Introduction to Hematopathology

July 14, 2014

Introduction

- *Working hours:* The residents are expected to be on duty from 8:00 am to 5:00 pm

- *Clinical Team:* Typically, two pathology residents are on the rotation each month, a senior and a junior level. The clinical team may also include other trainees on the rotation (one fourth-year medical students/week, one or two MDACC hematology-oncology fellow/month, four or five MDACC hemepath fellows/year, and two TMH hemepath fellows/year).

Introduction

- *Conferences:* Residents are required to attend the 8-9 am UTHMS teaching conferences. Other conferences, including AP conferences may be attended with the permission of the attending, if the clinical work is performed.

- Residents duties include present ing at the Hematopathology journal club (once a month), Hematopathology tumor board (Leukemia, Lymphoma and Multiple Myeloma, also once a month), and hematopathology cases at the Wed Case Review conference

- Resident may also attend / present at the Texas Medical Center Citywide Hematopathology Conferences.

Introduction

- *Service duties:* After the morning conference, the residents review pending materials and prioritize work.

- The residents will review cases on their own and prepare the reports draft in the Pathnet. Cases requiring emergent action (such as new/relapsed leukemia and TTP), should be brought to the attending's attention immediately.

Introduction

- The typical daily workload includes several areas:

  I. Wet hematology: review of peripheral blood smears and body fluid cytospins

  II. Bone marrow cases: performing bone marrow procedures, reading, interpreting and reporting the bone marrow cases in conjunction with the ancillary studies (flow cytometry and immunohistochemistry, if performed); integration of cytogenetics and molecular studies in addendum report.

  III. Interpretation and reporting of coagulation reports.

  IV. Consult cases (lymph node, outside cases etc)

Introduction

- *Daily schedule:* If bone marrow procedures are scheduled for the Pathology Team, the mornings may be at least partially occupied with the procedure.

- If no bone marrow procedures are scheduled for the Pathology team to perform, cases are previewed by the residents, then signed-out with the attending within the sign-out sessions, usually scheduled from 9:30 am-12:00 noon and 1-3 pm

- The resident is expected to participate in the clinical work by preparing the cases according to his/her level of proficiency and achieve increasing ability to recognize morphology and formulate correct interpretations.

Resources

- Web site:
  http://HemepathReview.com
  -Interp templates
  -Teaching/review files

- BD FACS Diva Software for flow data analysis

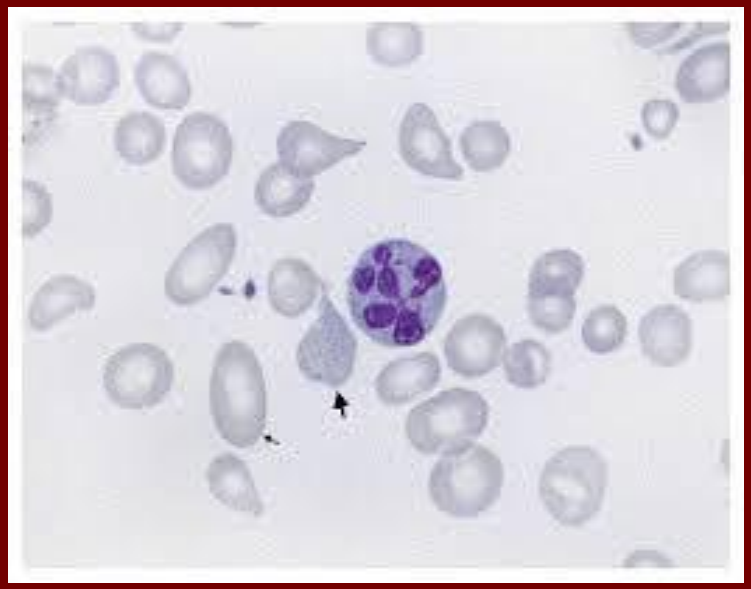
- Study set: 1,500 slides of interesting pathology

Introduction to Hemepath: I. Benign HemePath

Peripheral Blood Smear Examination

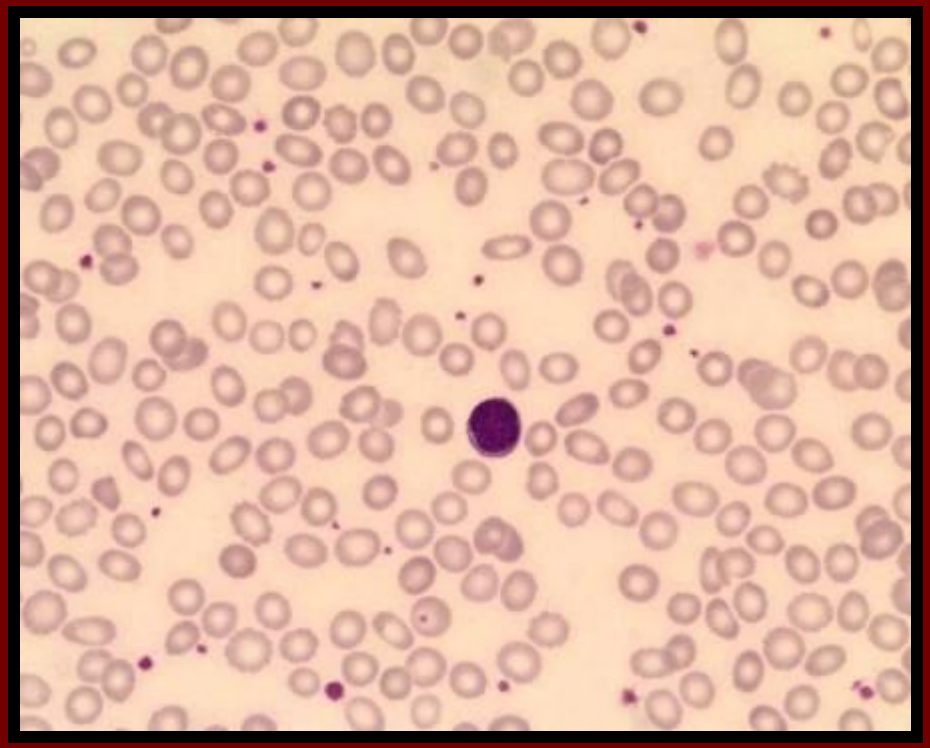
Elevated MCV = Macrocytosis
MCV > 100um^3

- B12/Folate deficiency, aplastic anemia, MDS
- Autoimmune hemolytic anemia
- Liver disease, hypothyroidism, alcoholism
- Cold agglutinin disease



Decreased MCV = Microcytosis
MCV < 80um^3

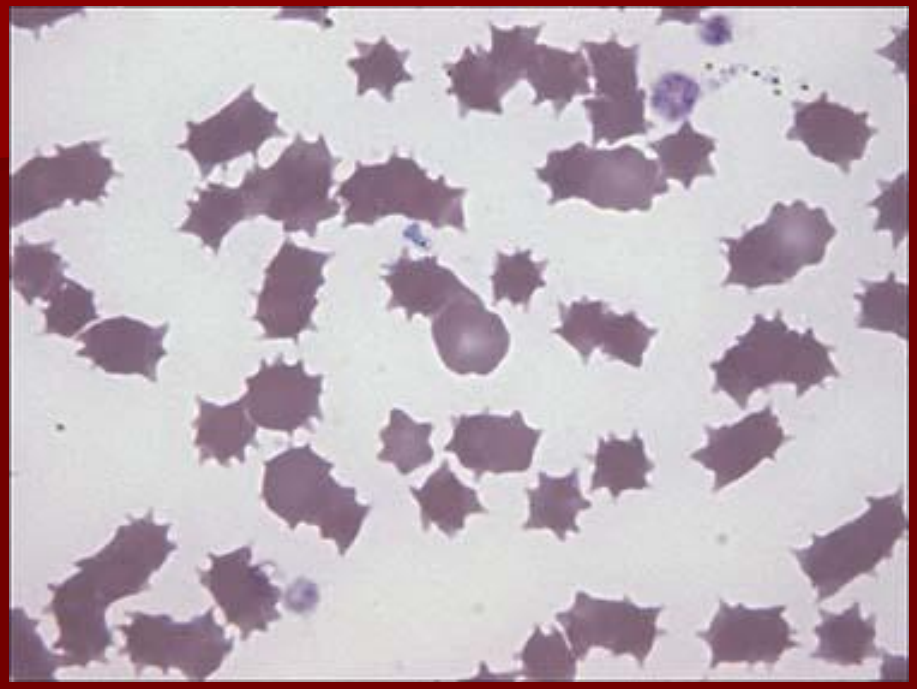
- Iron deficiency
- Thalassemias
- Anemia of chronic disease
- Hemoglobinopathies
  - C, E, S, D



Iron Panel Interpretation

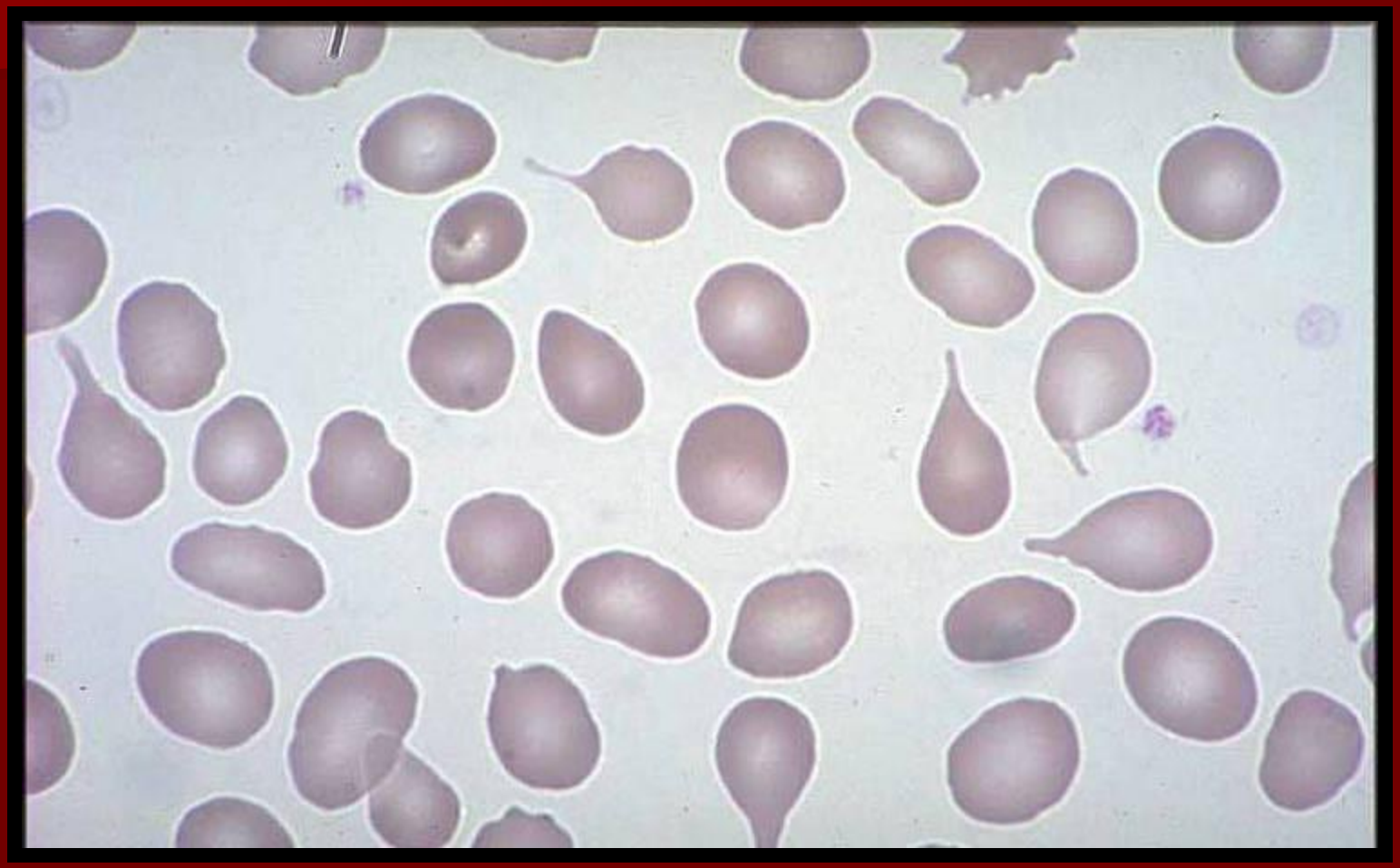
Cause of anemia	Serum iron	TIBC	Percent saturation
Iron deficiency	↓	↑	↓
Thalassemias	↑ / N	↓ / N	↑ / N
Sideroblastic anemia	↑	↓ / N	↑
Chronic disease	N/↓	↓	N

Acanthocytes (Spur cells)



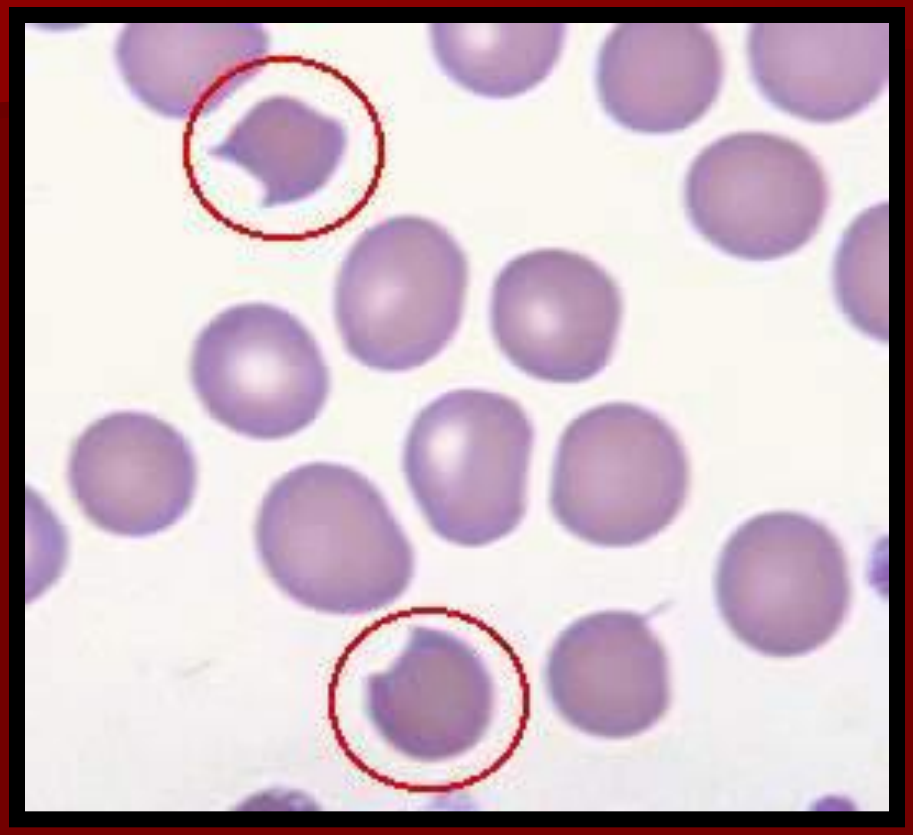
- Irregular, long, sharply pointed and bent spicules
- Absence of central pallor
- Most commonly seen in liver disease

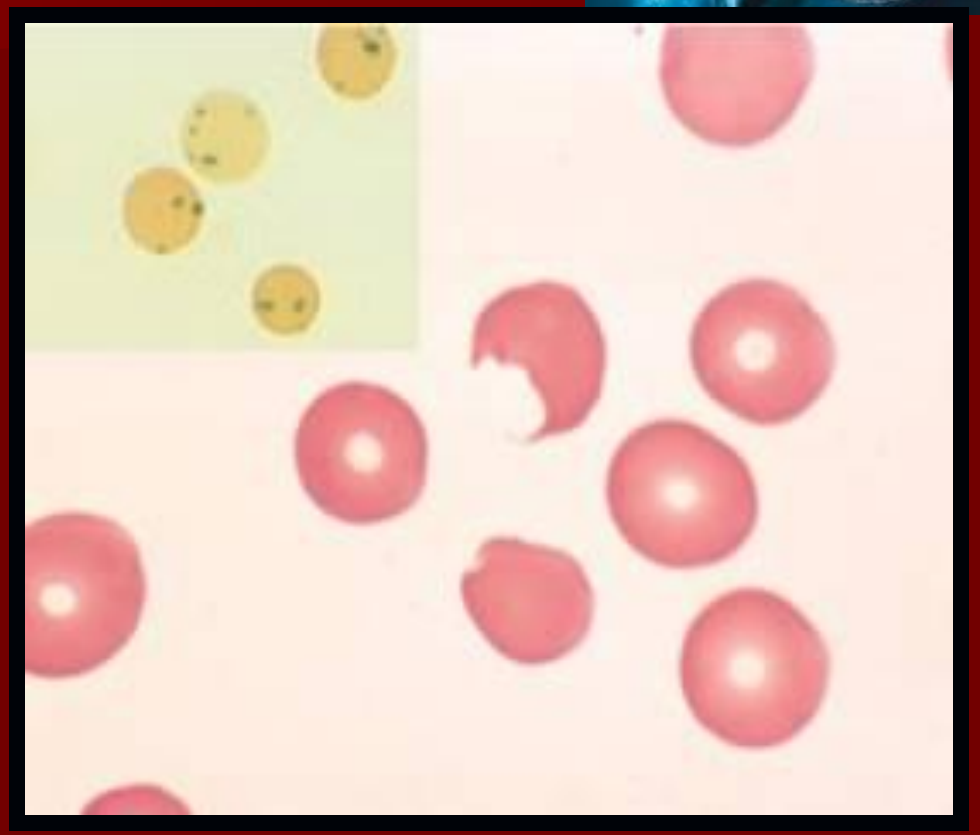
Tear Drop Cells (Dacrocytes)



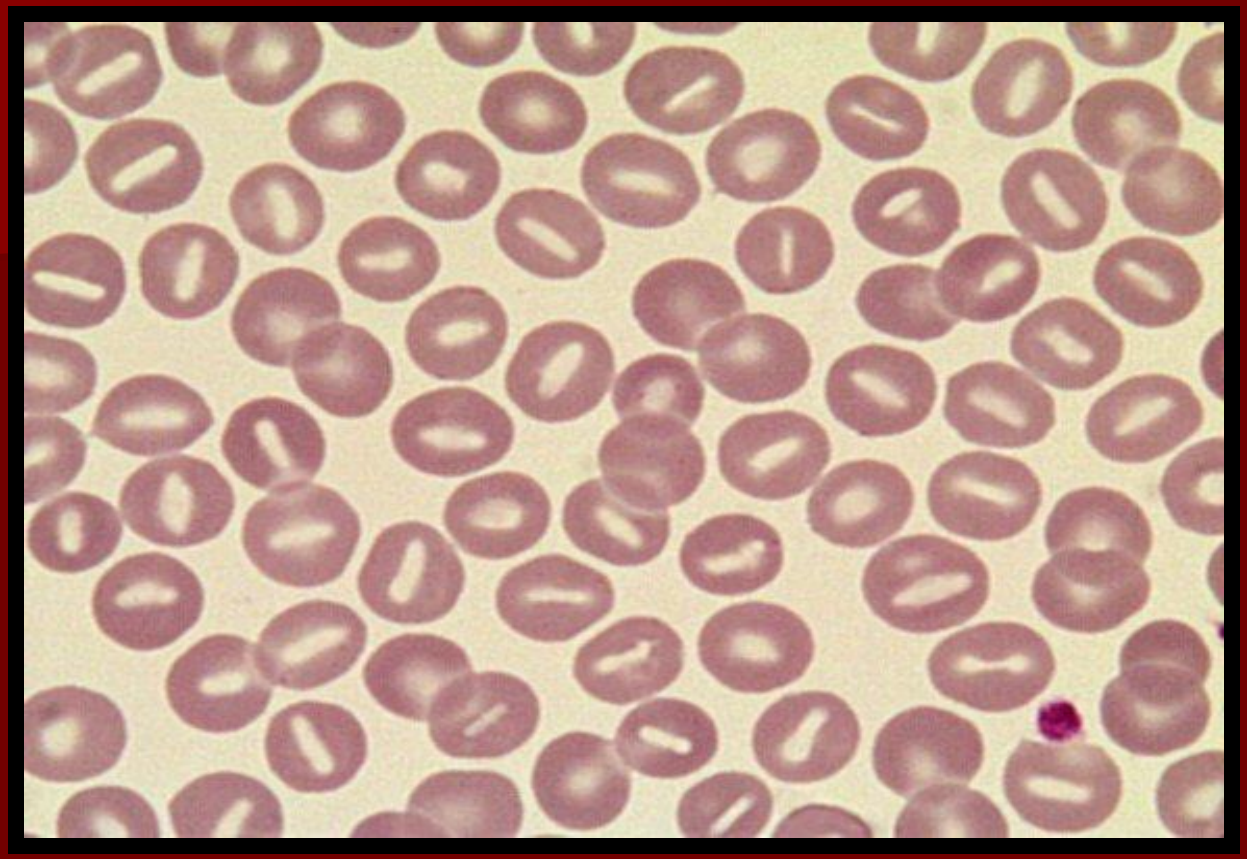
Myelofibrosis or bone marrow infiltrate

Bite Cells





G6PD deficiency

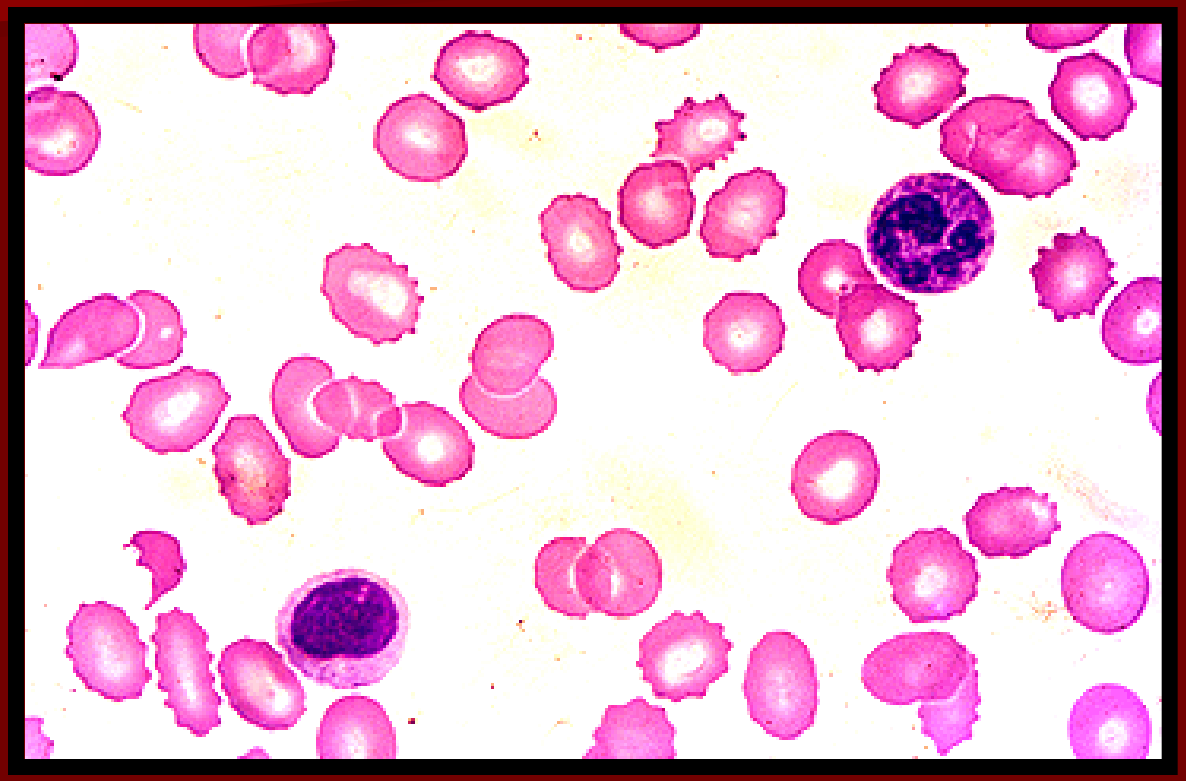


STOMATOCYTES

RBC with slit-like or rectangular area of central pallor, a mouth

Most often seen in liver disease

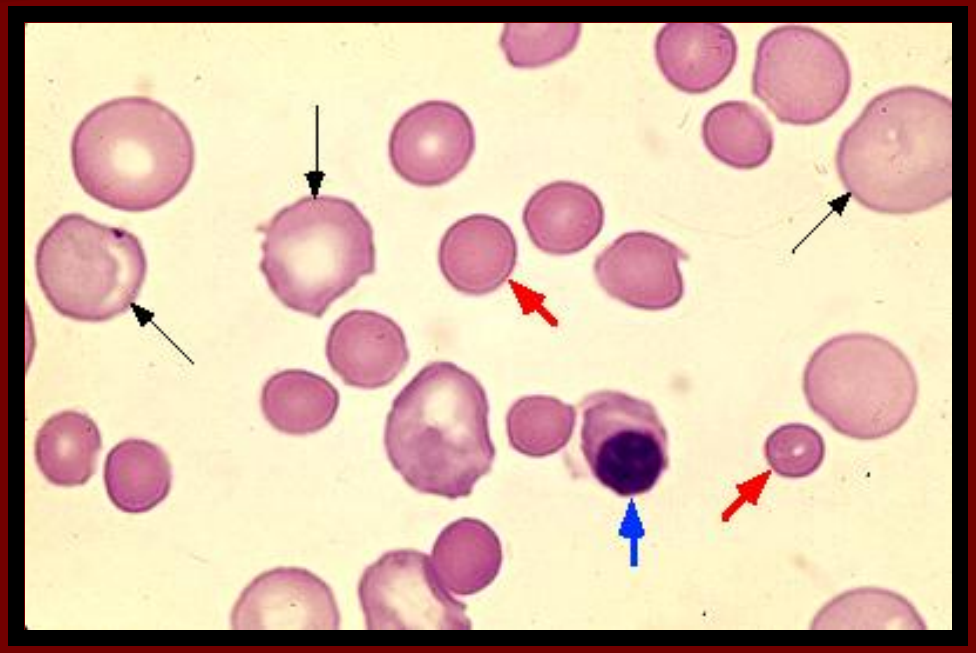
Burr Cells (Ecchinocytes)

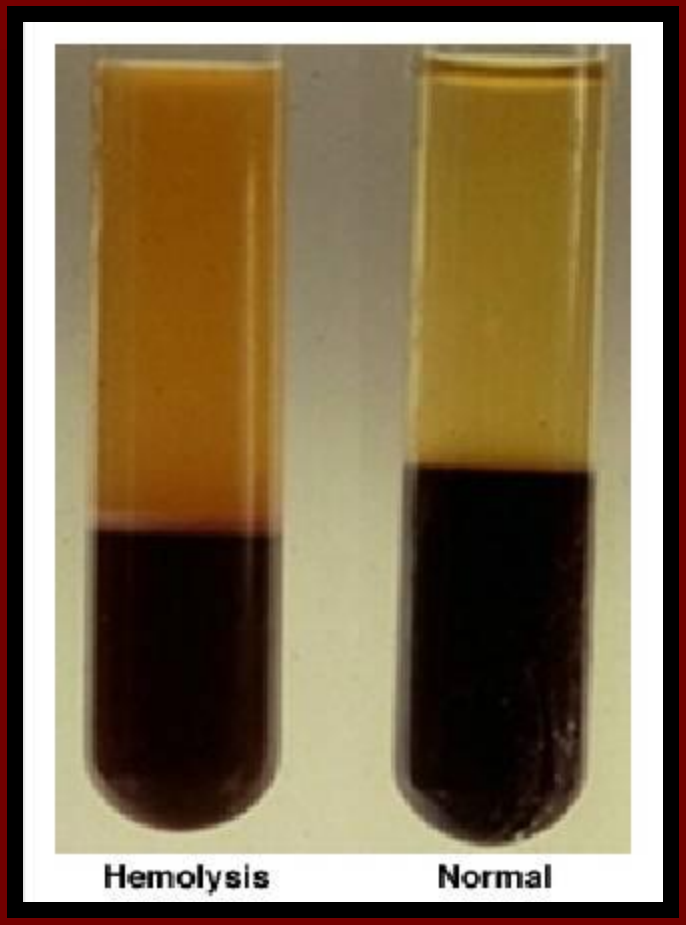


Projections- smaller more regular than acanthocytes

Often artifactual but may be seen in **UREMIA**

Spherocytes

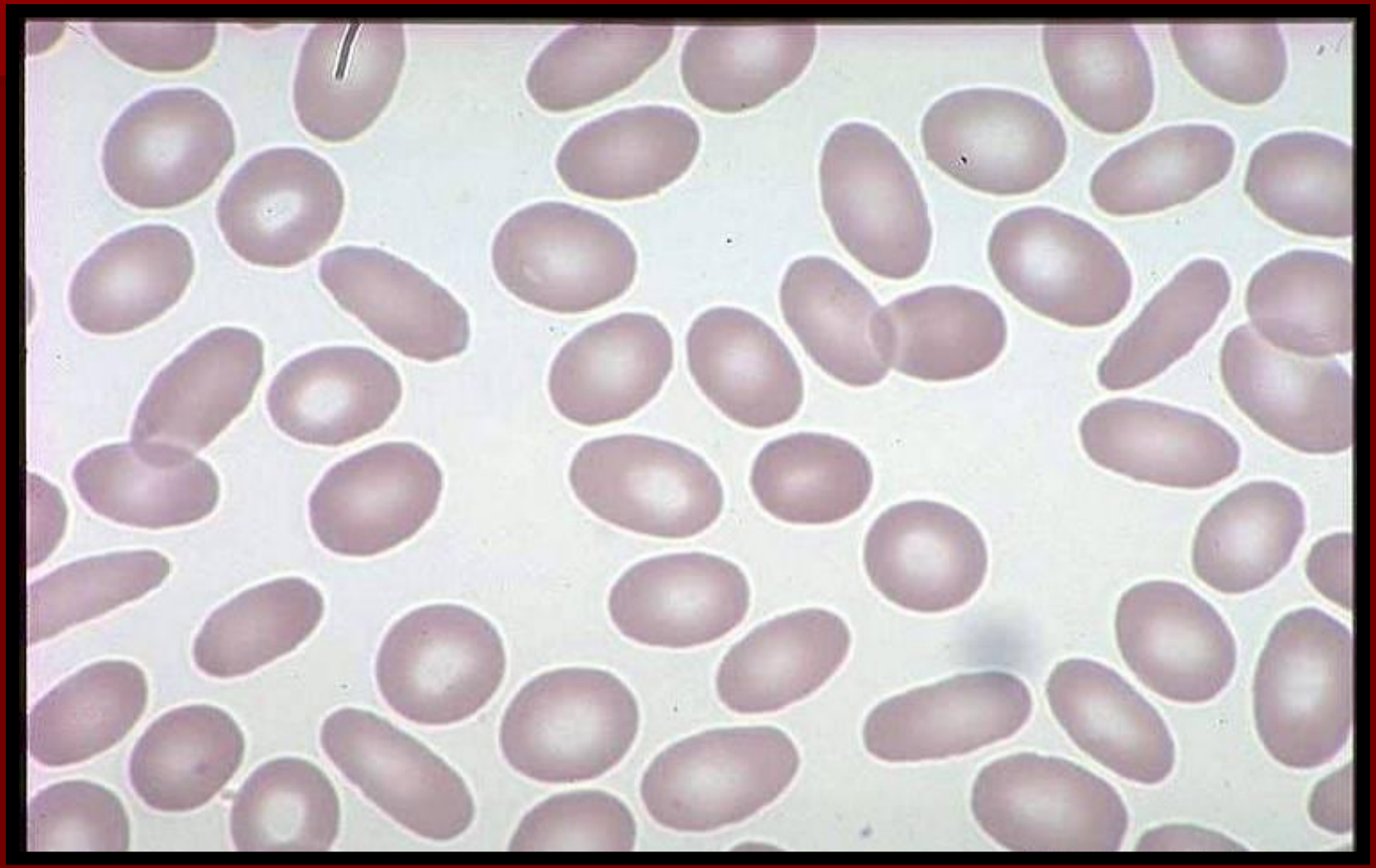




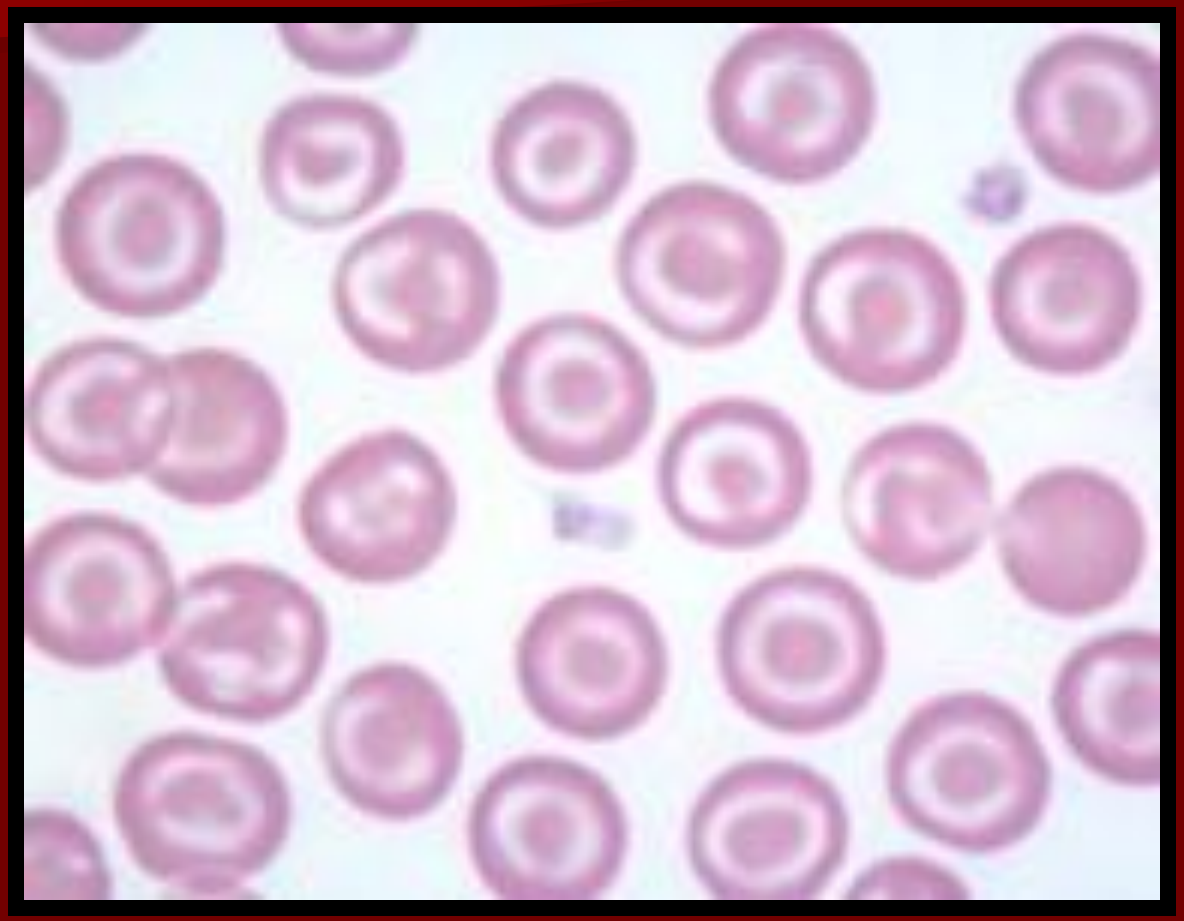
-Hereditary sphereocytosis,

-Immunohemolytic anemia (warm Ab)

