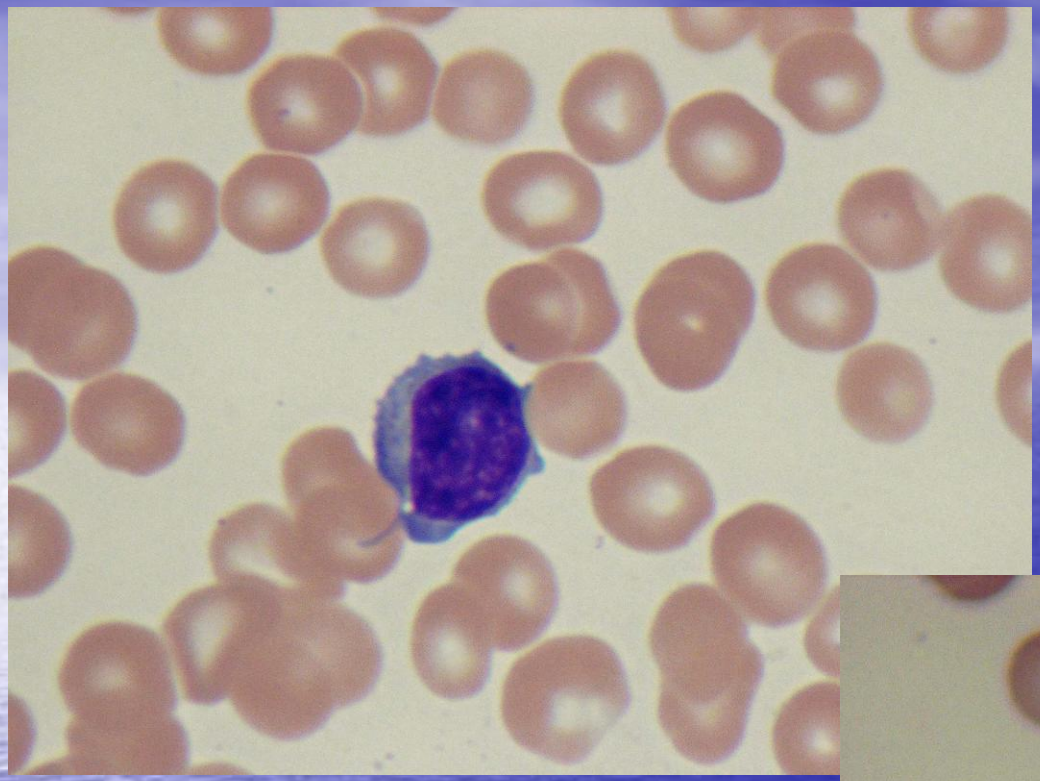
Hematology cases

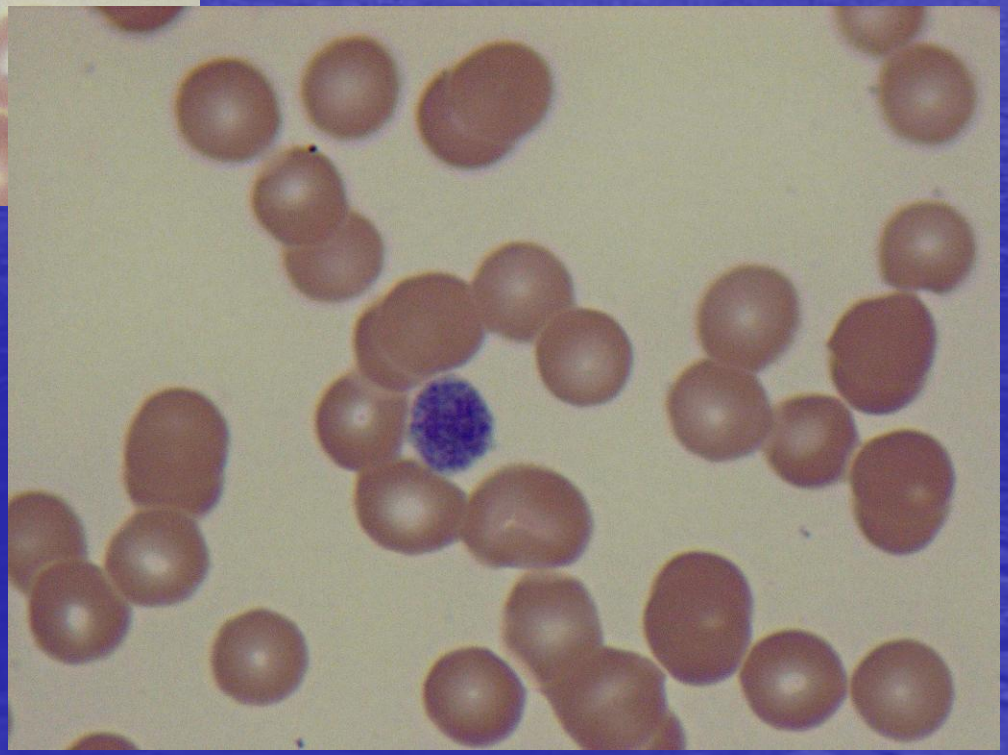
2nd March, 2004

Case-1: LB

- A 3 year old male with epistaxis and petechial hemorrhage.
- Labs:
- Hypochromic anemia
- Severe thrombocytopenia (5,000), with
- a few giant platelets
- Relative lymphocytosis, reactive
- lymphocytes



Reactive lymphocyte



Giant platelet

Thrombocytopenia

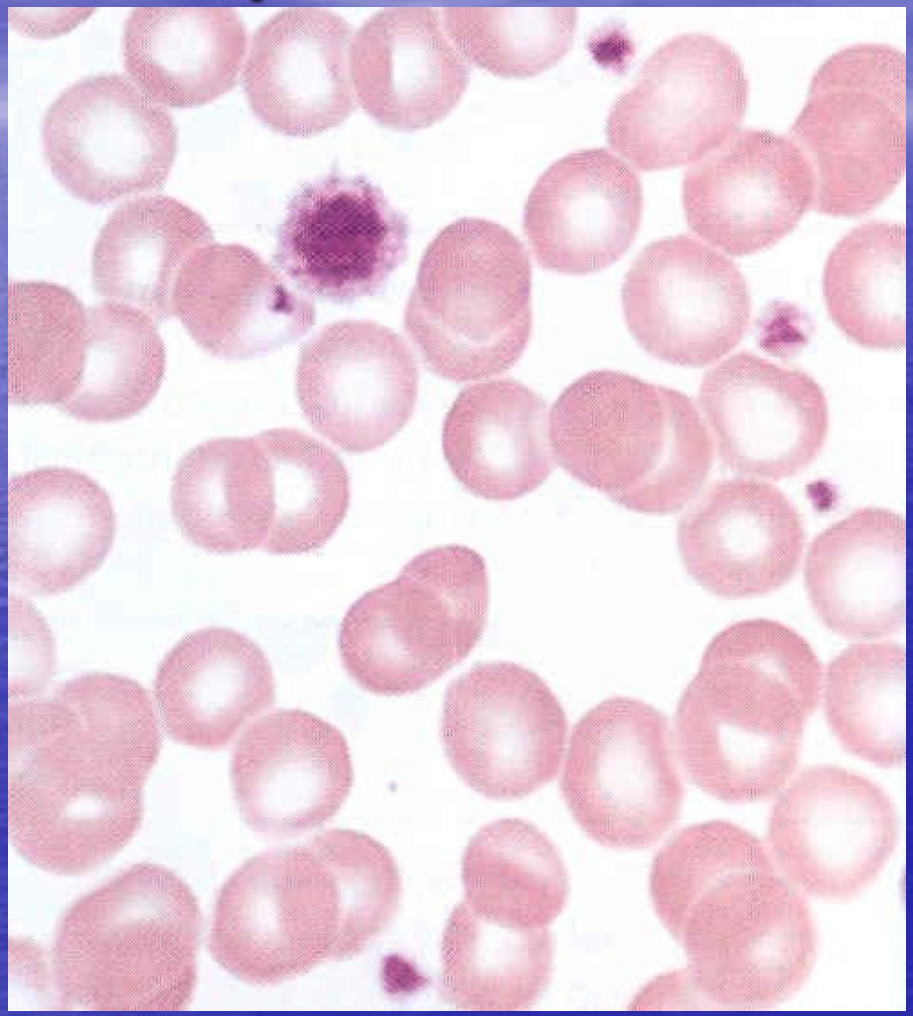
- Impaired production
- Increased platelet consumption, destruction
- Redistribution

- Isolated acquired thrombocytopenia is commonly due to peripheral destruction of platelets.
- Anti-platelet antibodies
- Drug dependent antibodies
- Autoimmune diseases
- Viral infections including HIV

Platelets

- With increased consumption or destruction, there is increased bone marrow output. MPV will be increased, with large and giant platelets.
- With bone marrow failure platelets are normal or small in size.

Large/giant platelets



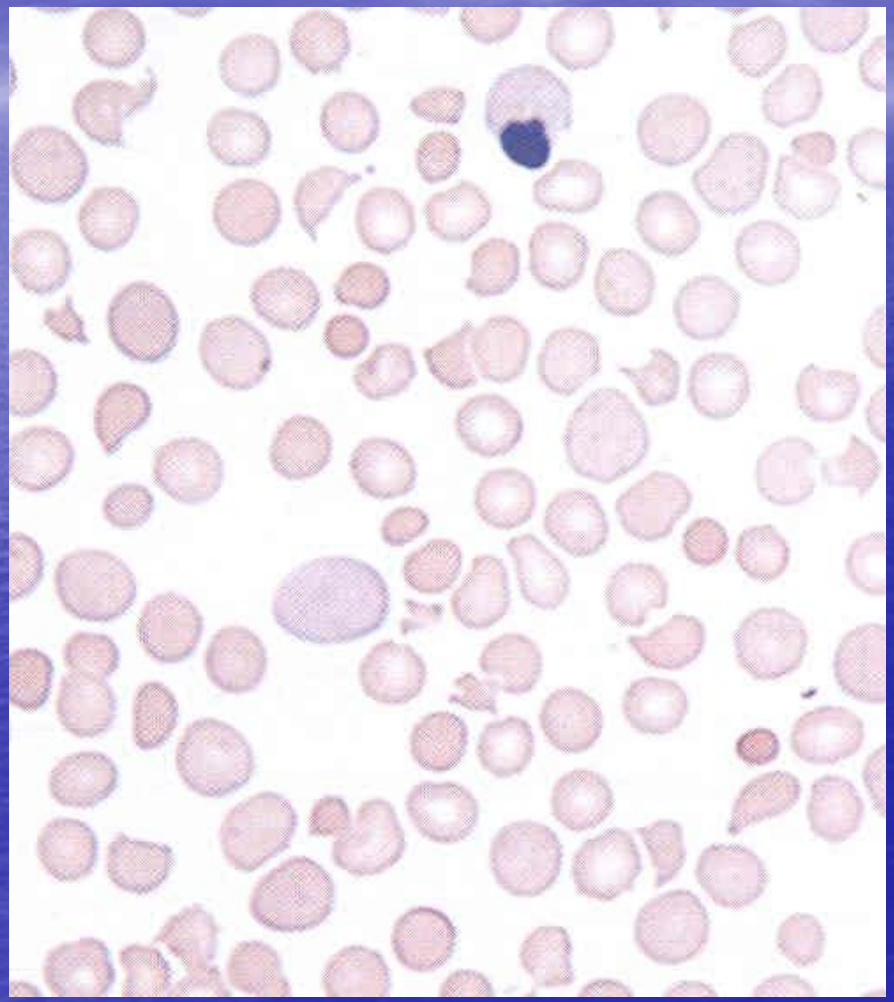
Peripheral smear

- Platelet size and granularity should be assessed.
- Red cells should be assessed for micro-angiopathic hemolytic anemia and bone marrow infiltration.
- Macrocytic anemia due to megaloblastic anemia may result in thrombocytopenia.
- Spherocytes with thrombocytopenia: Evan's syndrome

Red cells

- In microangiopathic hemolytic anemia schistocytes should be present.
- Tear drop RBCs and nucleated red cells may be indicative of bone marrow infiltration.

