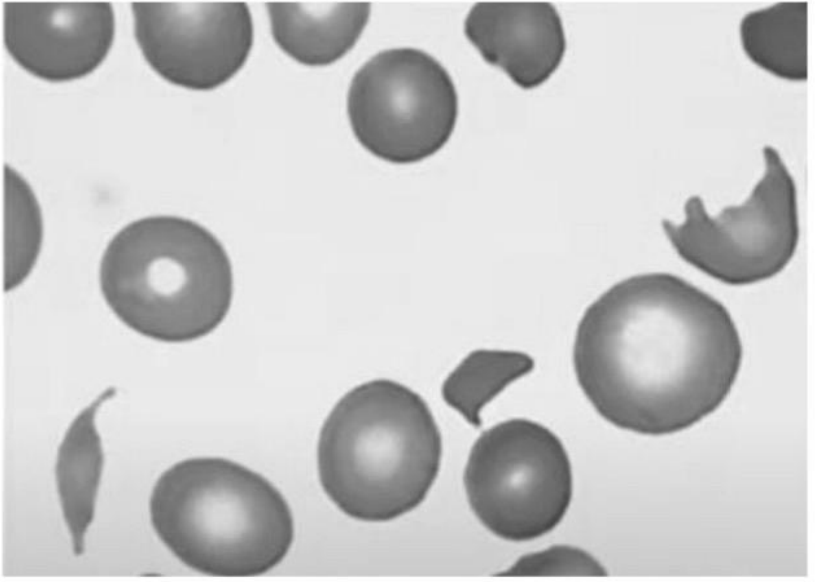
🔪Autosomal Dominant, sometimes recessive
• Mutation is RBC cell membrane skeleton
• Most commonly affects ankyrin, band 3 or spectrin
• Cell membrane becomes unstable, keeps losing parts of it as the RBC age
• Little amount of cytoplasm is lost
• With decreasing surface area, the RBC loses it normal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



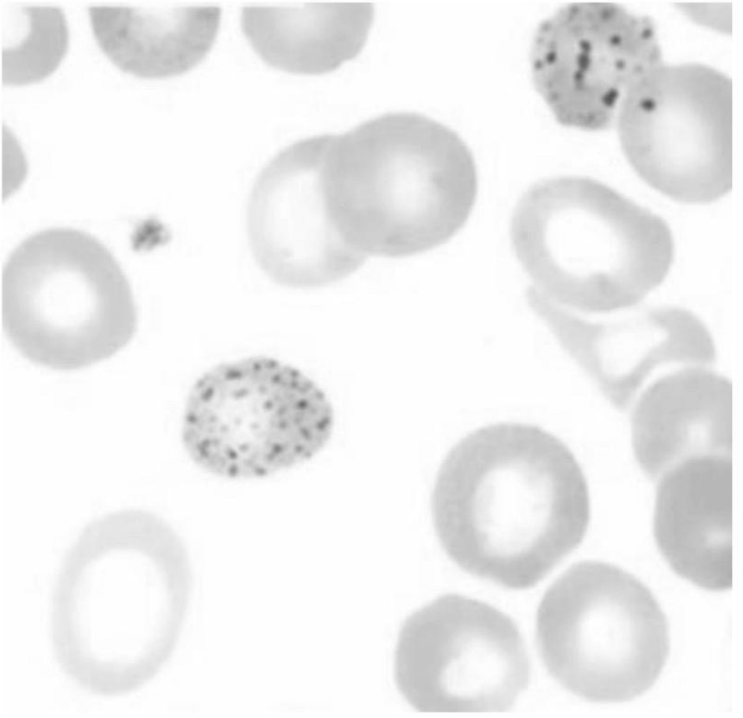
🔪Appearance of spherocytes in peripheral blood
• Spherocytes have a smaller size (low MCV)
• Little cytoplasm is lost, normal amount of Hg (normal MCH)
• MCHC is increased⬆️
• Spherocytes show increased fragility ⬆️when put in hypotonic solution (increased⬆️osmotic fragility)

🔪**TRAUMATIC HEMOLYSIS**

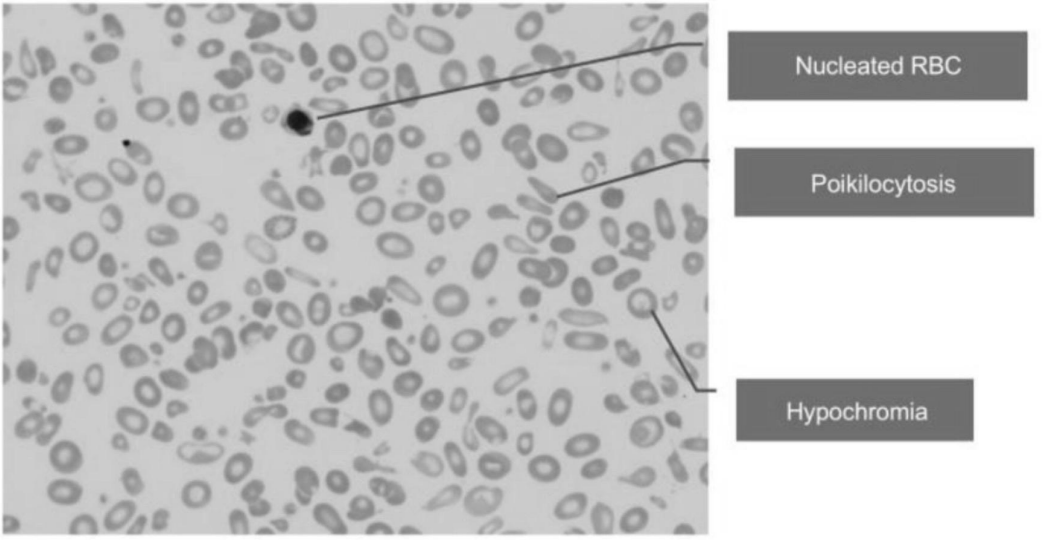
- **Direct physical force, or turbulence causing lysis of RBCs**
- **Prosthetic heart valves**
- **Repetitive physical pounding (marathon, boxing, marching)**
- **Disseminated thrombi (microangiopathic hemolytic anemia)**
- **Hallmark of traumatic hemolysis: schistocytes**



