Chronic Idiopathic Myelofibrosis (CIMF)

CIMF

Synonyms

- Agnogenic myeloid metaplasia
- Myelosclerosis with myeloid metaplasia
- Chronic granulocytic-megakaryocytic myelosis

CIMF

- Megakaryocytic proliferation
- Granulocytic proliferation
- Bone marrow fibrosis
- Extramedullary hematopoiesis

CIMF

- Initial prefibrotic stage - hypercellular bone marrow
- Fibrotic stage with leukoerythroblastic peripheral blood
- Hepatosplenomegaly with extramedullary hematopoiesis

Epidemiology

- 0.5-1.5 per 100,000 per year
- Seventh decade
- Men and women equally

Anatomic Sites

- Blood and bone marrow
- Spleen and liver with extramedullay hematopoiesis causing leukoerythroblastic features
- Lymph nodes (and other sites)

Clinical Features

- 30% asymptomatic, discovered by chance
- Splenomegaly (90%) (fibrotic stage)
- Hepatomegaly (20%) (fibrotic stage)
- Mild anemia
- Leukocytosis
- Thrombocytosis

Prefibrotic (Cellular) Stage

- 20-30% detected in this stage
- Peripheral blood with leukocytosis, thrombocytosis, anemia
- Naked megakaryocytic nuclei
- Leukoerythroblastic picture with "tear-drop" RBCs, nucleated RBCs, poikilocytosis, large platelets

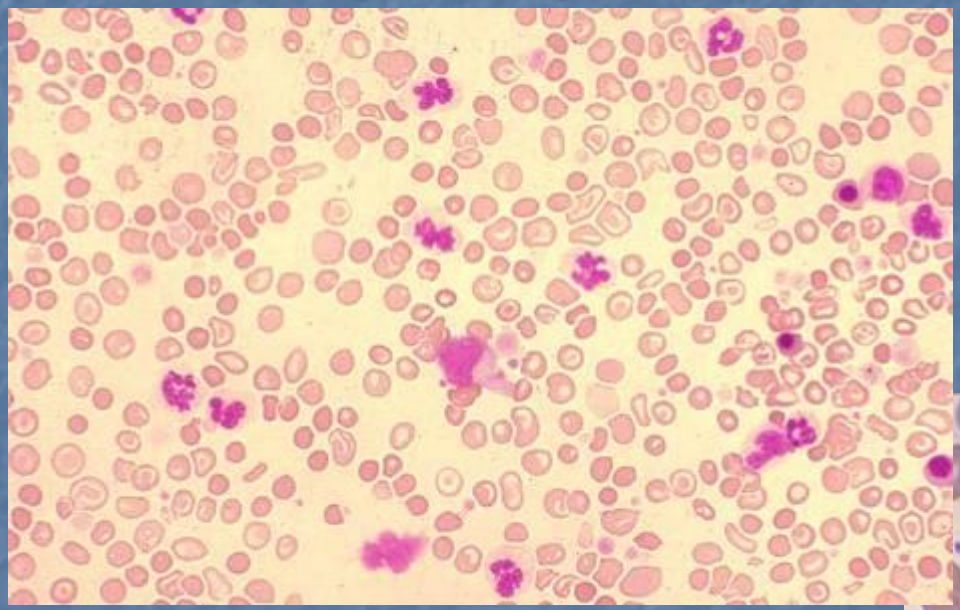
Prefibrotic (Cellular) Stage

- Bone marrow hypercellular
- Granulocytic hyperplasia
- Megakaryocytic hyperplasia
- Erythroid lineage variable