Elliptocytes

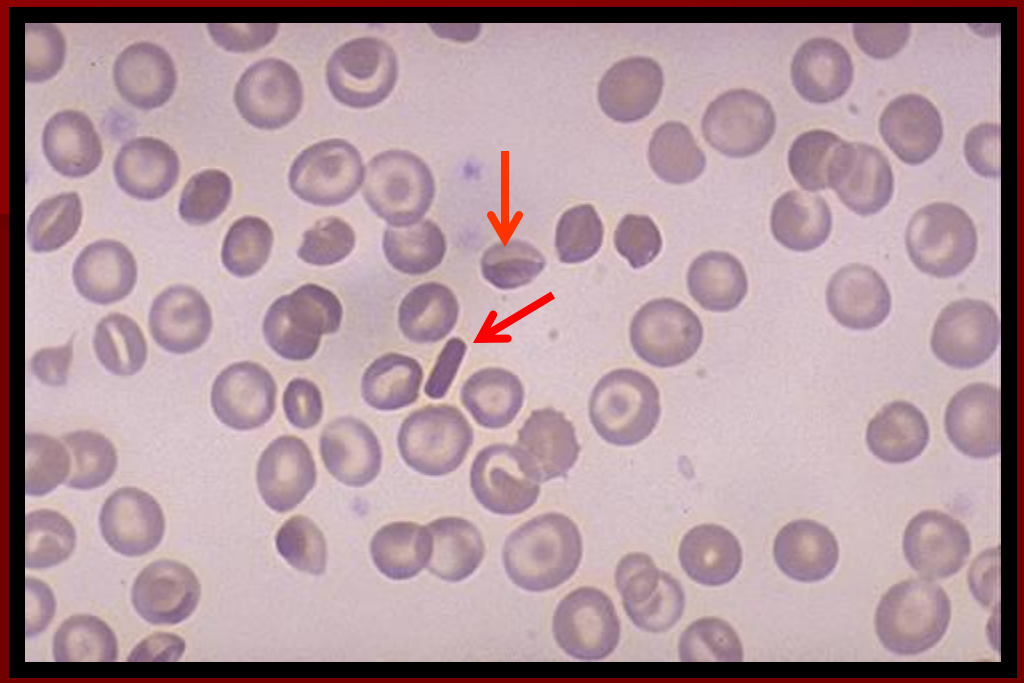


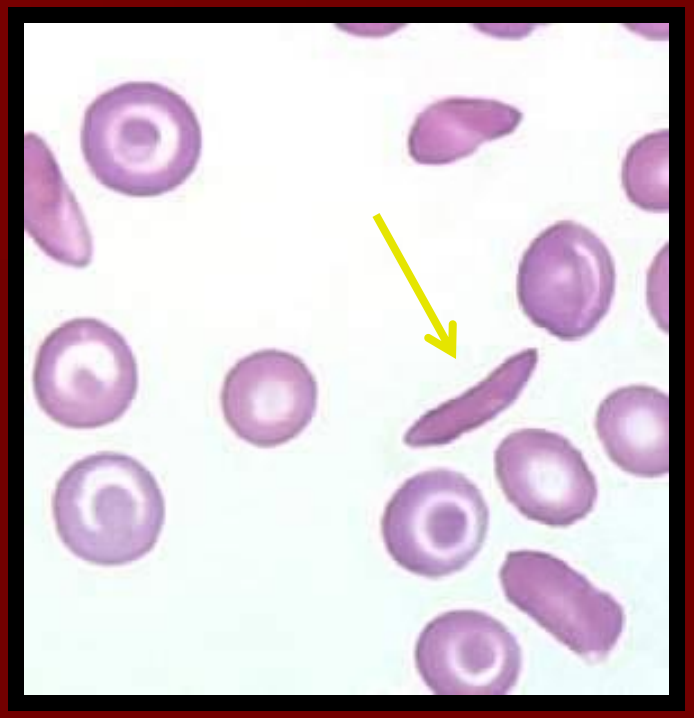
Target Cells



Characteristic of:

- Liver disease
- Post-splenectomy
- Hemoglobin disorders
  - Beta thalassemia
  - Hemoglobinopathy Hb S, C, D and E

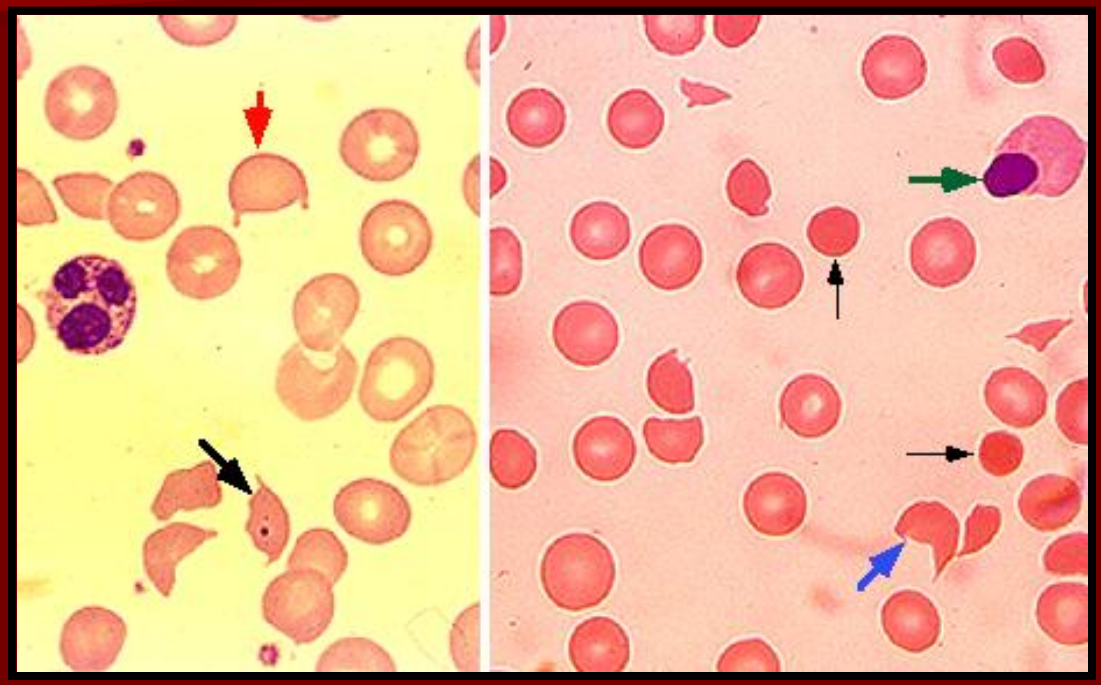




Hgb SC disease with C crystals,
Taco cells and sickle cells

“Washington Monument crystals”

Schistocytes

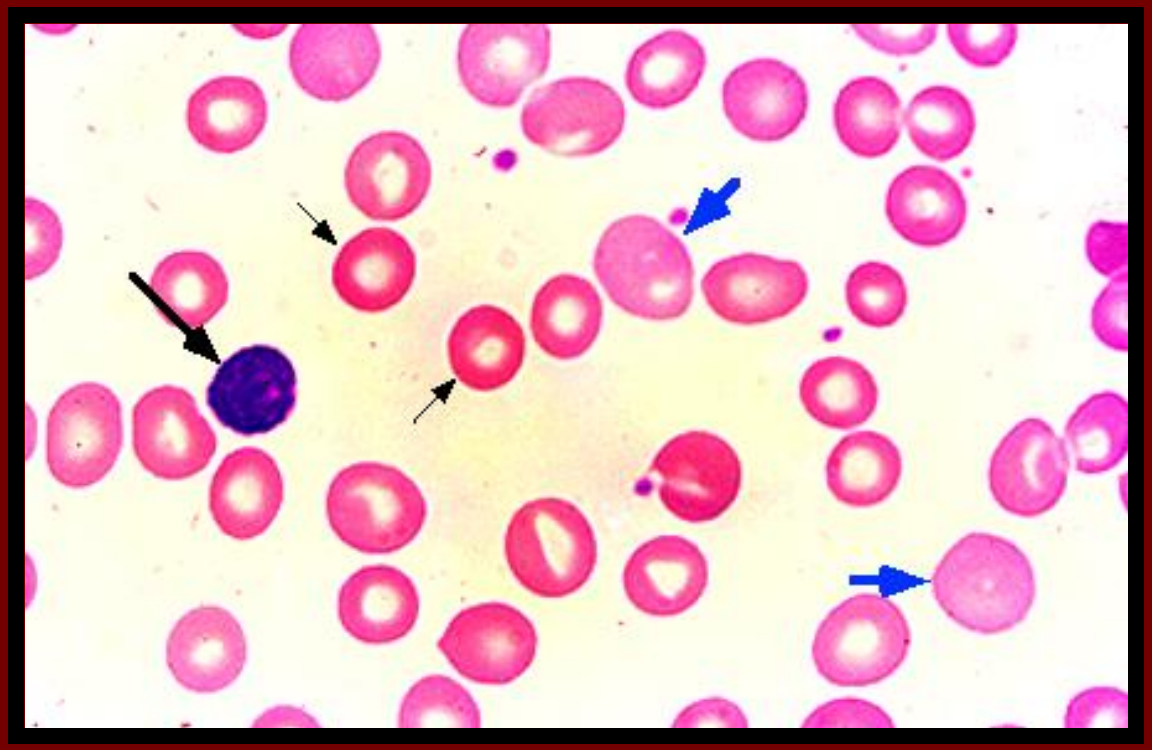


Microangiopathic hemolytic anemia

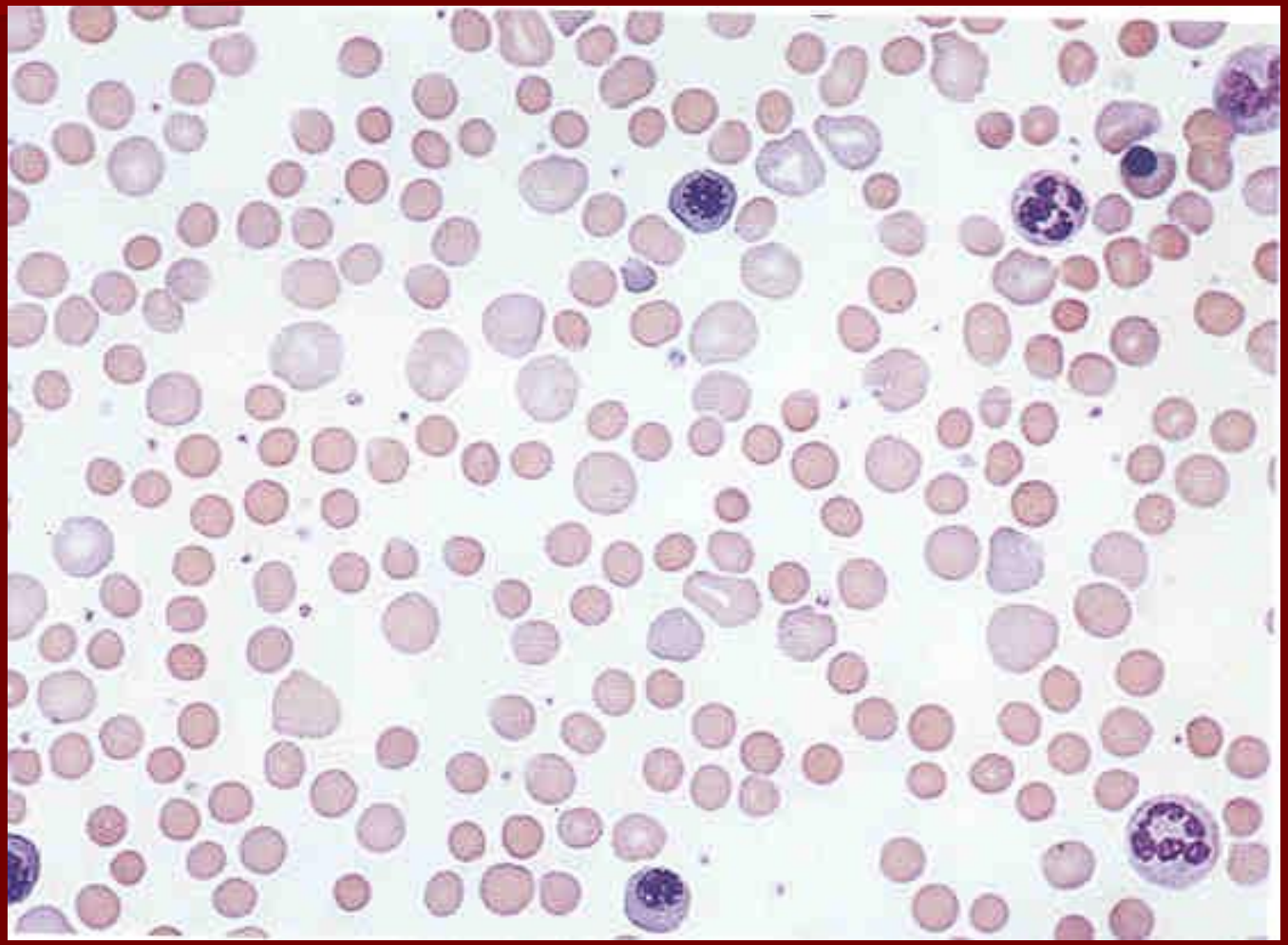
DIC, TTP, HUS

Reticulocytes

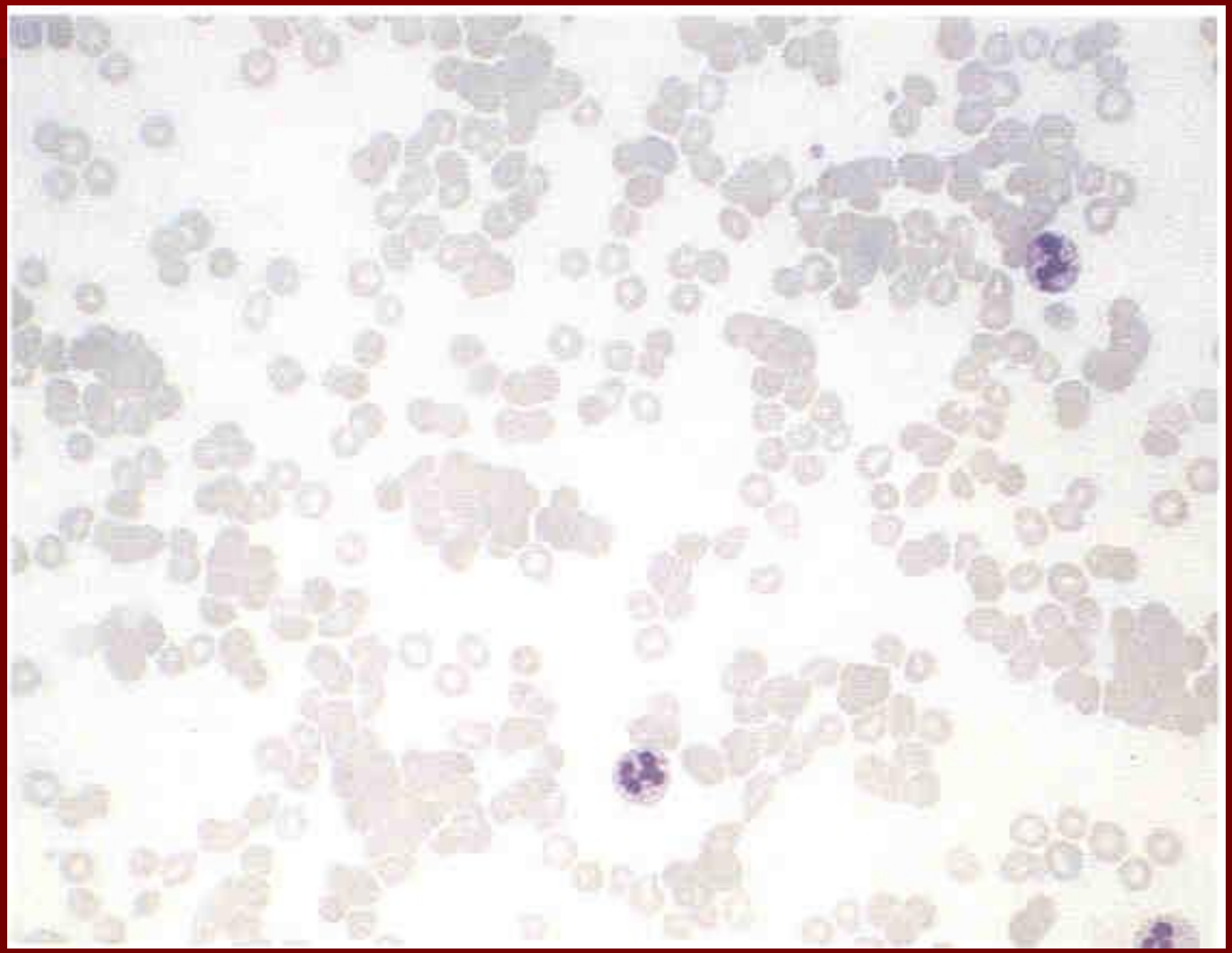
- Decreased cell survival
  - Blood loss
  - Autoimmune hemolysis
  - Nonimmune hemolysis
    - TTP, HUS, DIC
    - H. spherocytosis
    - G6PD
    - PNH
    - Hemoglobinopathy
    - Thalassemia



WARM AIHA



COLD AIHA

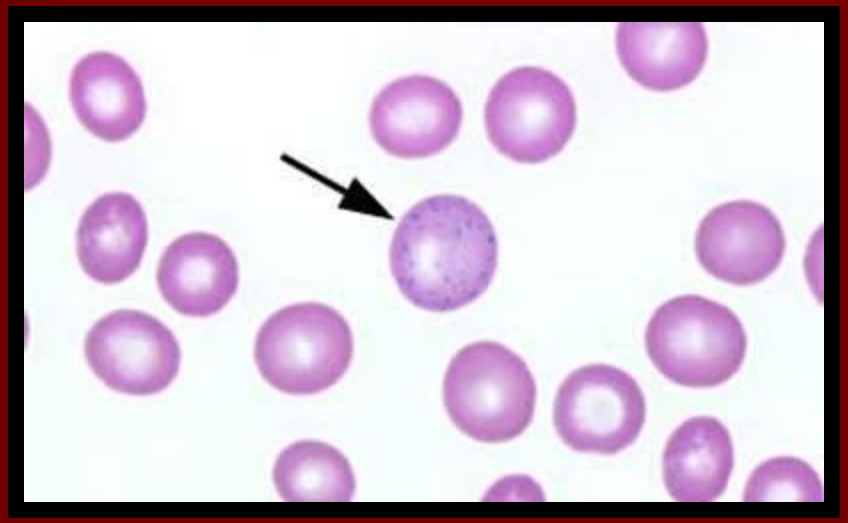


LAB PARAMETERS

	WARM	COLD
DAT	2+ TO 4+	2+ TO 4+
ANTI IgG	+	RARE
ANTI C3	RARE	+

Basophilic Stippling

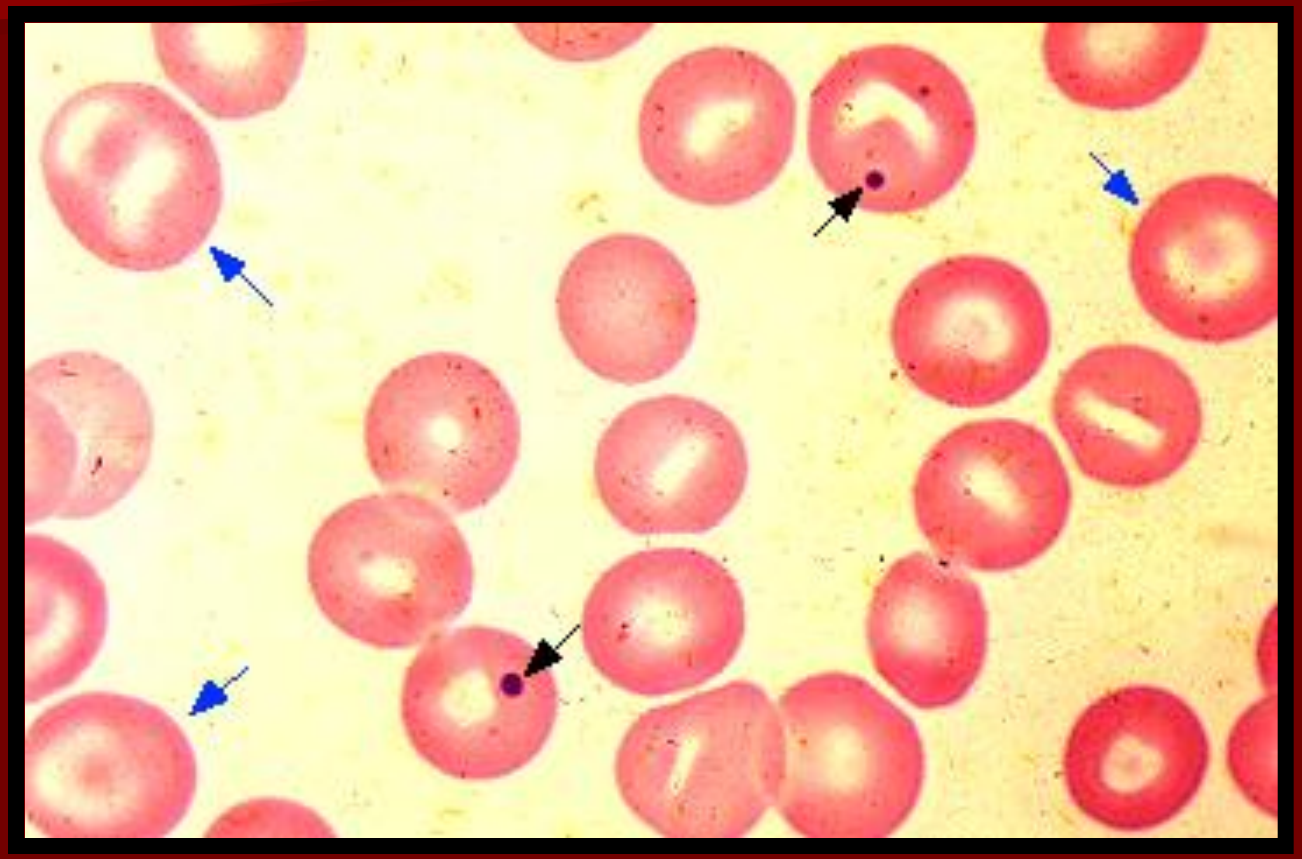
Precipitated ribosomes (RNA)



Fine – variety of anemias: Siderblastic, sickle cell, megaloblastic

Coarse – Lead intoxication, thalassemia

Howell Jolly Bodies



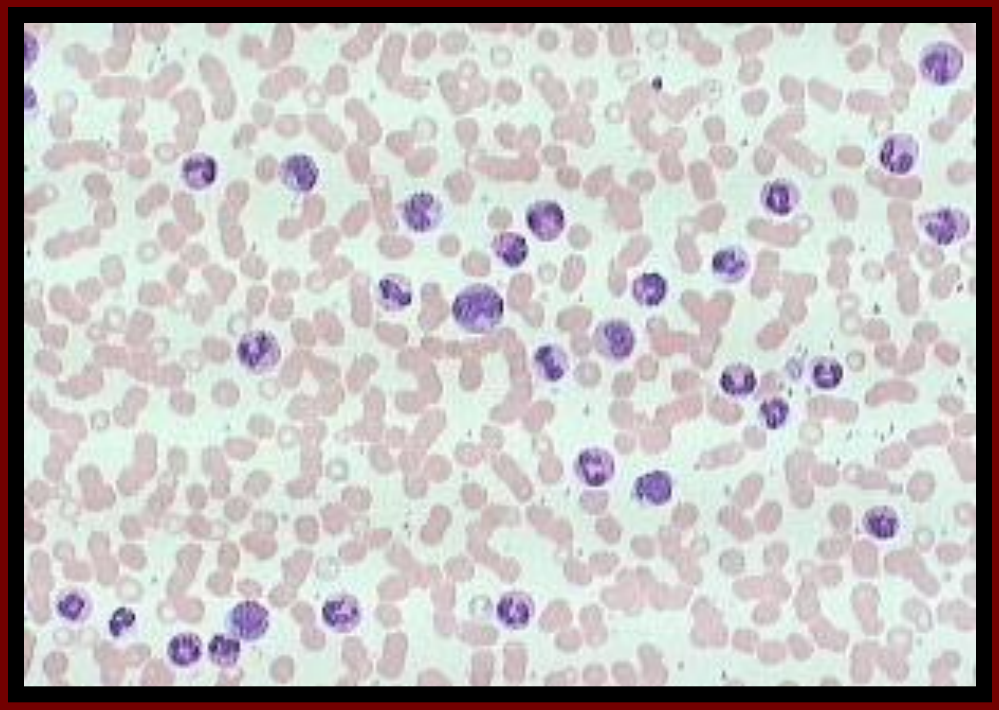
Dense,usually single

Nuclear remnant

Seen in:

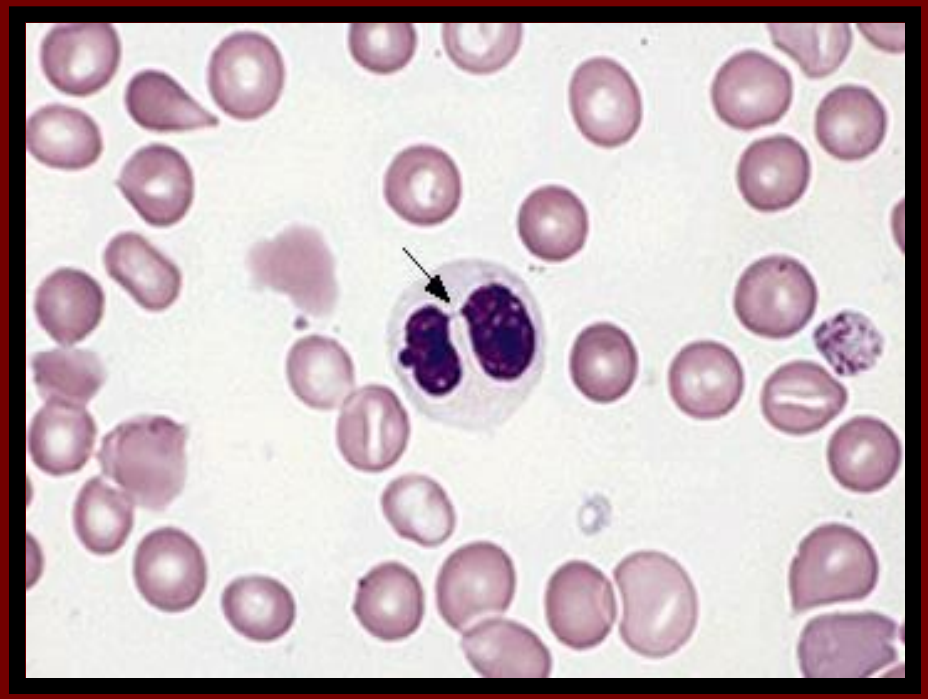
- Postsplenectomy
- Hemolytic anemia
- Megaloblastic anemia

The Malignant Mimicker: Leukemoid Reaction



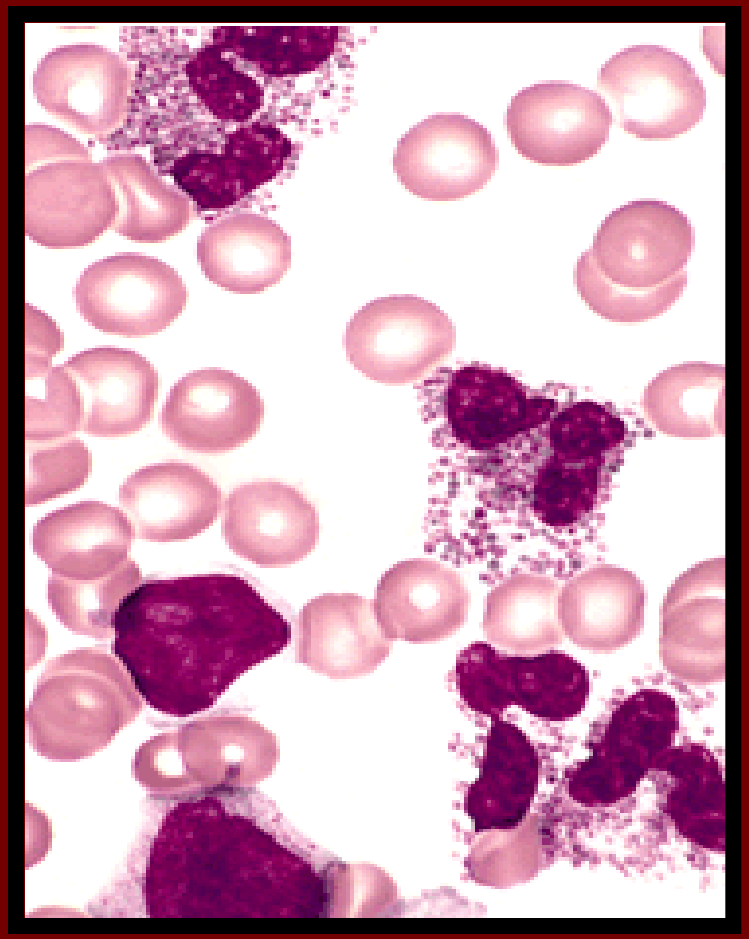
- Precursor granulocytes in the PBS
- WBC in the range up to 100K
- Response to severe stress or infection
- Other signs of malignancy not present (i.e. CML)