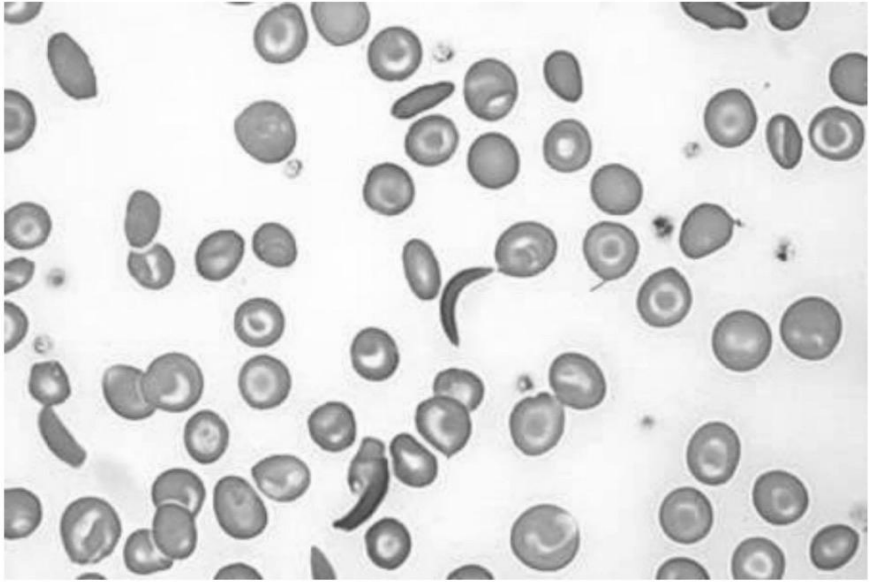
BASOPHILIC STIPPLING OF RBCS



✏️**Blue dots ⚫ are residual ribosomes that appear in the thalassemia**


Nucleated RBC
Poikilocytosis
Hypochromia

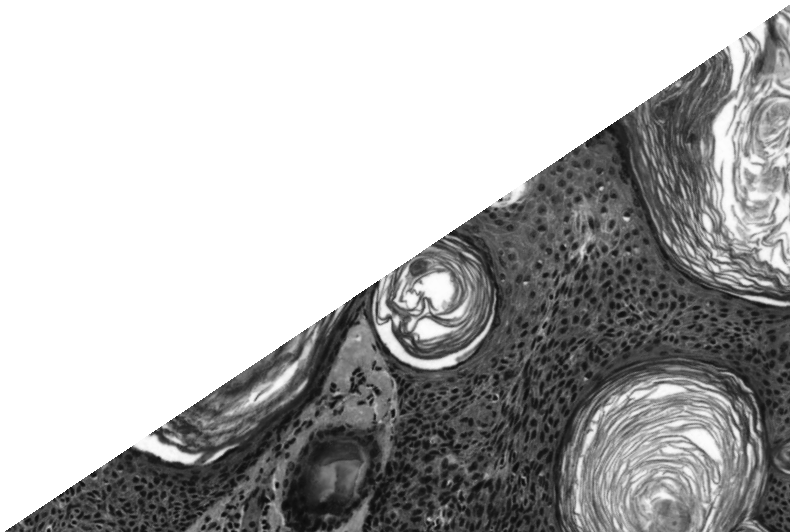
SICKLE CELL ANEMIA



✏️Routine blood smear: presence of sickle cells, target cells

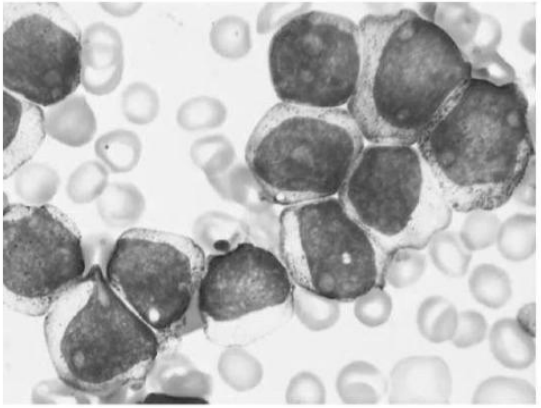
- Sickling test: adding hypoxic agent to RBCs promote sickling
- Hemoglobin electrophoresis
- In sickle cell trait, Blood smear is normal

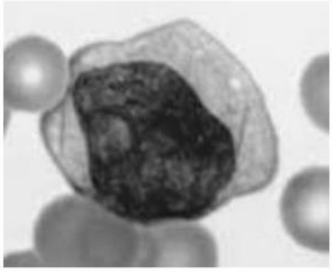
Final material



Acute myeloid leukaemia

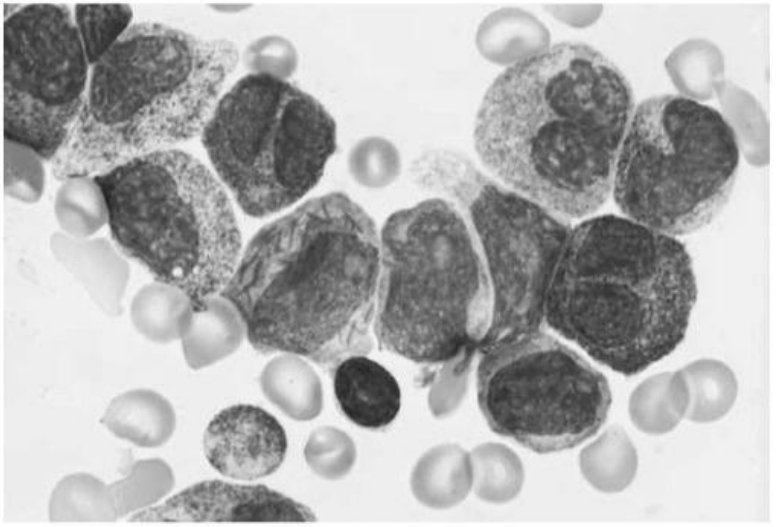
- Morphology: large cells, high N/C ration, fine granules in cytoplasm, fine chromatin,
prominent nucleoli
- Auer rods: small pink rods present in cytoplasm, represent peroxidase enzyme
- Myeloblasts express CD34, myeloperoxidase (MPO), CD13, CD33
- Sometimes: monoblast, erythroblast, megakaryoblast