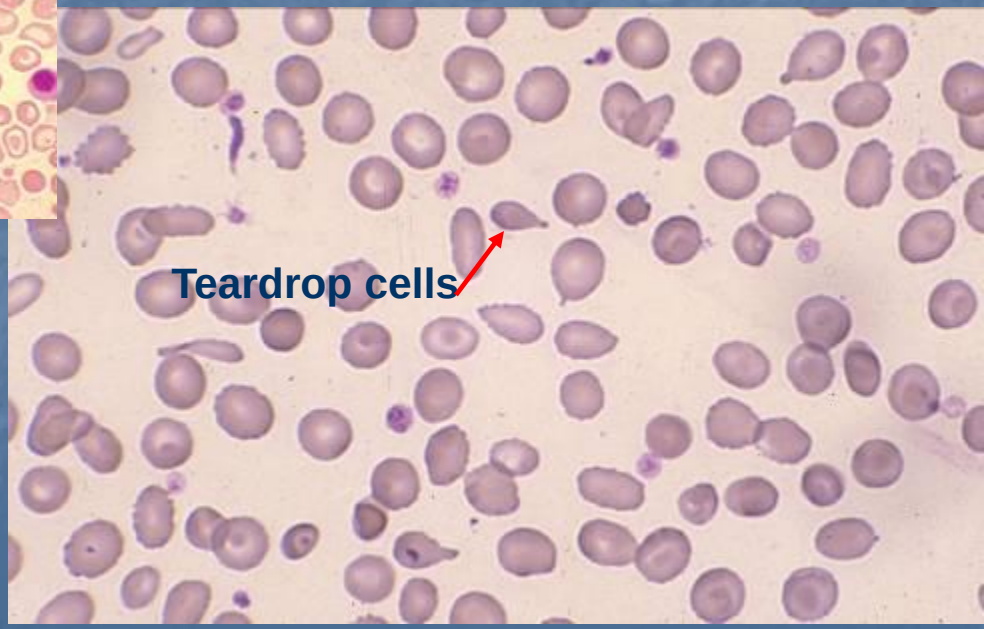
Prefibrotic (Cellular) Stage

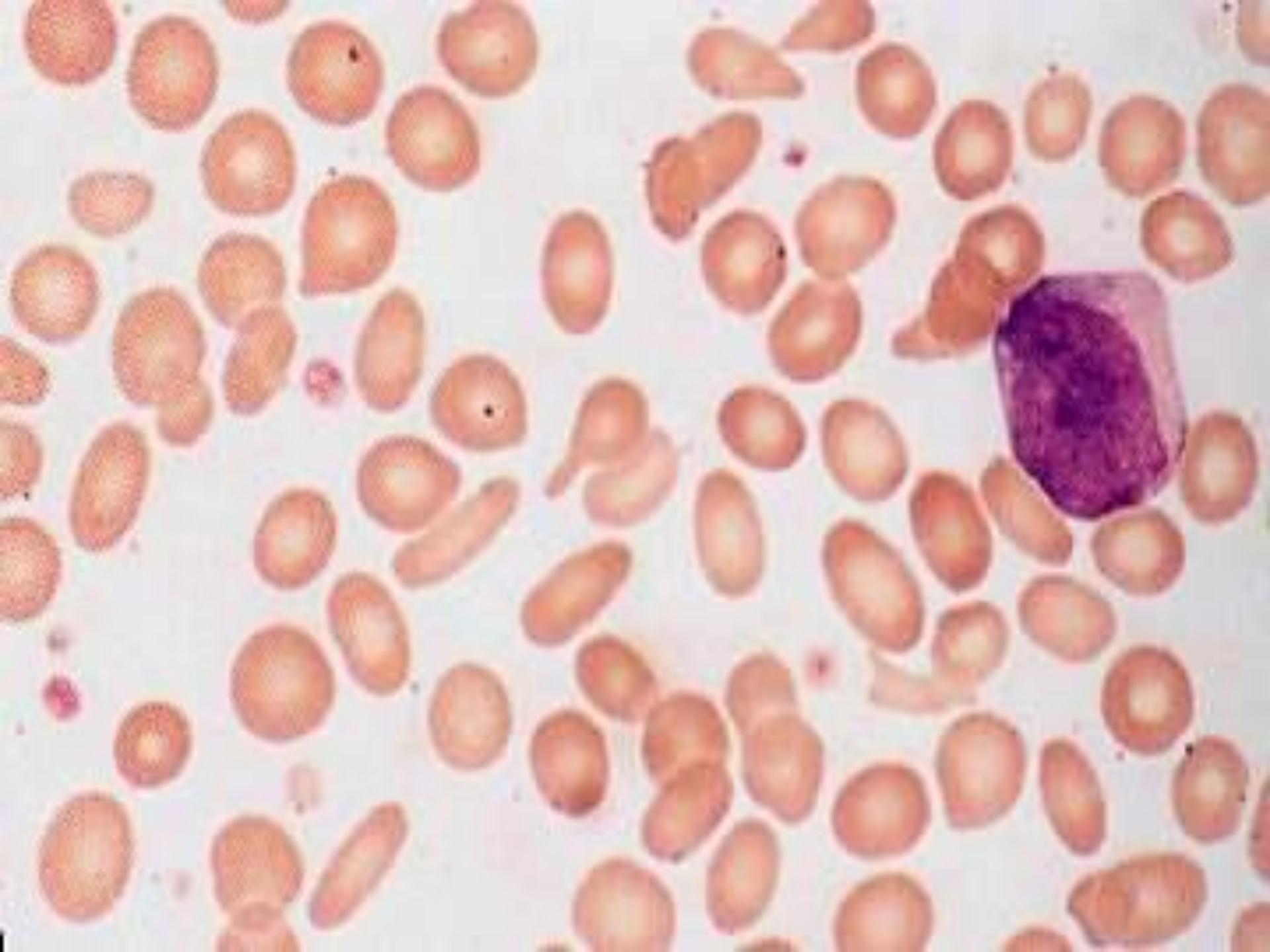
- Megakaryocytes large and dysplastic: "Cloud-like" or "balloon-like" lobulation of megakaryocytic nuclei
- Reticulin minimal or variable
- Blasts not increased