Pelger-Huet Anomaly



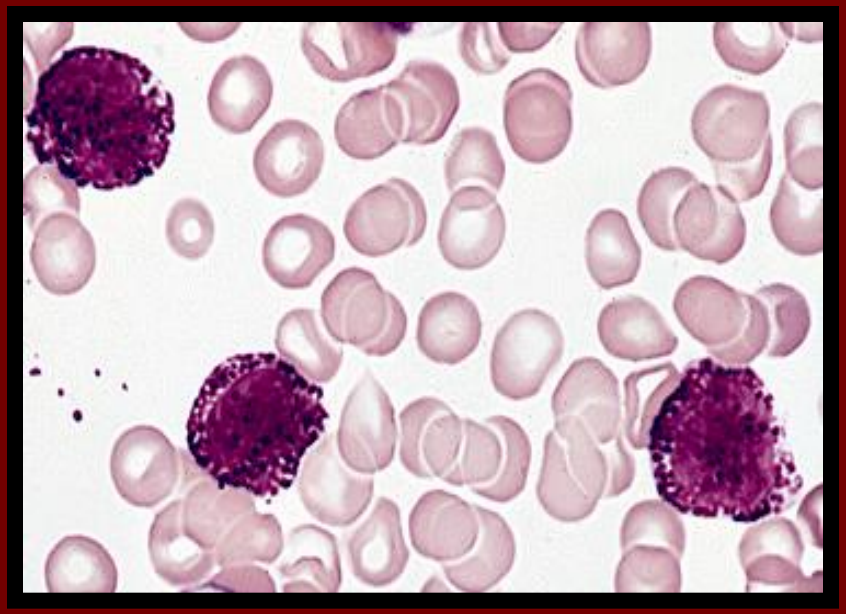
- Inherited, AD
- Acquired = "pseudo" Pelger-Huet as in MDS

Eosinophilia

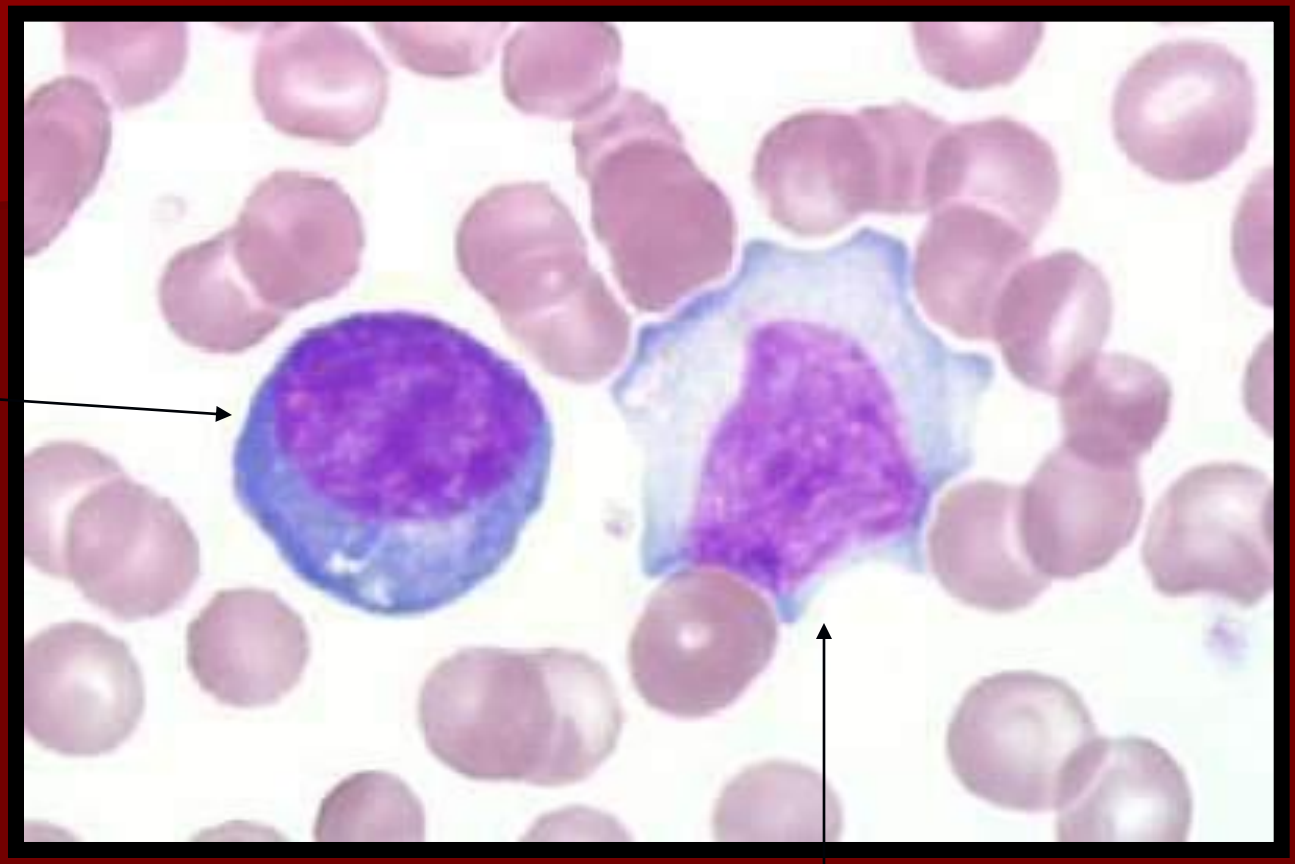


- Allergic/hypersensitivity reactions
- Drug allergies
- Parasitic infections
- Connective tissue/collagen vascular disease
- Neoplasms
  - T-cell lymphoma
  - Hodgkin lymphoma
- Sarcoidosis
- Hypereosinophilic syndrome/Chronic eosinophilic leukemia
- Chronic/acute leukemia a/w PDGFRRA or PDGFRB mutations

Basophilia

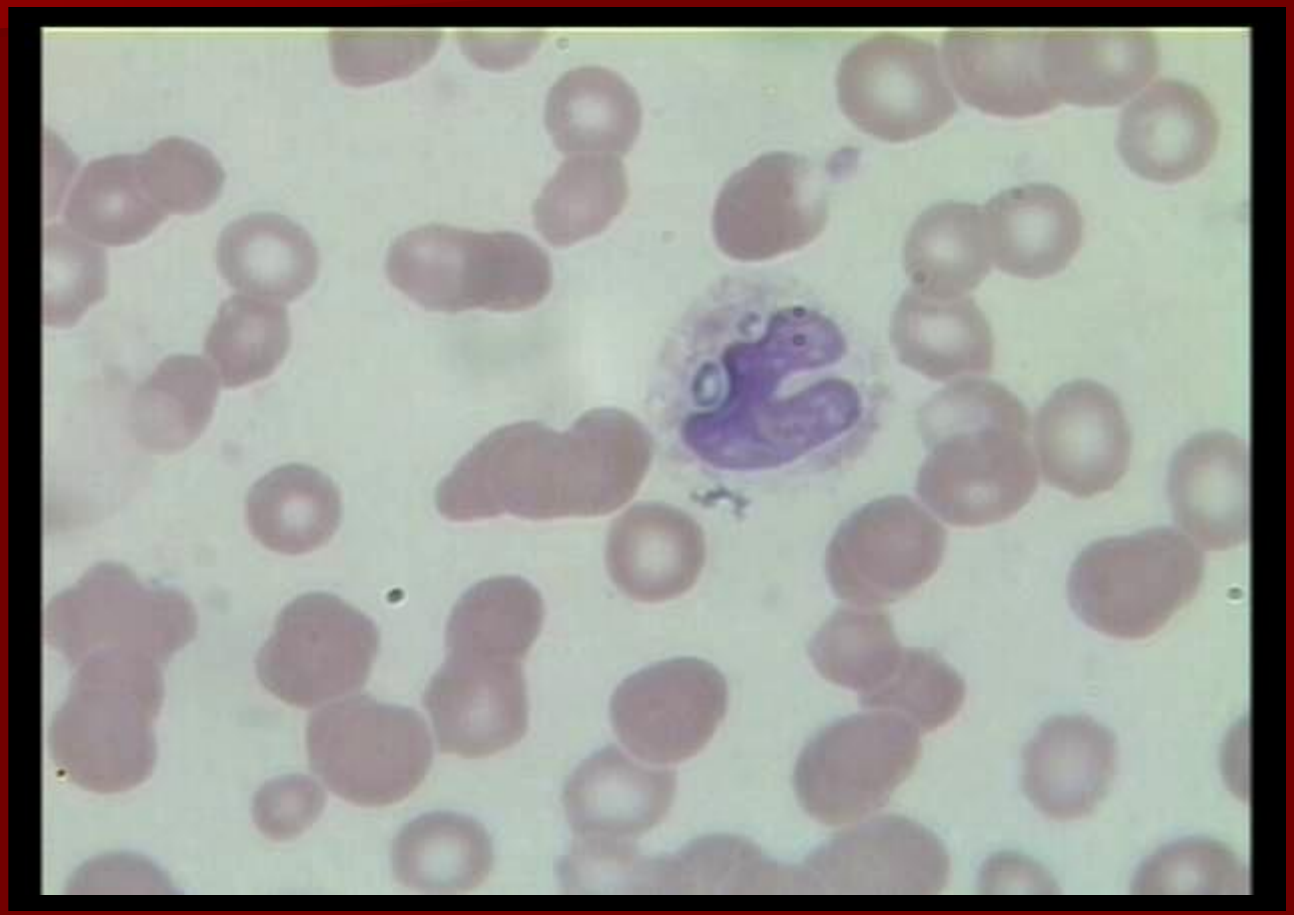


- Much more common in malignancies like CML vs. reactive



Reactive Lymphocytosis

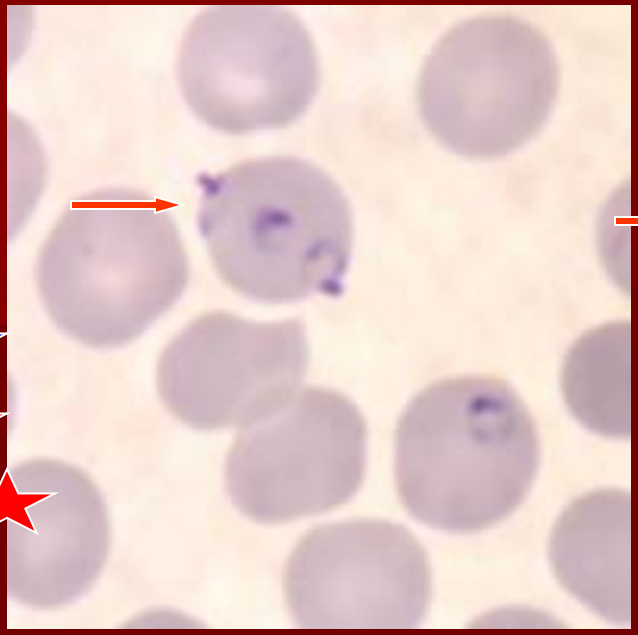
Histoplasma

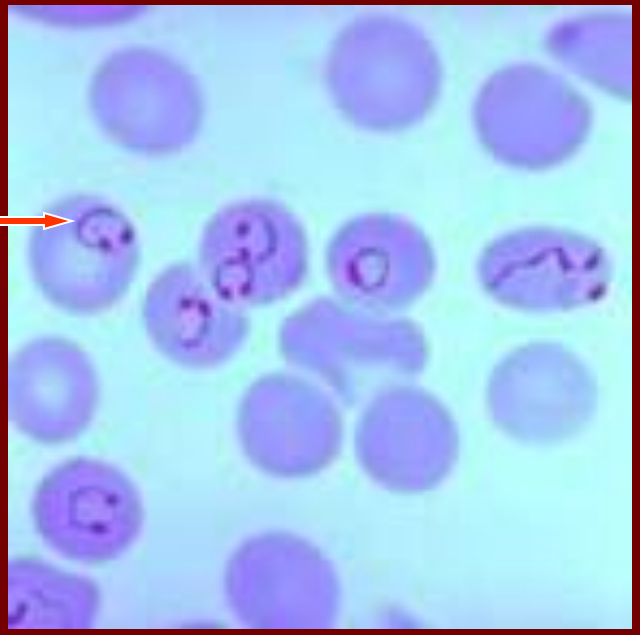


Malaria

Trophozoites (rings)

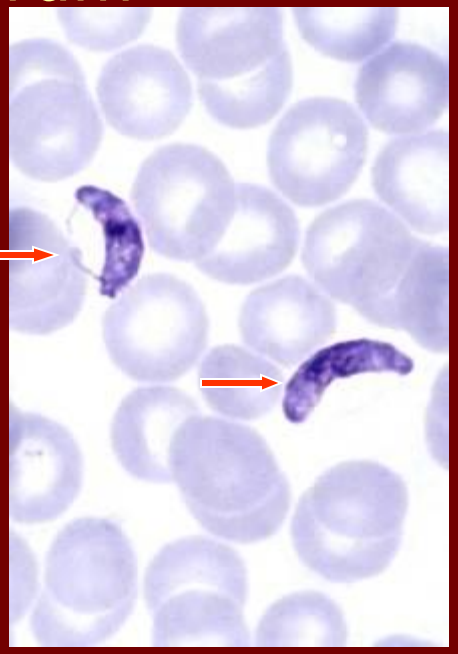
- Multiple rings/cell
- Appliqué forms
- 1-2 chromatin dots

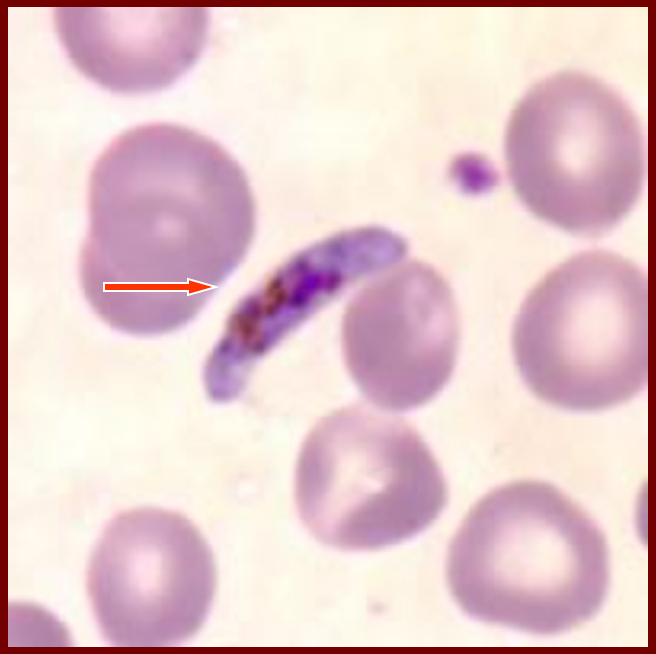




Plasmodium falciparum

Gametocytes





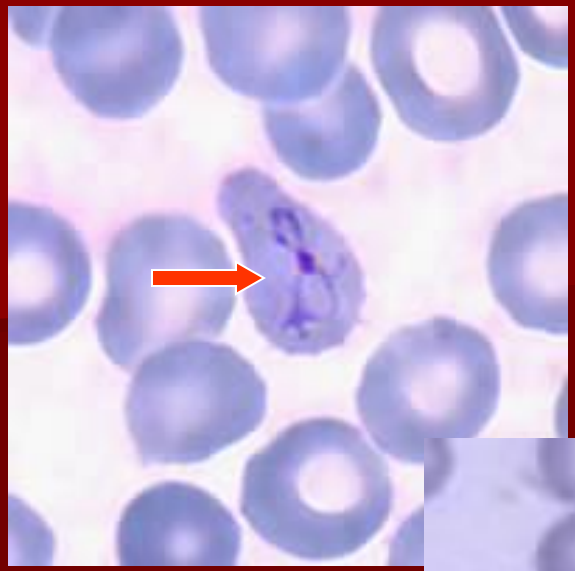
Plasmodium vivax

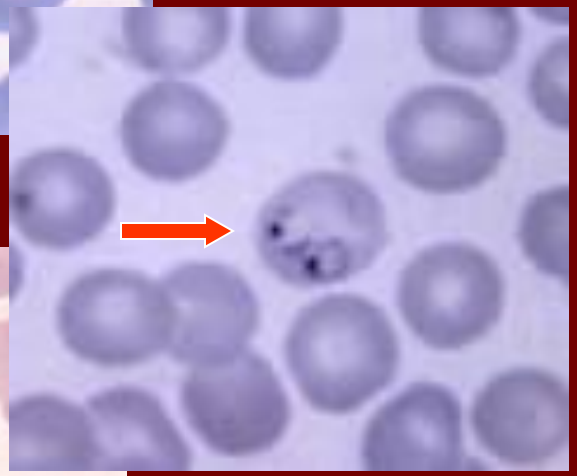
Early Trophozoites (rings)

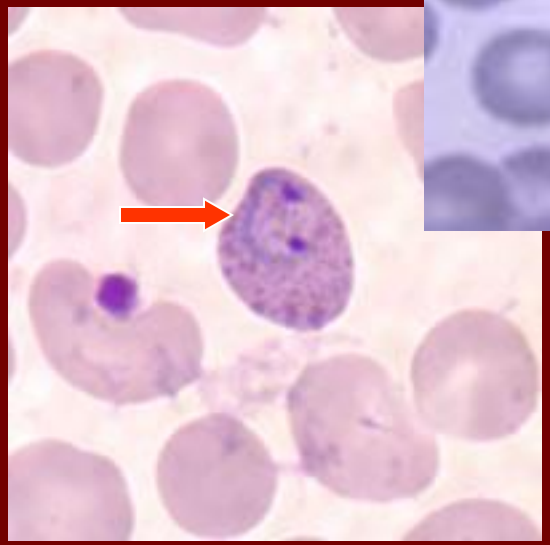
Ameoboid rings

Enlarged RBCs

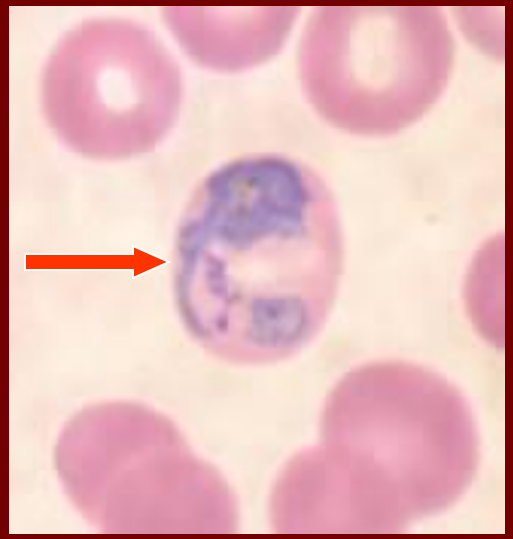
Schuffner's Dots



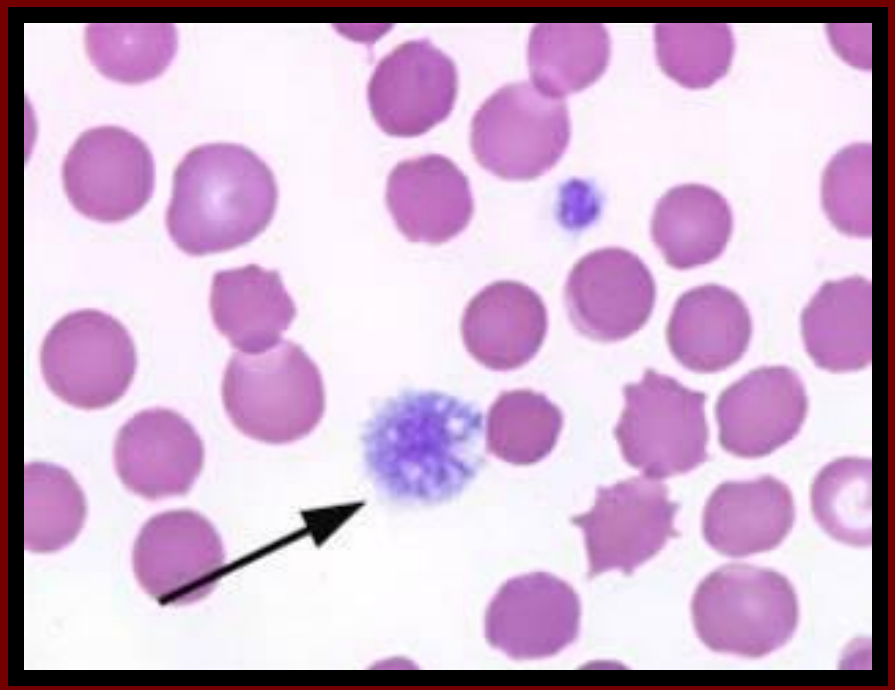




Mature trophozoite ->schizont

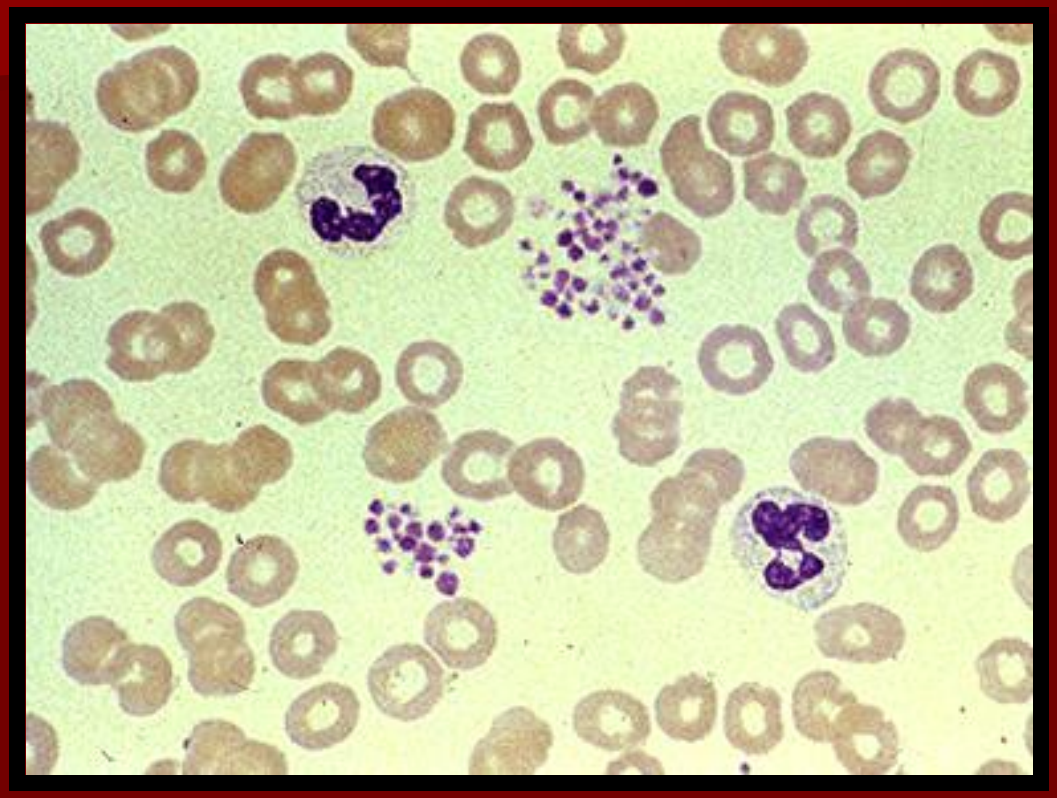


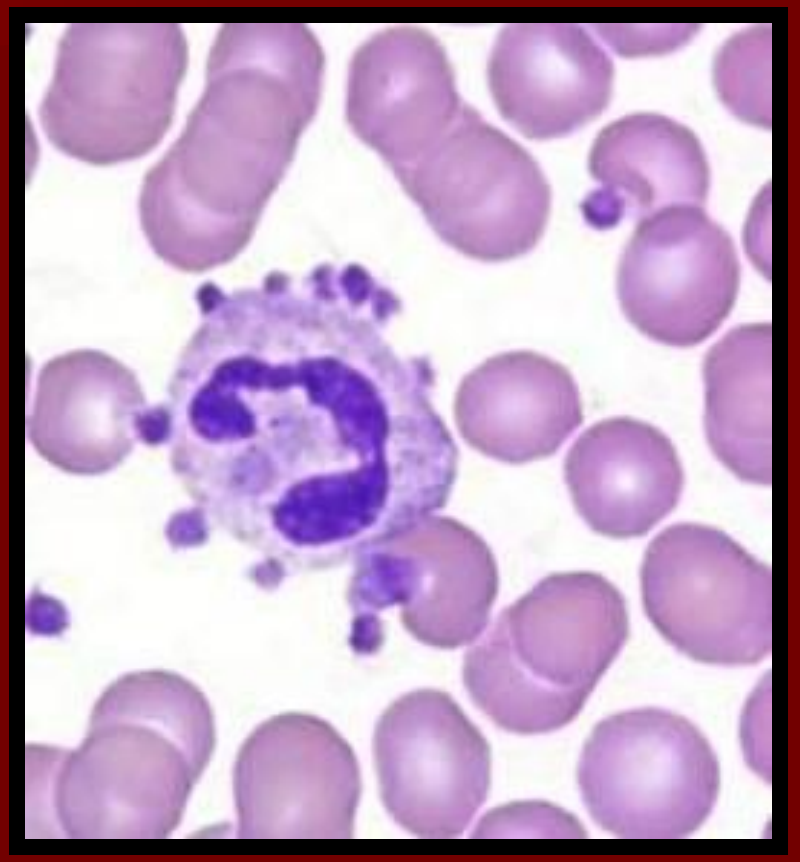
Giant Platelets



- Size of an RBC
- Usually indicates a hyperreactive bone marrow 2^{o} to underlying condition
  - ITP, TTP, DIC
- Can be inherited in the form of Bernard-Soulier syndrome, May-Heglin anomaly

Platelet Clumping and Satellitelosis

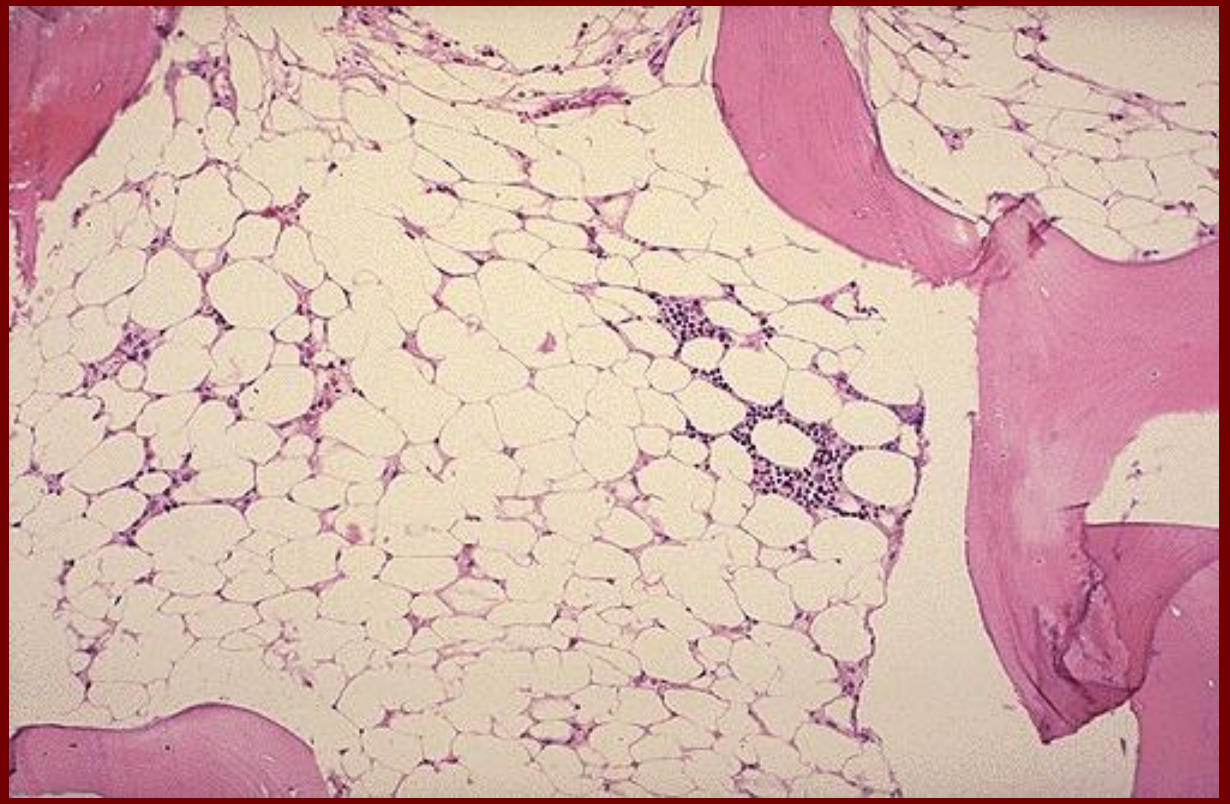


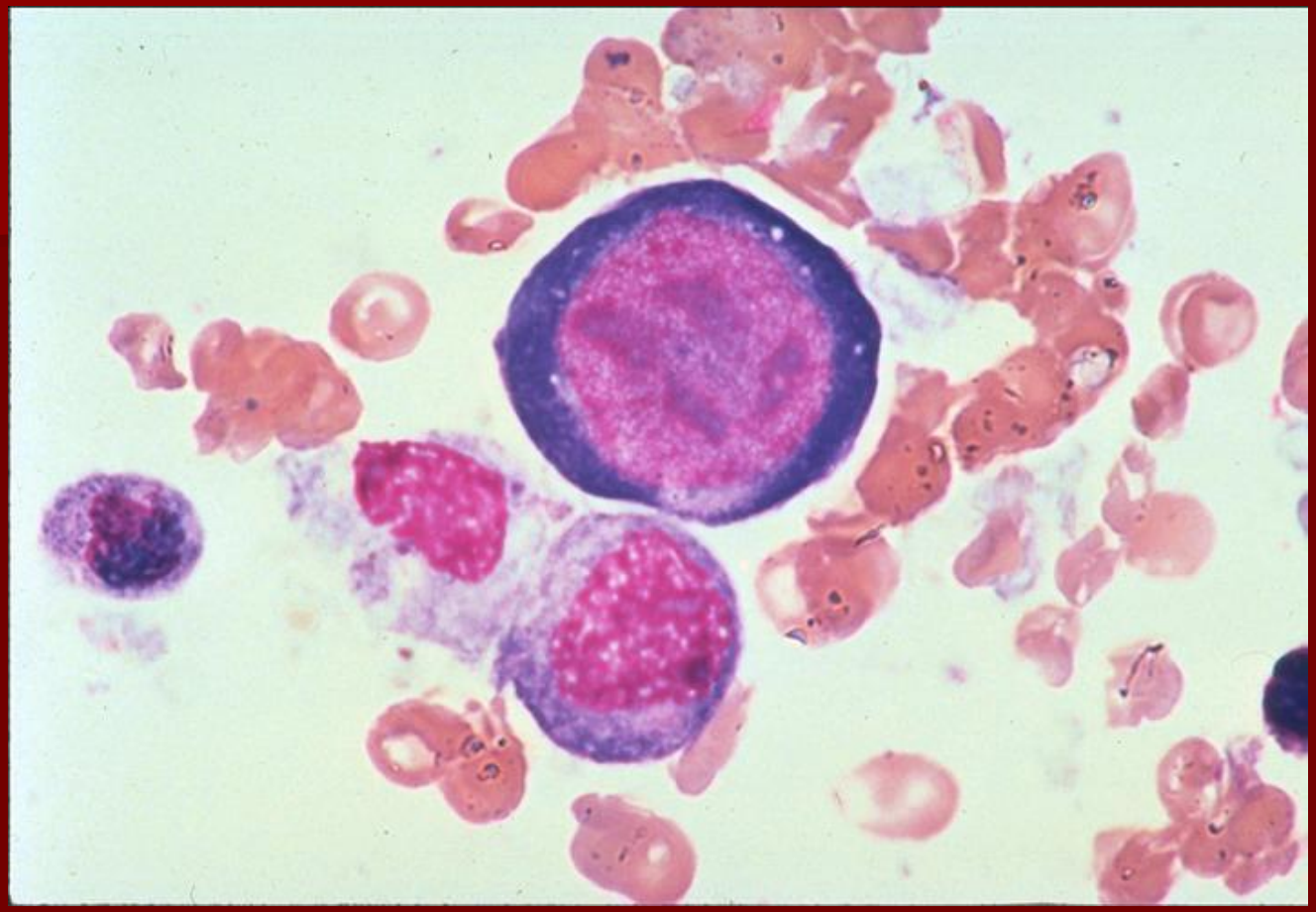


- Causes artificially low platelet counts
- 2^{o} to EDTA used in collection tubes