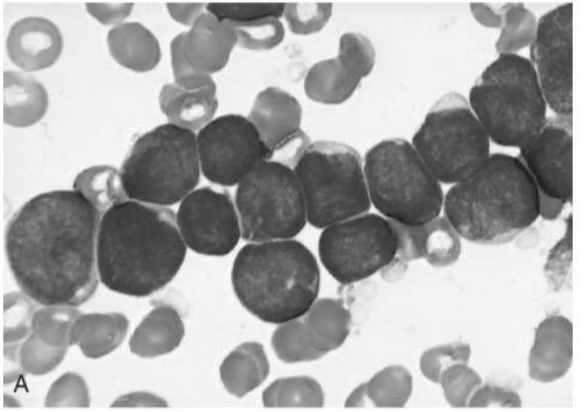
Acute ProMyelocytic Leukemia (APL)

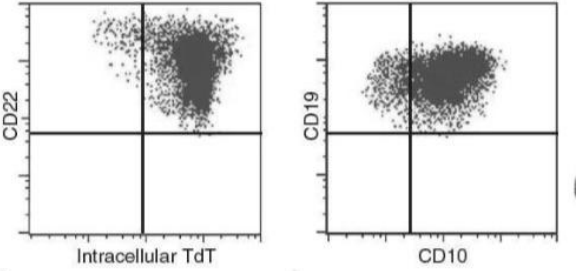
✏️APL: malignant promyelocytes show numerous cytoplasmic granules and Auer rods.
✏️The nuclei are commonly cleaved.