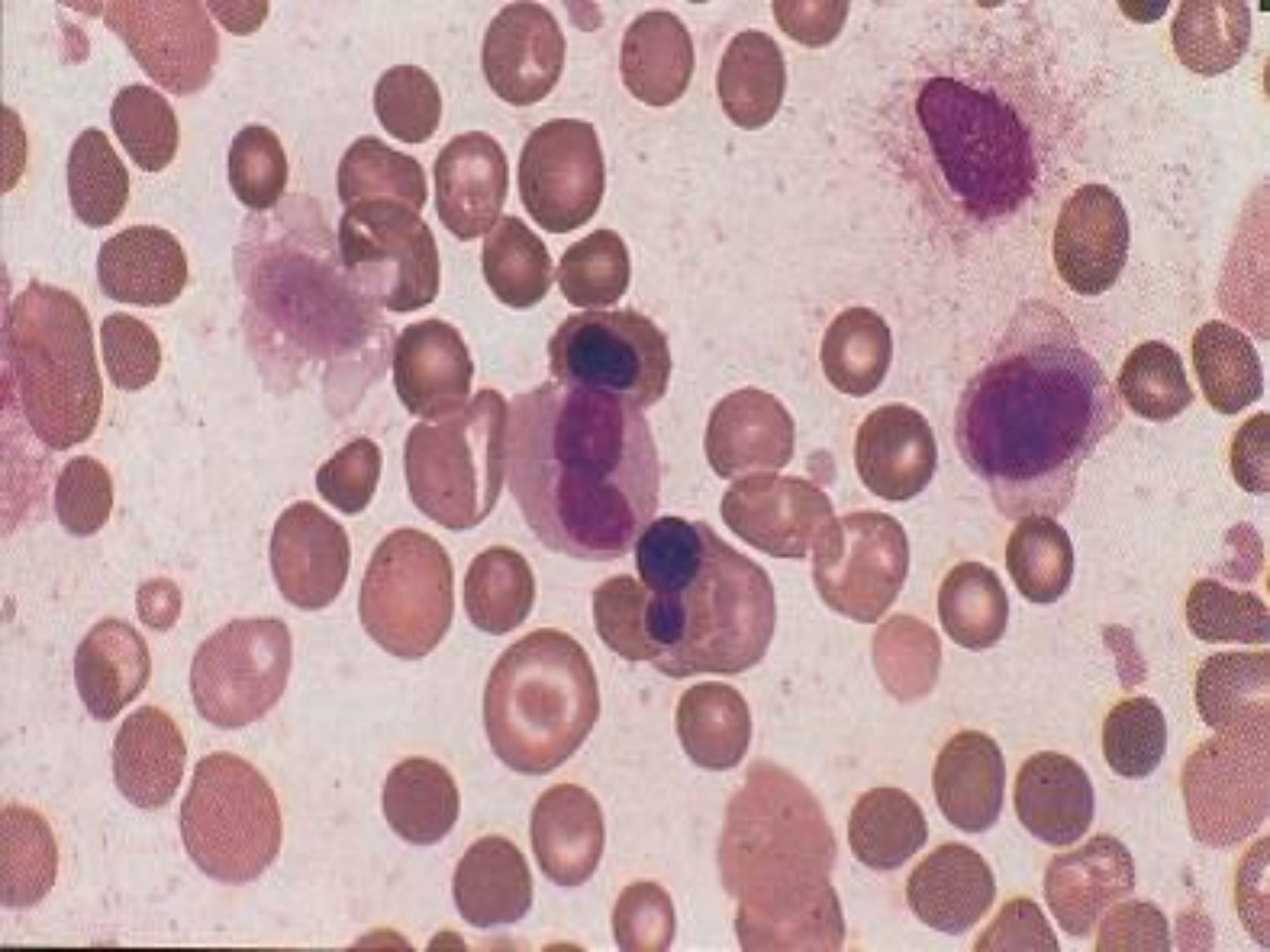
Agnogenic Myeloid Metaplasia (Idiopathic Myelofibrosis)



Peripheral blood smear







Fibrotic Stage

- Most diagnosed in this stage (70-80%)
- Splenomegaly and hepatomegaly
- Extramedullary hematopoiesis
- Leukoerythroblastic peripheral blood smear with 'tear-drop" RBCs and nucleated RBCs
- Leukocytosis or leukopenia

Fibrotic Stage

- Bone marrow fibrosis (reticulin increased)
- Dilatated marrow sinuses with intrasinusoidal hematopoiesis
- Marrow cellularity decreases
- Osteosclerosis