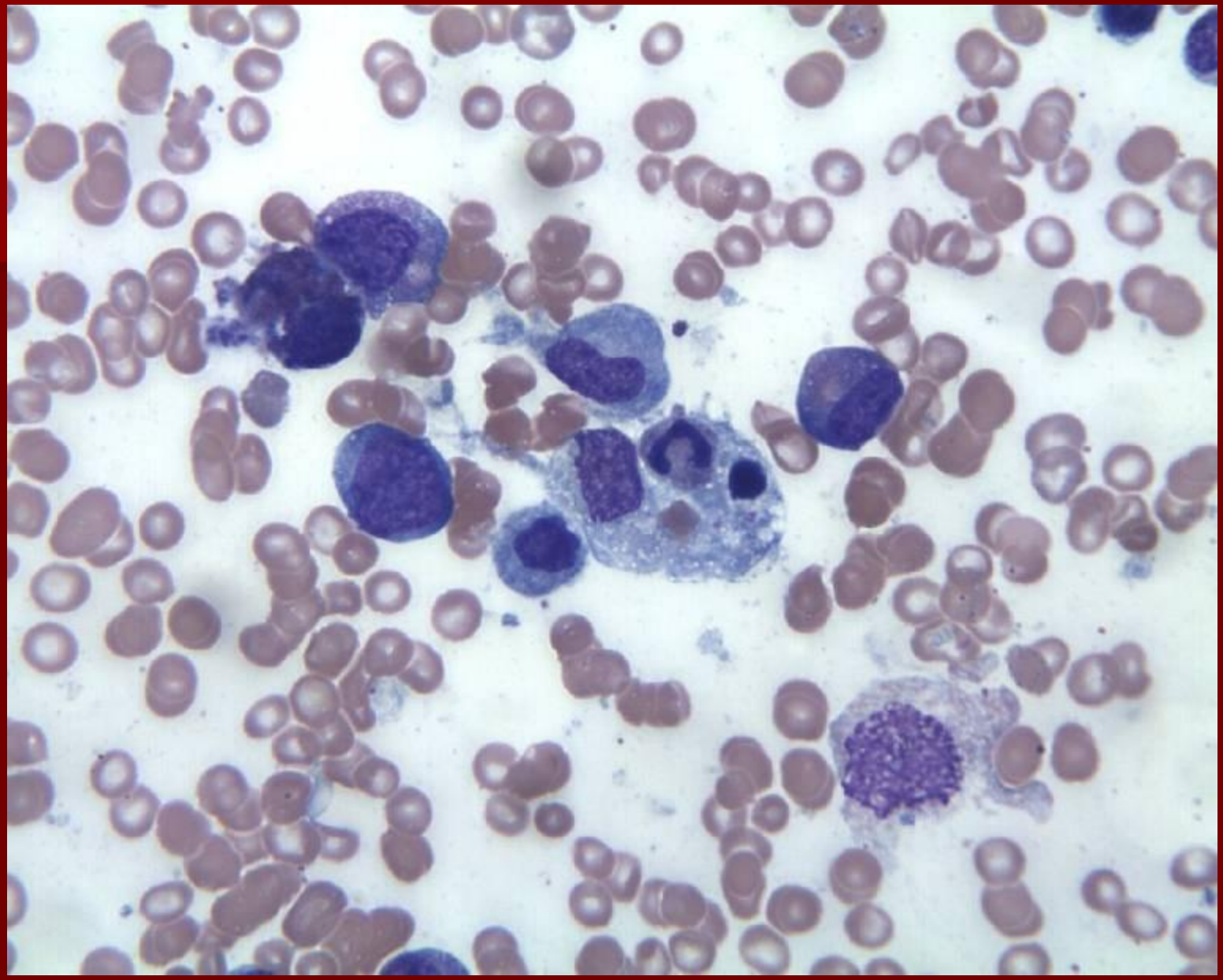
Solution is to use sodium citrate instead of EDTA

Hypocellular Bone Marrow





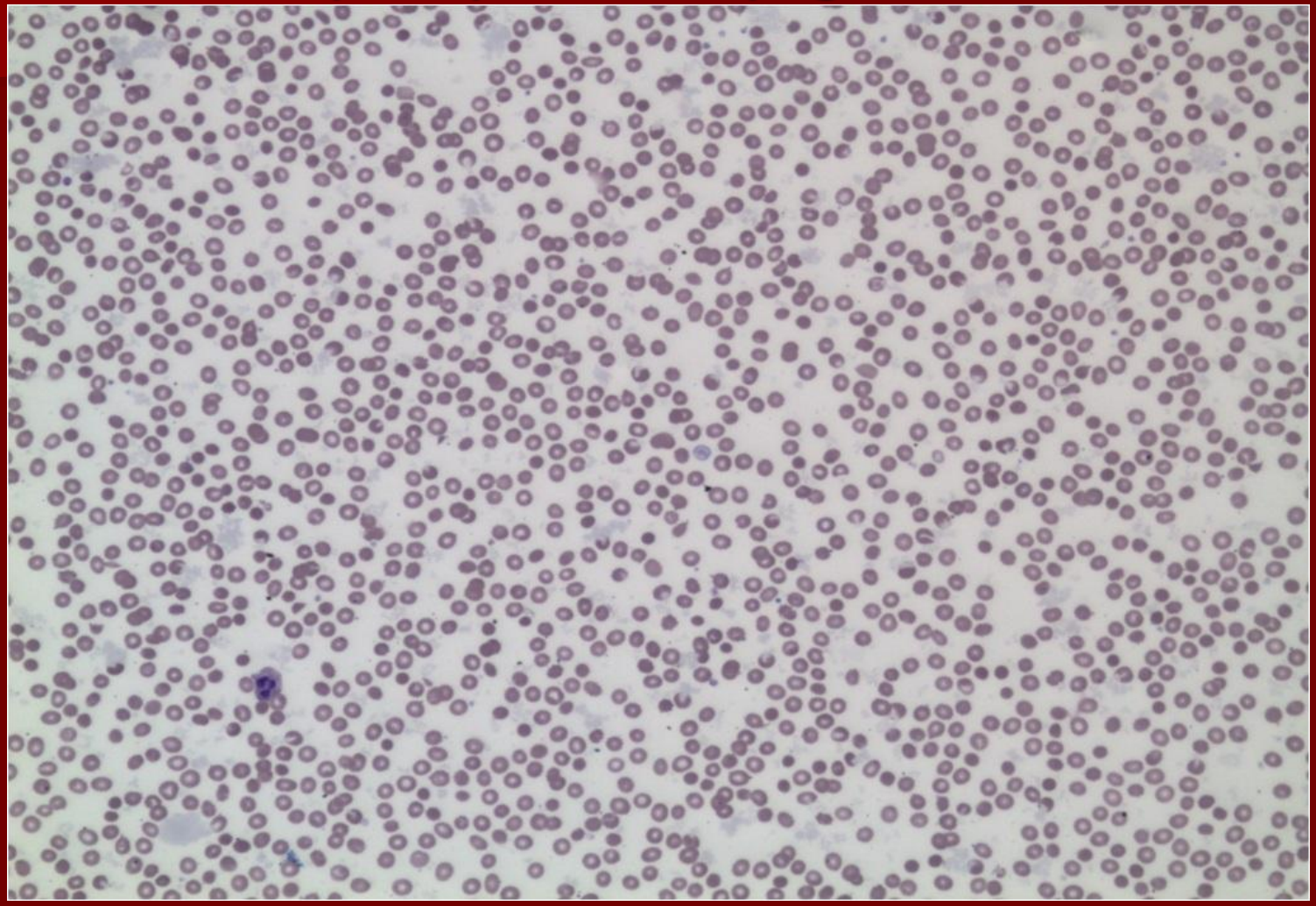
Parvovirus B19



Hemophagocytic lymphohistiocytosis (HLH) : Bone marrow aspirate

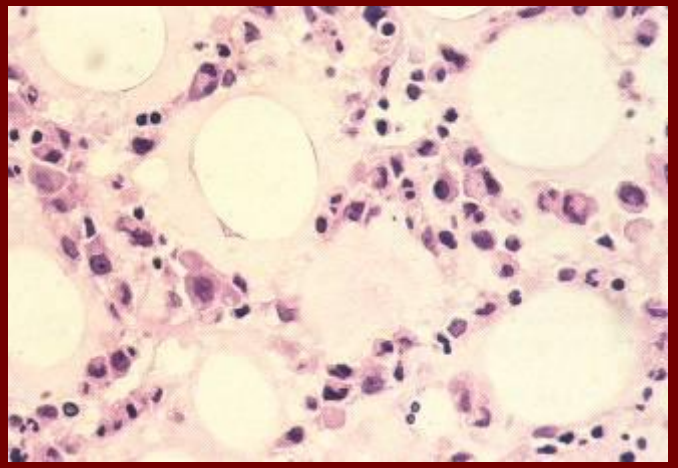
CRYOGLOBULINAEMIA

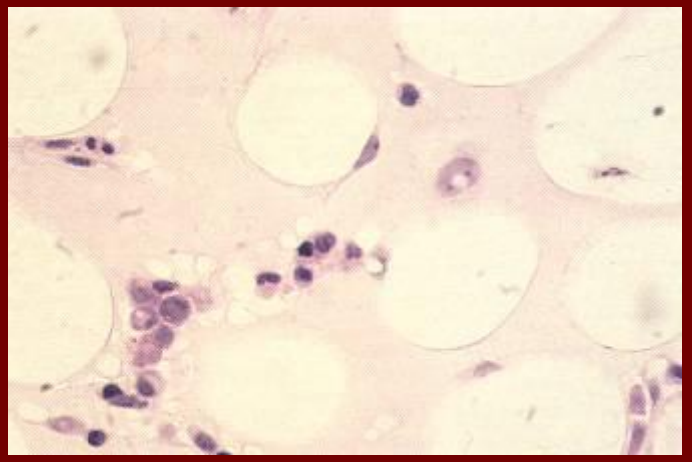
Peripheral blood smear with clumps of precipitated cryoglobulin



Serous Fat Atrophy

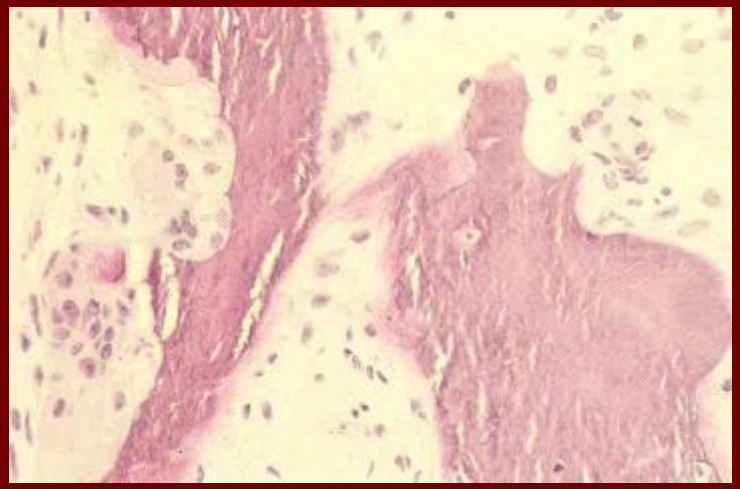
- AKA gelatinous transformation
- Associated with starvation and wasting diseases
- Homogenous extracellular substance with "gelantinous" appearance

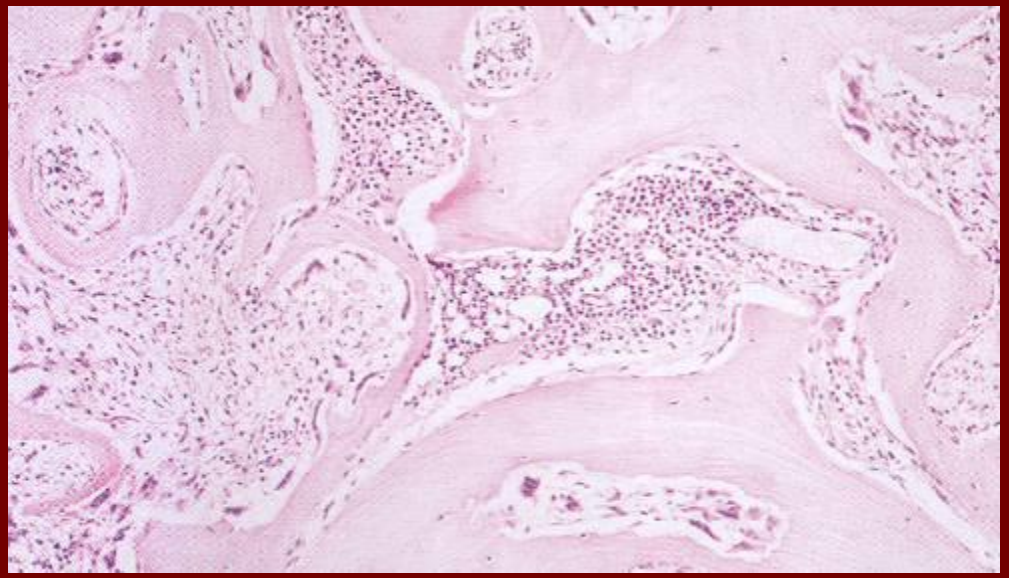




Renal Osteodystrophy

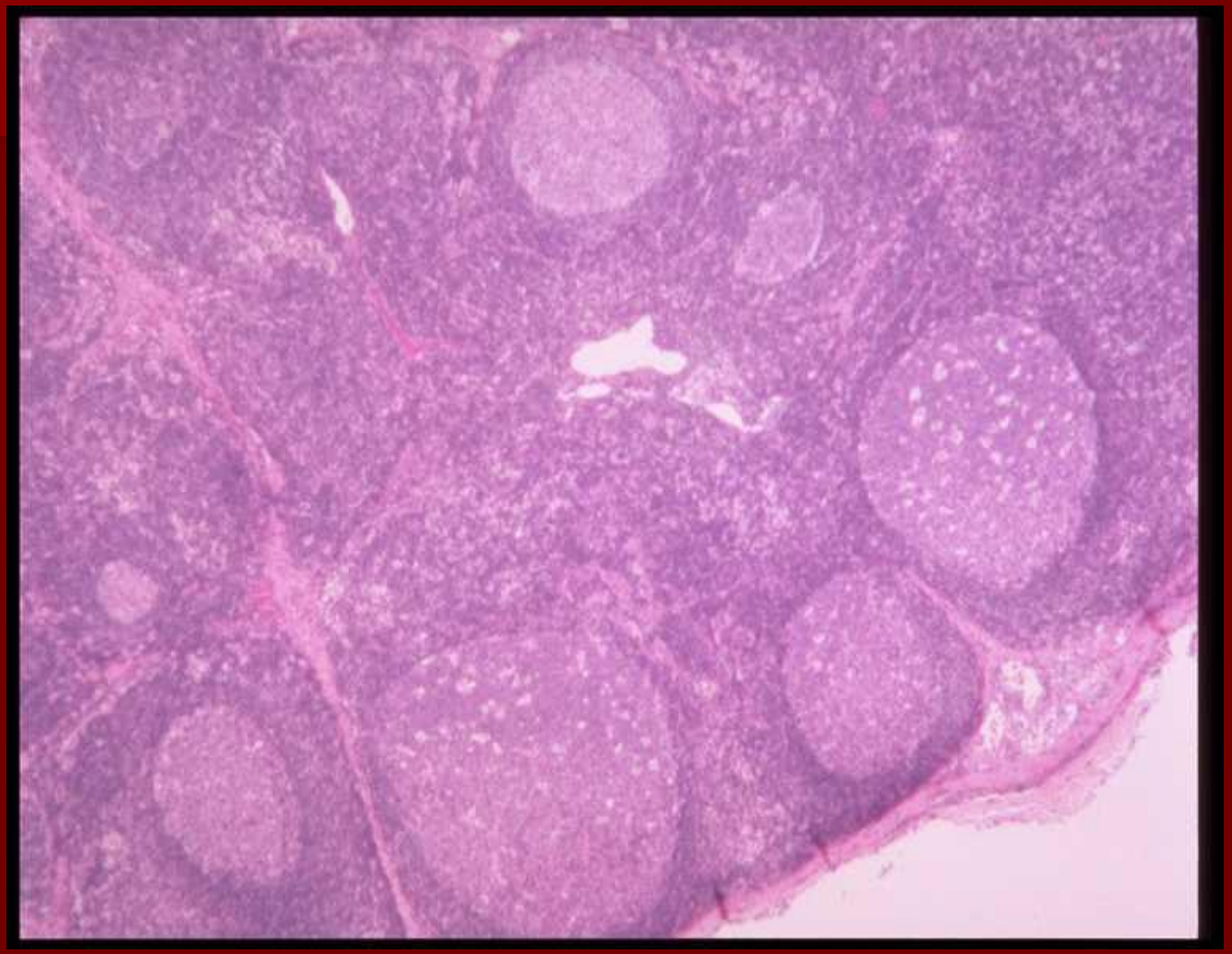
- "Scalloping" of bony trabeculae
- Peritrabecular fibrosis

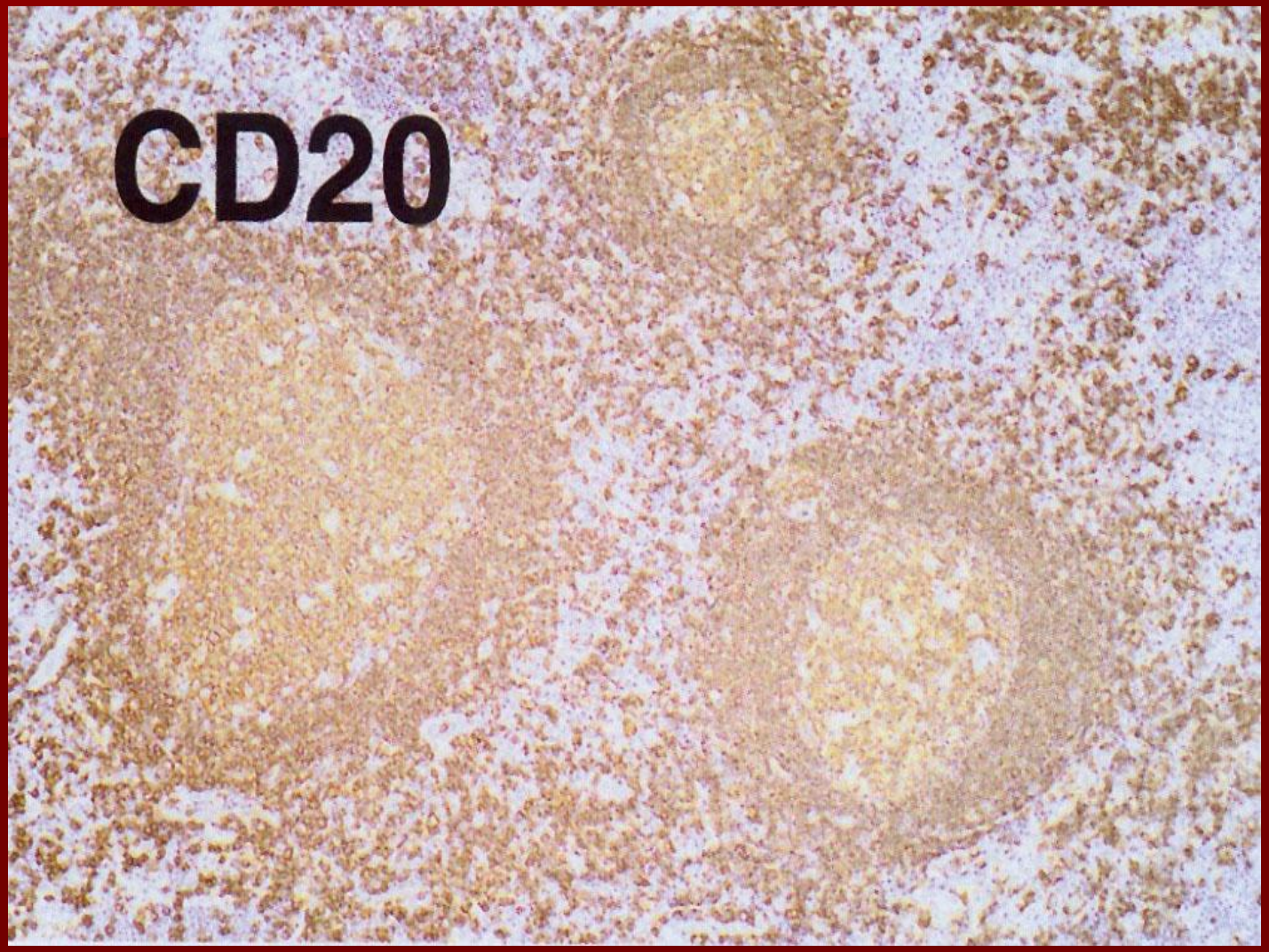


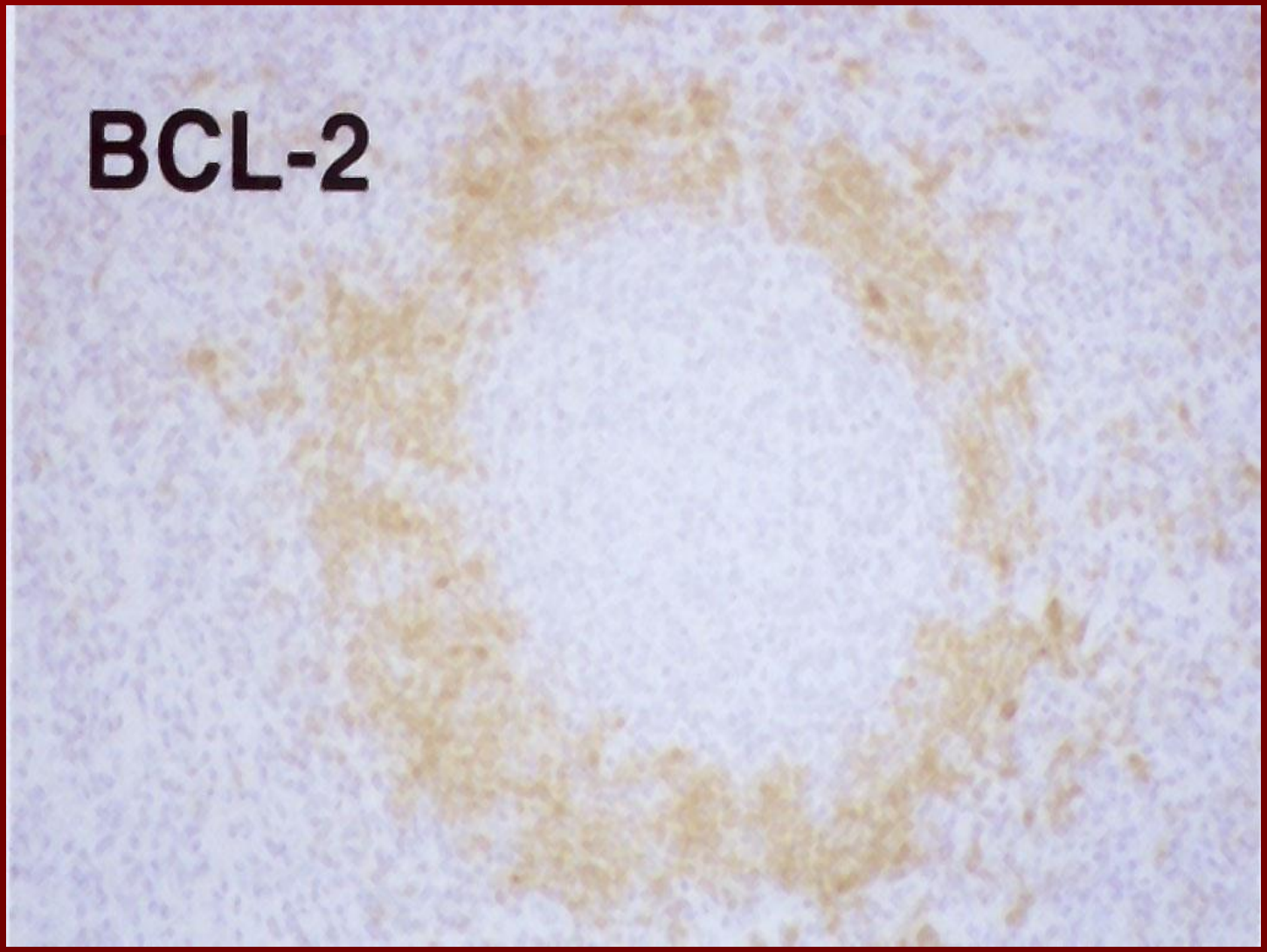


Nonmalignant Lymphadenopathy

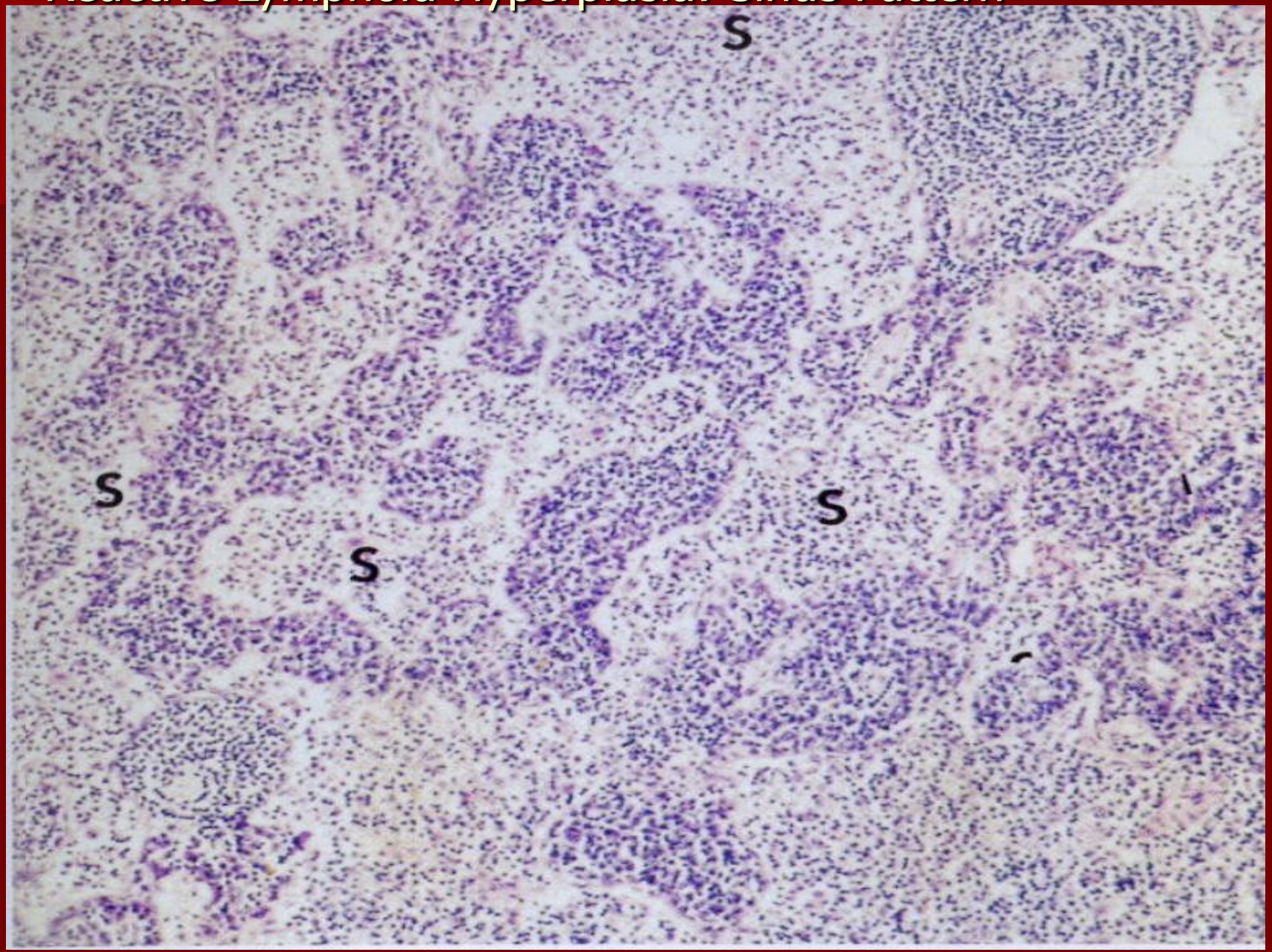
Reactive Lymphoid Hyperplasia
Follicular Pattern