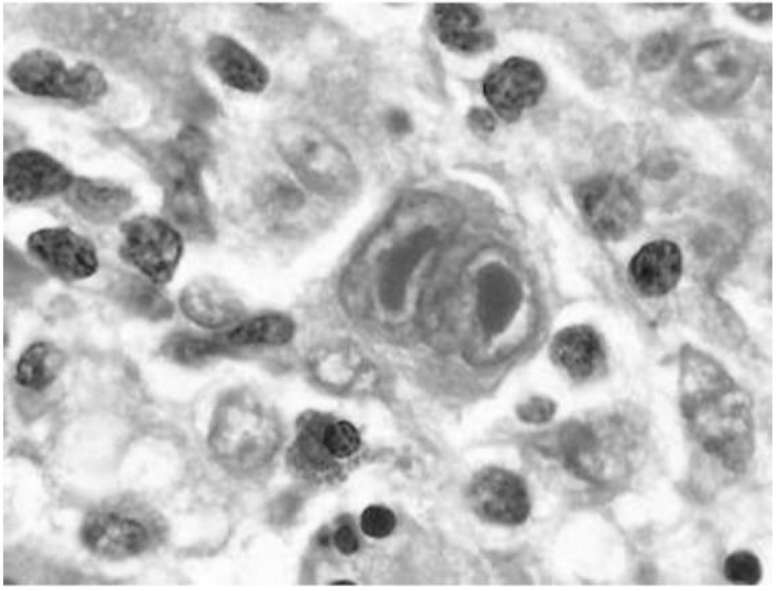
Precursor B and T cell neoplasm

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



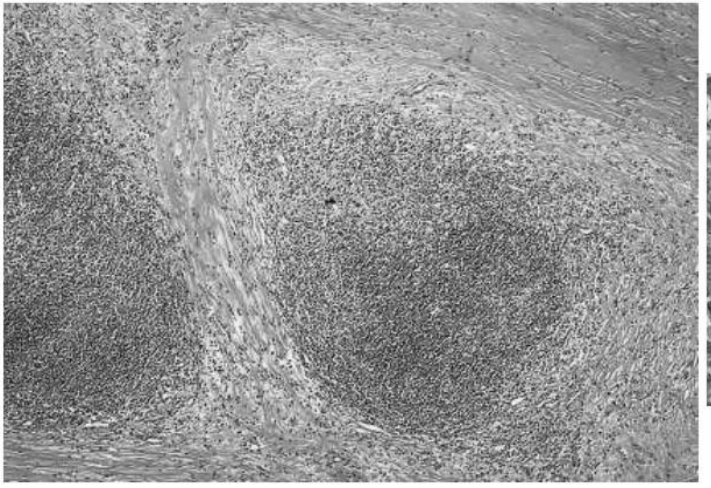


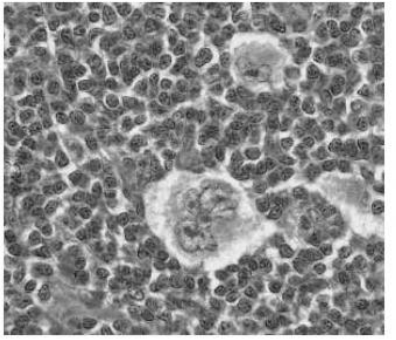
Hodgkin lymphoma



✏️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

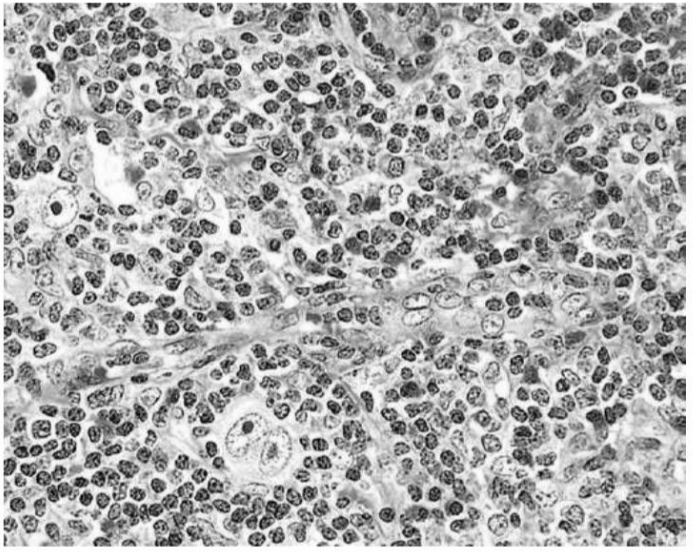




- Common in children and young adults
- Thick fibrous bands separating nodules of lymphocytes
- RS cells show clear cytoplasm, as a retraction artifact from formalin, called Lacunar cells

Mixed cellularity HL

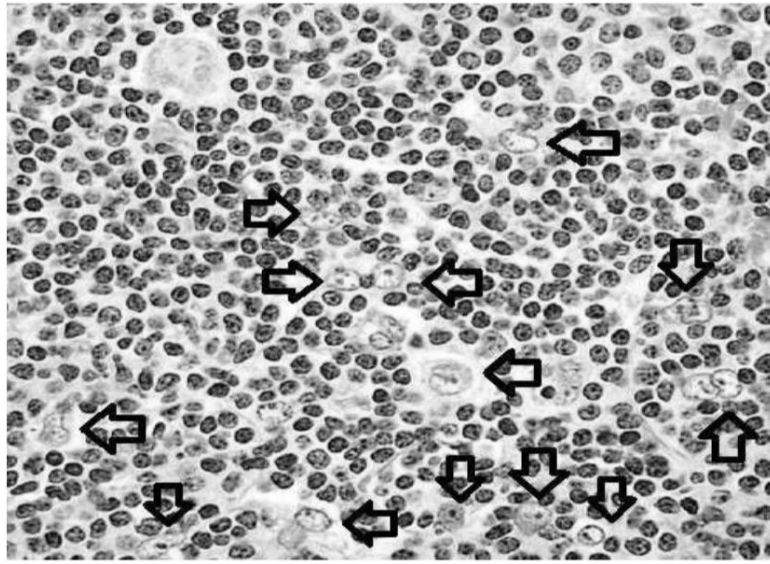
- Common in old people
- Numerous RS cells
- Lacks fibrous bands
- Associated with EBV
- Background: mixed neutrophils, eosinophils, lymphocytes,plasma cells and histiocytes



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

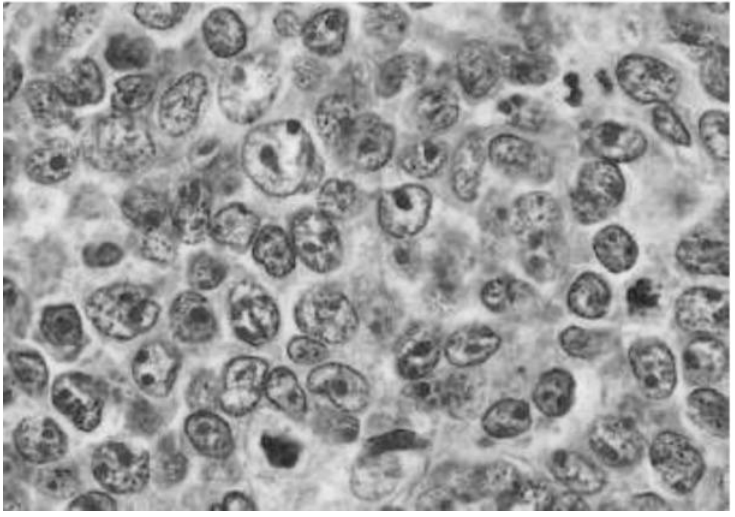
! Excellent prognosis



Popcorn cells

Diffuse Large B cell Lymphoma

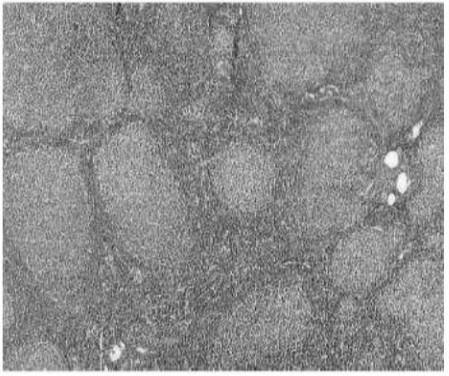
- Most common NHL
- Predominantly in adults
- High-grade (rapidly growing mass)
- Most common non-cutaneous extranodal lymphoma (GI most common)
- 2/3 have activating mutation of Bcl6 promotor gene, which is an important regulator of gene expression in germinal center B-cells
- 30% have t(14;18) (Bcl2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

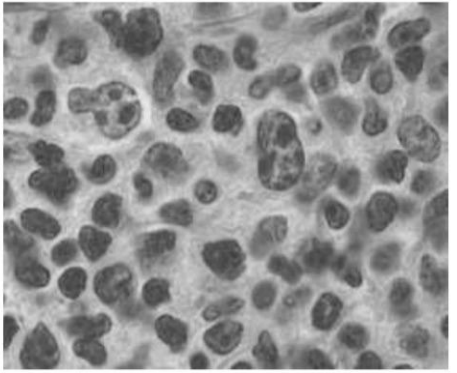


- DLBCL: cells are large (3x normal lymphocytes), irregular nuclei, small nucleoli, frequent mitosis. Positive for CD20