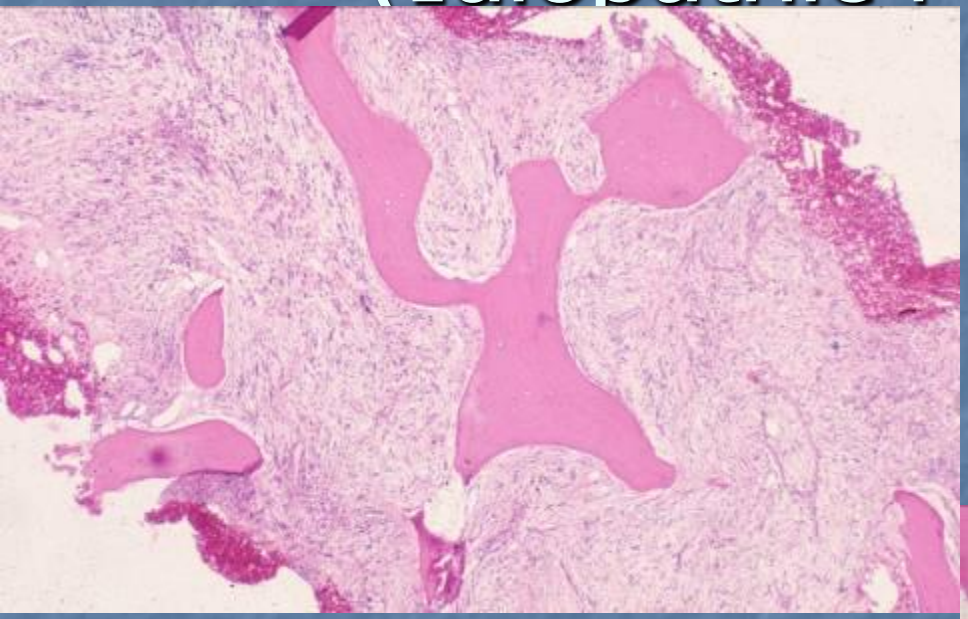
Fibrotic Stage

- Blasts <10%; if more, then consider accelerated phase
- If blasts >20%, then acute leukemia (or acute panmyelosis with myelofibrosis if organomegaly is not prominent)

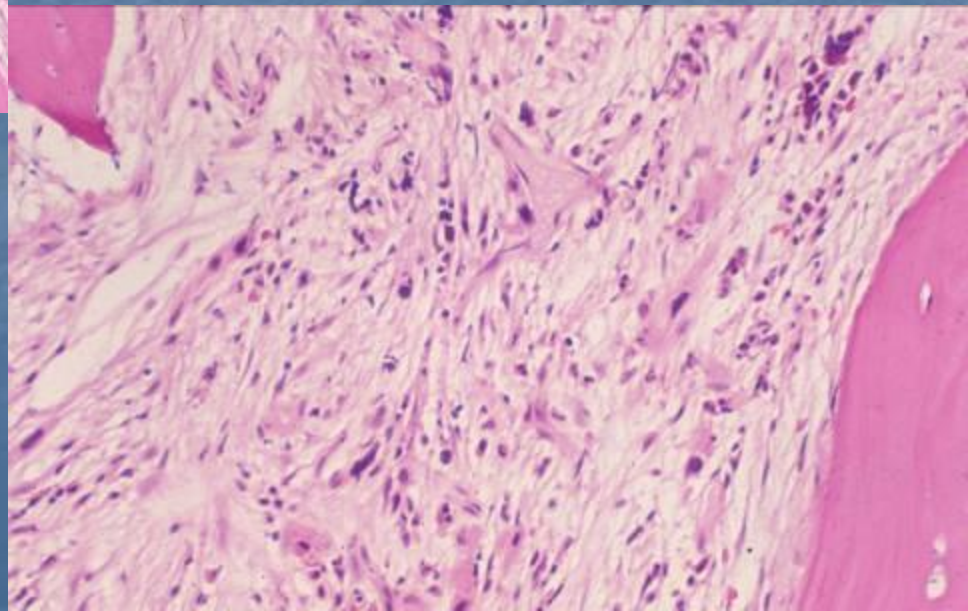
Fibrotic Stage

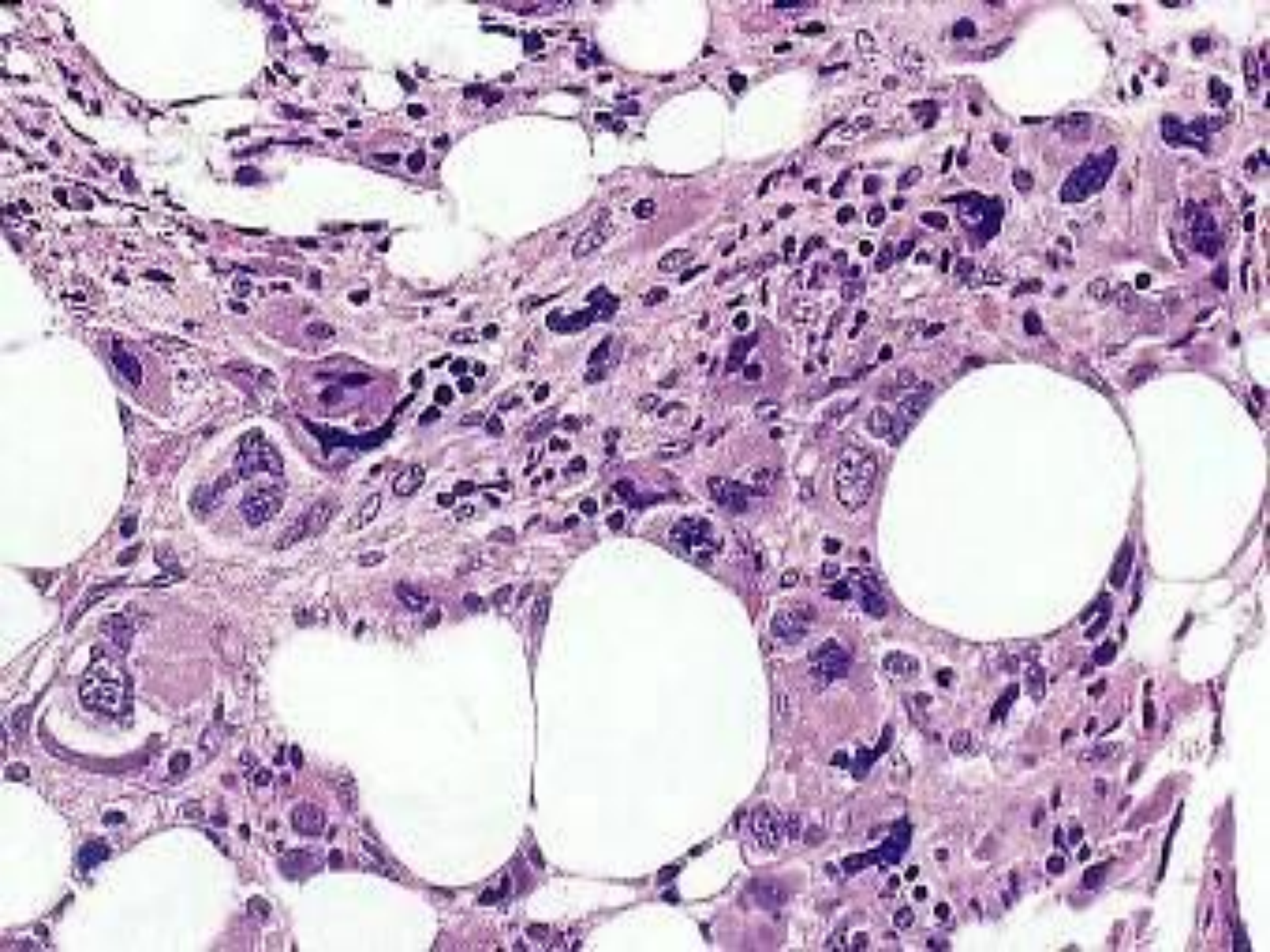
- Extramedullary hematopoiesis in splenic red pulp and hepatic sinusoids
- Fibrosis and cirrhosis