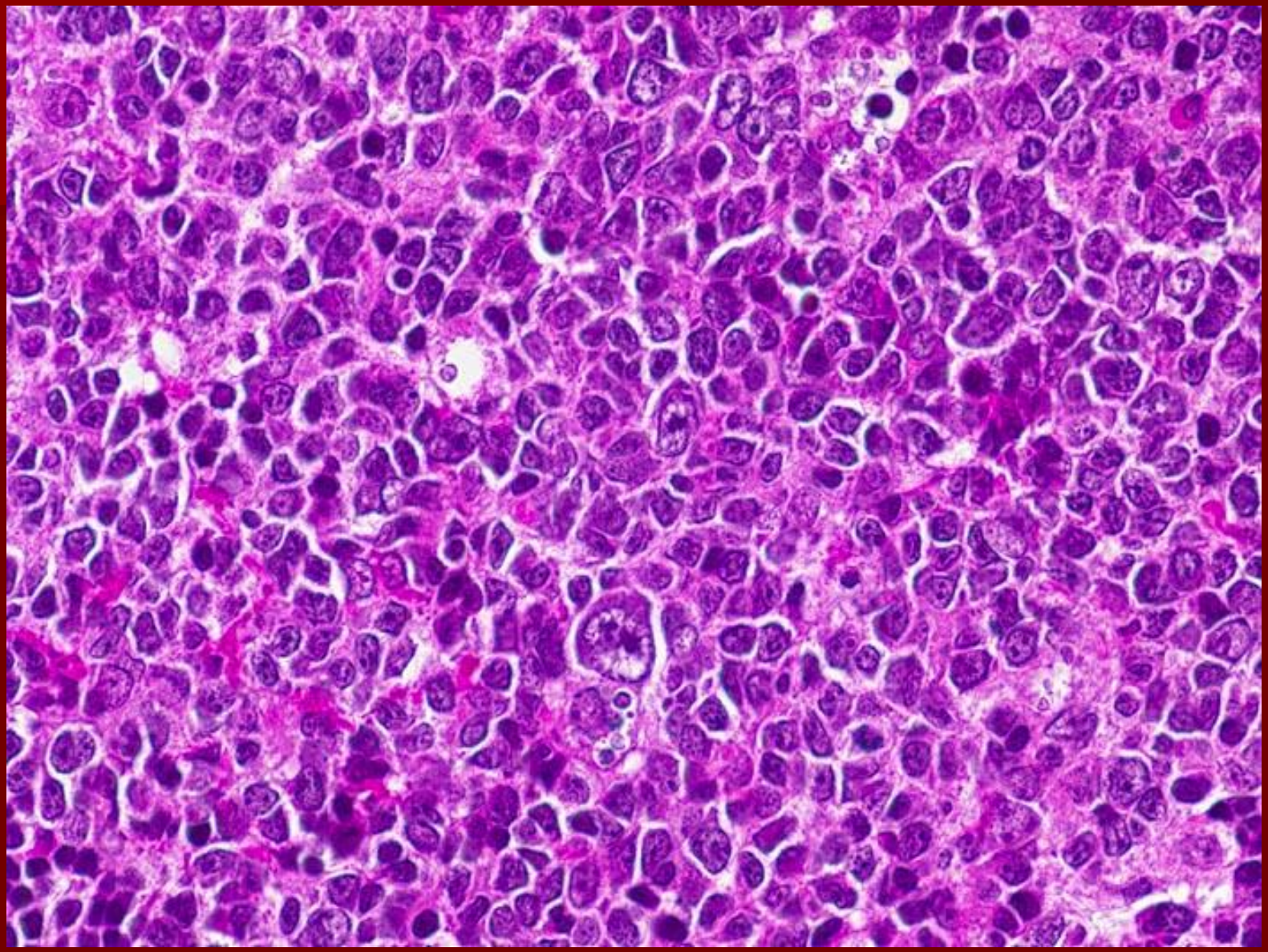

CD20

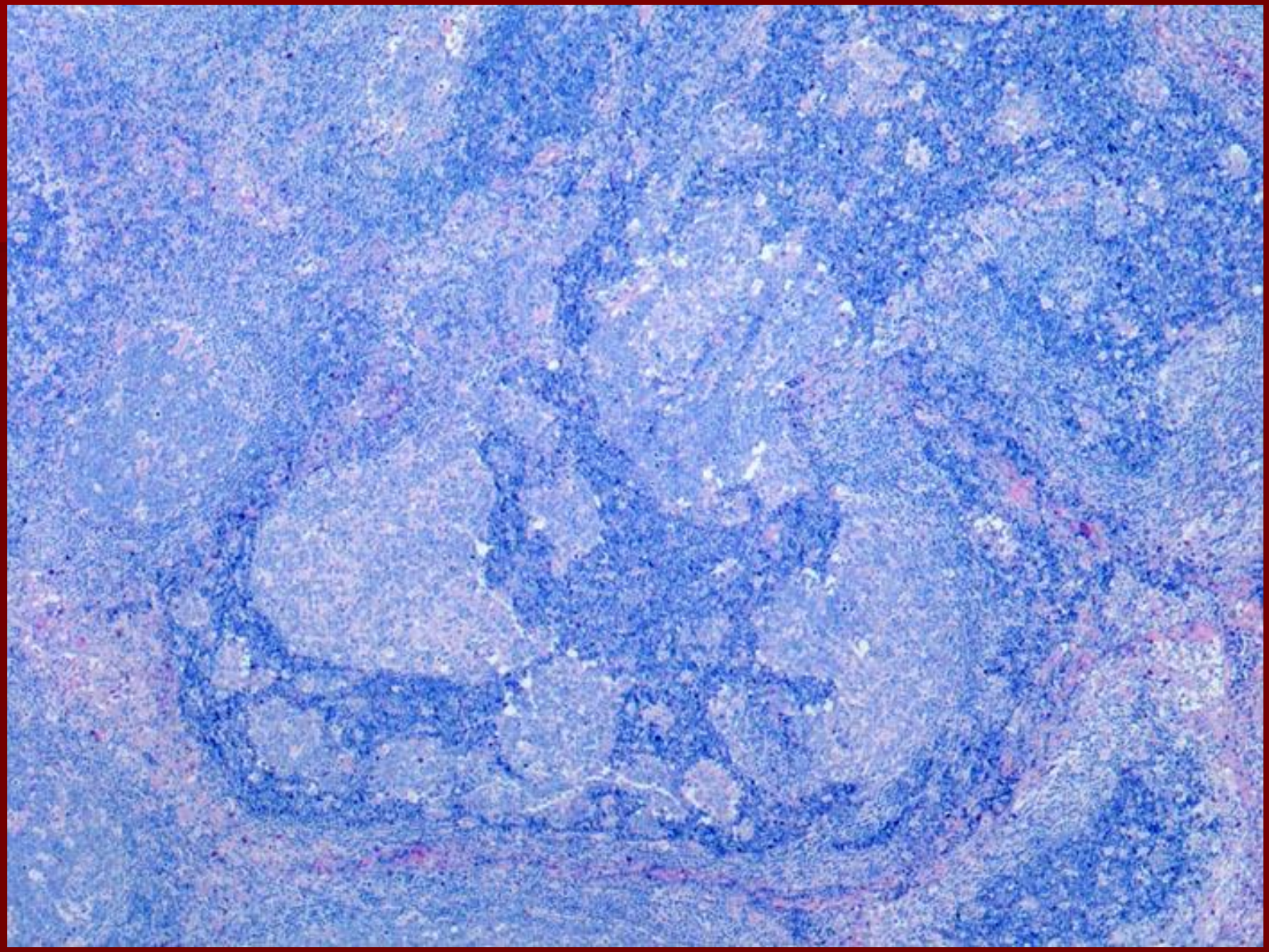

BCL-2

Reactive Lymphoid Hyperplasia: Sinus Pattern



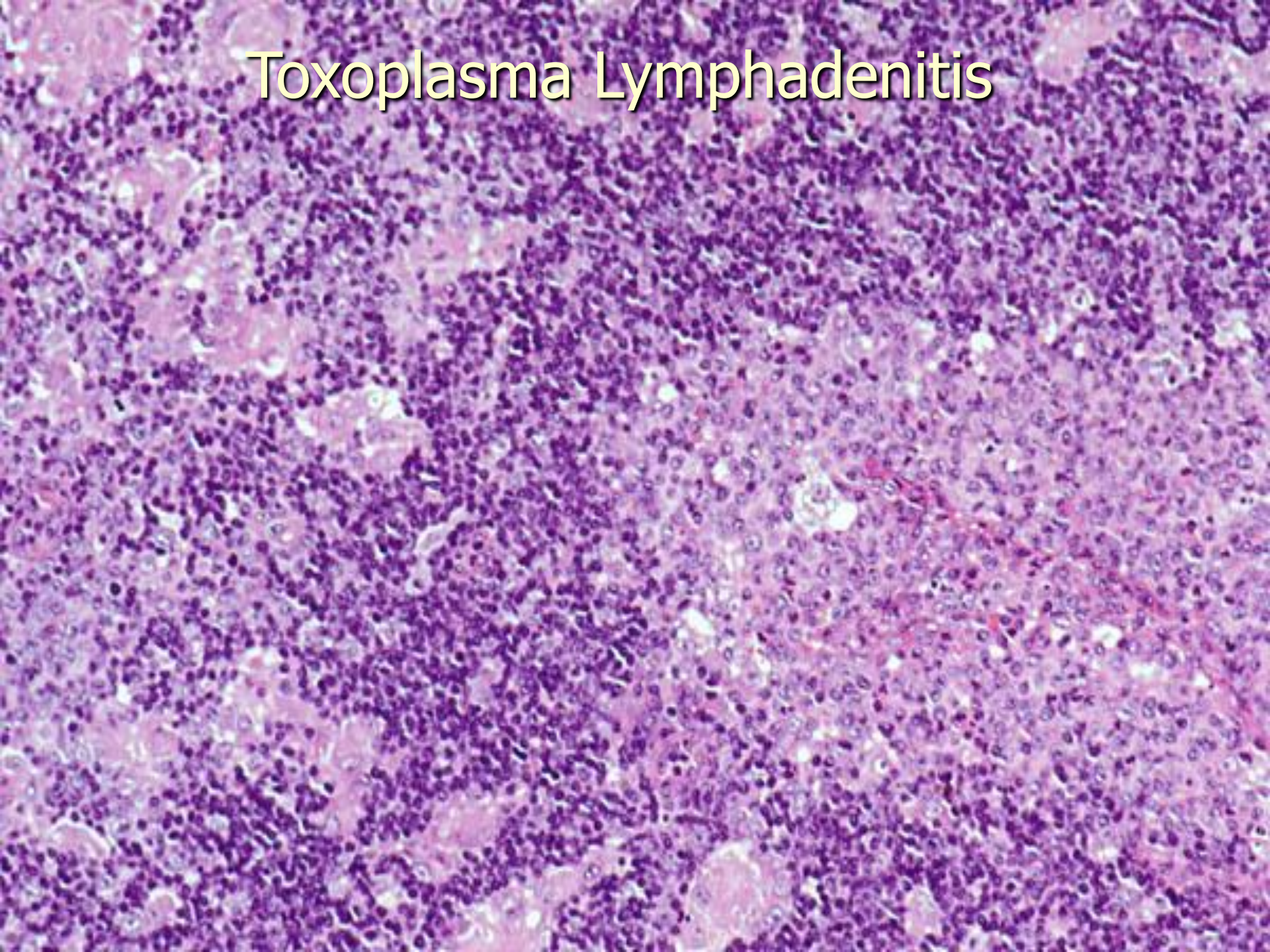
Infectious Mononucleosis



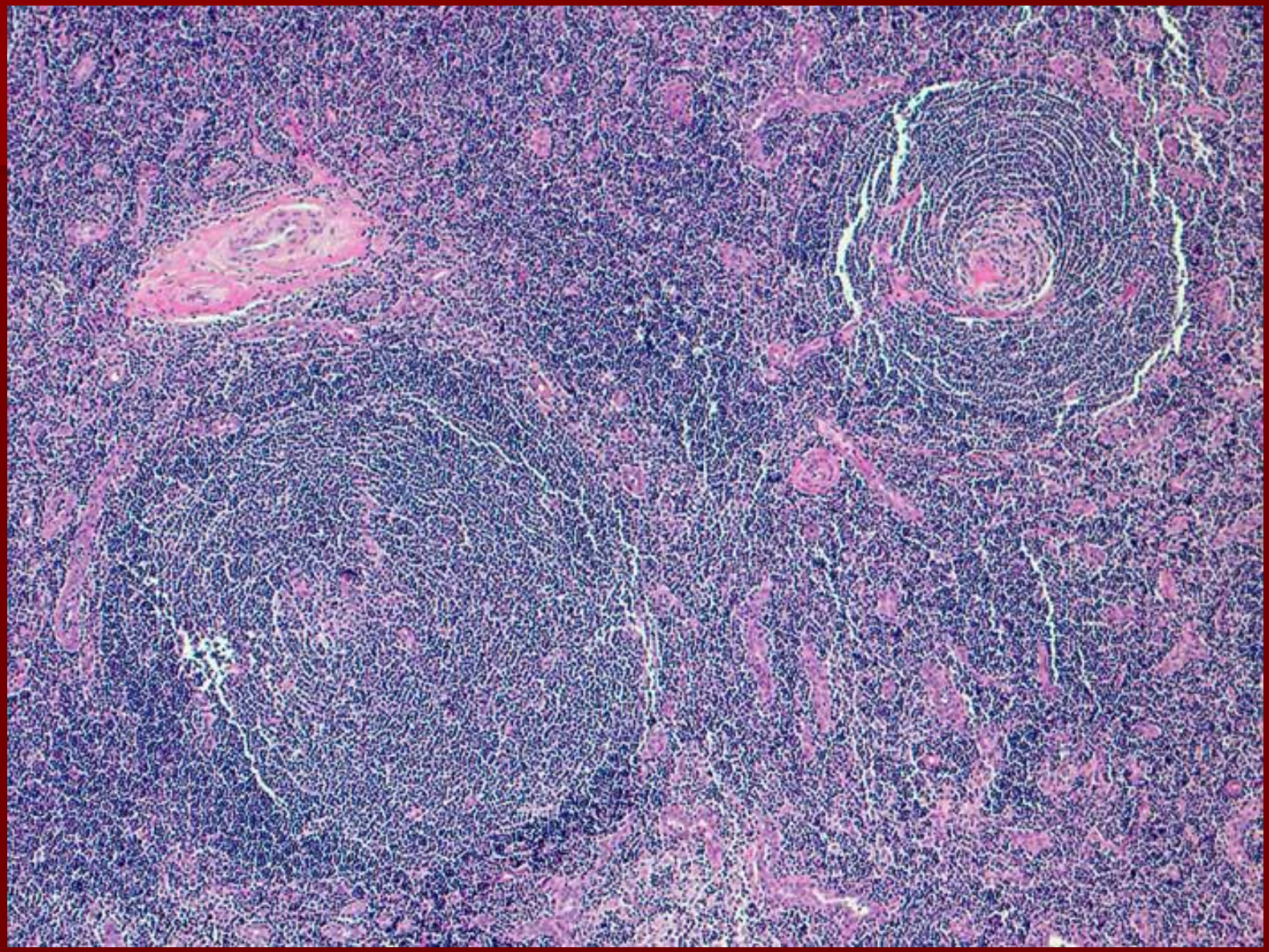


HIV Lymphadenitis (persistent generalized lymphadenopathy)