Schistocytes



White cells

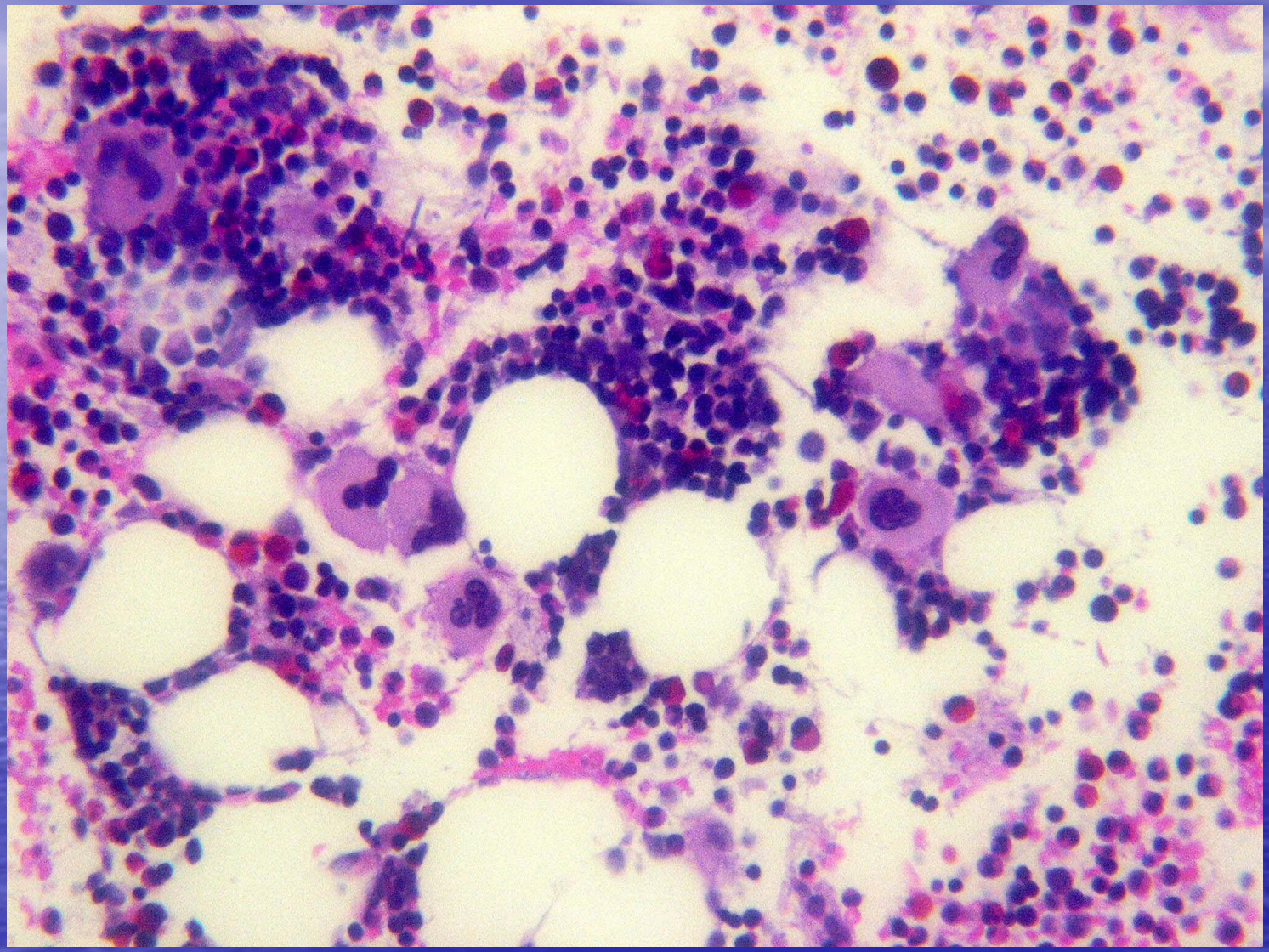
- Presence of blasts
- Left shifted myeloid cells
- Reactive or atypical lymphocytes
- Evidence of dysplasia
- White cell morphology
- e.g. Dohle bodies in May Hegglin
- anomaly; giant neutrophil granules
- in Chediak Higashi syndrome

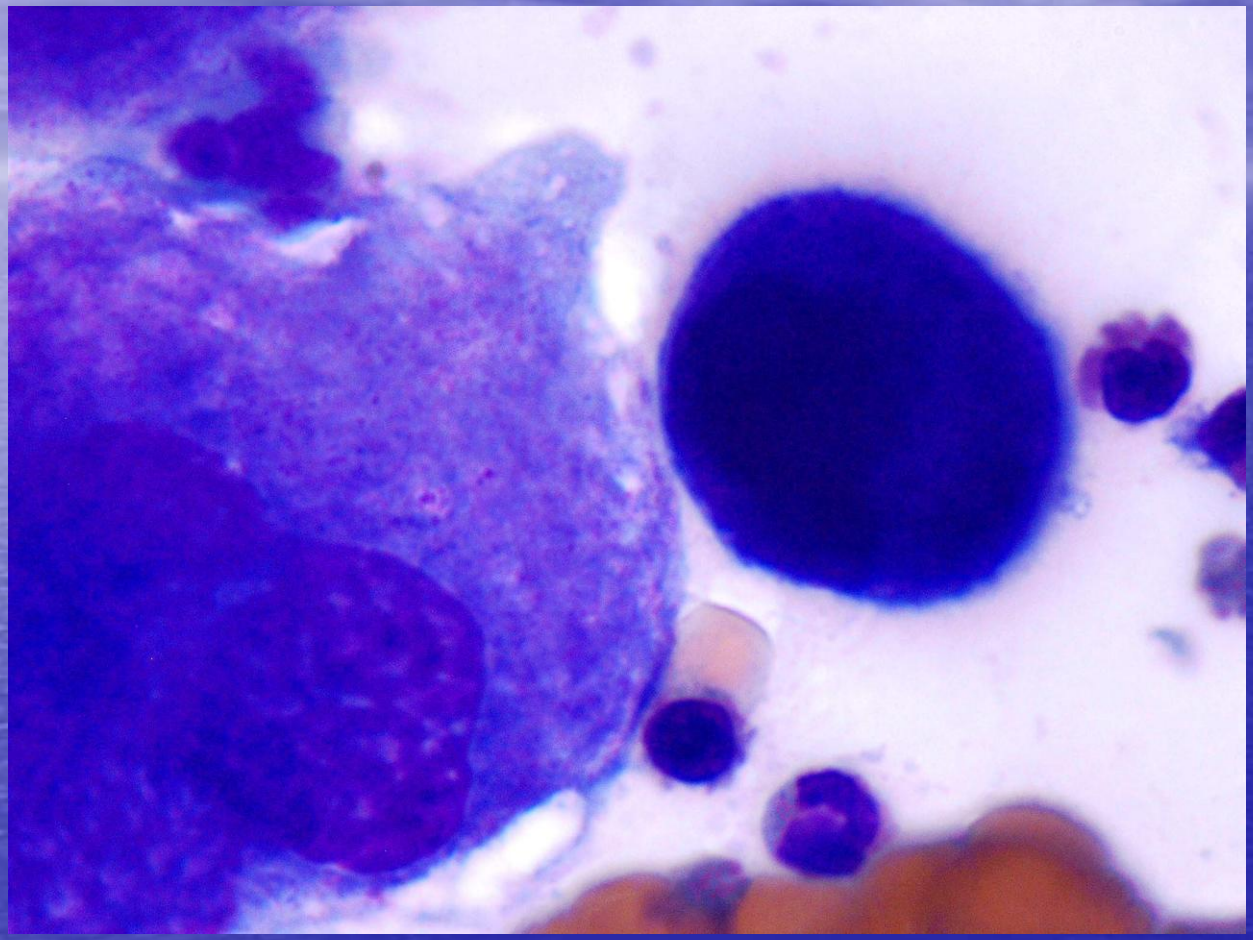
Peripheral smear of LB

- Hypochromic anemia
- Severe thrombocytopenia (5,000), with
- a few giant platelets
- Relative lymphocytosis, reactive
- lymphocytes

Bone marrow of LB

- Markedly increased megakaryopoiesis with immature forms (hypolobated with basophilic cytoplasm).
- Comment: Findings support the diagnosis of ITP.





Bone marrow examination of ITP

- Normocellular trilineage hematopoiesis
- Increased number of megakaryocytes
- Immature forms are seen
- No abnormal localization of megakaryocytes or clusters are seen

ITP

- Immune destruction of platelets.
- Antibody coated platelets are removed following binding to Fc receptors on macrophages.
- Antibodies often have specificity for GpIIb/IIIa and/or Ib
- Acute : children; viral infection
- Chronic: adult women

Rx of ITP

- Spontaneous remission
- Steroids
- IVIG
- Splenectomy
- Immunosuppressive agents

Case 2: LS

- A 61 y.o. AA male with TTP, alcohol abuse, osteomyeltis, elevated serum ferritin, iron and iron saturation.
- Labs:
- Neutrophilic leukocytosis with left shift.
- N.N. anemia, schistocytes,
- polychromasia, NRBCs.
- Thrombocytopenia, increased MPV,
- giant platelets

Case 2

- Labs:
- LDH: 1680
- Normal DIC panel
- Haptoglobin: not done
- Elevated creatinine and BUN

TTP

- Pentad:
- Micro-angiopathic hemolytic anemia
- Thrombocytopenia
- Fever
- Renal impairment
- Neurological abnormalities

TTP

- Endothelial damage associated with the presence of very high molecular weight multimers (ULvWF) of vWF.
- Absence or impaired function of metalloprotease enzyme.

TTP

- Most often the enzyme activity is hindered by an IgG inhibitor to the enzyme
- Deficiency of the enzyme is rare

TTP

- Increased binding of ULvWF multimers to platelets and endothelial cells results in thrombosis in arterioles and capillaries

TTP

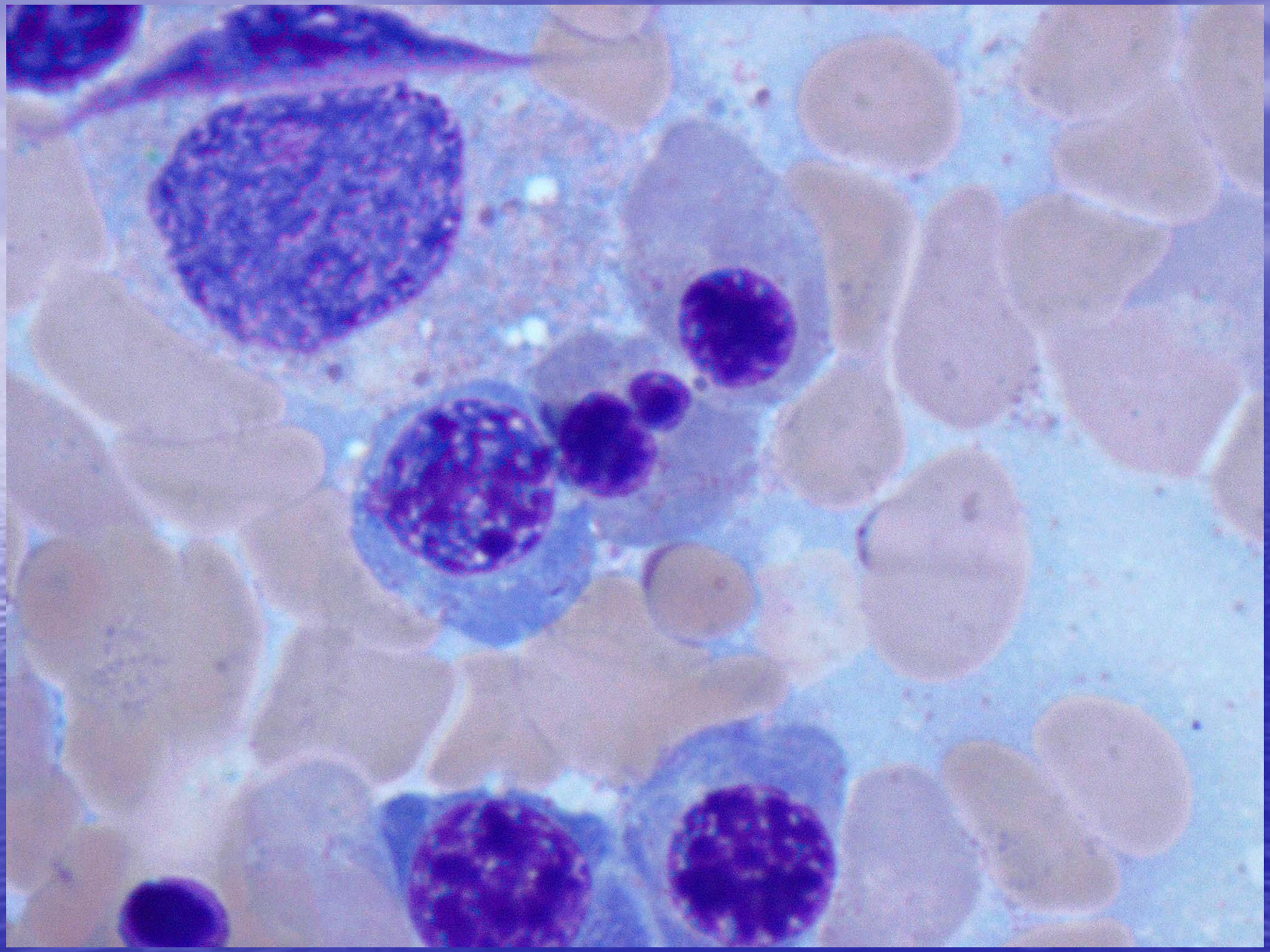
- Peripheral blood:
- Thrombocytopenia with increased
- MPV, large and giant platelets;
- schistocytes
- Other lab values:
- Increased LDH, decreased haptoglobin
- Normal DIC panel