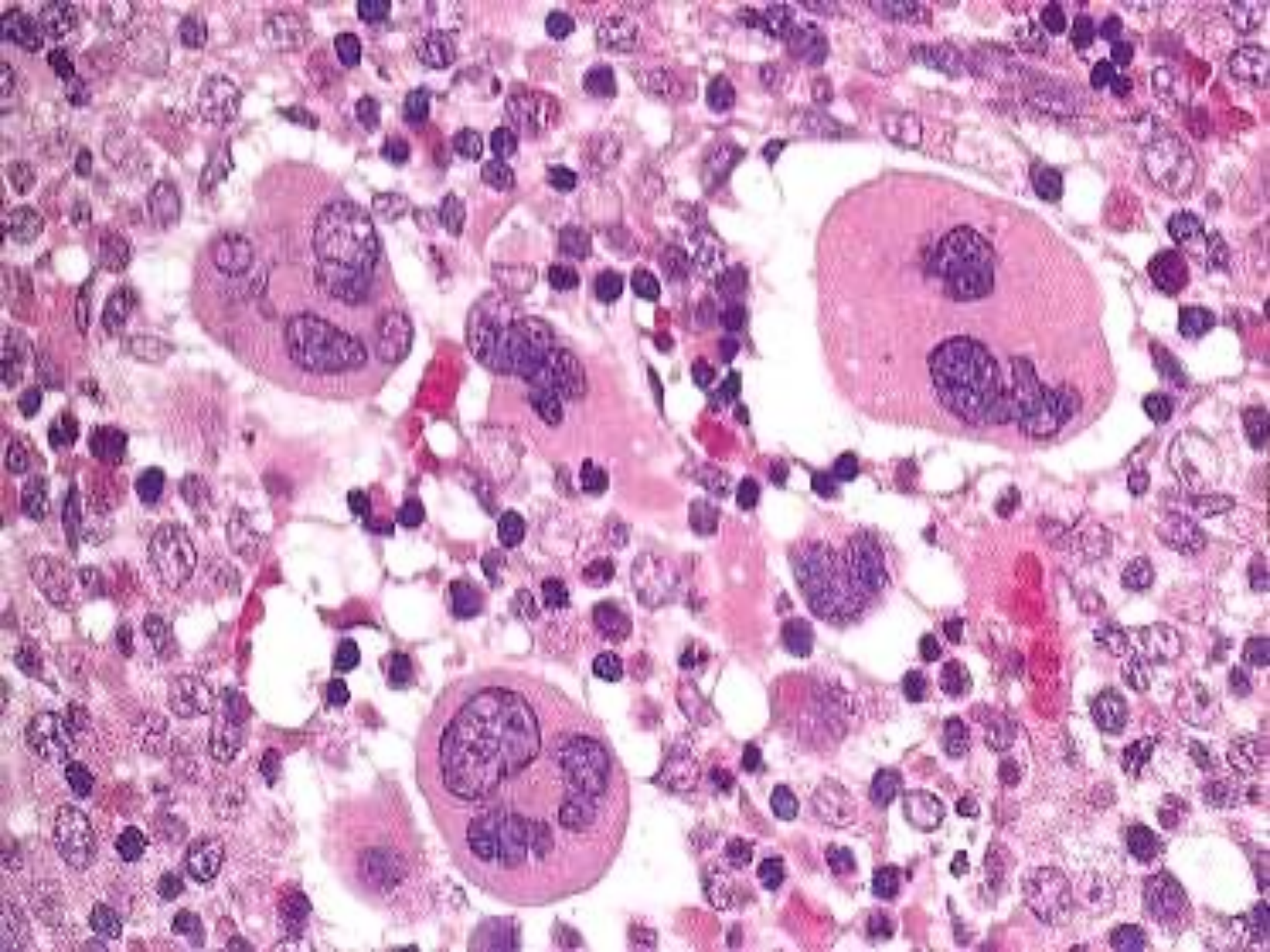
Agnogenic Myeloid Metaplasia (Idiopathic Myelofibrosis)