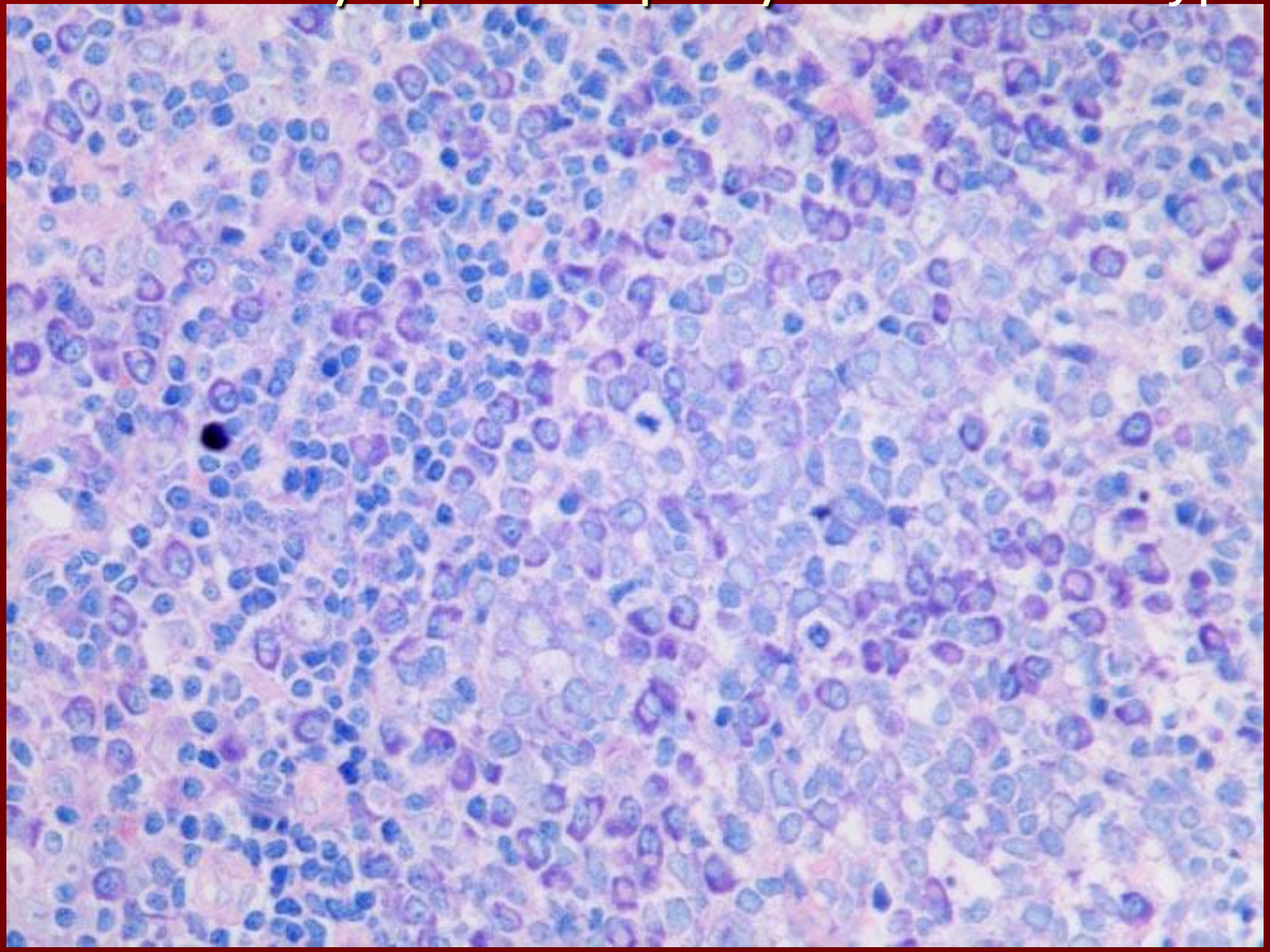
Toxoplasma Lymphadenitis

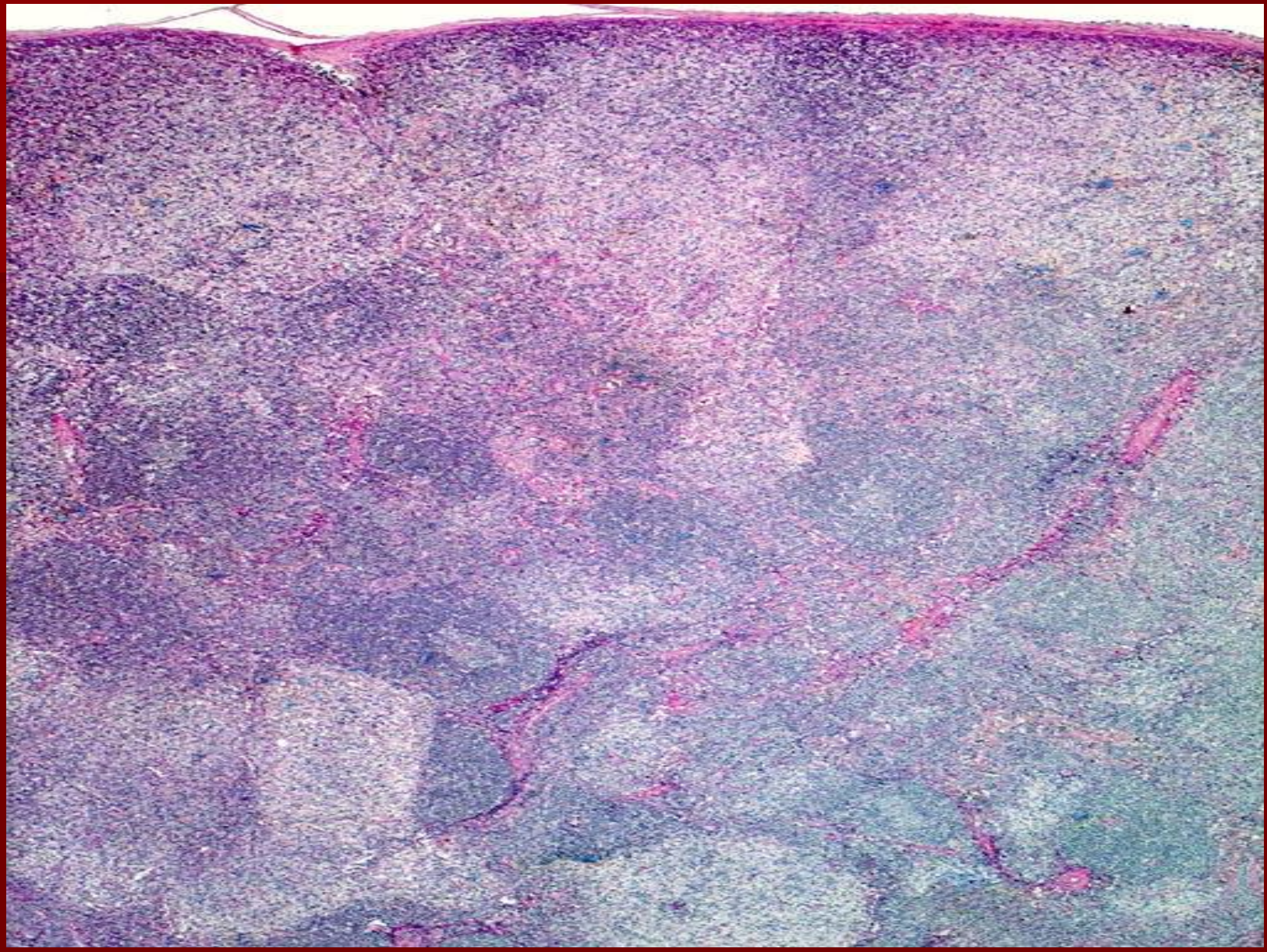


Castleman Lymphadenopathy: Hyaline-vascular type



Castleman Lymphadenopathy: Plasma cell type

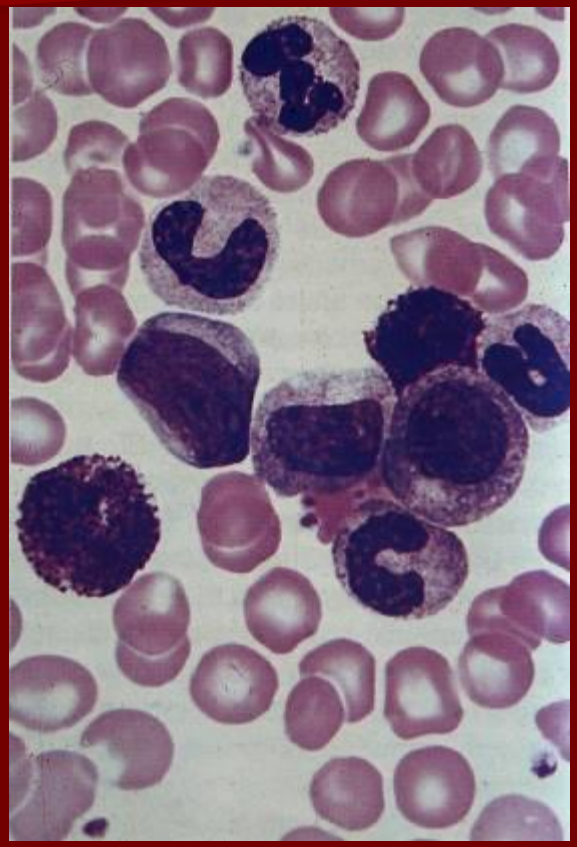




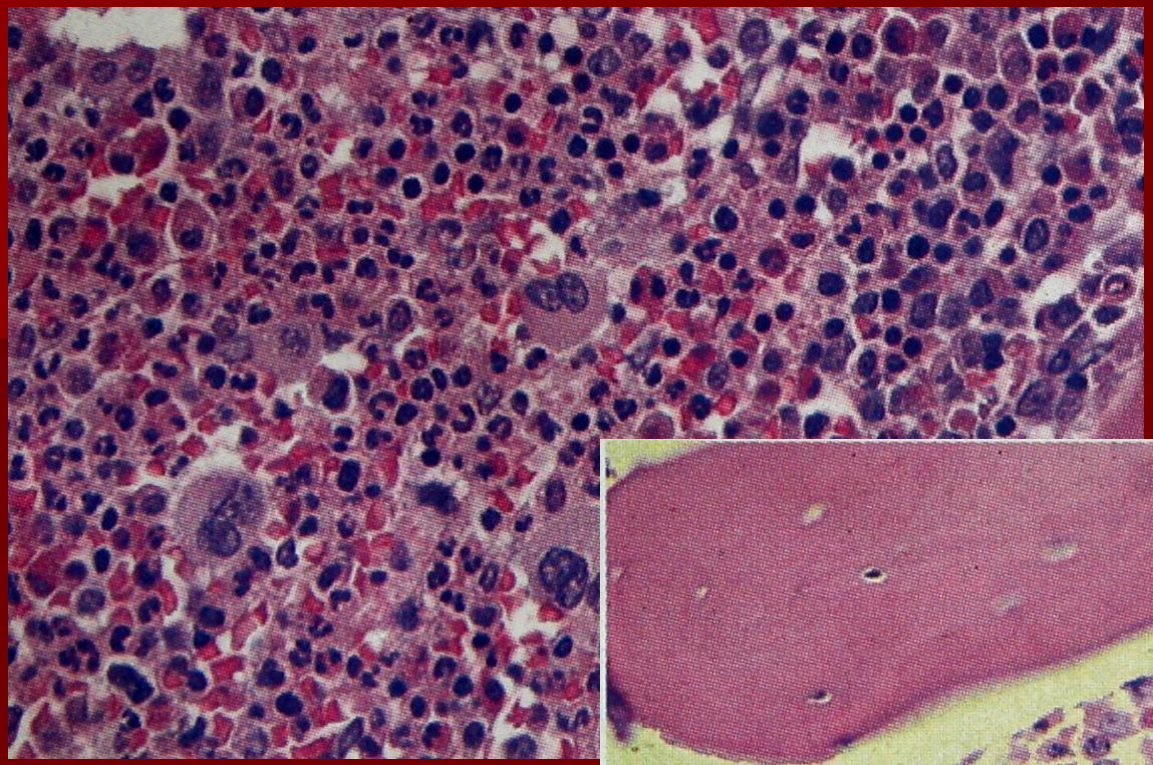
Dermatopathic Lymphadenopathy

Introduction to Hemepath: II. Malignant HemePath

Chronic Myelogenous Leukemia, bcr/abl1 pos

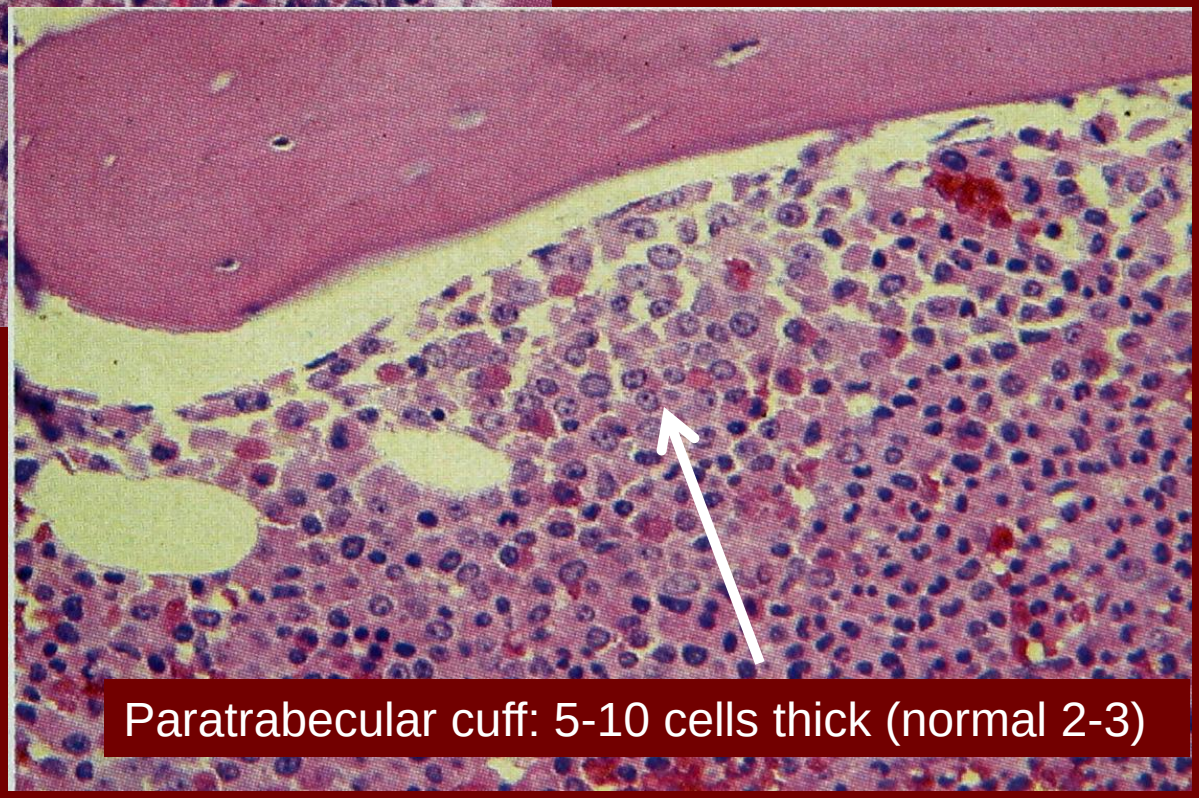


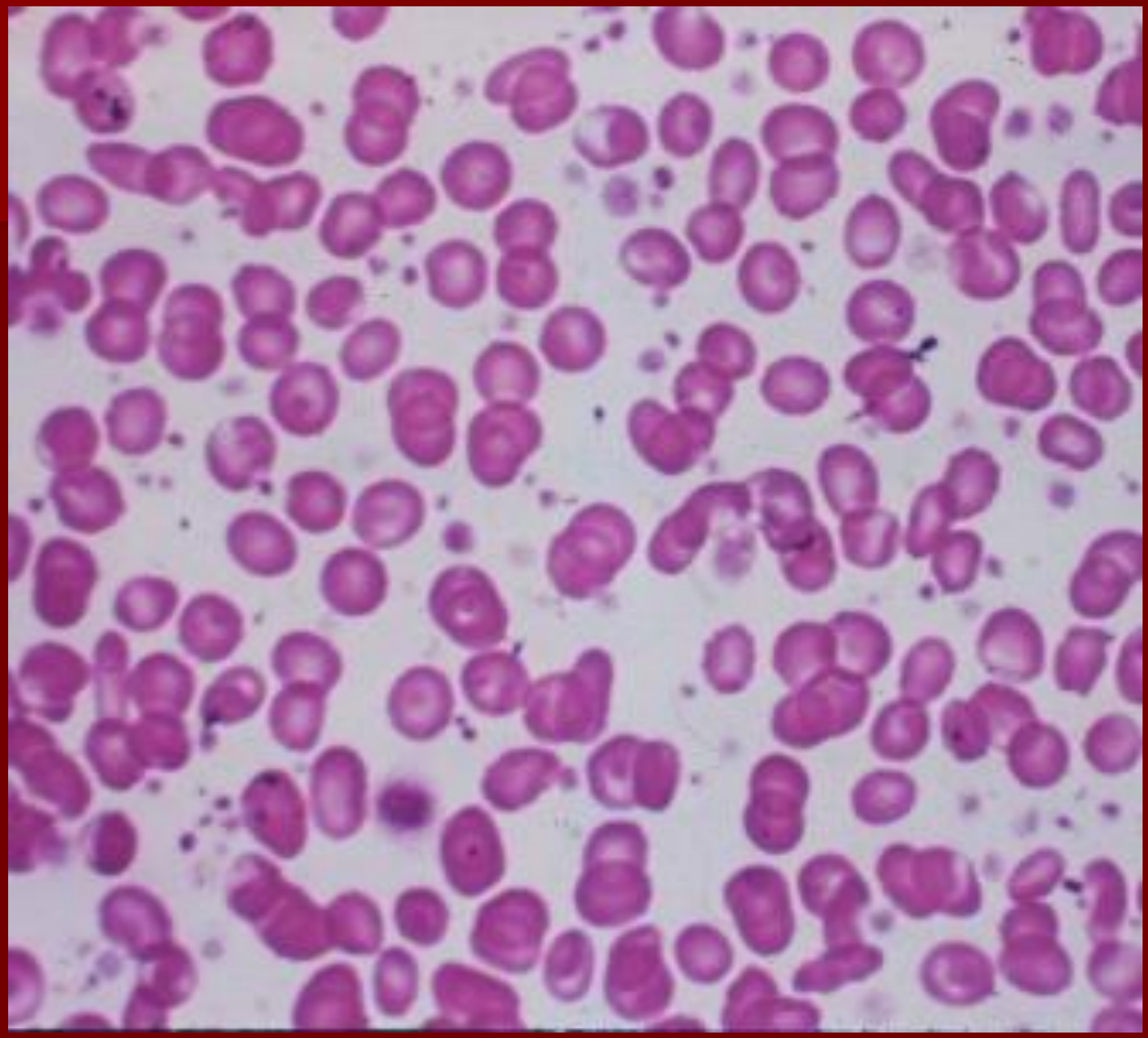
Peripheral Blood



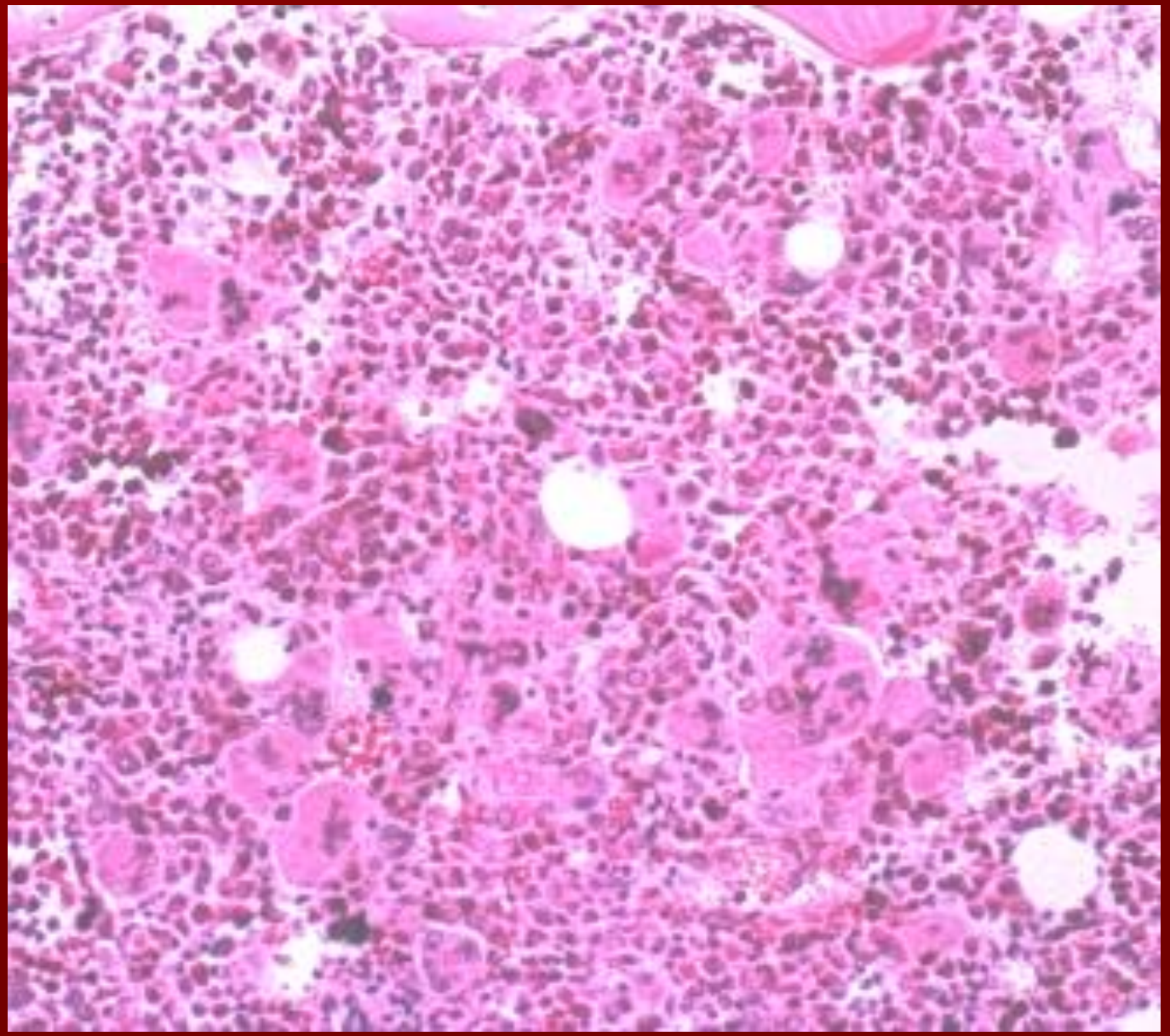
BM: hypercellular

BM: increased immature cells



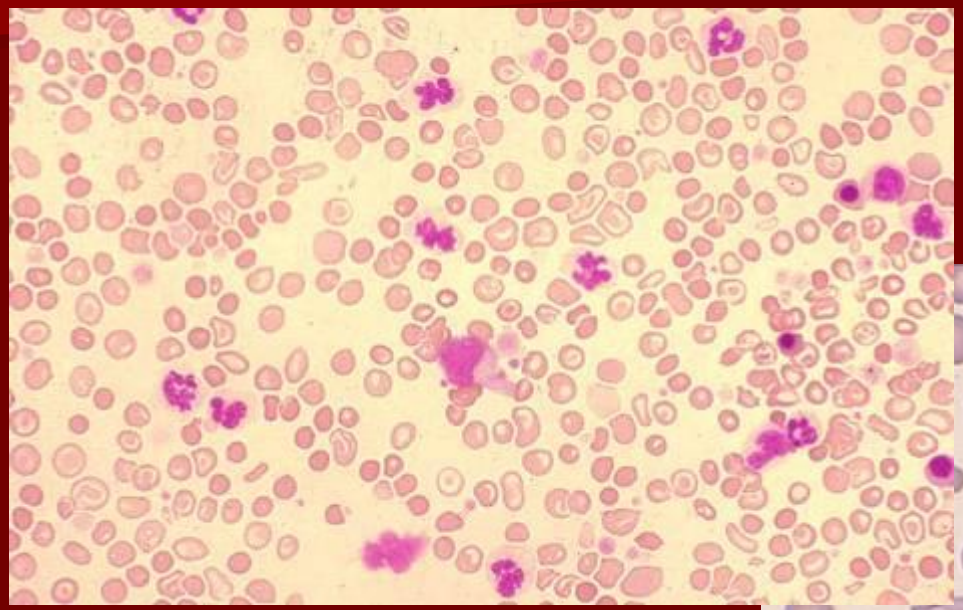


Essential Thrombocythemia: Peripheral Blood

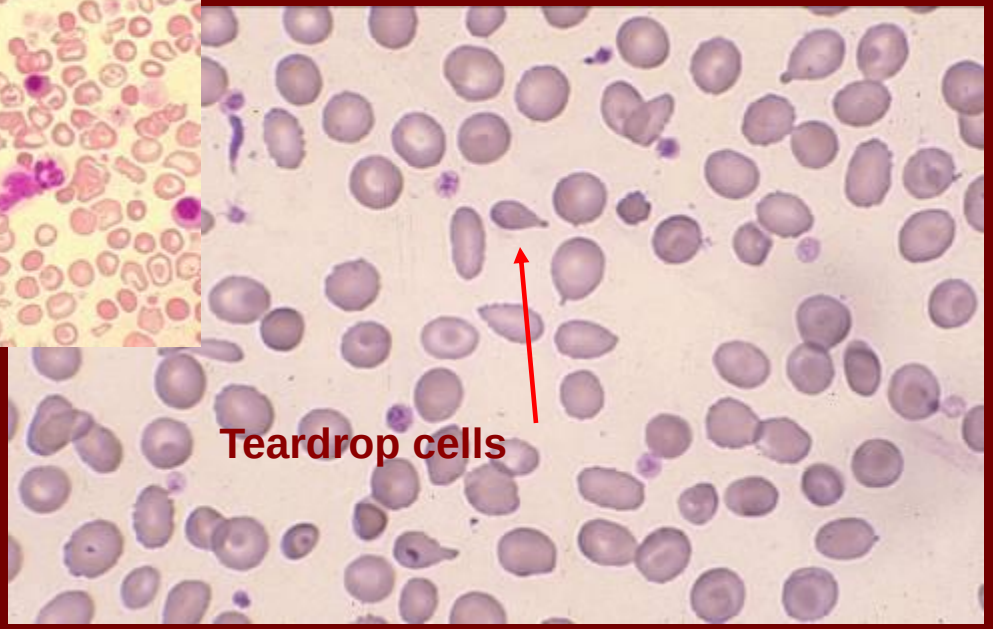


Essential Thrombocythemia: Bone Marrow

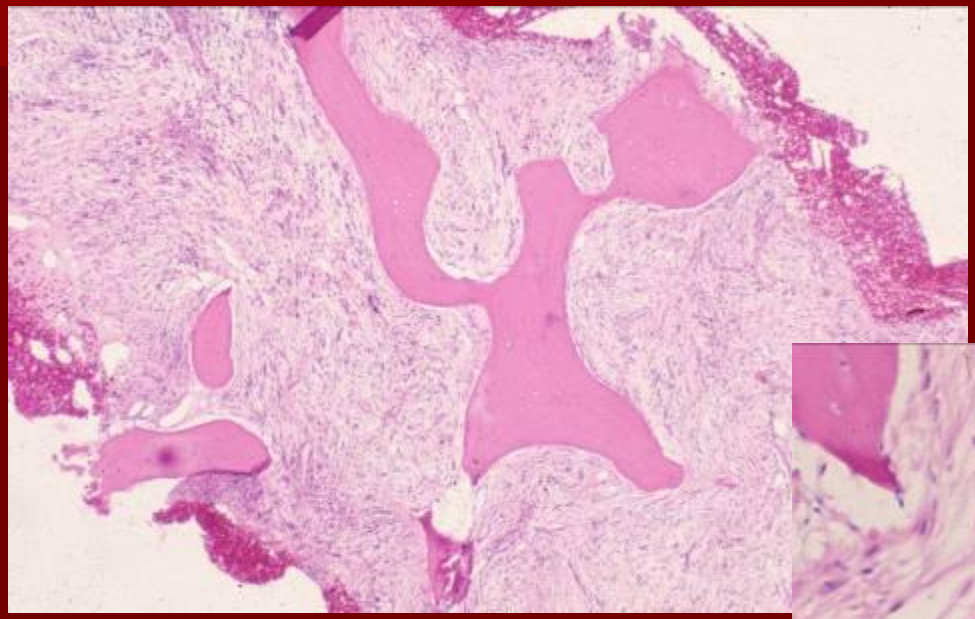
Primary Myelofibrosis



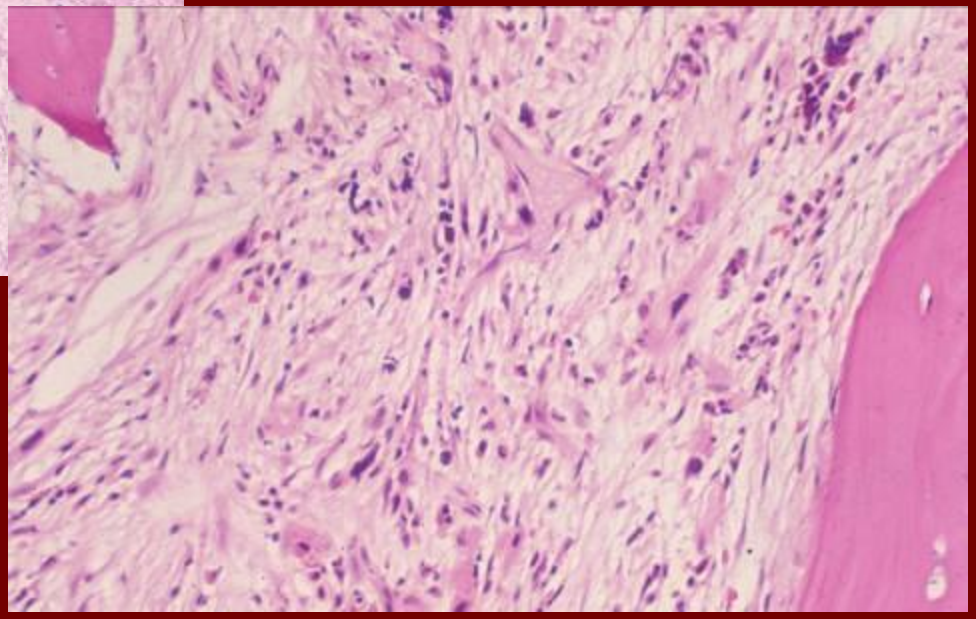
Peripheral blood smear



PM



Bone marrow biopsy



Myelodysplastic syndrome

General:

-Stem cell disorder

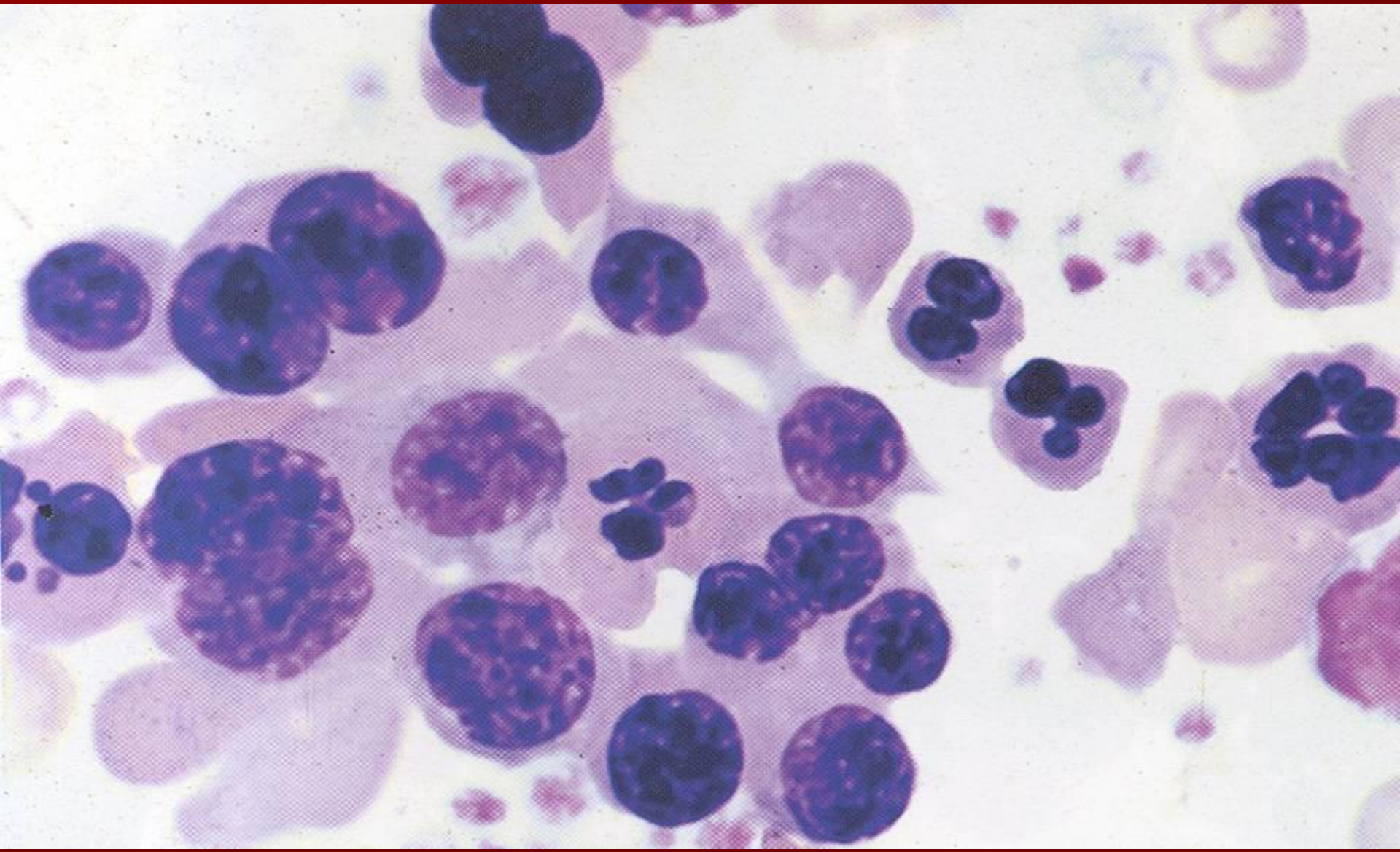
-Dysplasia

-Ineffective hematopoiesis

-Blasts <20% in blood and BM

- Median age: 70 y/o

- Incidence: 3-5/100,000

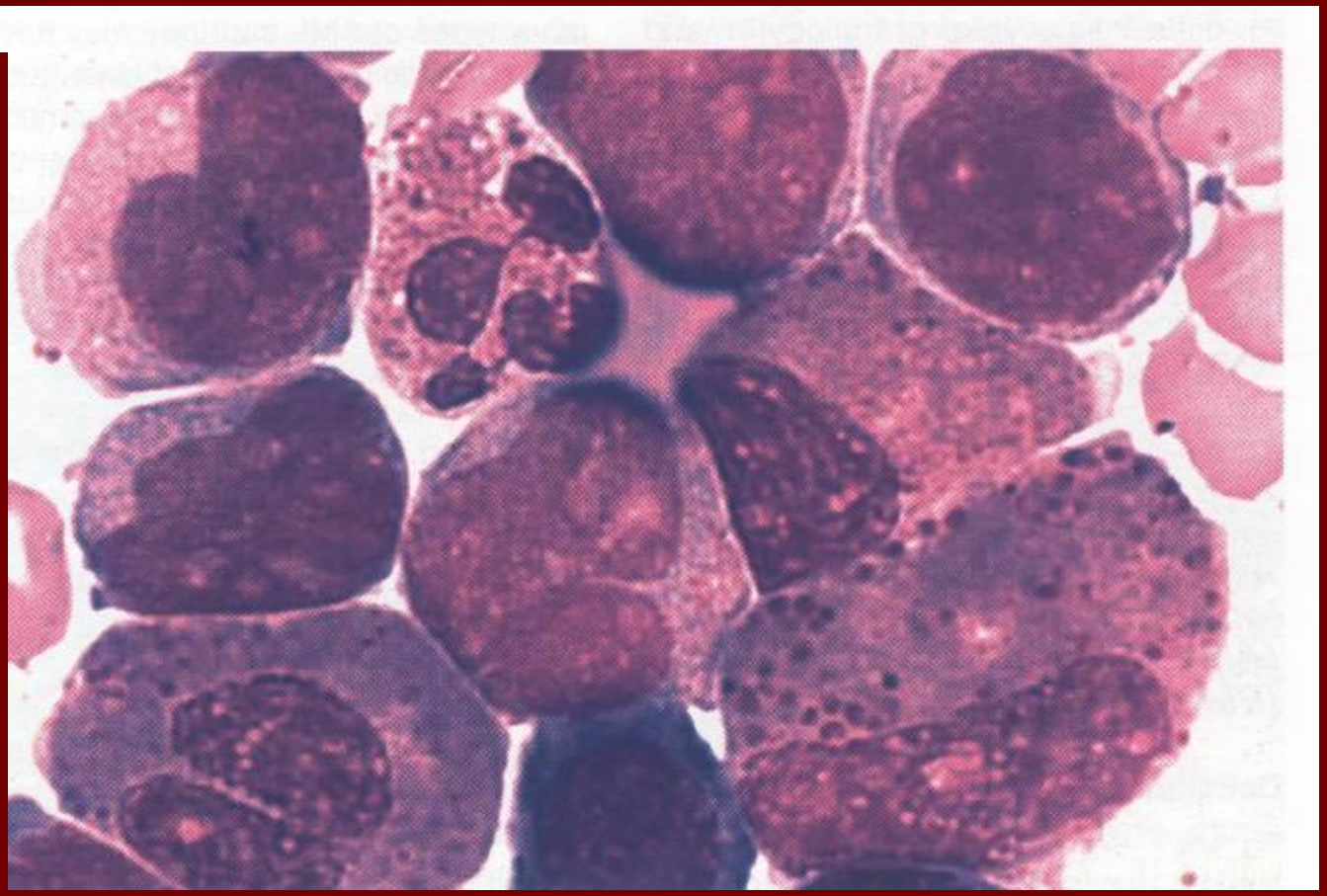


Dyserythropoiesis, Bone marrow aspirate

Acute Myeloid Leukemia with recurrent cytogenetic abnormalities t(8;21)(q22;q22)

- 5-12% of all AMLs,
  1/3 of AML-M2 cases
- May present with myeloid sarcoma

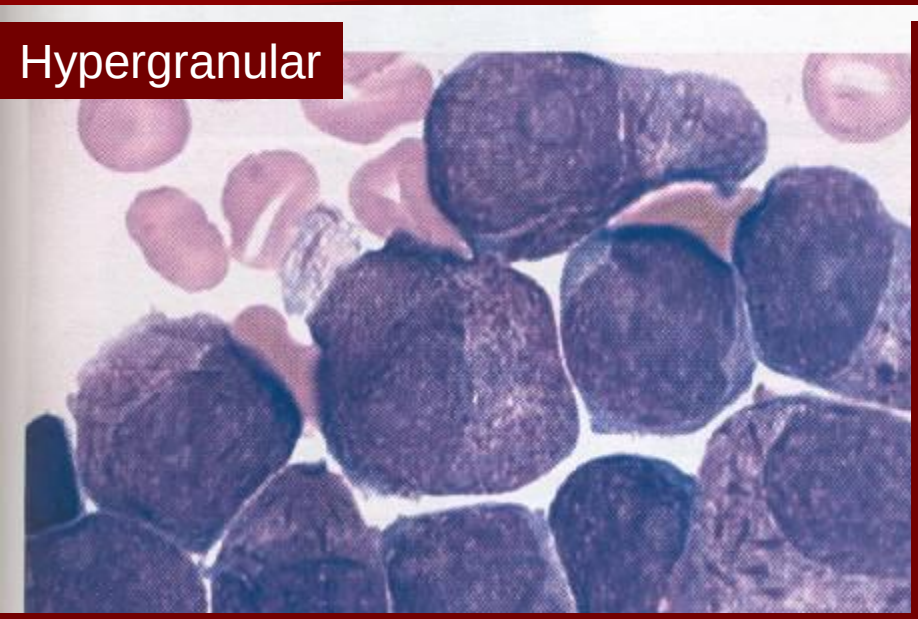
Acute Myeloid Leukemia with inv(16)(p13q22)



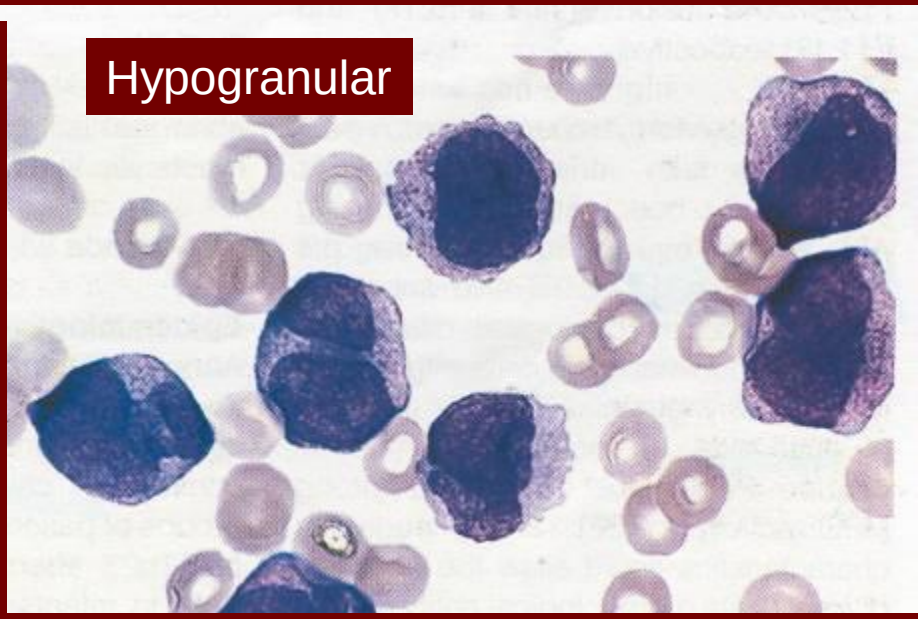
Acute promyelocytic leukemia,

t(15;17)(q22;q21);(PML/RARa)

Hypergranular



Hypogranular



Acute myeloid leukemia with 11q23(MLL) abnormalities

Typically AML, with monocytic / myelomonocytic feature (M4, M5), occasional M1, M2

Epidemiology: 5-6% of AML, more in children
Two clinical groups:
-infants
-therapy-related, topoisomerase II inhibitors (translocation of chromosome 11 and 4, 9, or 19)

AML with Gene Mutations: FLT3

- FLT3: Member of the class III receptor tyrosine kinase family
- Mutated gene leads to a constitutive activation of protein (leukemic transformation)
- FLT3-ITD Found in 28–34% of cytogenetically normal AML
- Associated significantly to worse clinical outcome

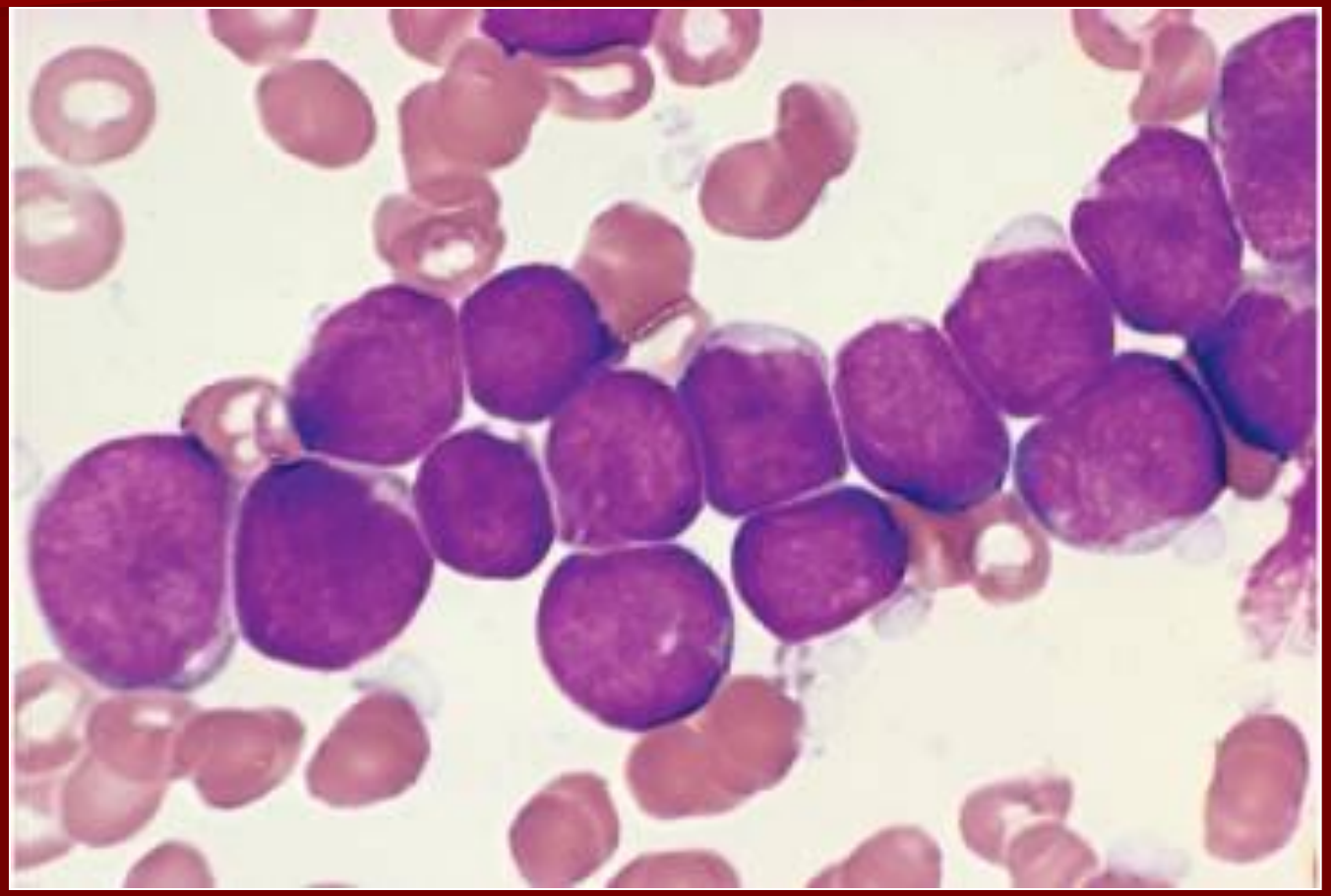
AML with Gene Mutations: NPM1

- NPM1: Nuclear protein with oncogenic and tumour-suppressive function
- Found in 25–35% of AML and predominantly in cytogenetically normal AML
- Associated to favorable prognosis (in absence of FLT3-ITD mutations)

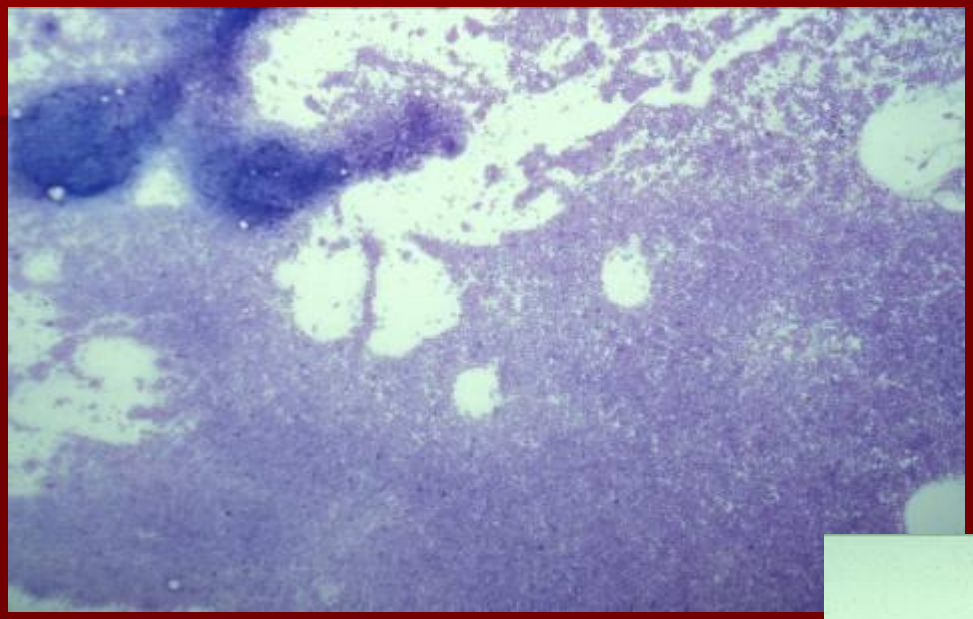
AML with Gene Mutations: CEBPA

- CEBPA: Transcription factor for differentiation of myeloid progenitors into neutrophilis
- Found predominantly in cytogenetically normal AML and in AML with 9q deletion
- Associated with higher CR rate and better DFS and OS