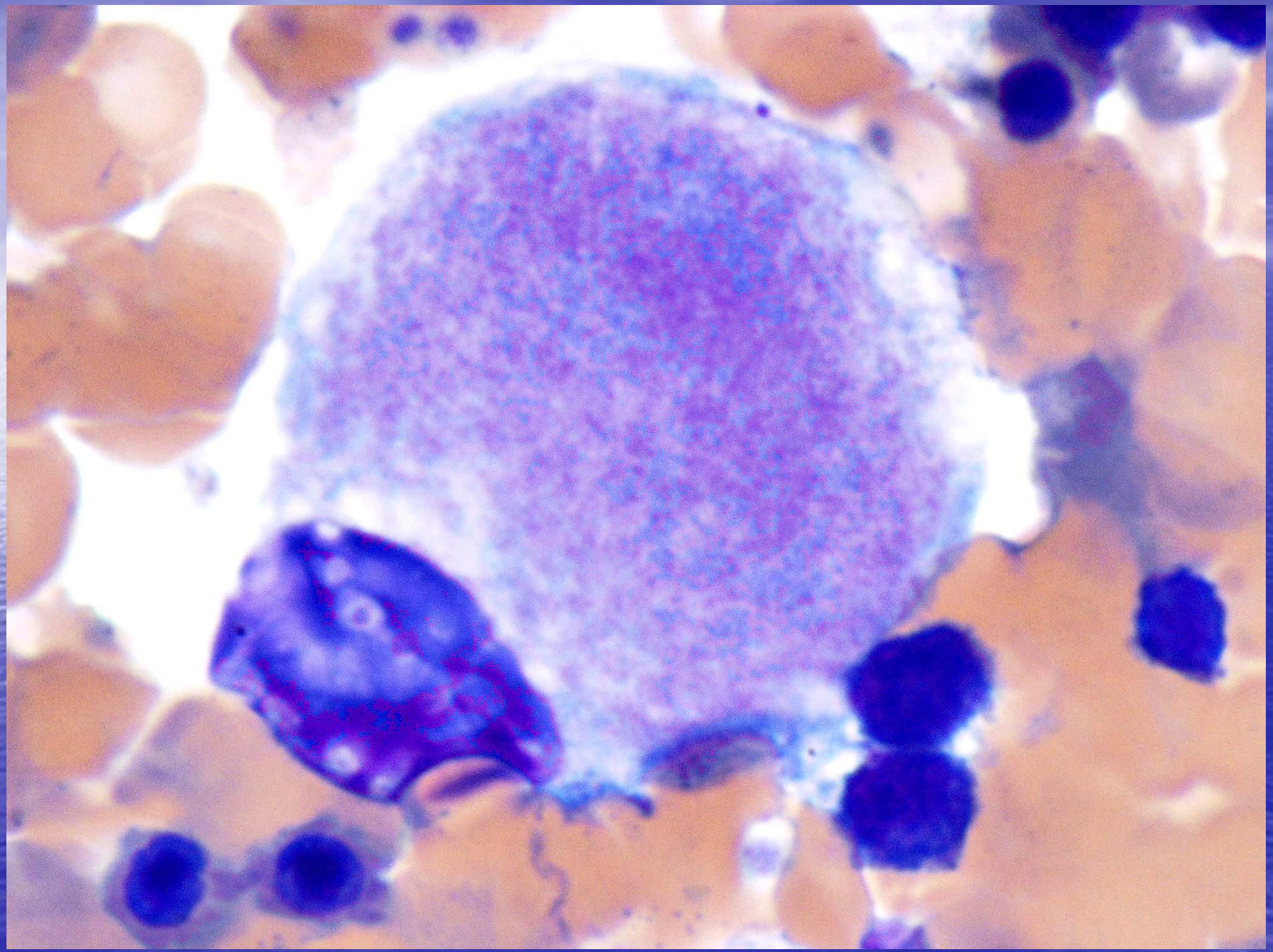
TTP

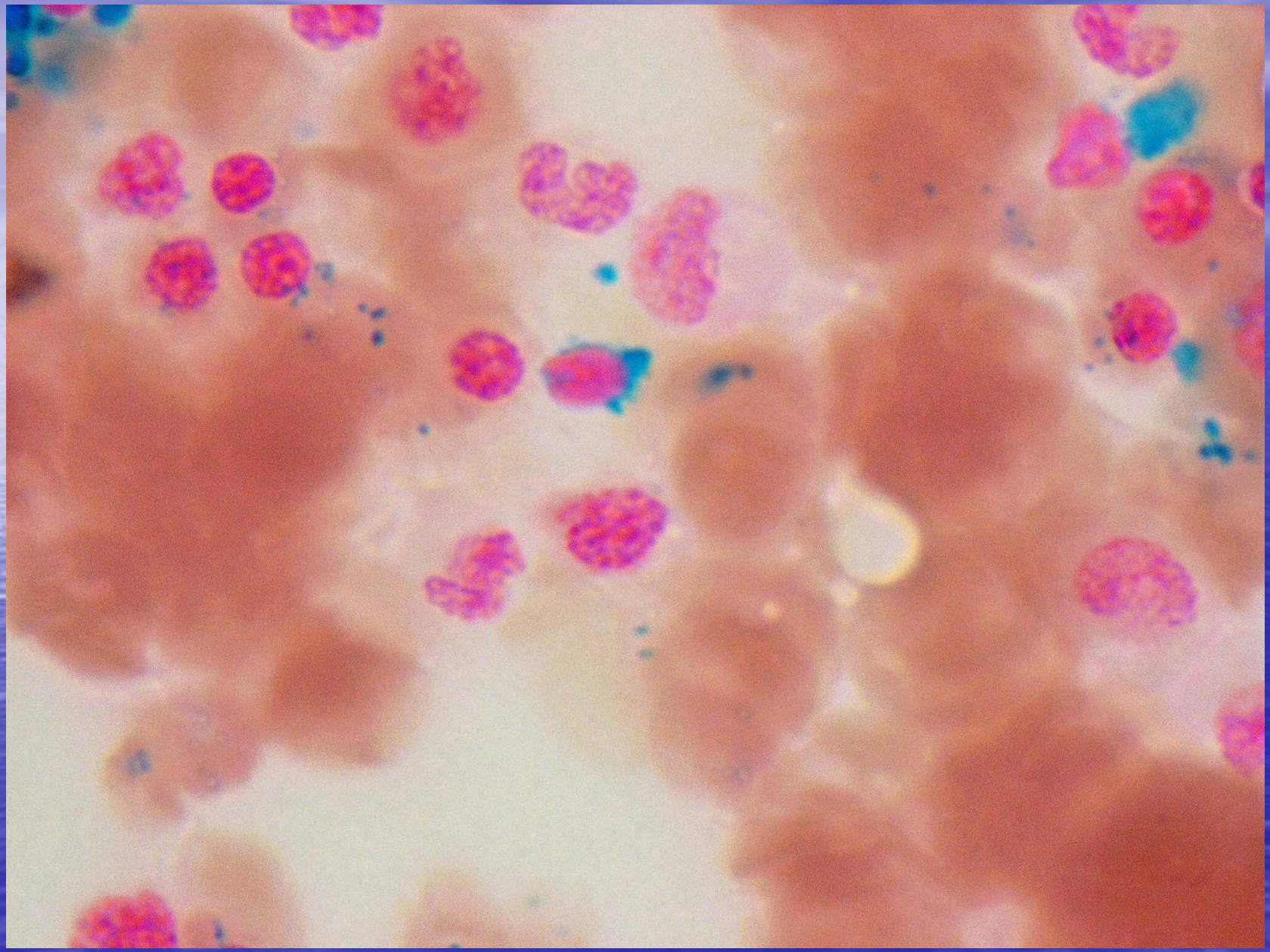
- TPE (with FFP), performed daily is the cornerstone of therapy
- TPE resistant TTP:
- Cryo poor FFP
- Vincristine
- Splenectomy

Bone Marrow of LS

- Hypercellular marrow for age (50-70%)
- Marked increased in erythropoiesis (M:E=0.4:1) with mild dyserythropoiesis
- Increased megakaryopoiesis with rare dysplastic forms
- Markedly increased Iron stores with ringed sideroblasts