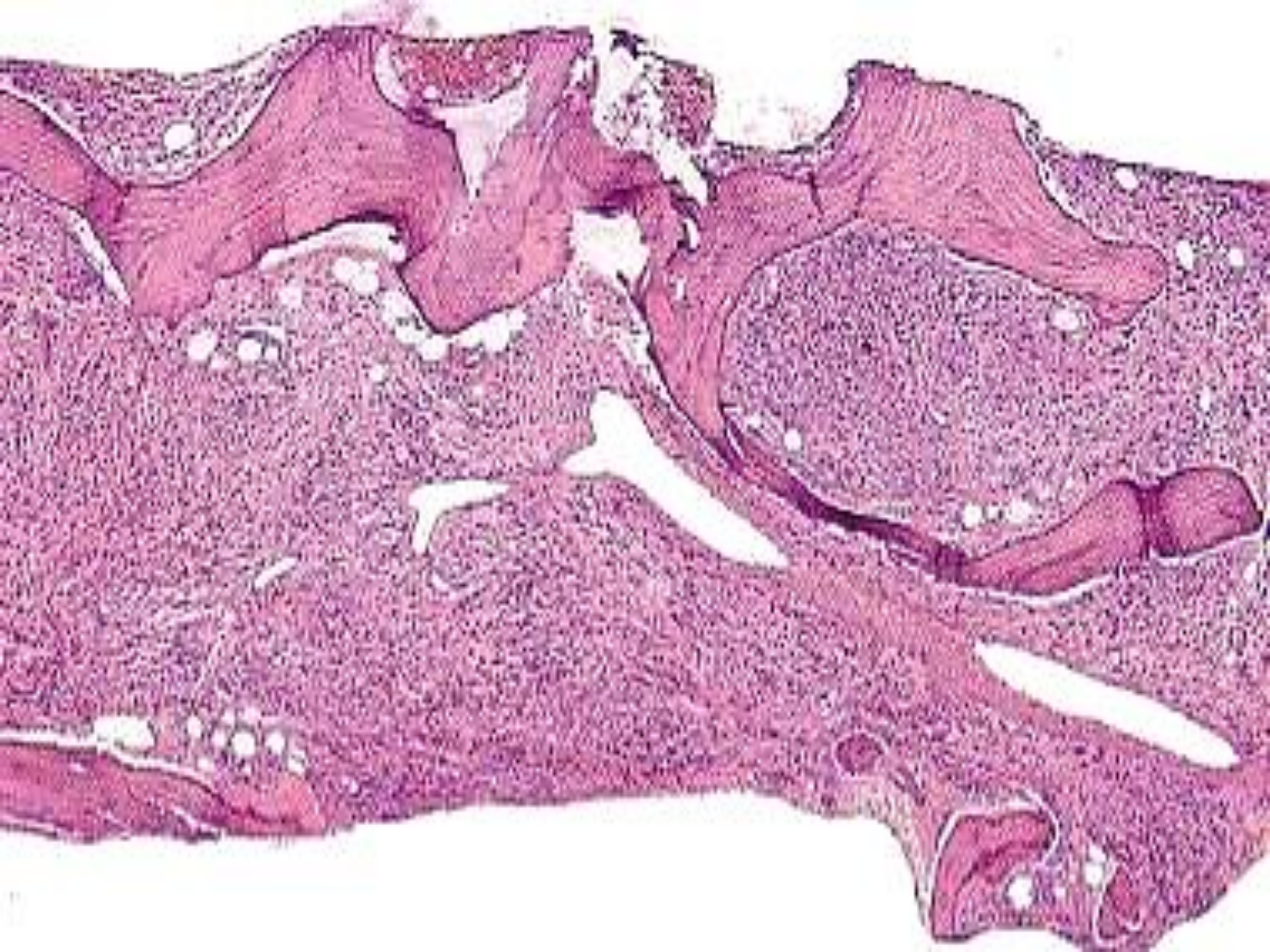


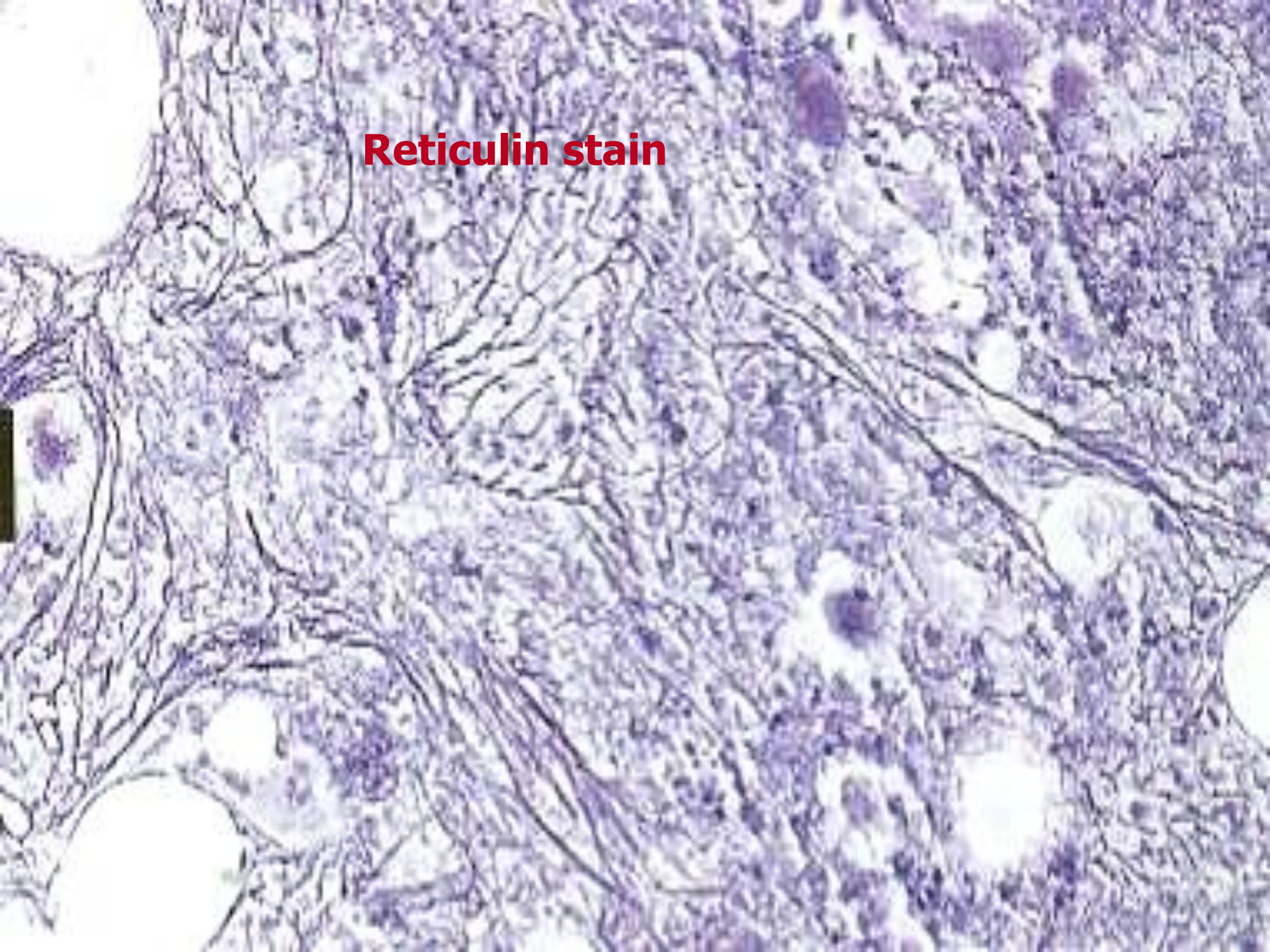
Bone marrow biopsy

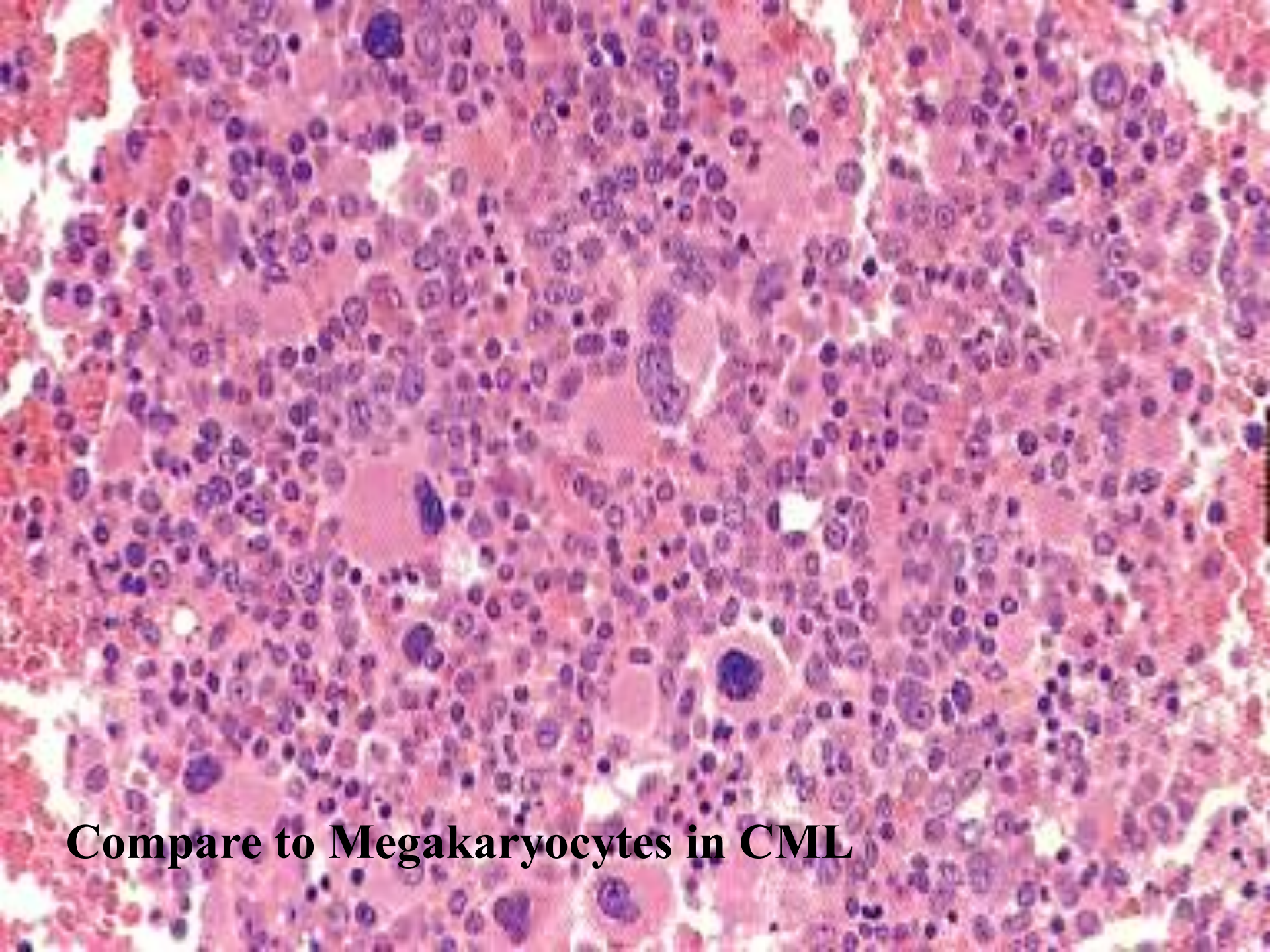









Reticulin stain



Compare to Megakaryocytes in CML

Genetics

- Cytogenetic abnormalities in 60%
- None specific for CIMF
- No Philadelphia chromosome or BCR/ABL fusion gene
- 13q, del(20q), partial trisomy 1q most common

Diagnostic Aids

JAK-2 mutation (V617F) for:

polycythemia vera (sensitivity 65-97%), essential thrombocythemia (sensitivity 30-57%), and chronic idiopathic myelofibrosis (sensitivity 35-95%),

Prognosis

- Survival range: months to decades
- Median survival: 3 to 5 years from Dx
- Adverse factors: >70 years, Hb <10g/dL, platelets <100 x 10^6/L, granulocytic immaturity, abnormal karyotypes

Prognosis

- Morbidity and mortality: bone marrow failure, infection, thromboembolic events, portal hypertension, cardiac failure, and transformation to acute leukemia