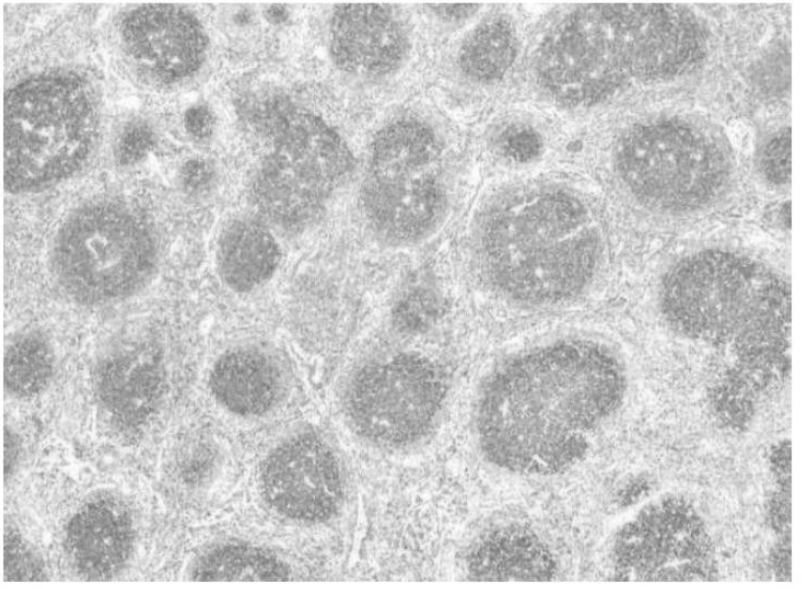
Follicular Lymphoma

- 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





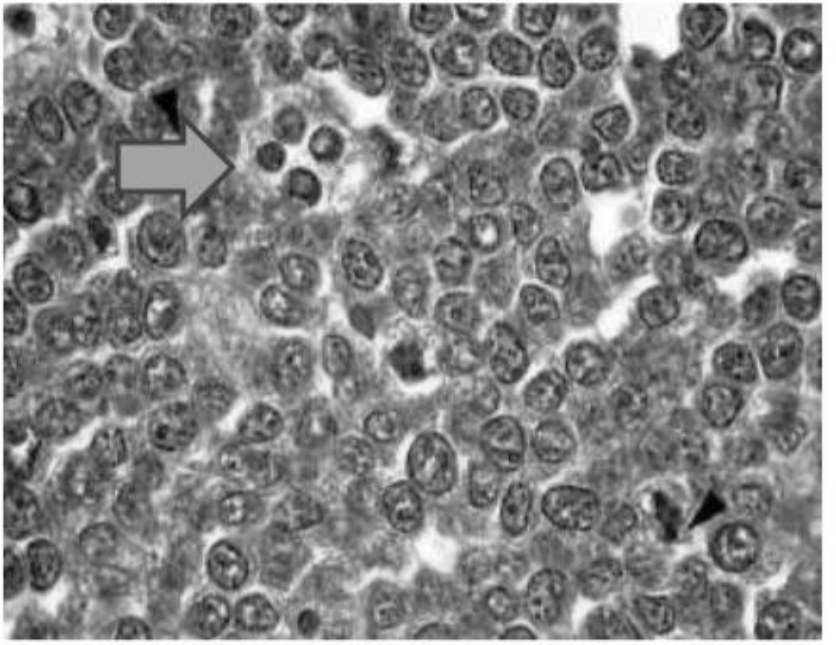
Morphology of FL,
=> left: nodular (follicular growth of neoplastic cells effacing the entire lymph node architecture.
=> Right: most cells in this field are centrocytes, appear as small fark cells with cleaved nuclei.
• There are few large cells with multiple nucleoli, corresponding to centroblasts



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

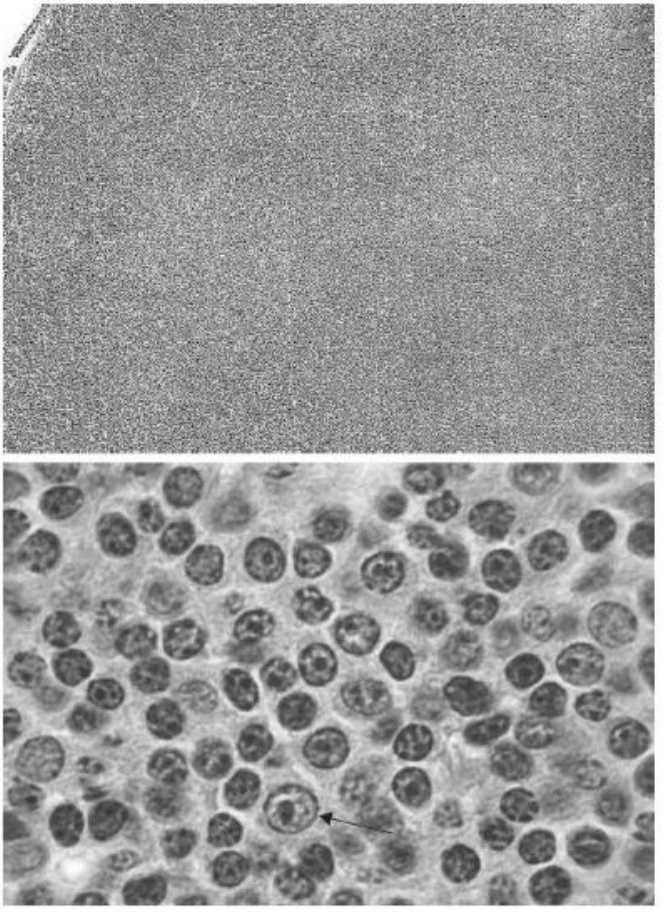
LN shows effacement of architecture

- Most of neoplastic cells

are small in size, round, dark chromatin, along with few large cells with central prominent nucleolus (prolymphocyte)