Cytogenetics

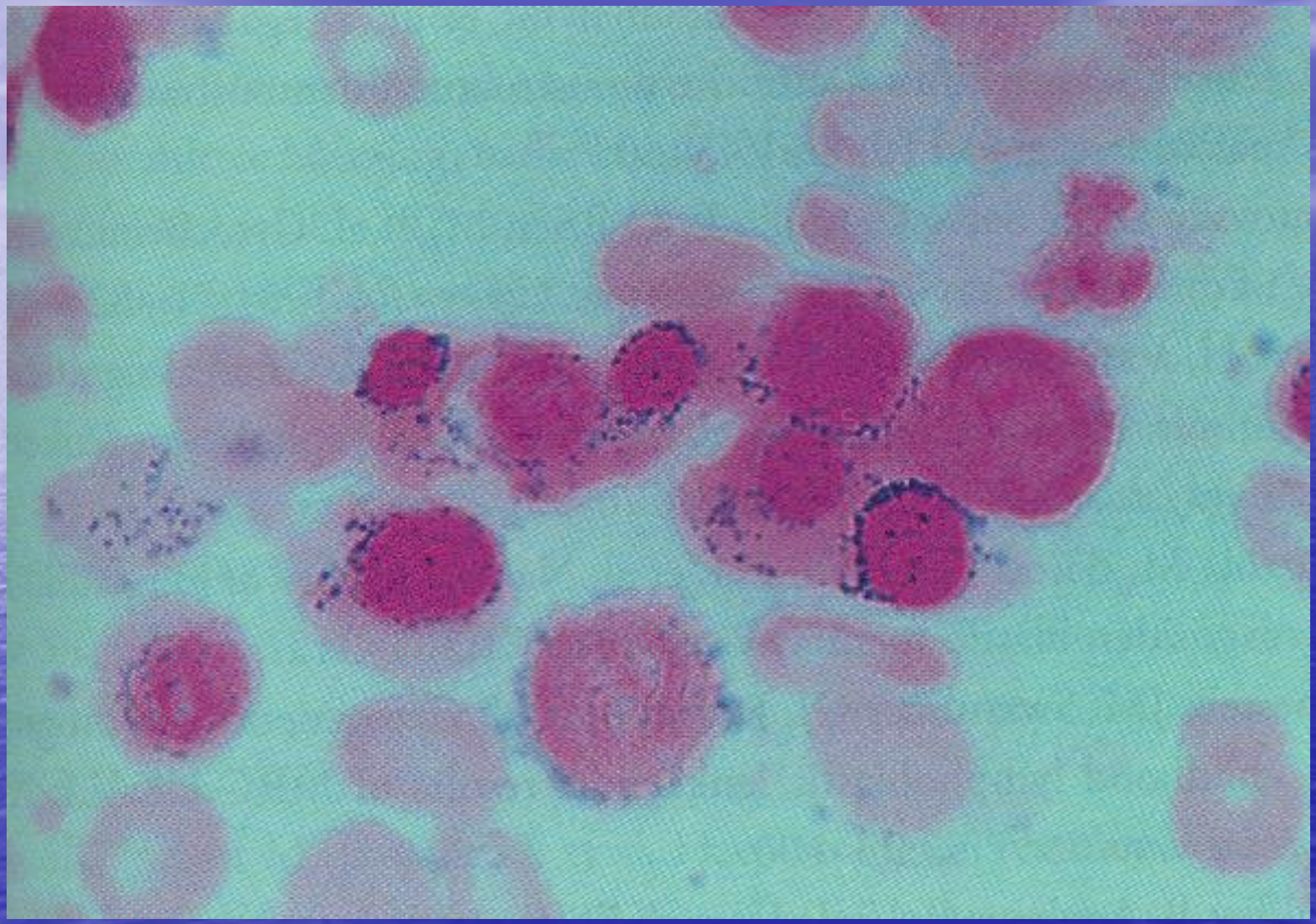
- Normal study

Dx

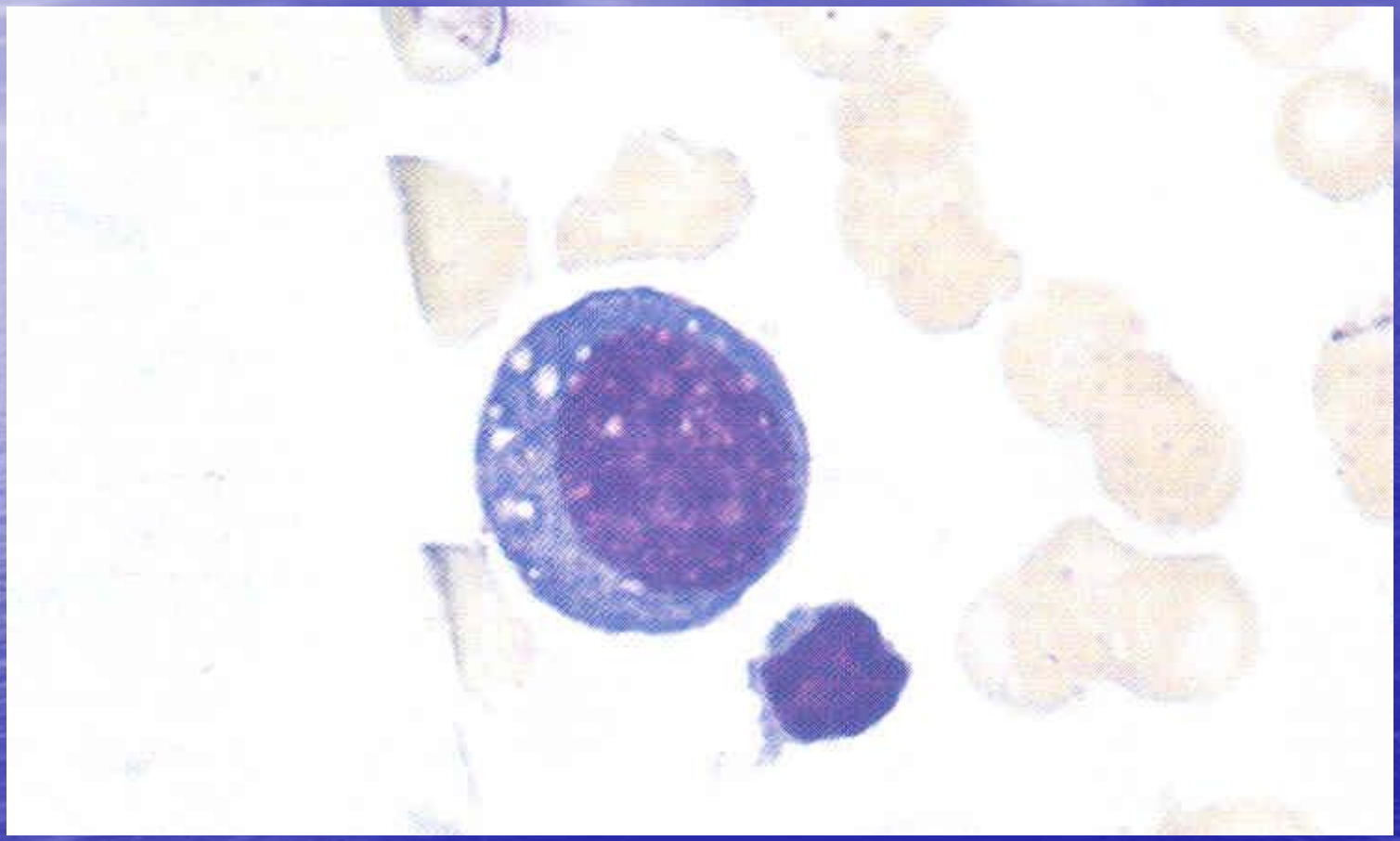
- TTP
- Sideroblastic anemia secondary to alcohol

Sideroblastic anemia

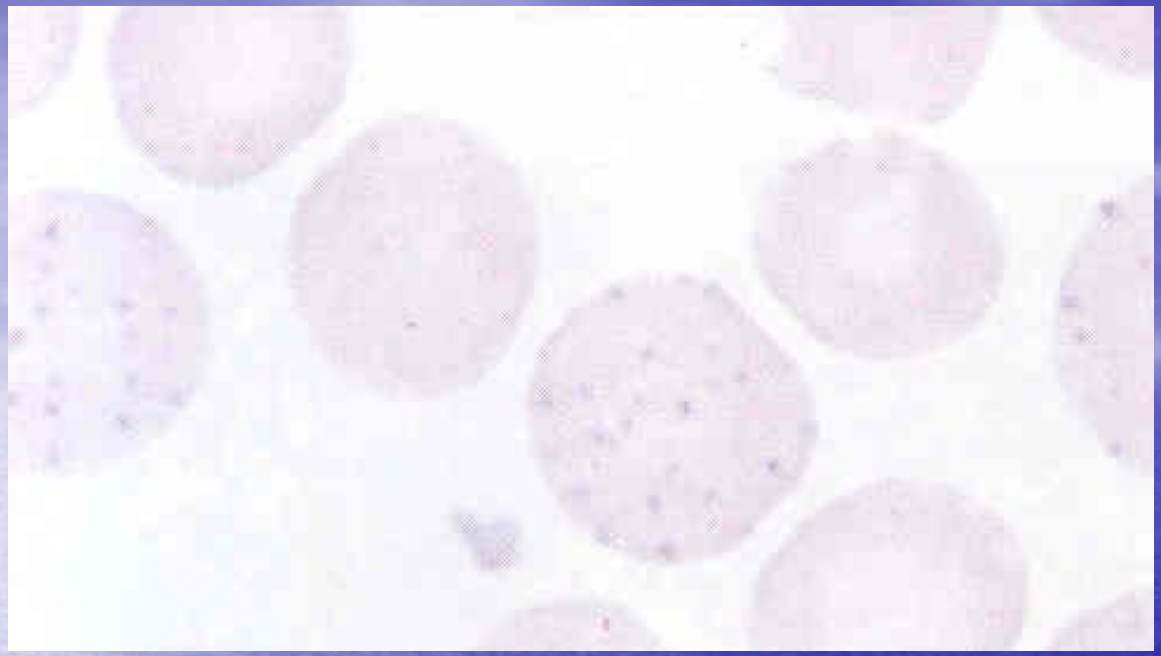
- Abnormal Iron metabolism within RBC.
- Iron is sequestered in the mitochondria and unavailable for heme synthesis.
- Types:
- Hereditary (X-linked or autosomal
- Acquired, idiopathic (MDS)
- Acquired, toxic (drugs, Pb, alcohol)



Ringed sideroblasts: 10 granules;1/3 of nucleus



Vacuoles in an erythroid precursor due to alcohol



Causes of punctate basophilia

Thalassaemia (α and β)