Acute Lymphoblastic Leukemia

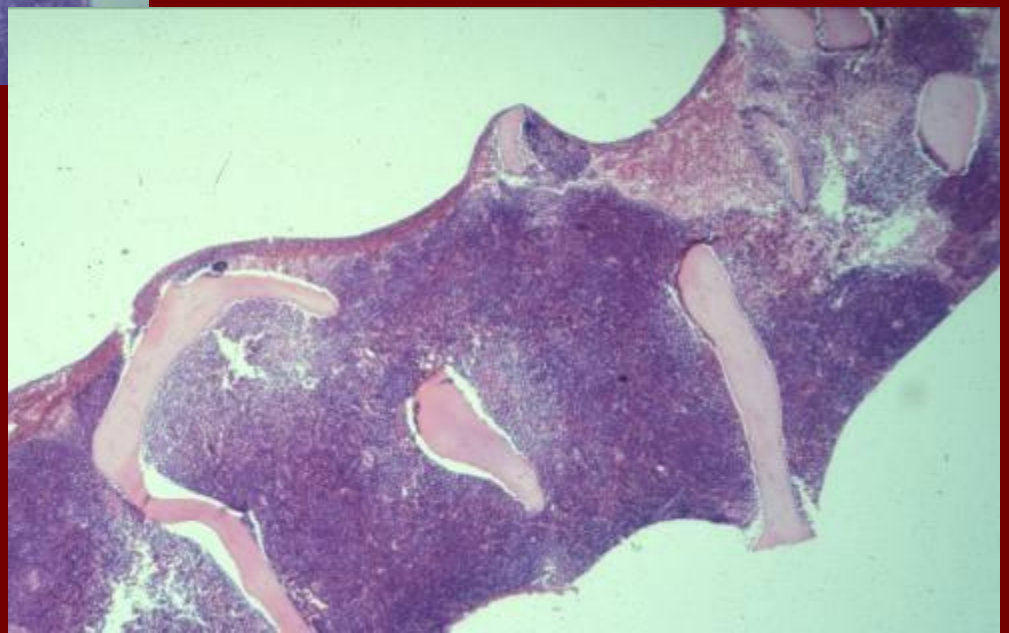


Acute Lymphoblastic Leukemia
Bone Marrow

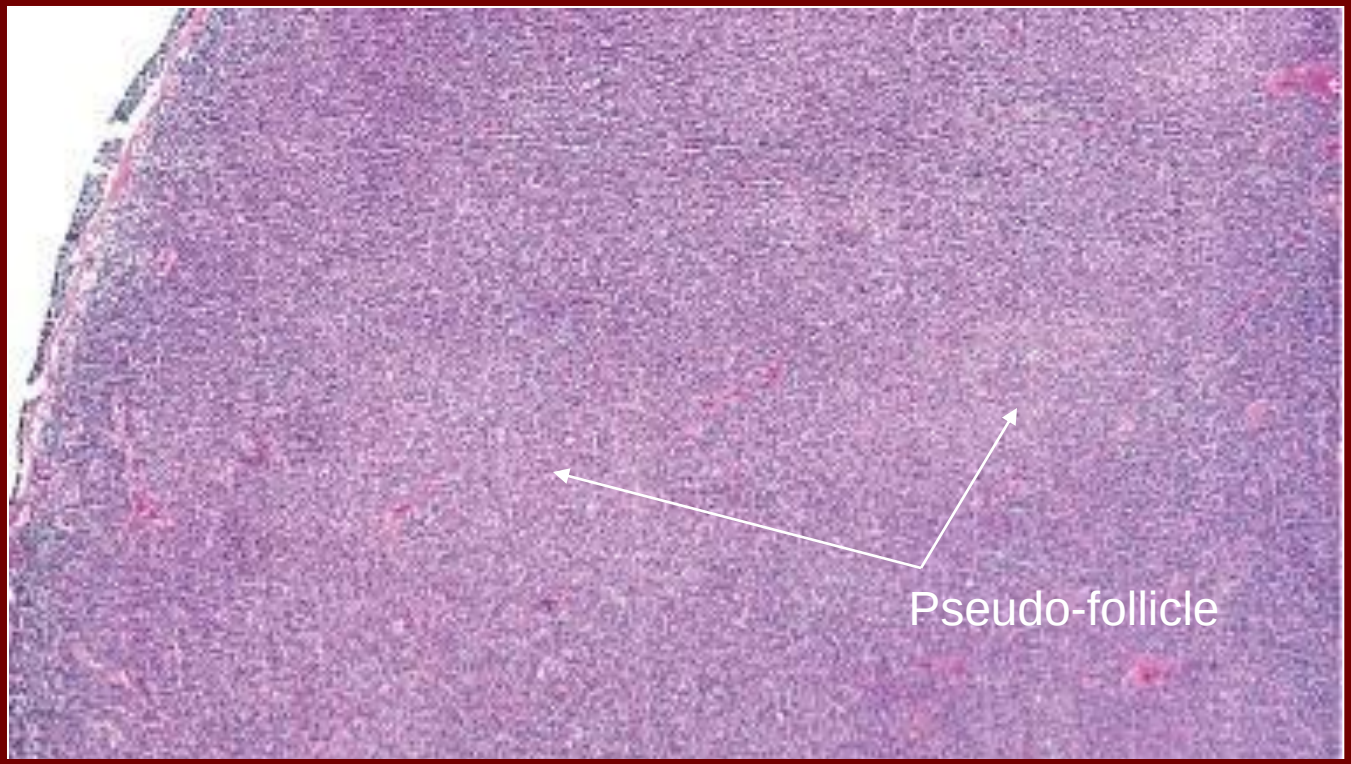


Bone marrow aspirate smear

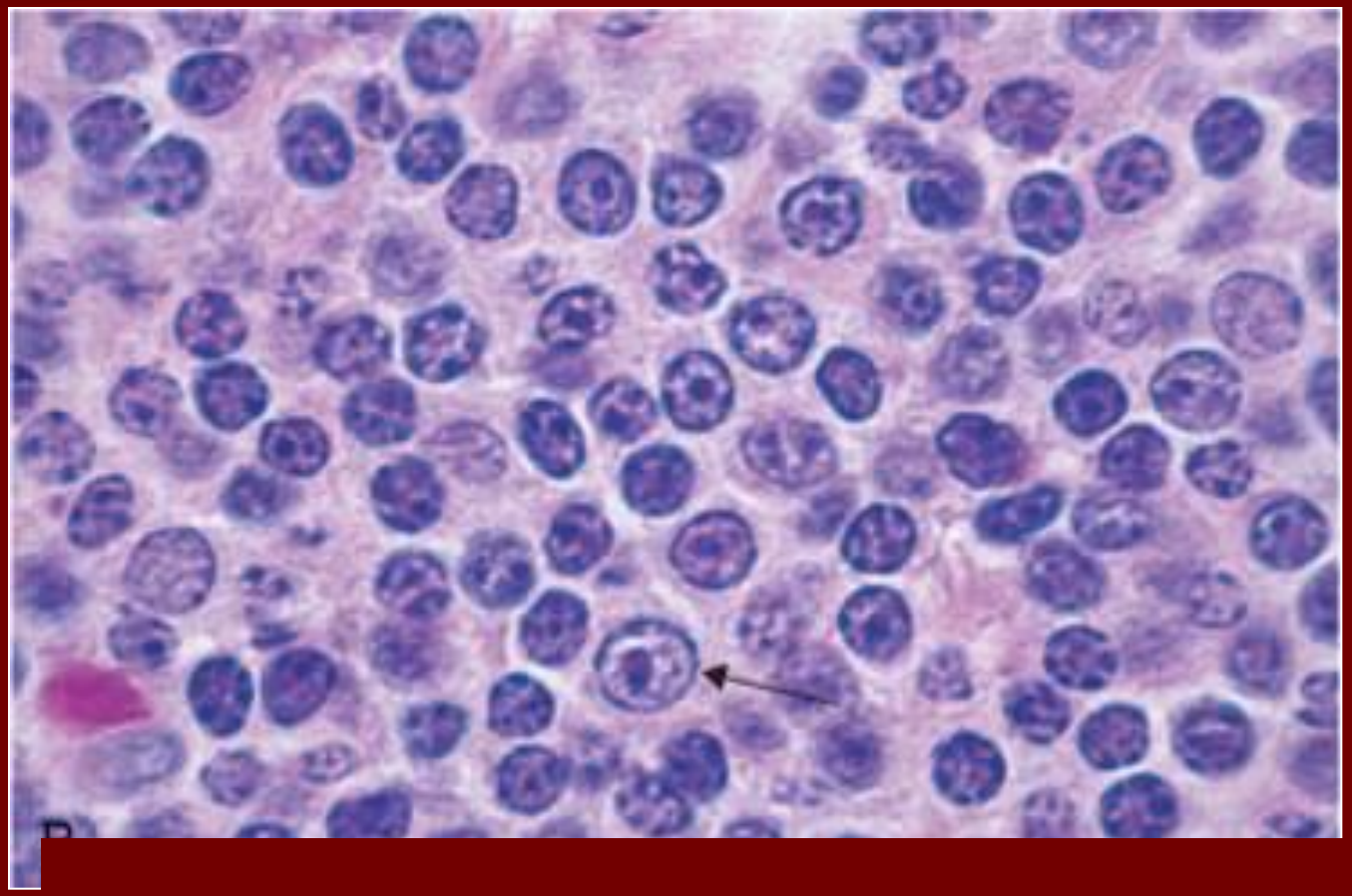
Bone marrow biopsy



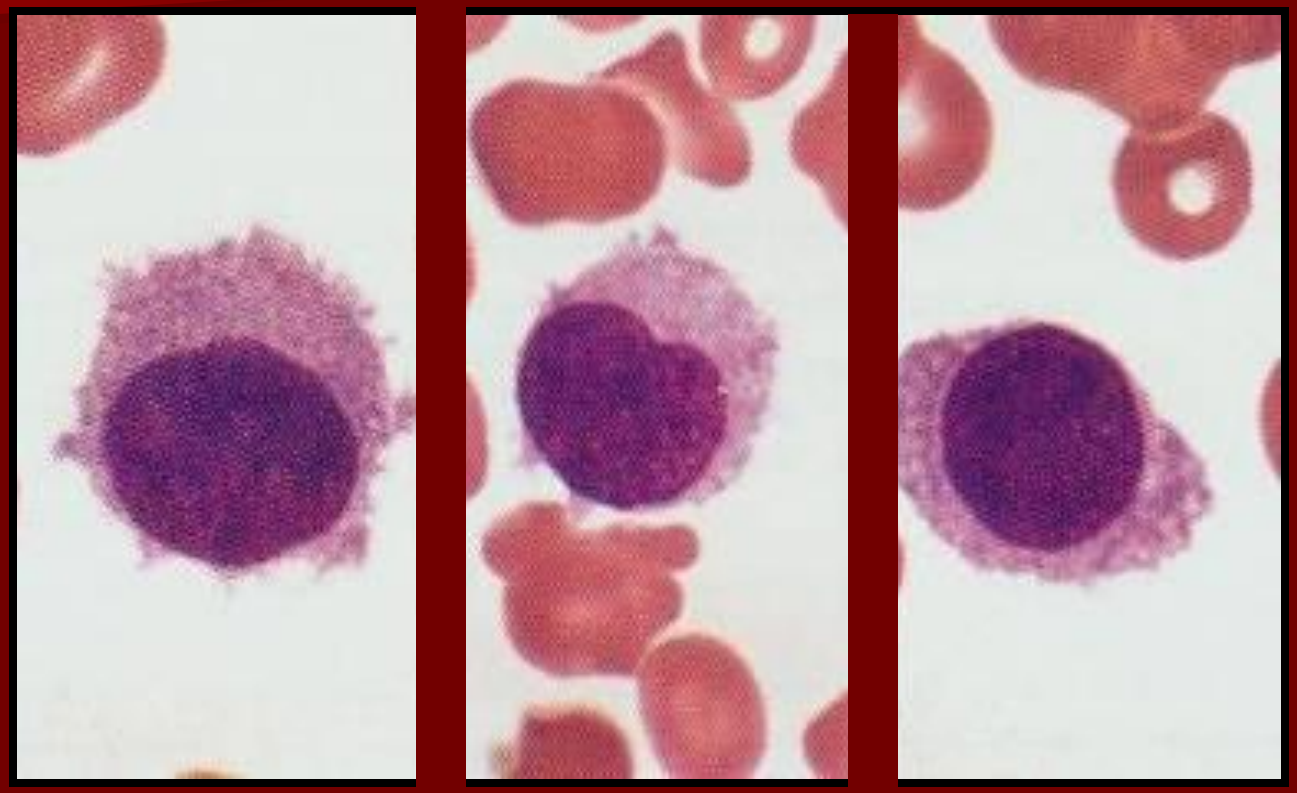
Small Lymphocytic Lymphoma



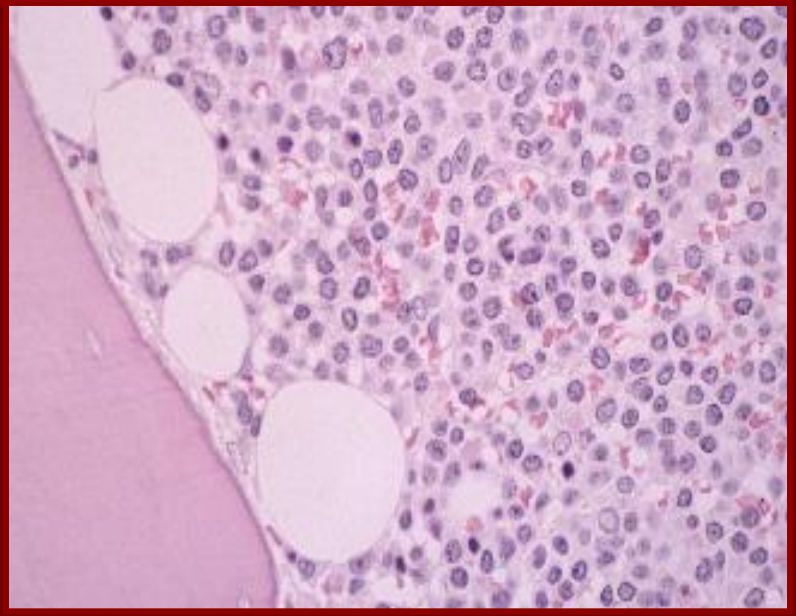
Small Lymphocytic Lymphoma



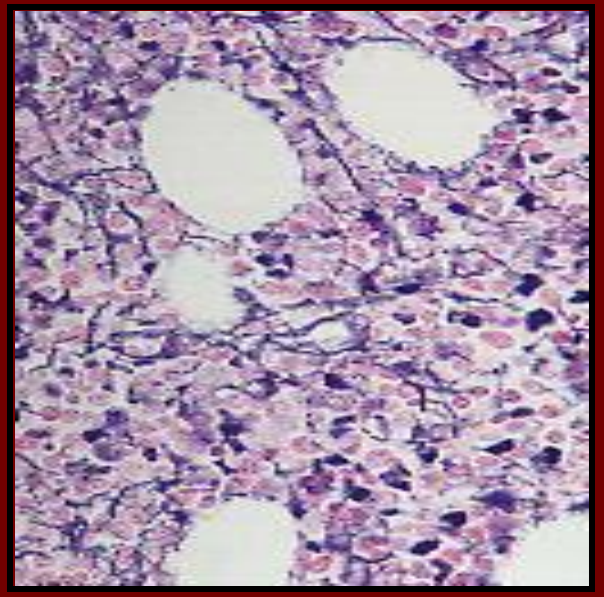
Hairy Cell Leukemia



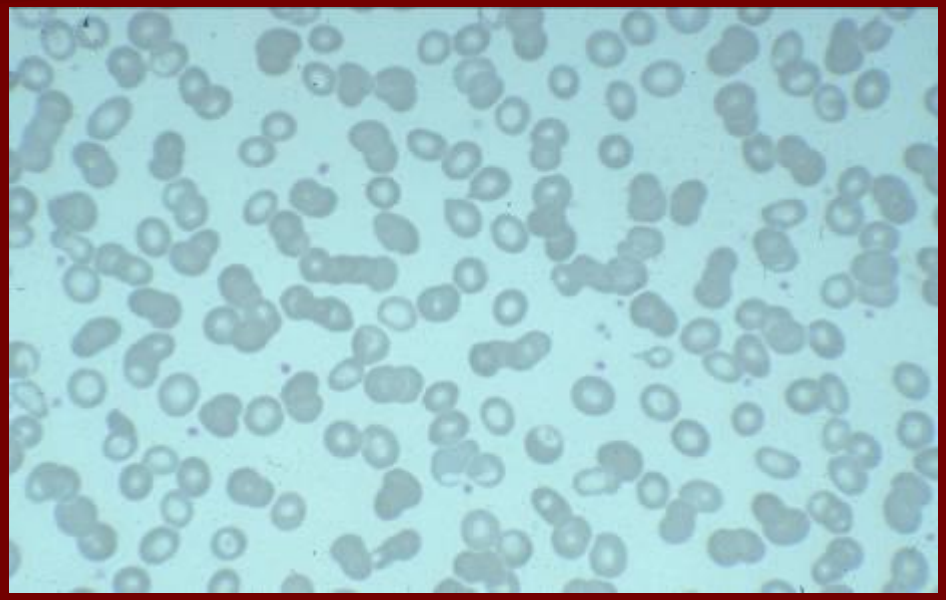
Hairy Cell Leukemia

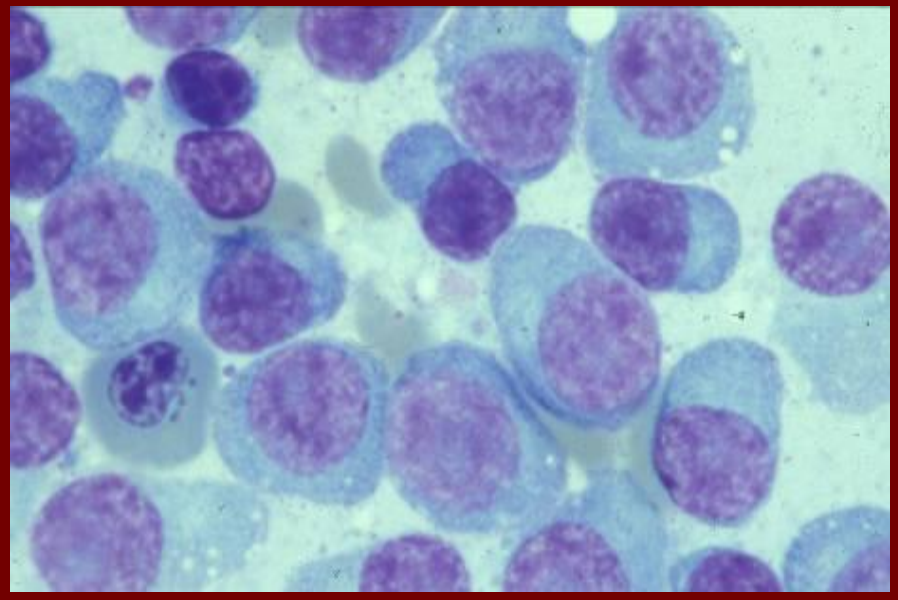


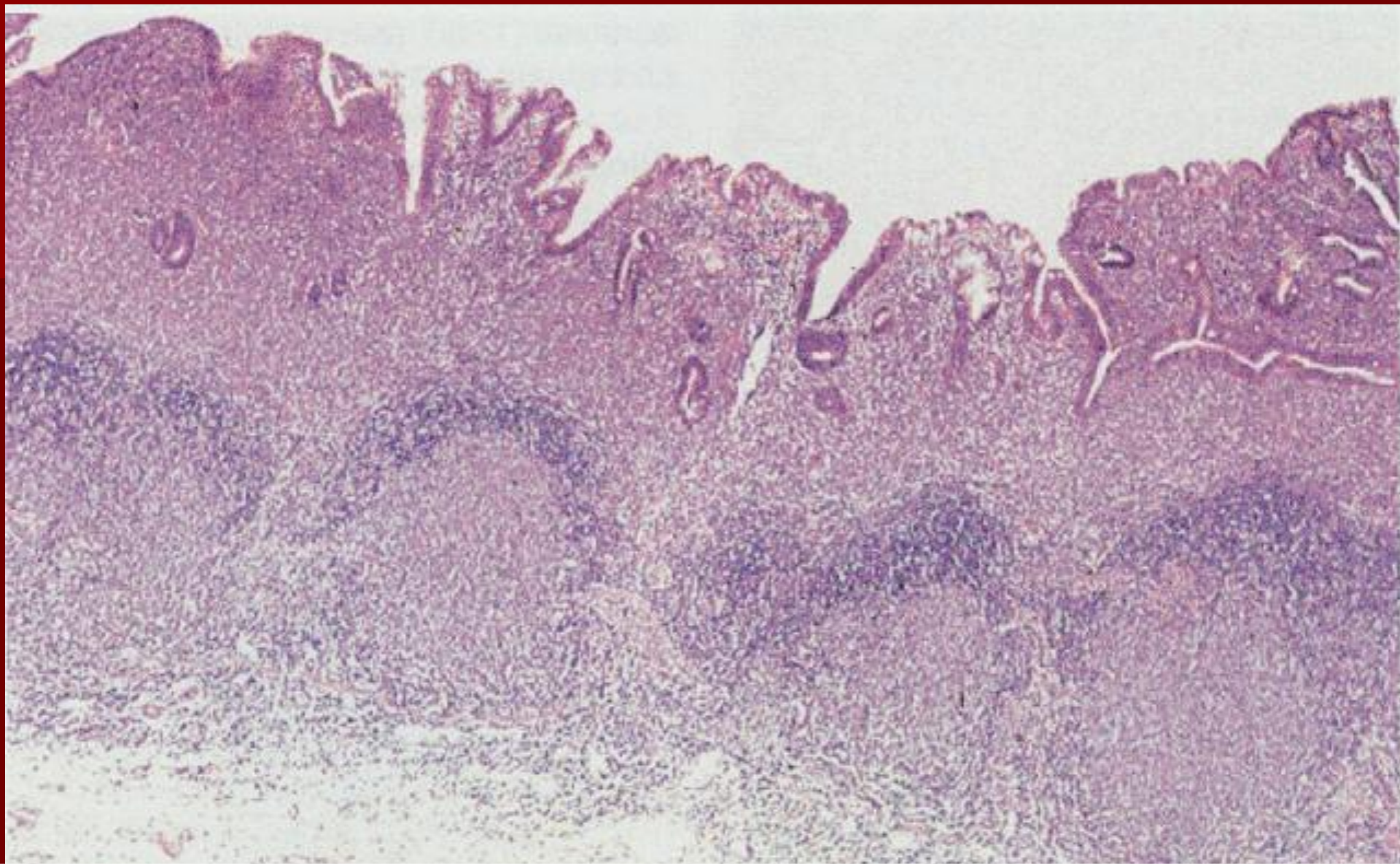
Reticulin



Multiple Myeloma



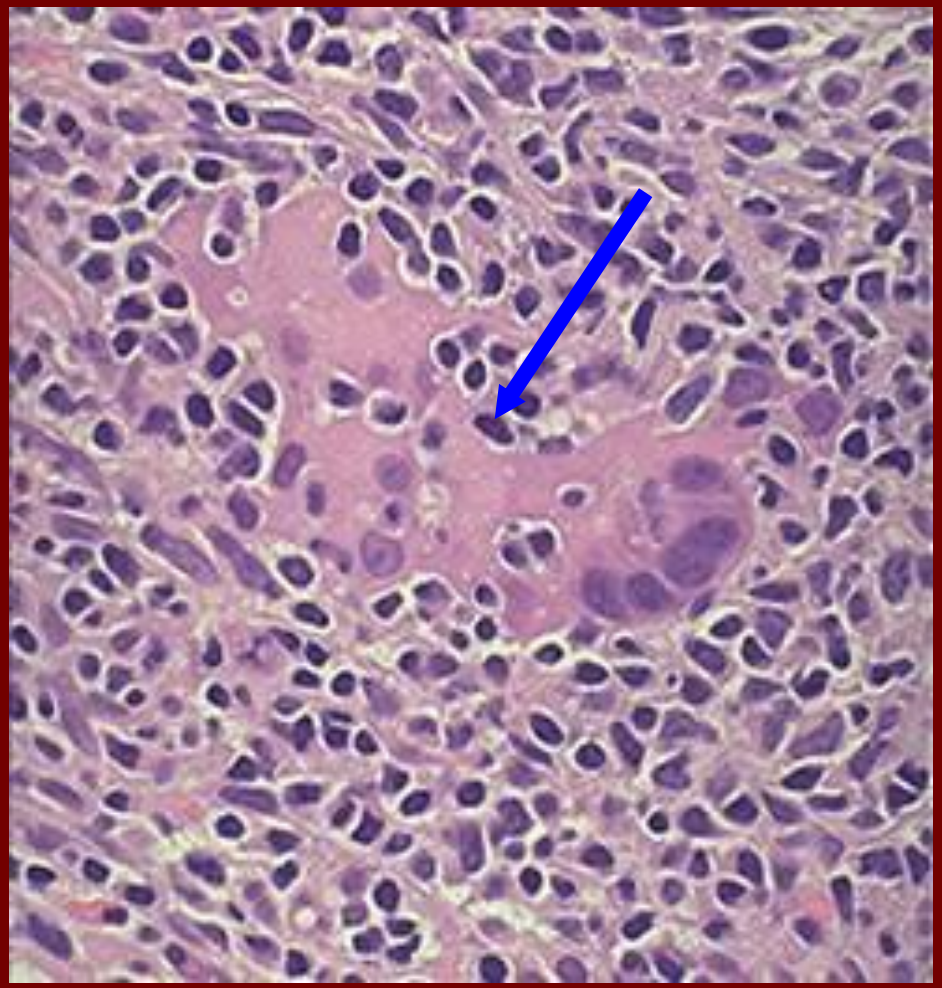




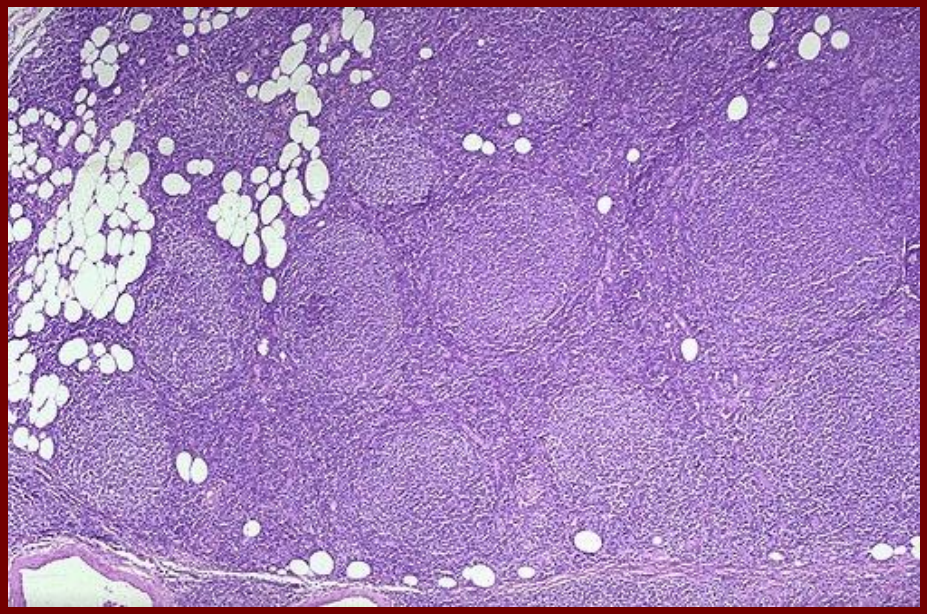
Gastric MALT lymphoma, tumor cells colonize the follicles

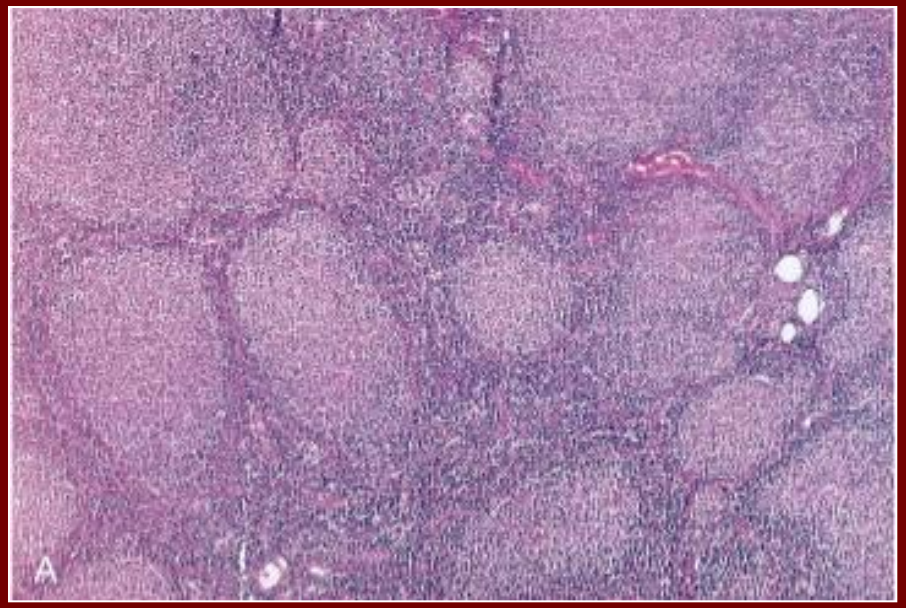
Microscopic findings

- Lymphoepithelial lesions:
  - ≥3 marginal zone lymphocytes with distortion or distruction of epithelium

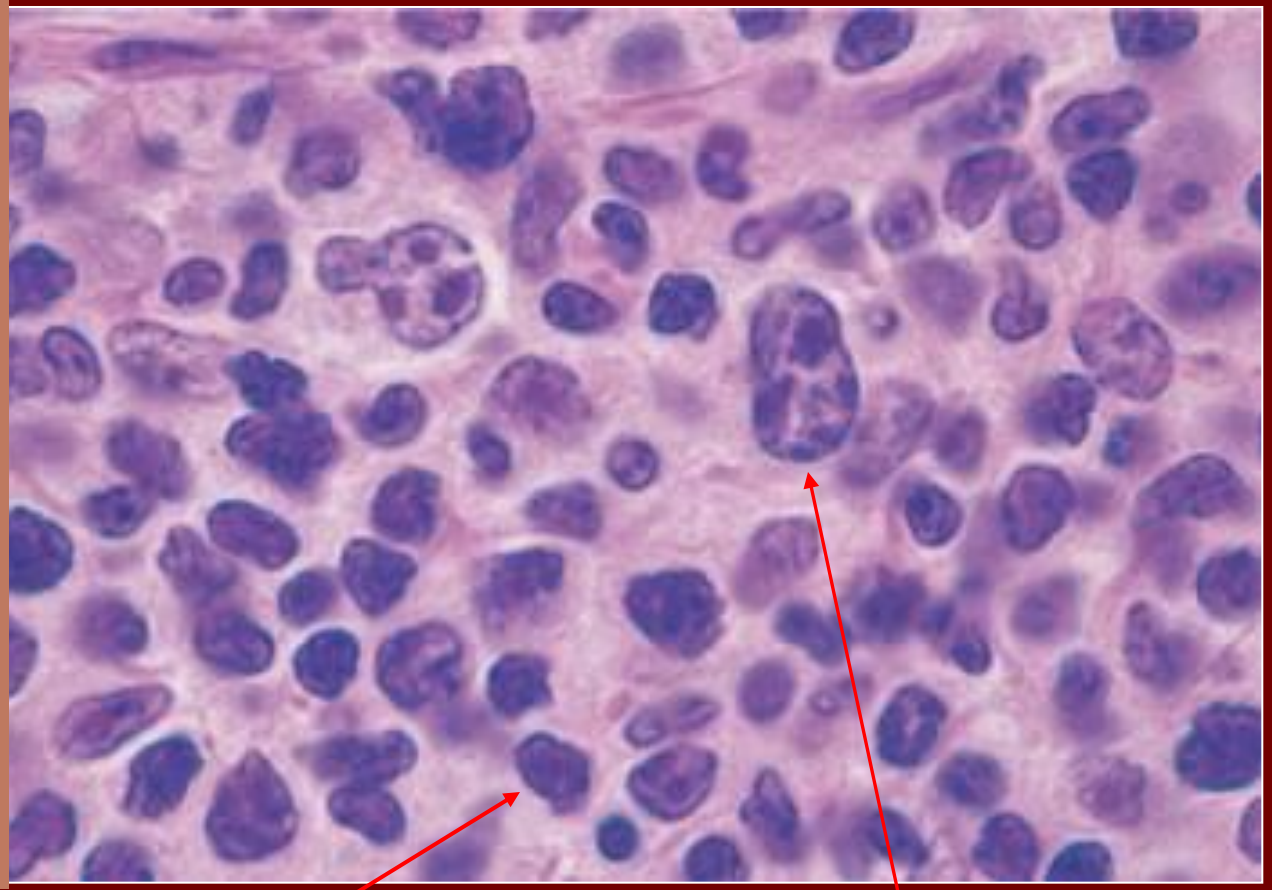


Follicular Lymphoma



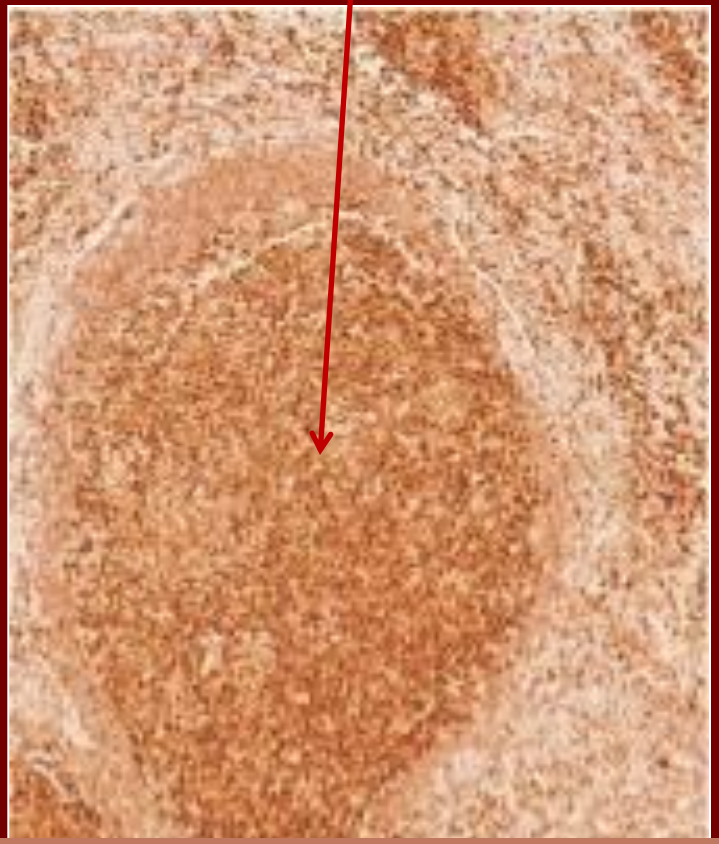


Follicular Lyphoma

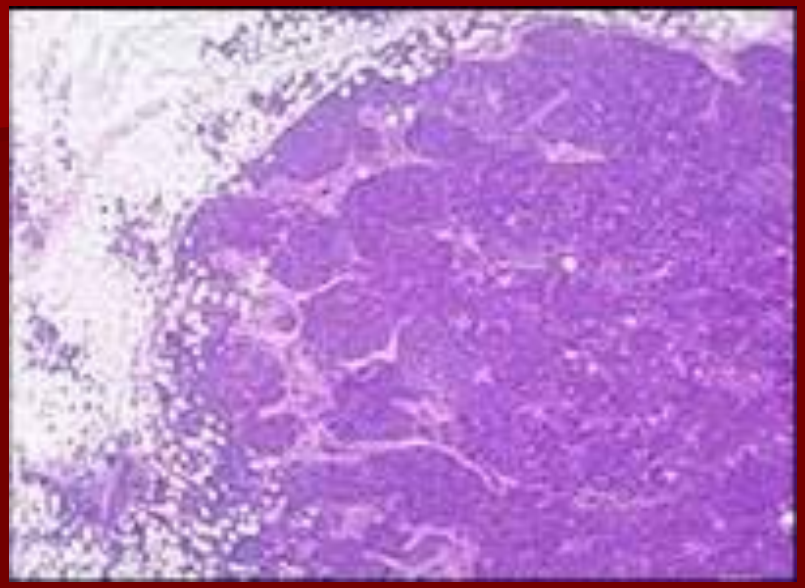


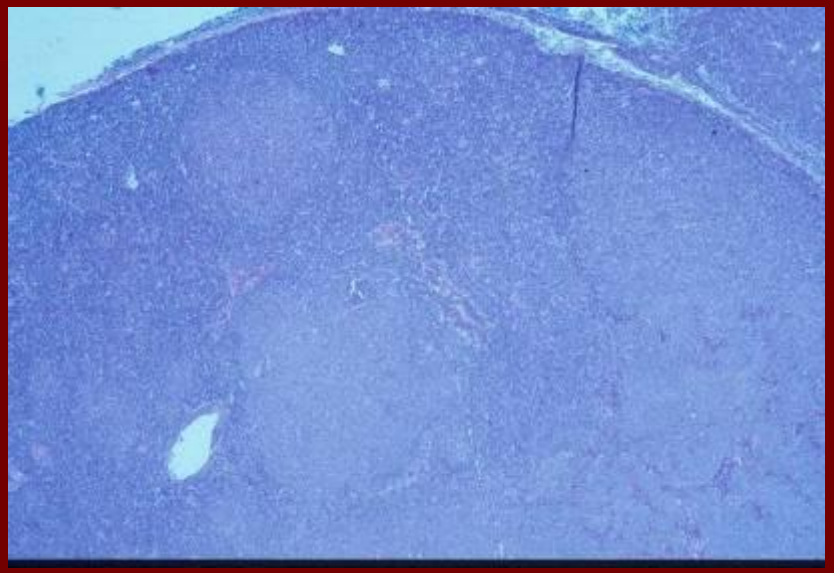
BCL2 Staining

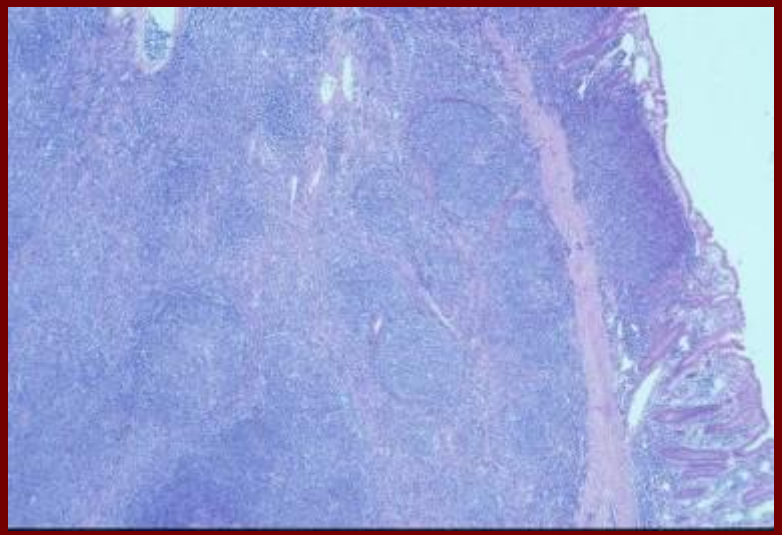
Use in distinguishing reactive follicular hyperplasia from follicular lymphoma