- Proliferation centers: focal

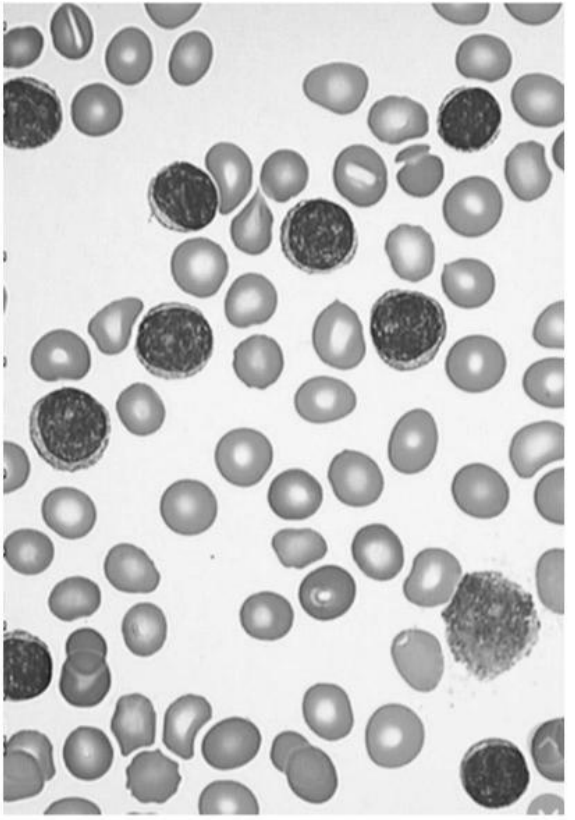
areas containing large number of prolymphocytes and increased mitosis



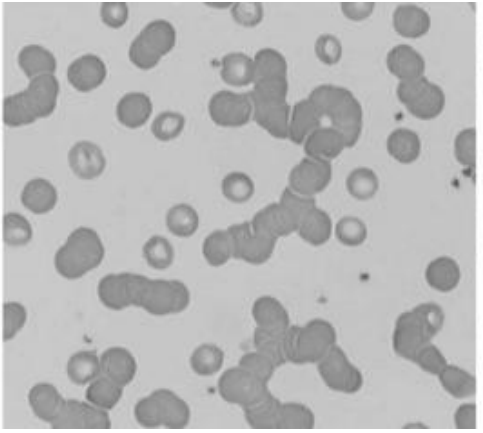
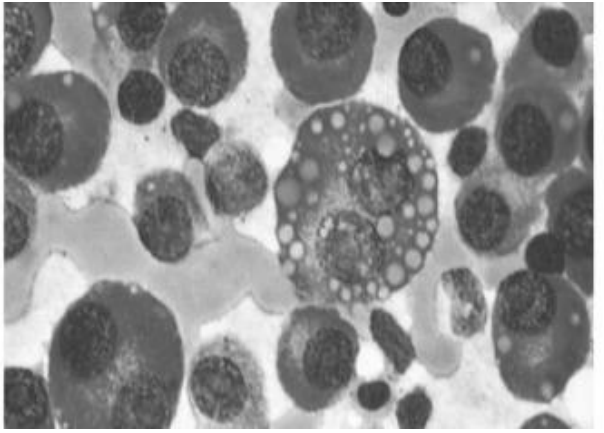
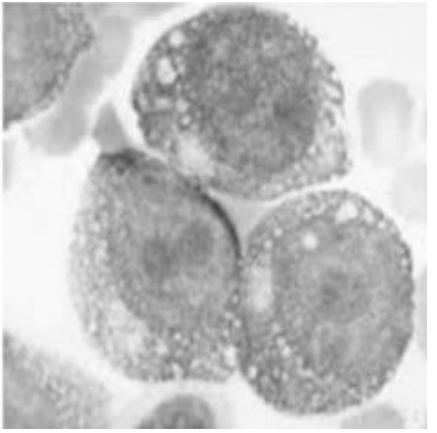
chronic lymphocyticl leukemia (CLL)morphology

Leukemic cells appear similar to lymphocytes

- Occasional prolymphocytes
- Smudge cells



Plasma cell Myeloma

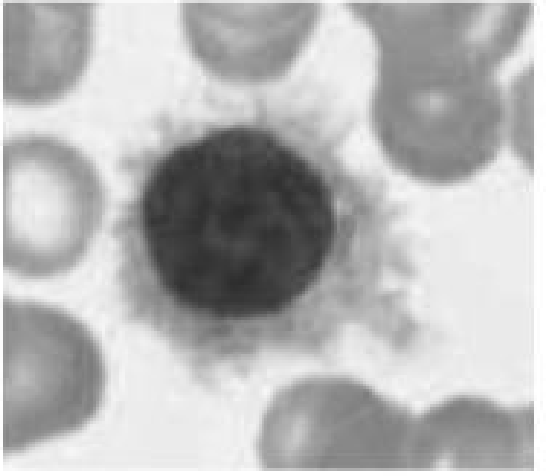
Peripheral blood: RBCs show rouleaux formation

- 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

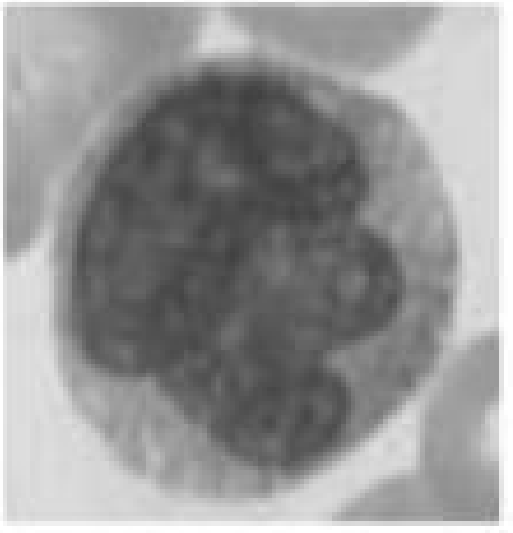
- Affects older patients, more common in men, smokers
- Leukemic cells are few in number, have prominent cytoplasmic projections
- Splenomegaly, pancytopenia (Leukemic cells heavily infiltrate BM and spleen)
- Leukemic cells are biologically active, inhibit hematopoiesis and cause bone marrow fibrosis
- 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