Acquired sideroblastic anaemia and other myelodysplasias

Lead poisoning

Severe megaloblastic anaemia

Pyrimidine 5′-nucleotidase deficiency

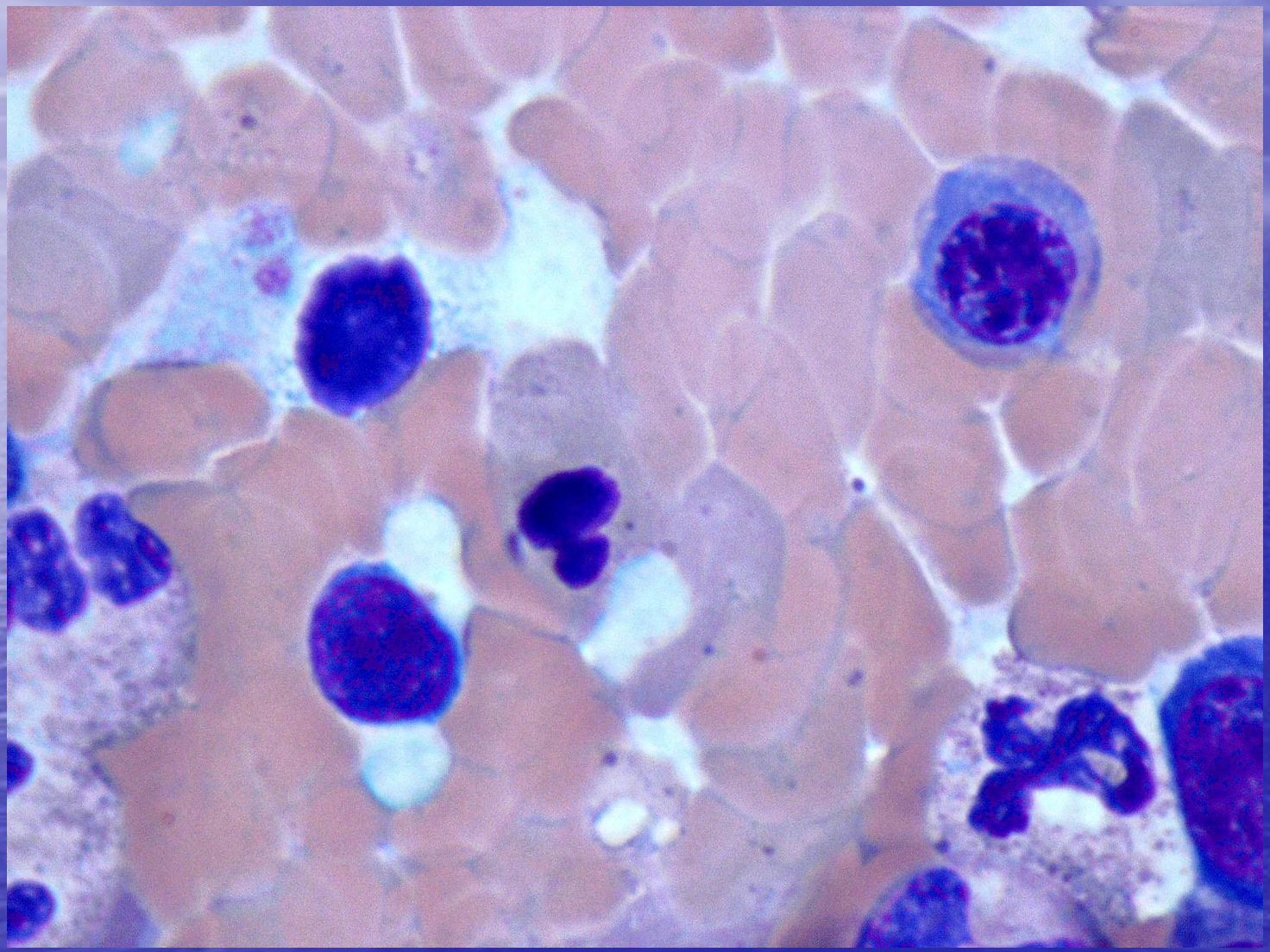
Congenital dyserythropoietic anaemia

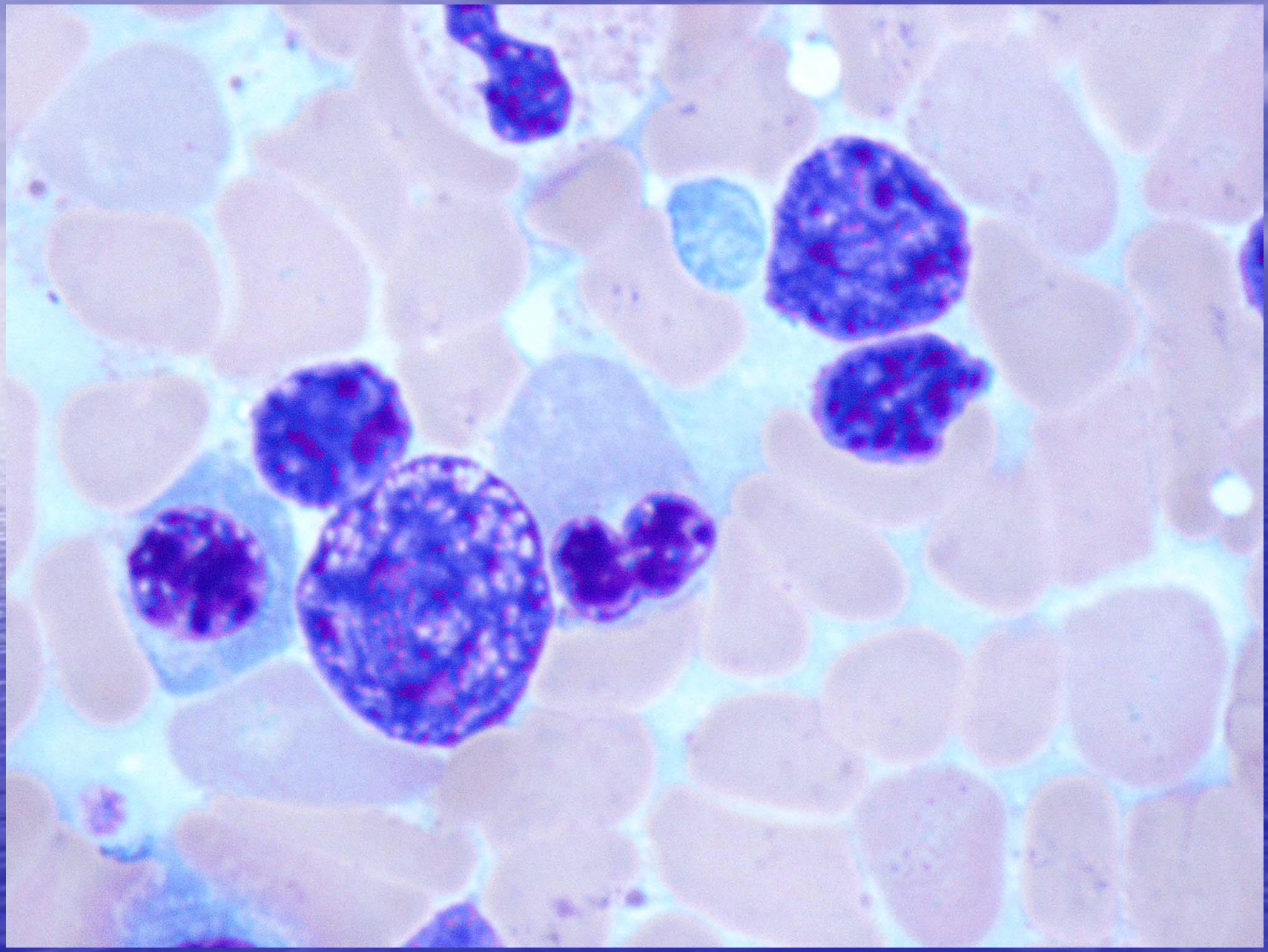
Case 3:BE

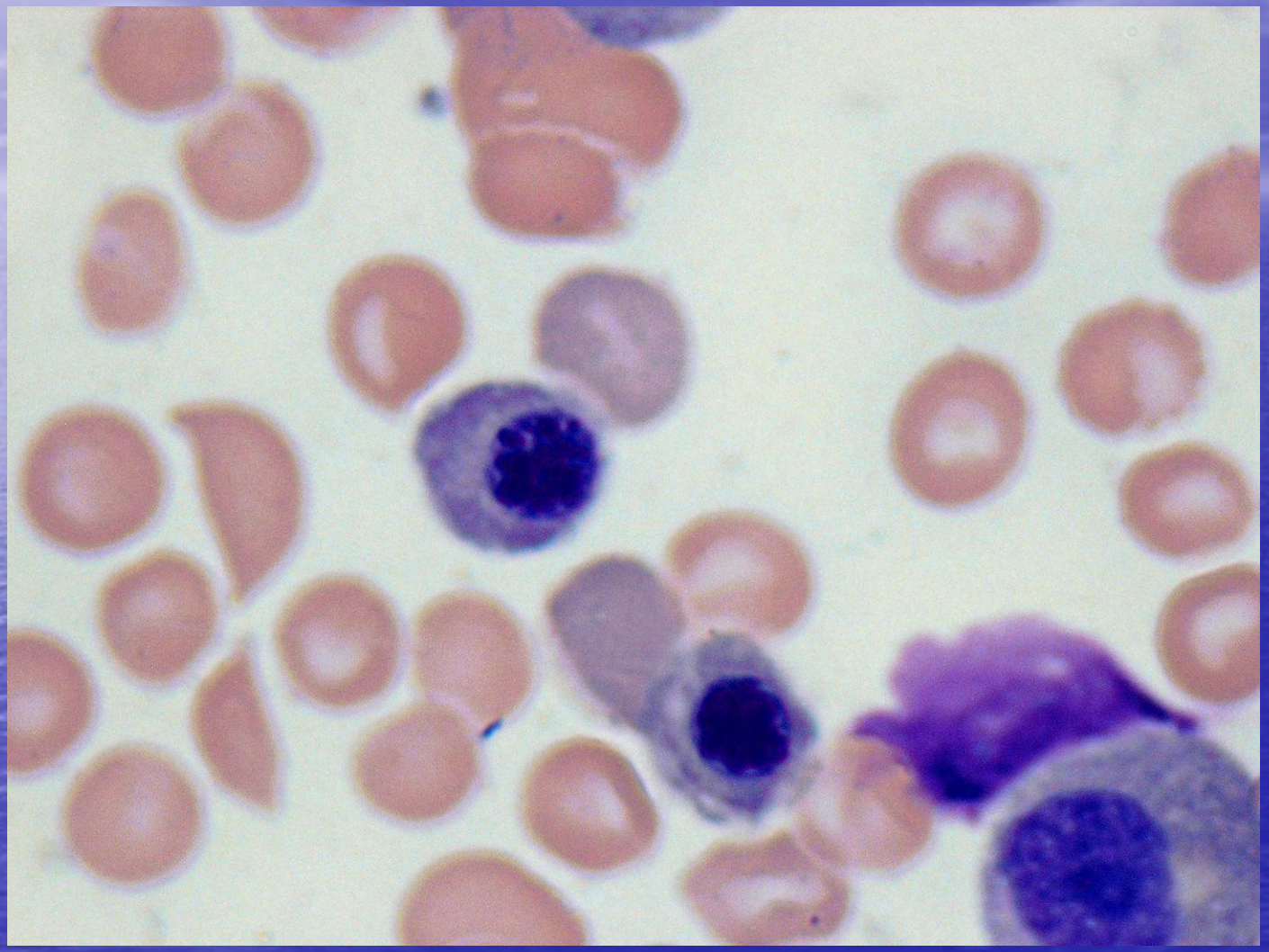
- A 65 y.o. male with DM, HTN, CAD, CHF, RF and pancytopenia.
- Labs:
- Hgb: 7.6; Hct: 22.5; WBC: 2.0;
- Platelets: 32,000
- RBC: Normocytic normochromic, few
- NRBCs

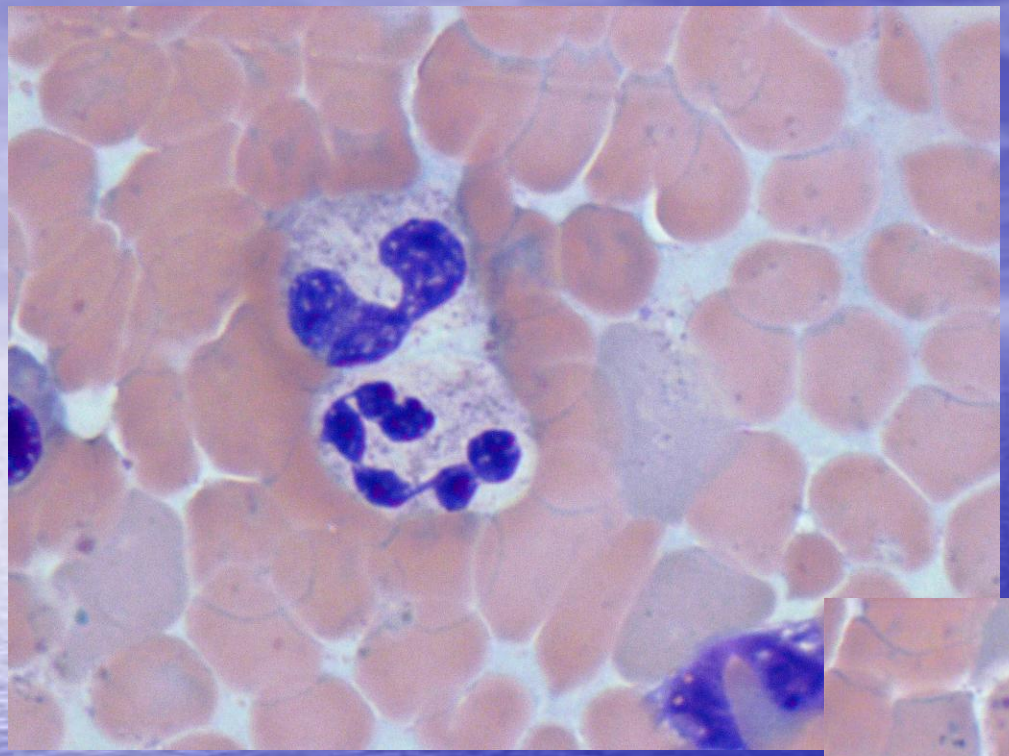
Bone Marrow

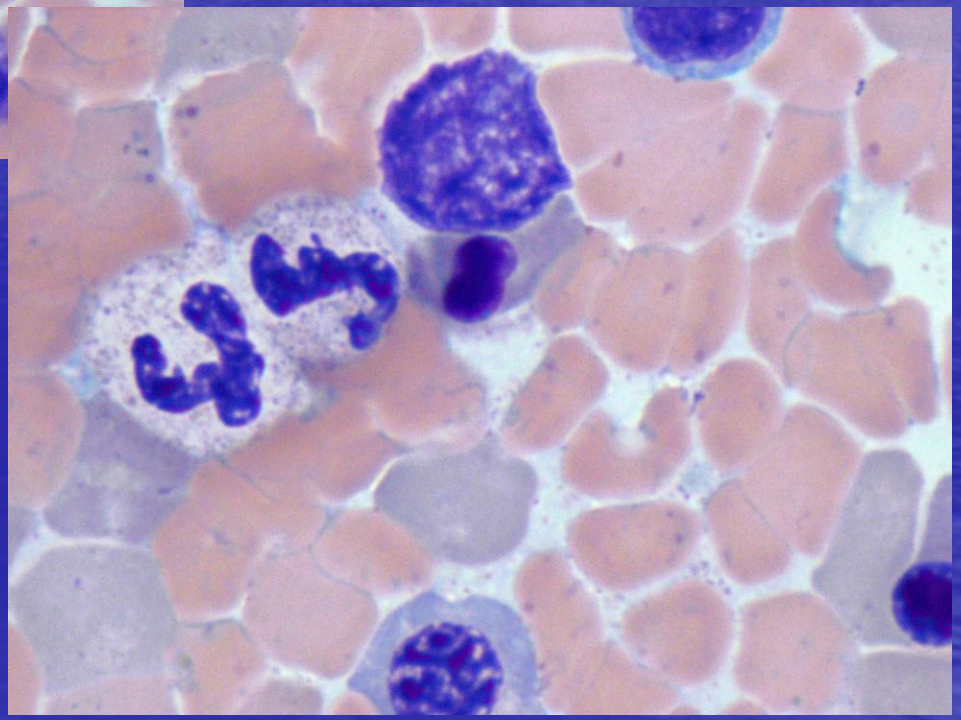
- Hypercellular for age (70-80%)
- Erythroid hyperplasia (M:E=0.7:1) with dysplastic cells
- Iron stores are increased with no ringed sideroblasts