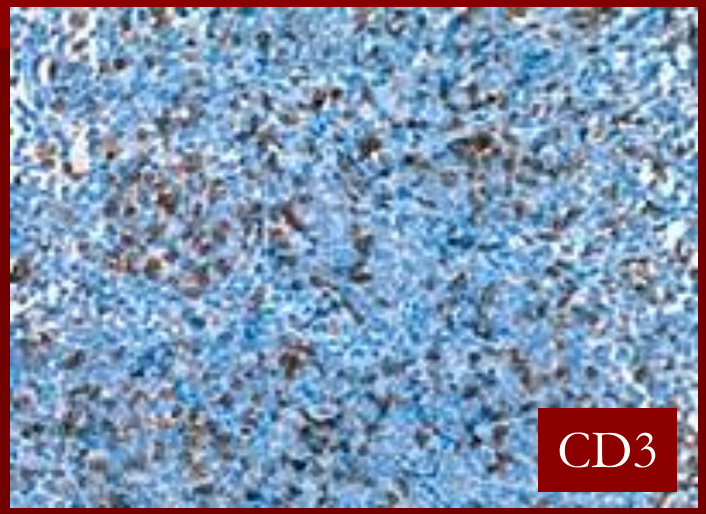
Mantle Cell Lymphoma

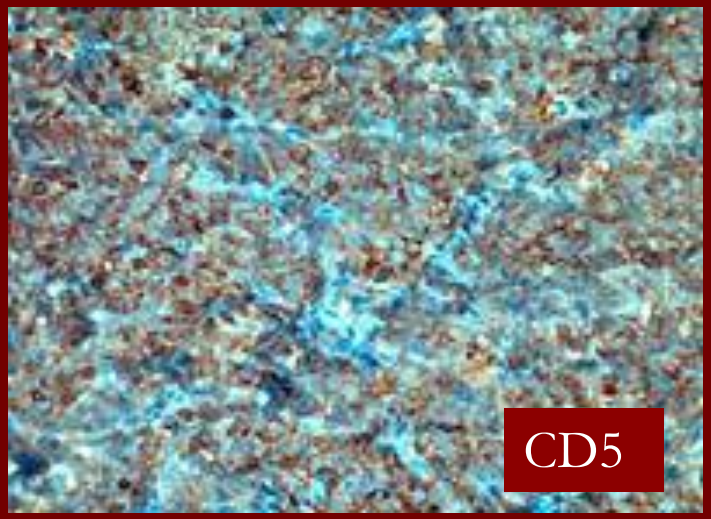


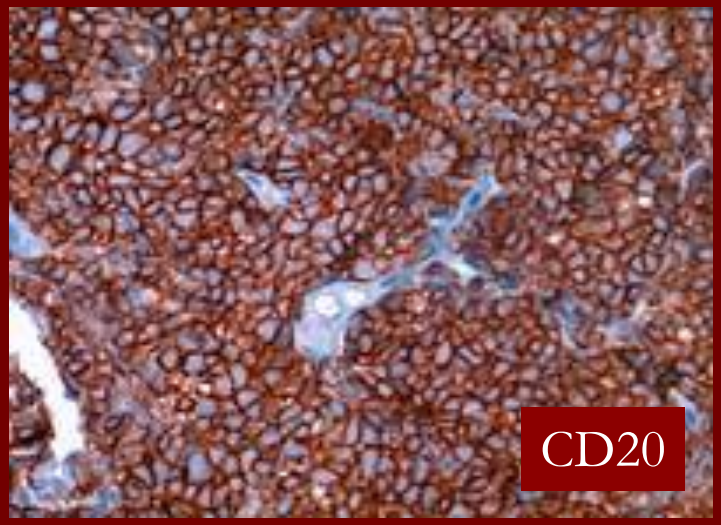


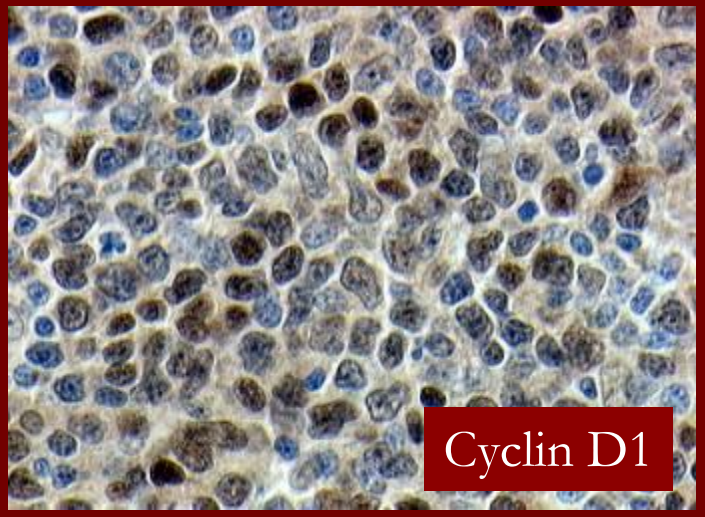


Mantle Cell Lymphoma

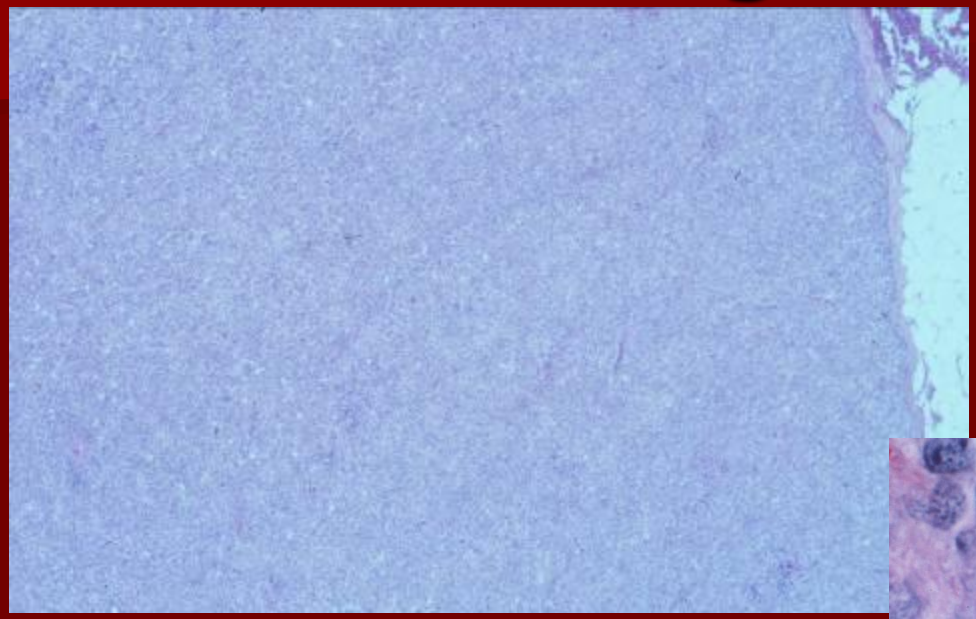


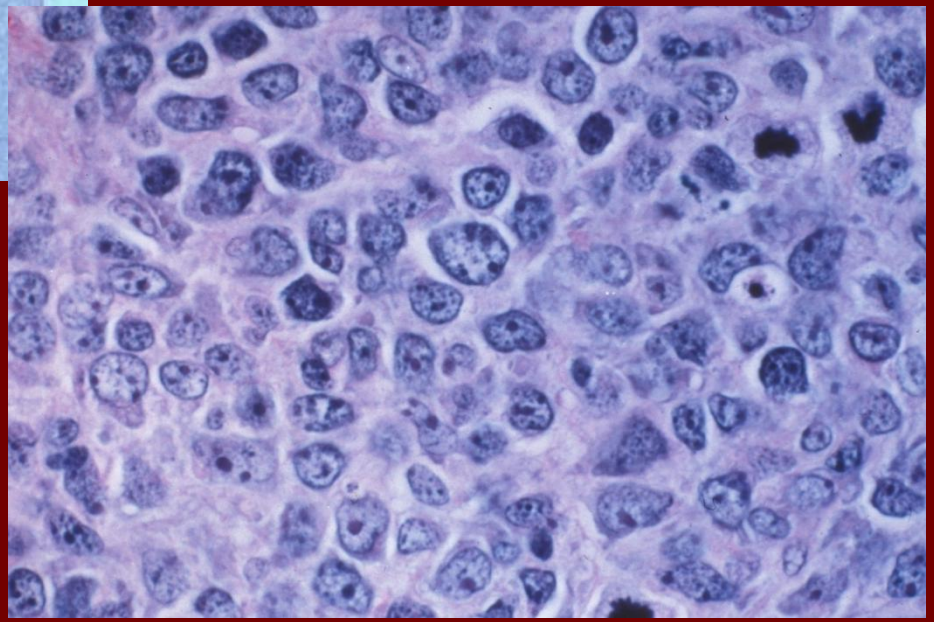




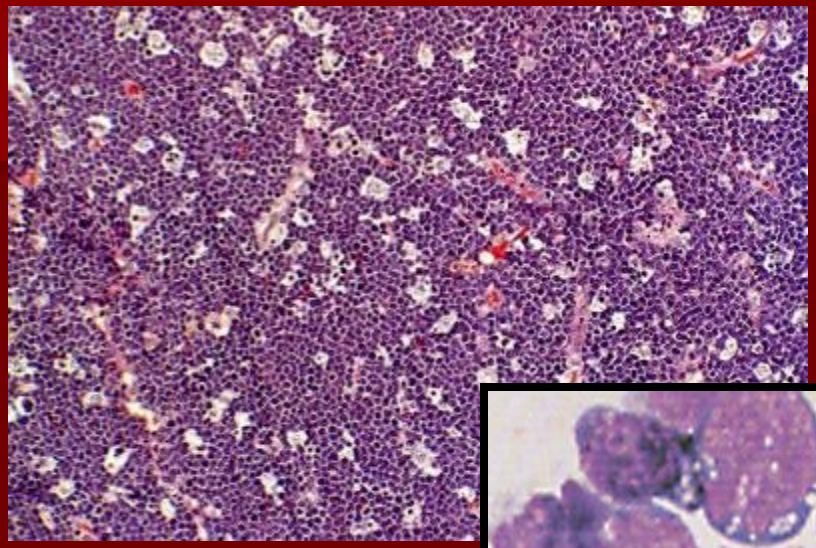


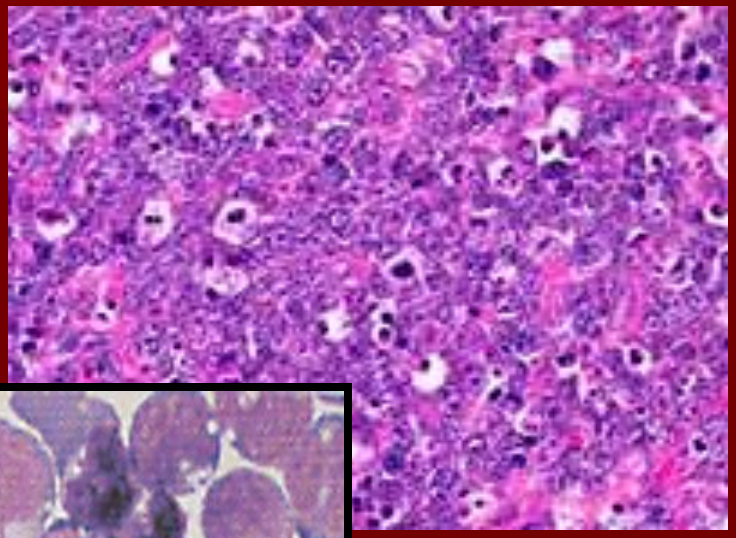
Diffuse Large Cell Lymphoma

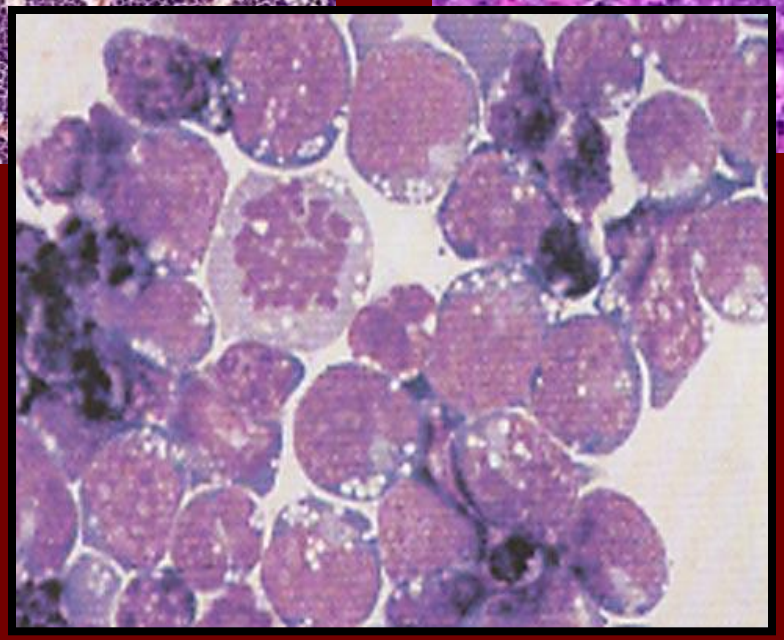




Burkitt Lymphoma

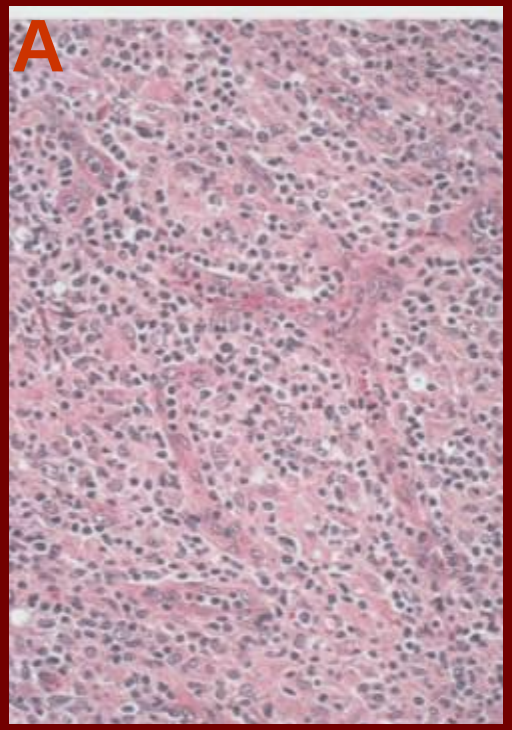


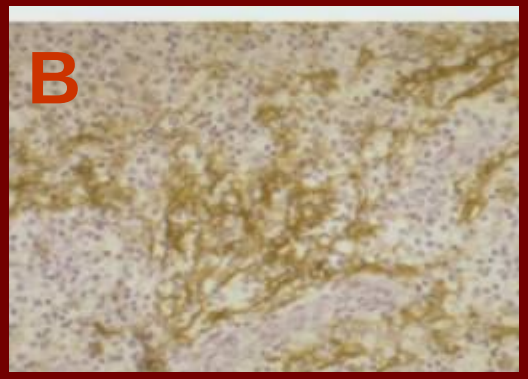


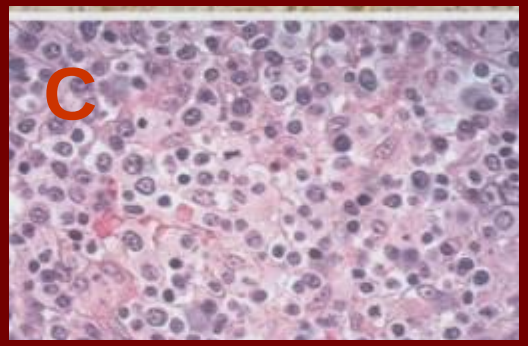


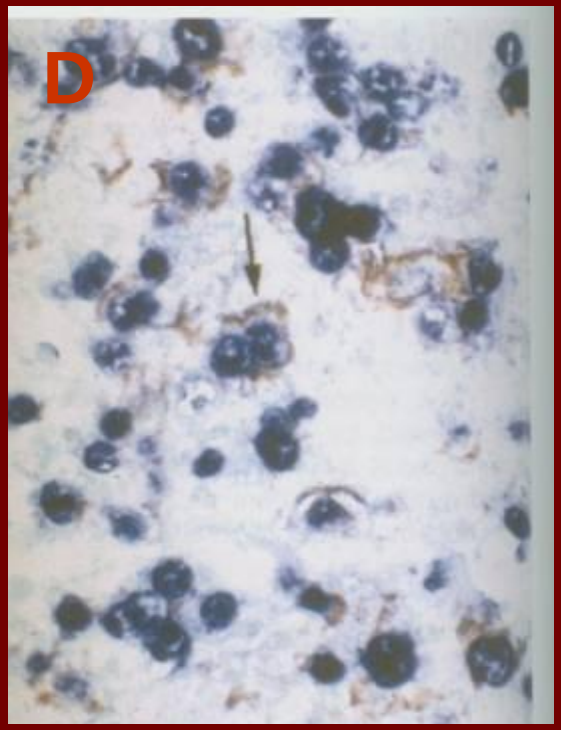
Angioimmunoblastic T-cell lymphoma

-A: Arborizing blood vessels
-B: Dentric cells abut and extend from venues(CD21)
-C: medium-sized lymphoytes with clear cytoplasm/distinct membrane
-D: Double staining: EBER/CD20

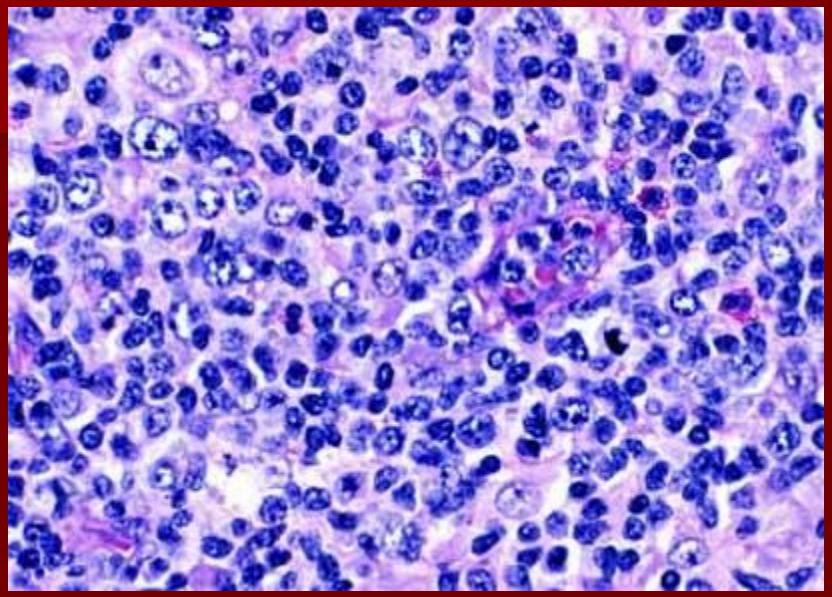


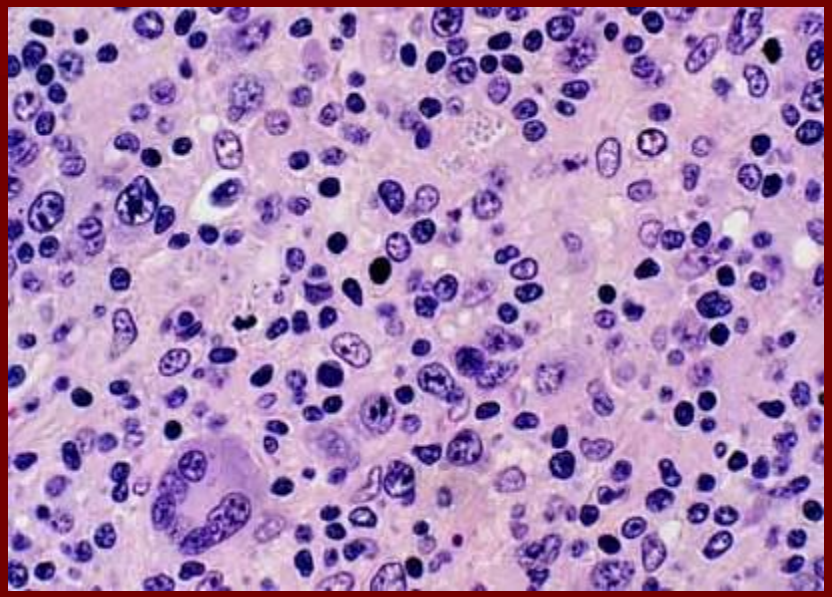


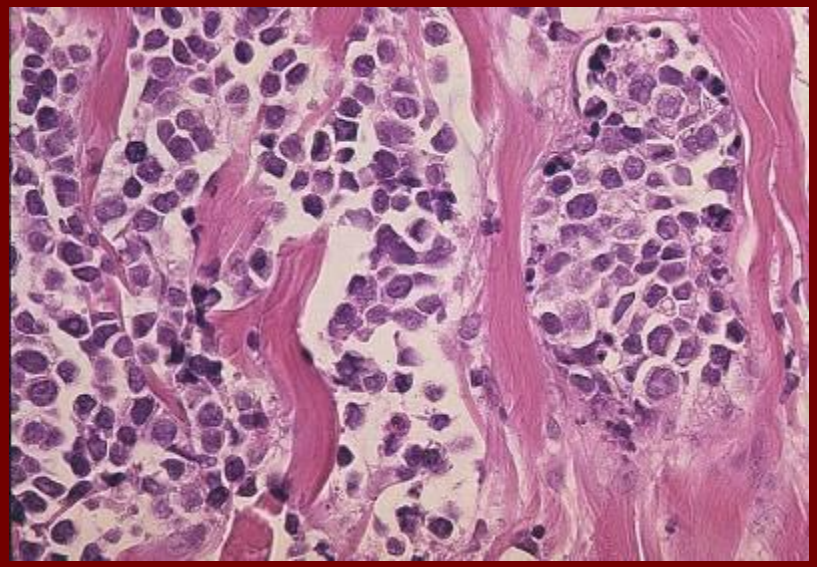


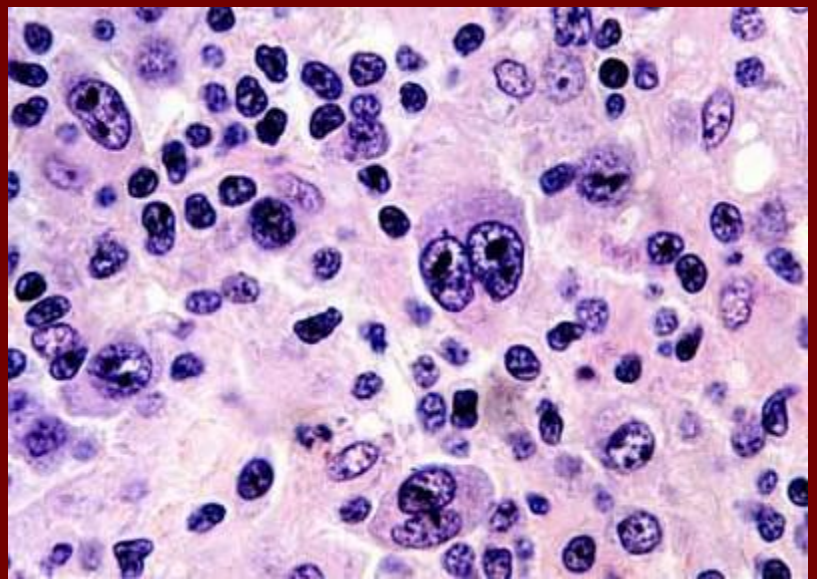


Peripheral T-Cell Lymphoma, unspecified

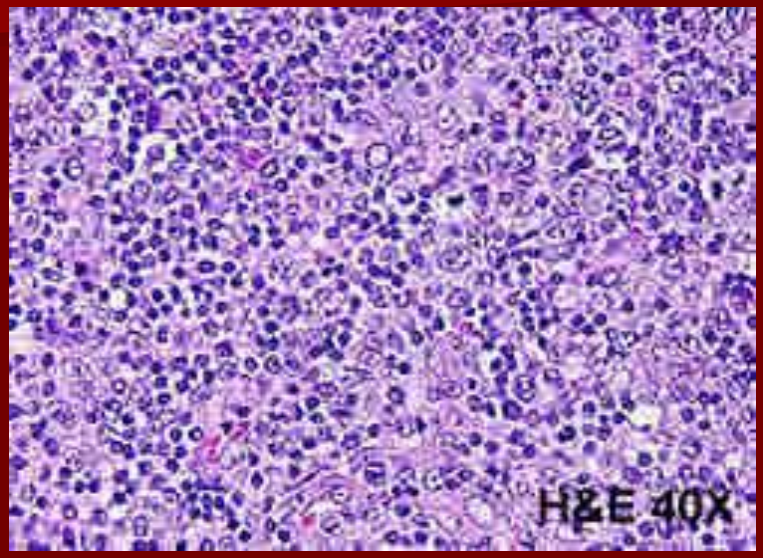


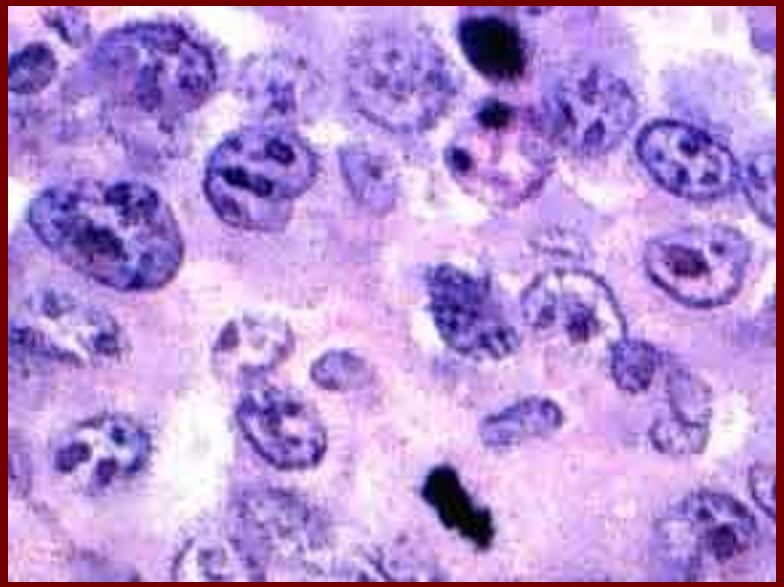




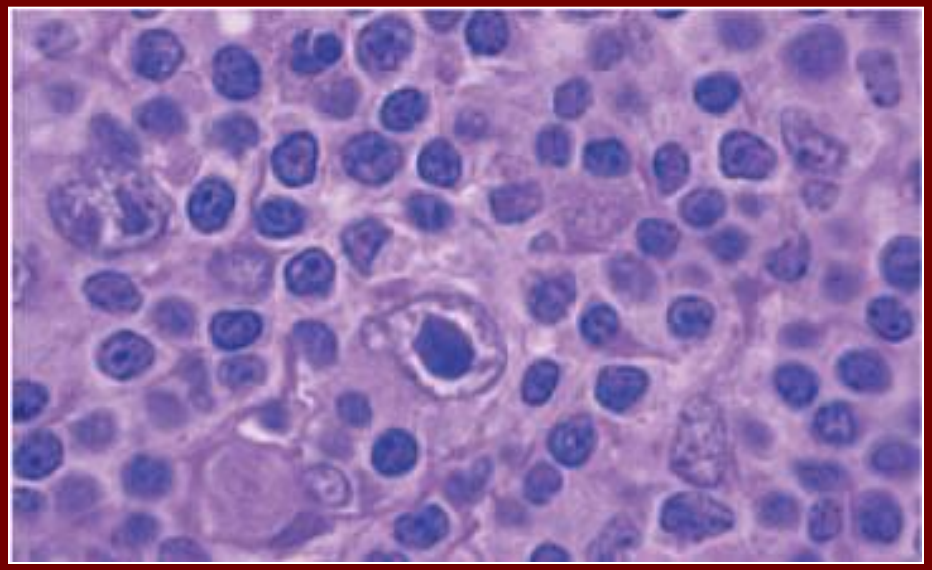


ALCL, common variant

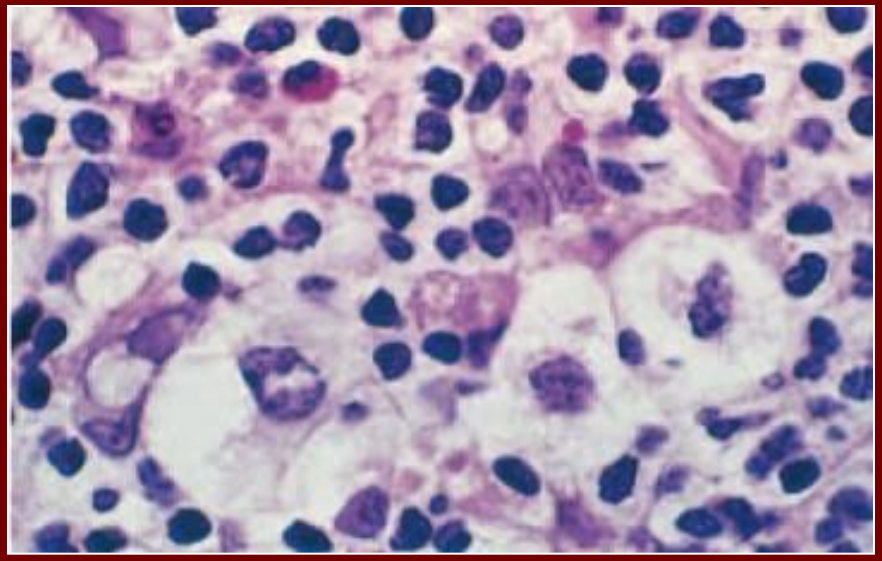




Hodgkin Lymphoma
Malignant Cell Variants



Mononuclear Hodgkin Cell



Lacunar cells seen in nodular sclerosis Hodgkin lymphoma