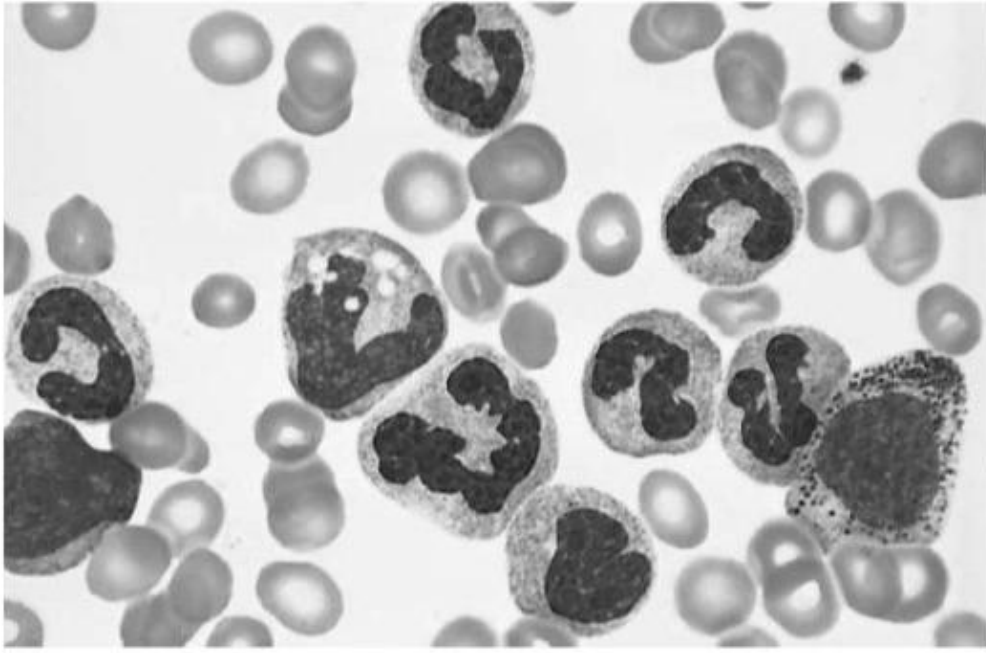
- Patients present with erythema, progressive to plaque then tumor
- Neoplastic lymphocytes have irregular nuclear membrane (cerebriform), affecting epidermis and dermis.
- With disease progression, lymphoma disseminates to LNs and viscera
- Sezary syndrome: a variant of MF, patients present initially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



Chronic Myeloid Leukemia (CML)

Leukocytosis, can be >100K

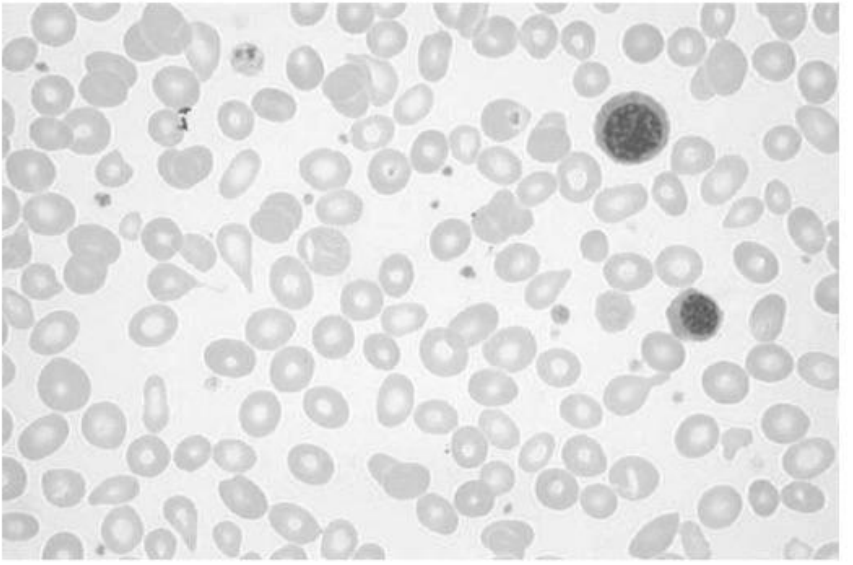
- Shift to left
- Basophilia, eosinophilia
- Thrombocytosis
- Anemia
- BM: increased nyeloid and megs
- Spleen: EMH
- Blasts: low
- Leukemoid reaction: high WBC and shift to left, occurs in severe inflammation