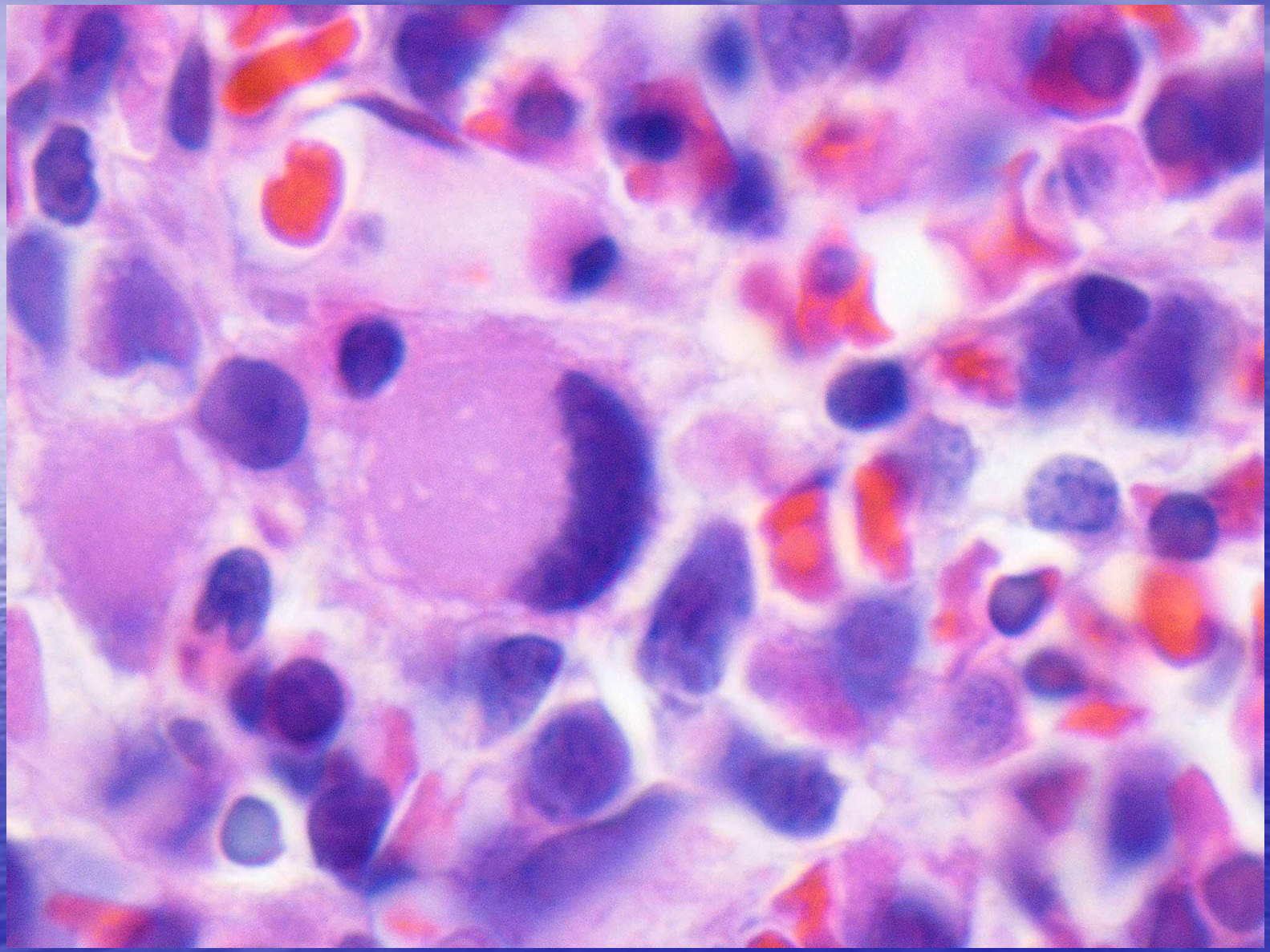


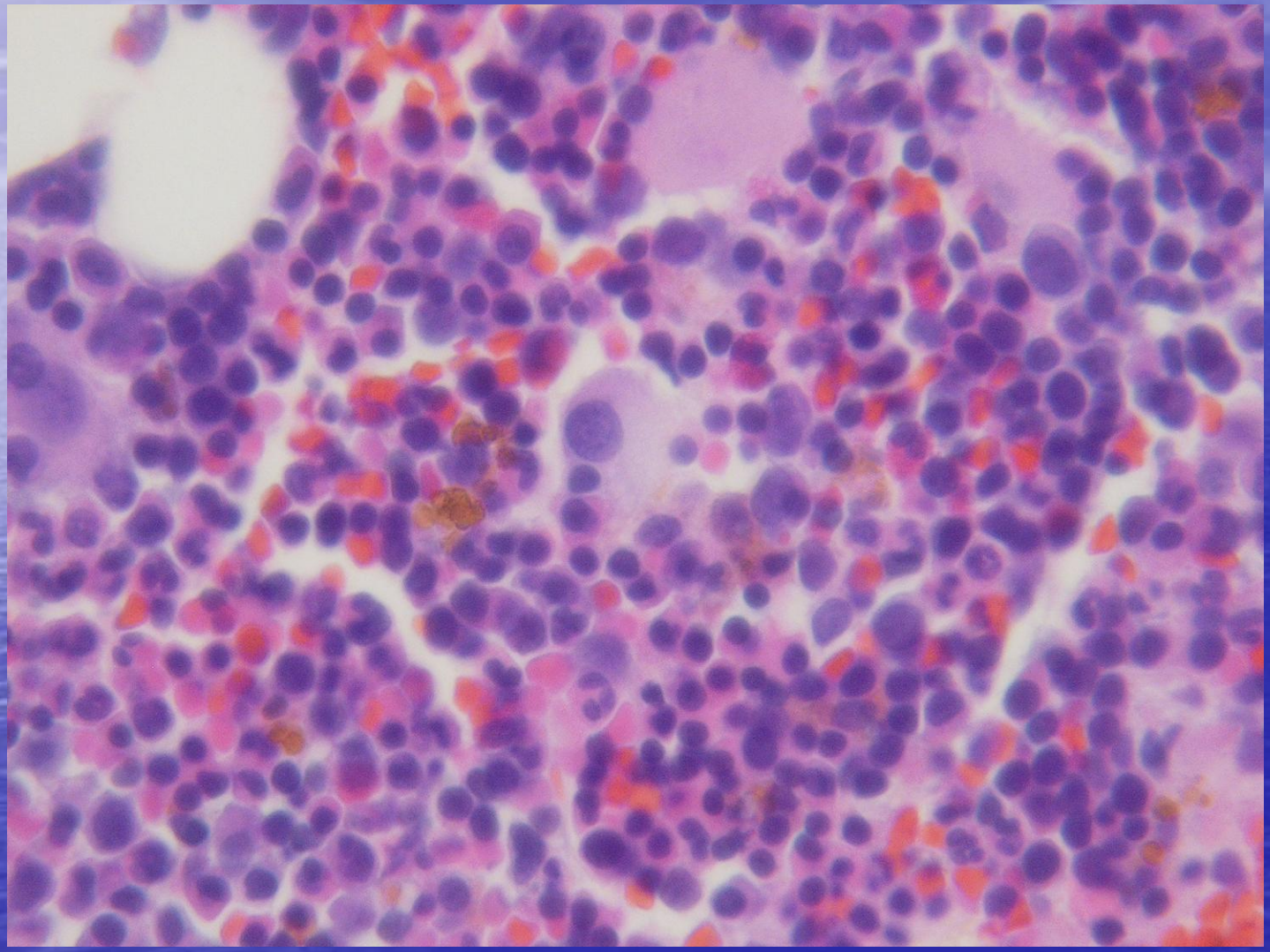


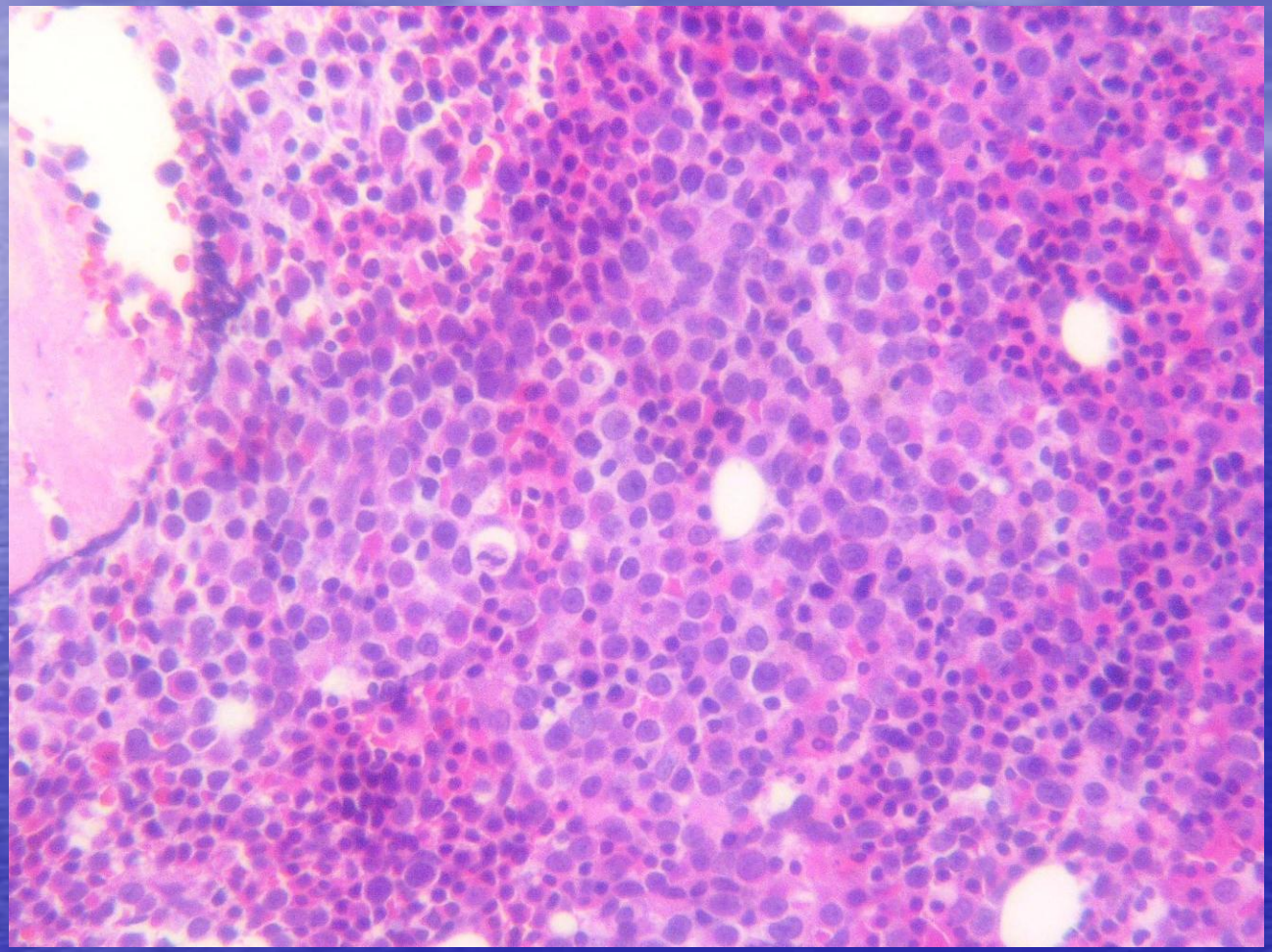












Cytogenetics

- 46,XY, del(5) (q11), -6, add (10) (q22), add (11) (q23), add (17) (p12)

Dx

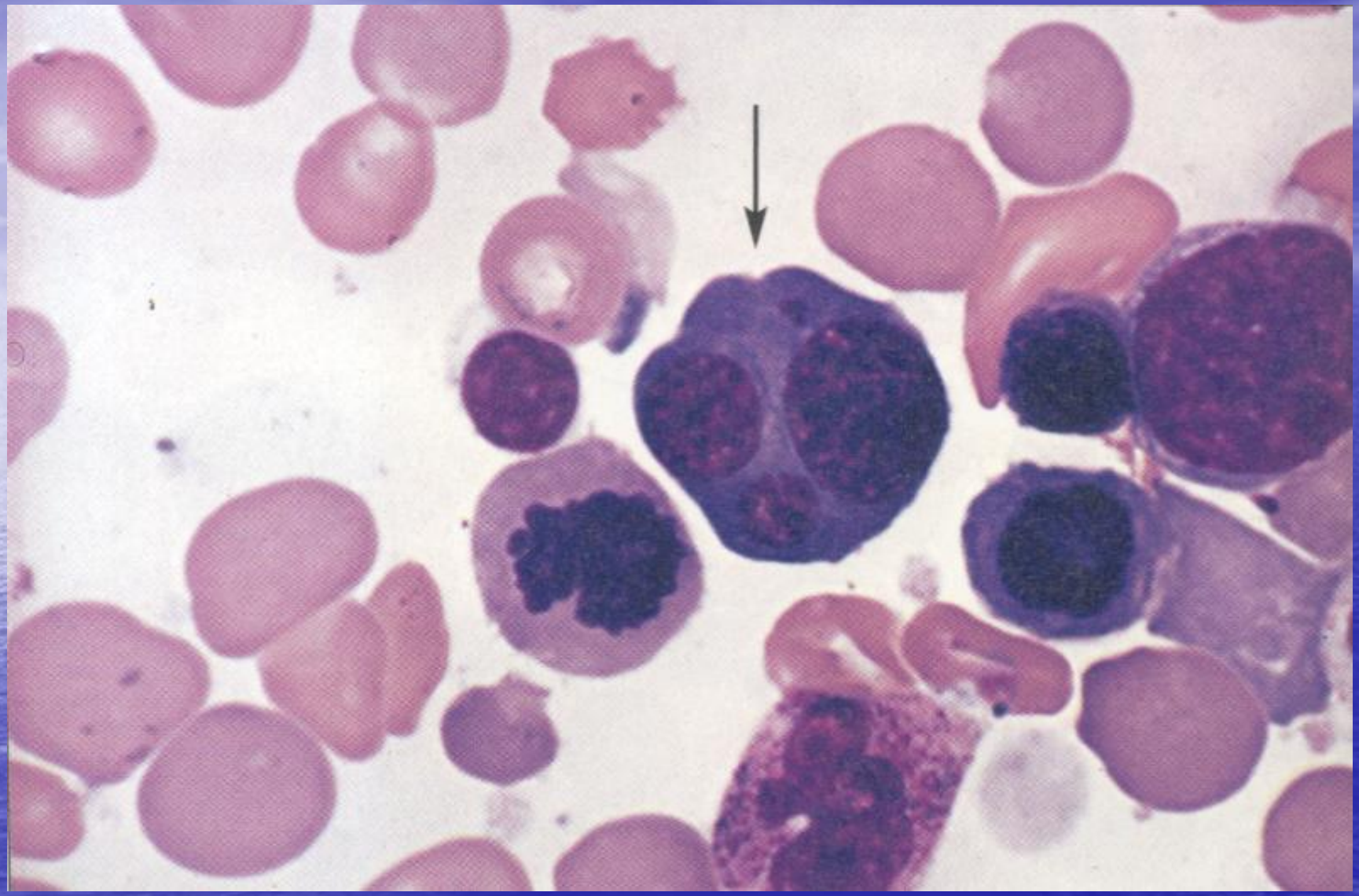
- FAB: refractory anemia
- WHO: refractory cytopenia with multilineage dysplasia (RCMD)