Prognosis

- Acute leukemia: 5-30%
- Some, but not all, may be cytotoxic therapy-related

Chronic Myeloproliferative Disease, Unclassifiable (Undifferentiated) (CMPD, U)

Chronic Myeloproliferative Disease, Unclassifiable, Undifferentiated) (CMPD, U)

- Fail to meet criteria of any one disease
- Overlap with several specific diseases
- No Philadelphia chromosome or BCR/ABL fusion gene

CMPD, U

- Initial stages of polycythemia vera, essential thrombocythemia, chronic idiopathic myelofibrosis
- Late stages of MPD diseases after myelosclerosis and osteosclerosis

CMPD, U

- Term used after exclusion of specific diseases
- Must exclude other non-CMPD diseases
- Proper sampling must be performed with adequate follow-up

CMPD, U

Rule out non-myeloproliferative processes:

- Infection, chemotherapy, toxins, growth factors, immunosuppressive agents
- Lymphomas and metastatic tumors

CMPD, U

- CMPDs do have overlapping characteristics
- Variations occur
- 10-20% of all CMPDs

CMPD, U

- Clinical and morphologic features similar to other CMPDs, but without clear-cut categorization
- Many cases in early stages are finally categorized after adequate follow-up

CMPD, U

- If blasts between 10-19%, then accelerated stage of CMPD, U
- If blasts >20%, then AML (suggestive of transformation of previous CMPD, U)
- If dysplasia present, then MDS/CMPD, U

Genetics and Immunophenotype

- Similar to other CMPDs
- Philadelphia chromosome or BCR/ABL fusion product gene must be excluded

Diagnostic Aids

JAK-2 mutation (V617F) for:

polycythemia vera (sensitivity 65-97%), essential thrombocythemia (sensitivity 30-57%), and chronic idiopathic myelofibrosis (sensitivity 35-95%),

Prognosis

- Patients with marrow fibrosis have advanced disease and poor outcome
- Patients in early stages have outcome similar to those of the group into which their disease evolves