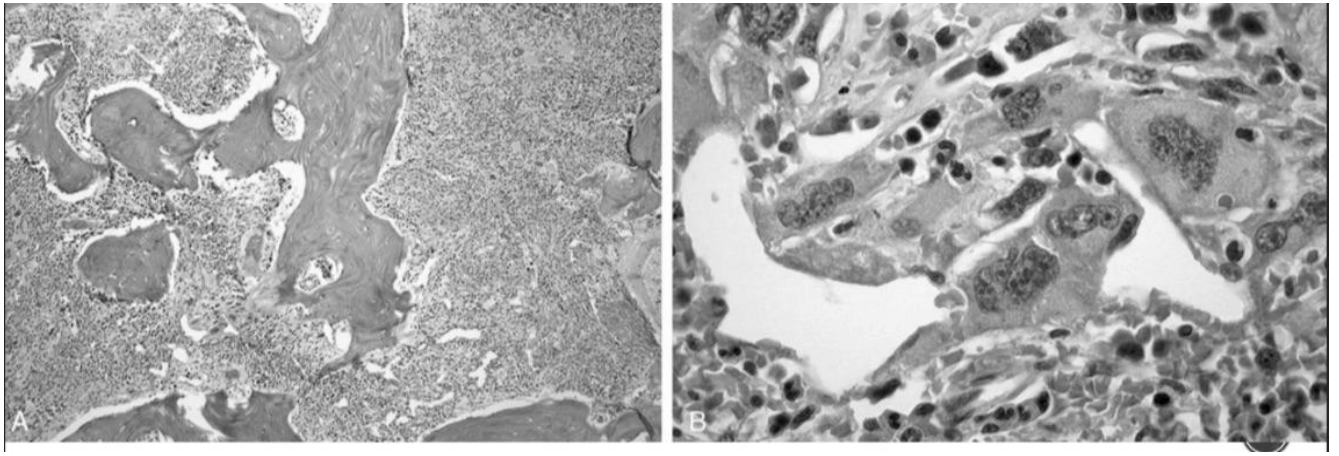


Primary Myelofibrosis (PMF)

✏️ Peripheral blood: tear-drop cells, nucleated RBCs, shift to left (leukoerythroblastic anemia)

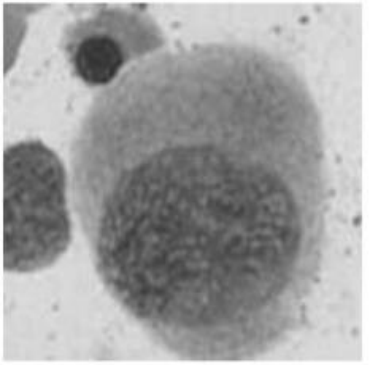
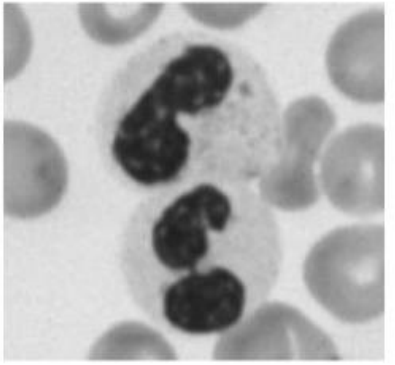
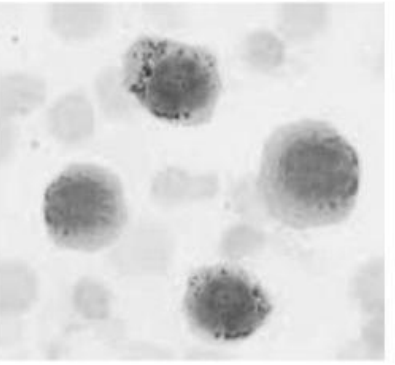
- WBC: can be normal of increase
- Plt: high, then low





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

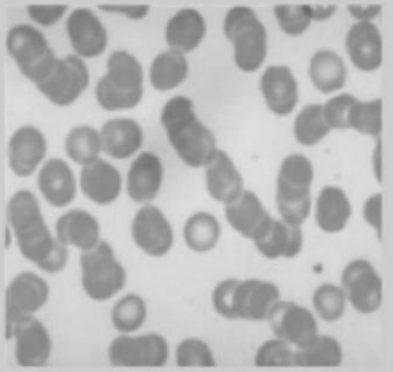
✎Erythroid: macrocytic anemia, megaloblastoid nuclei, ring sideroblasts (iron accumulation inside mitochondria)

- 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?

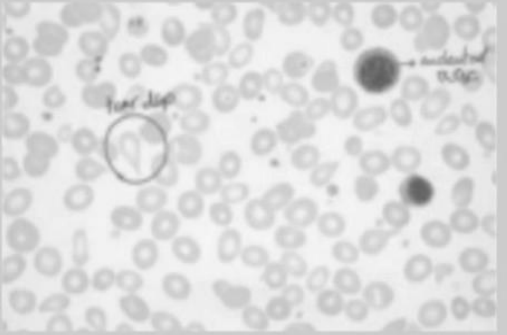
A. Hypercalcemia
B. Amyloidosis
C. Renal failure
D. Bone fractures
E. Plasma cells are less than 5% of bone marrow cells.



ANSWER : E

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

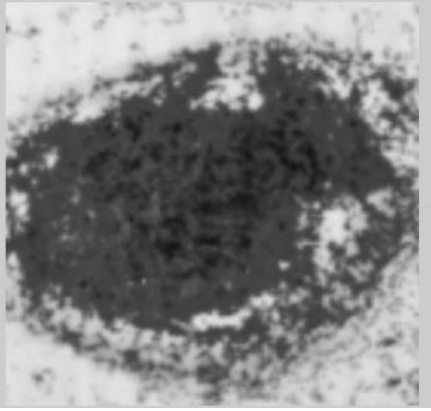
A. JAK2 mutation
B. Shift to the left Neutrophils
C. Mild splenomegaly
D. Thrombocytopenia
E. Anemia



ANSWER : C

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

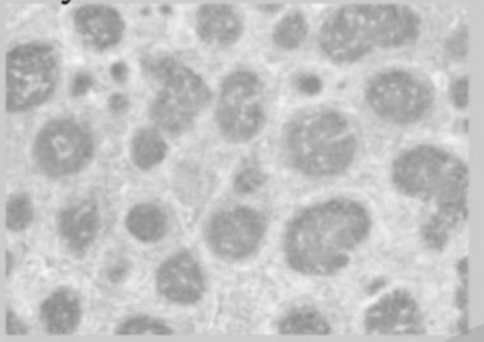
A. Elevated HgA2
B. Decrease in ferroportin
C. Increase hepcidin level
D. High TIBC (total iron binding capacity)
E. Long history of cancer



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