Myelodysplastic syndrome

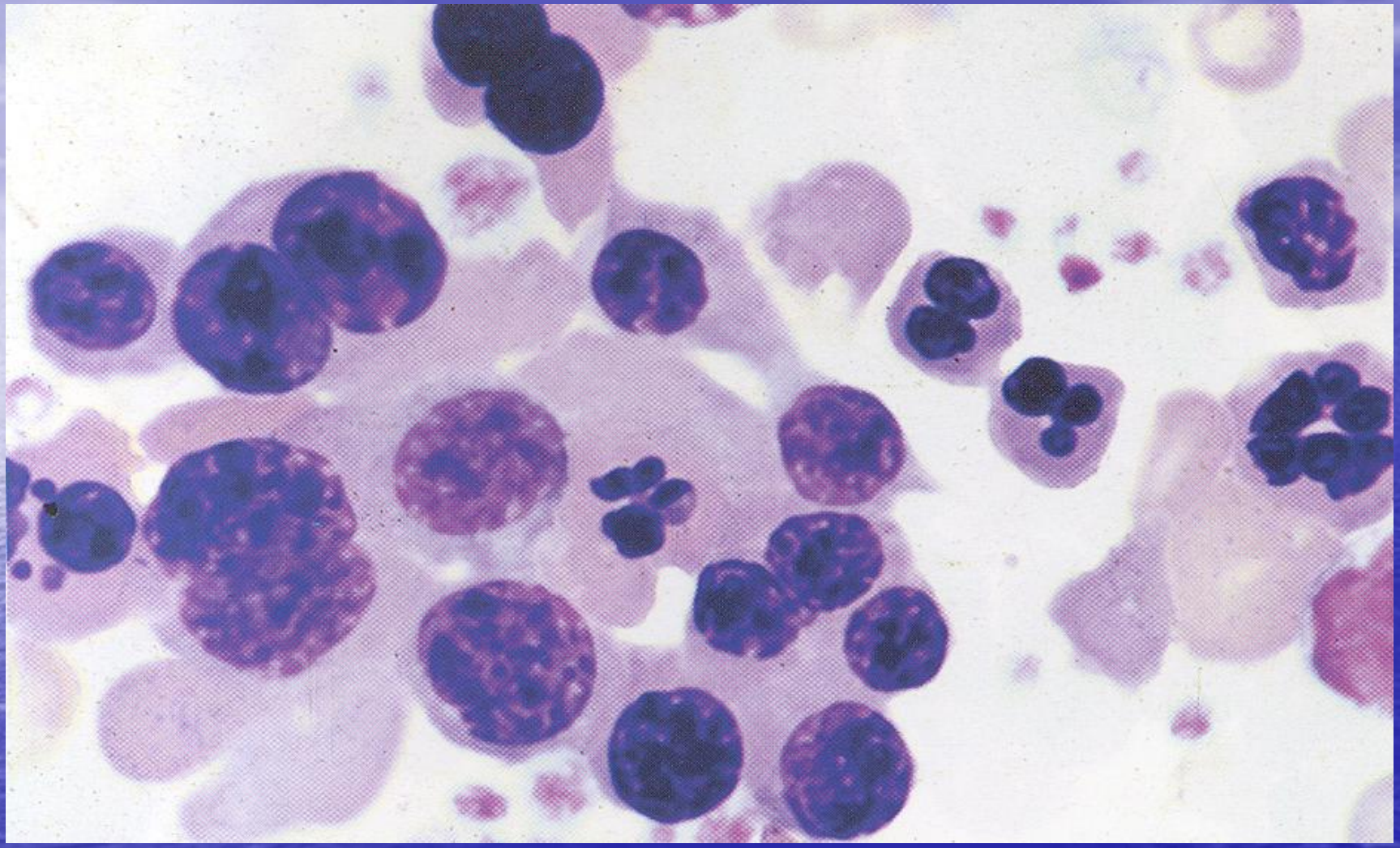
- Cytopenia
- Hypercellular bone marrow
- Dysplasia (1 or more myeloid cell lineages)
- Myeloblasts in BM < 20%
- May evolve to AML

Morphological Classification

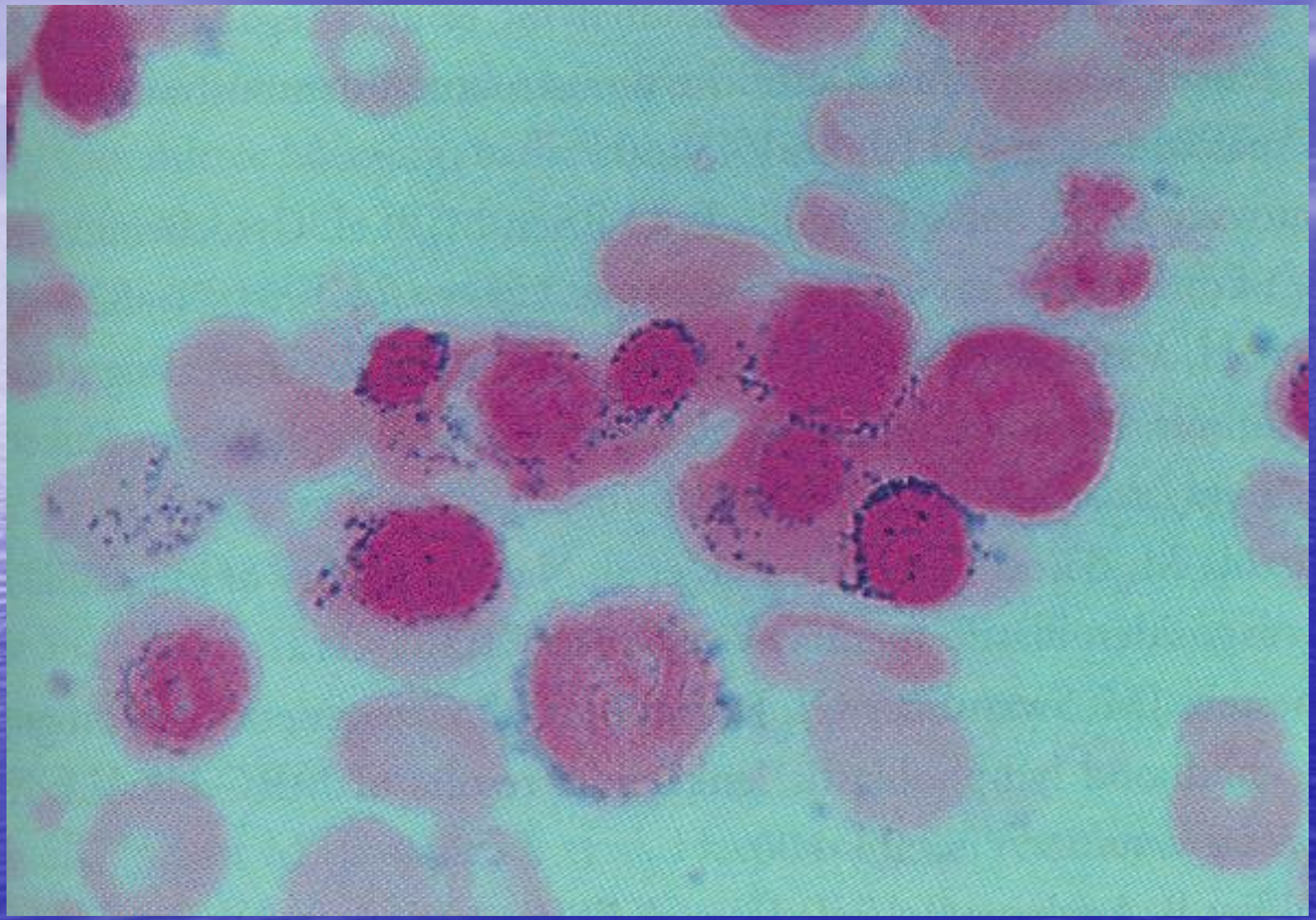
- % of Blasts
  - Marrow (500 cell differential)
  - Blood (200 leukocyte differential)
- Type and degree of dysplasia
  - 1) Dyserythropoiesis
  - 2) Dysgranulopoiesis
  - 3) Dysmegakaryopoiesis
- Presence of ringed sideroblasts

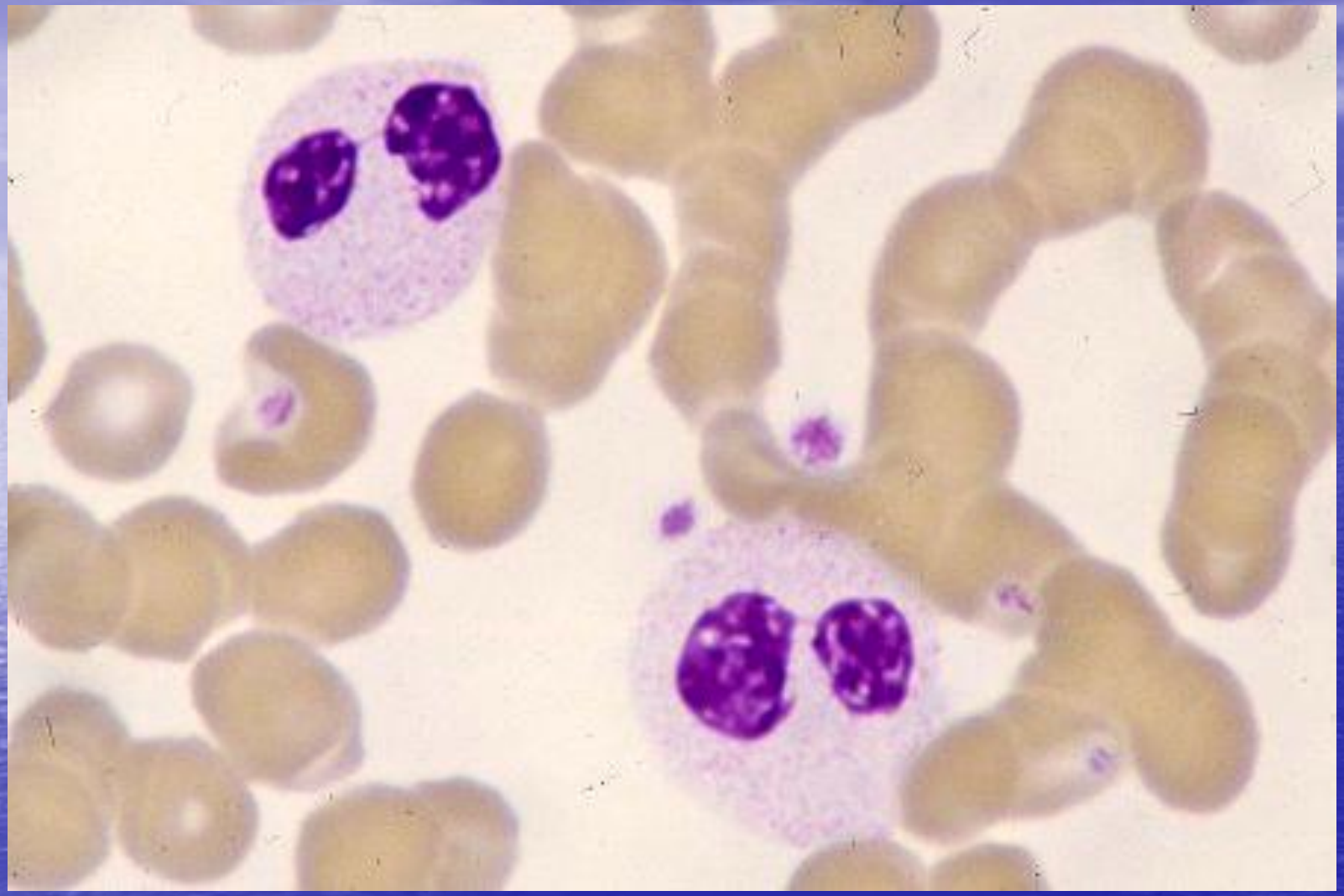


Multinucleated megaloblastoid erythroid precursor.
Bone marrow smear.

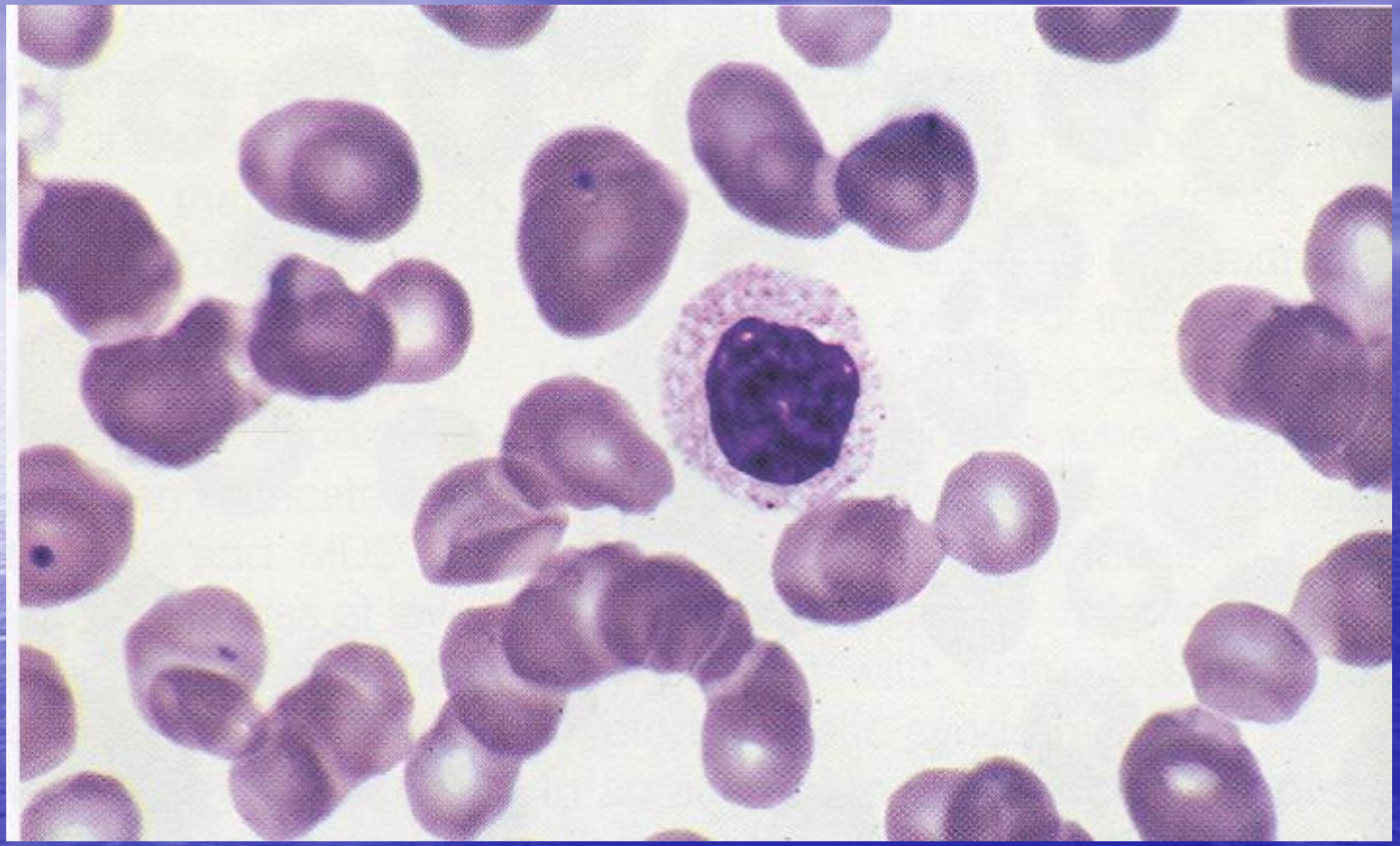


Dyserythropoiesis. Bone marrow smear.

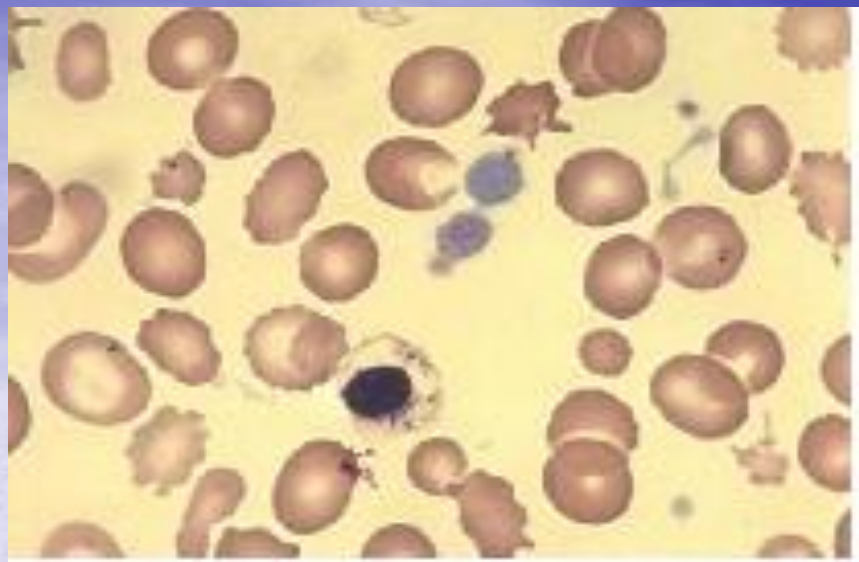




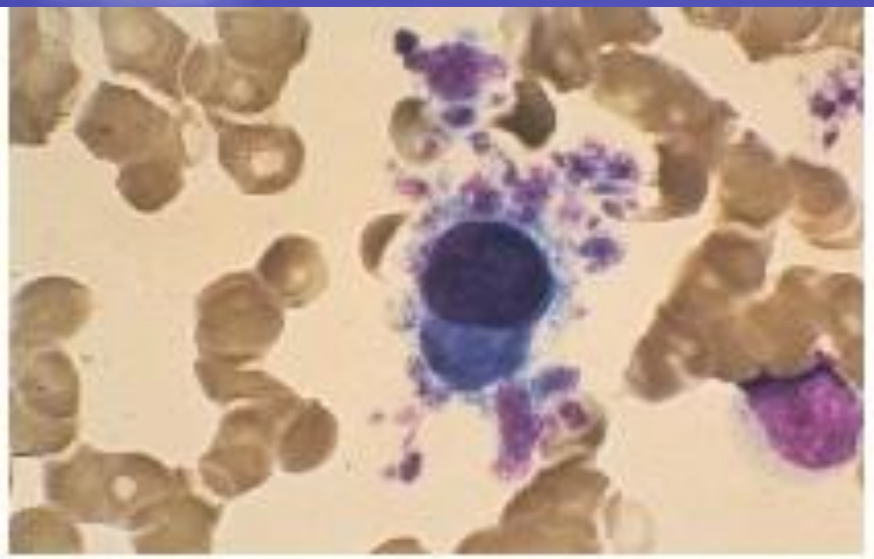
Circulating pseudo-Pelger-Huet neutrophils. Hypogranular cytoplasm, bilobed 'spectacle' nuclei. Blood smear.



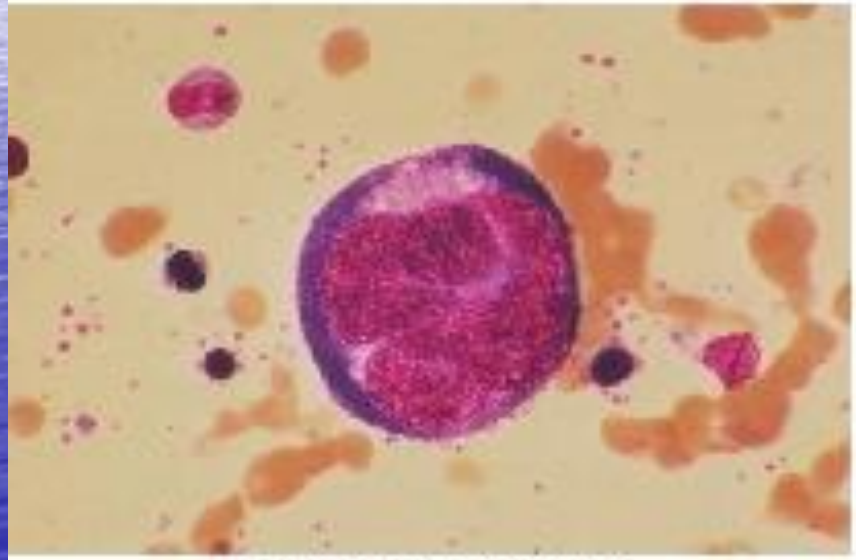
Neutrophil with non-lobulated nucleus. Blood smear.



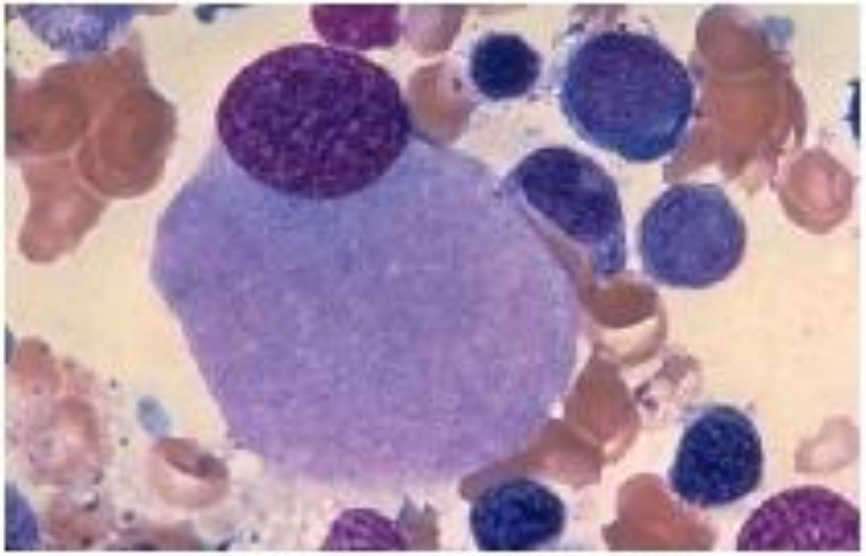
Hypogranular platelets



Micromegakaryocyte in blood



Abnormal megakaryocyte



Mononuclear megakaryocyte

FAB classification

Subtype	Blood	Marrow[a]
Refractory anemia (RA)	Blasts <1%	Blasts <5%
Refractory anemia with ringed sideroblasts (RARS)	Blasts <1%	Blasts <5%
Refractory anemia with excess blasts (RAEB)	Blasts $\leq$5%	Blasts 5-20%
Refractory anemia with excess blasts in transformation (RAEB-t)	Blasts >5%	Blasts 20-30% or Auer rods
Chronic myelomonocytic leukemia (CMML)	$\geq 1 \times 10^9$/L monocytes	Any number

WHO classification

- Reduced blast requirement for AML from 30% to 20%
- Eliminated RAEB-t category
- Split RAEB into RAEB-1 and RAEB-2
- Added
  - Multilineage dysplasia
  - Unclassified
  - 5q-syndrome
- Shifted CMML to new group
  - MDS/myeloproliferative syndromes

Low risk

High risk

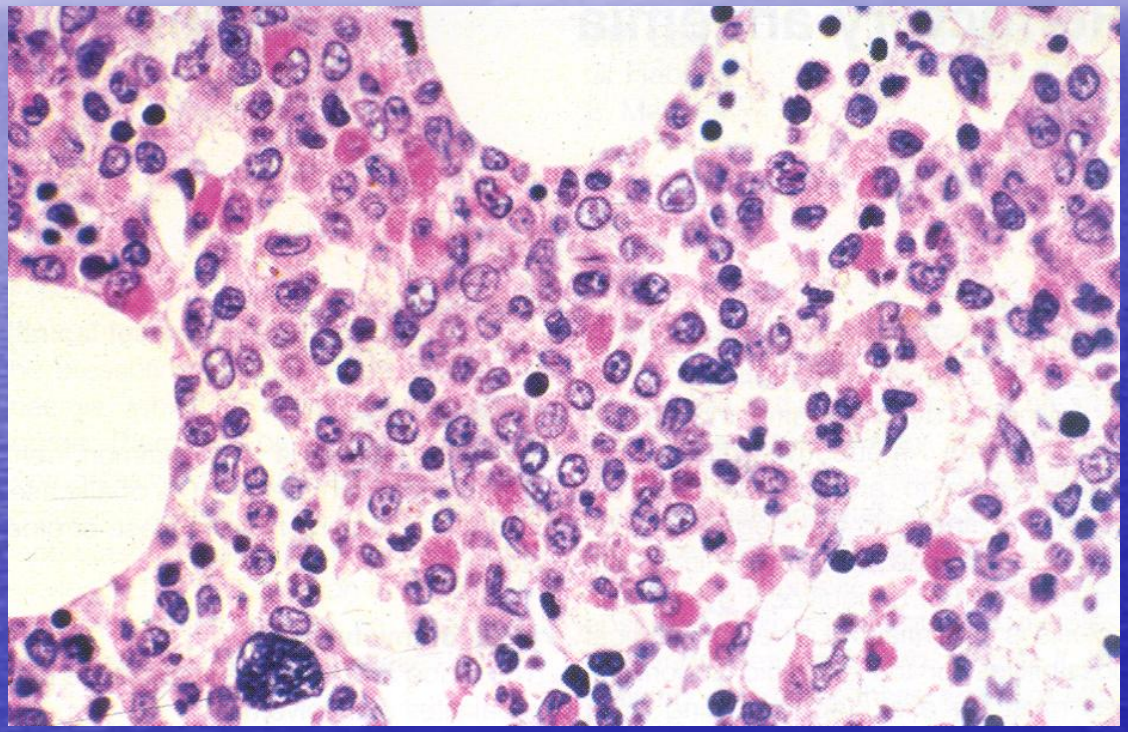
High risk

Low risk

Peripheral blood and bone marrow findings in myelodysplastic syndromes.

Disease	Blood findings	Bone marrow findings
Refractory anaemia (RA)	Anaemia No or rare blasts	Erythroid dysplasia only <5% blasts <15% ringed sideroblasts
Refractory anaemia with ringed sideroblasts (RARS)	Anaemia No blasts	≥15% ringed sideroblasts Erythroid dysplasia only <5% blasts
Refractory cytopenia with multilineage dysplasia (RCMD)	Cytopenias (bicytopenia or pancytopenia) No or rare blasts No Auer rods <1x10^9/L monocytes	Dysplasia in ≥10% of the cells of two or more myeloid cell lines <5% blasts in marrow No Auer rods <15% ringed sideroblasts
Refractory cytopenia with multilineage dysplasia and ringed sideroblasts (RCMD-RS)	Cytopenias (bicytopenia or pancytopenia) No or rare blasts No Auer rods <1x10^9/L monocytes	Dysplasia in ≥10% of the cells in two or more myeloid cell lines ≥15% ringed sideroblasts <5% blasts No Auer rods
Refractory anaemia with excess blasts –1 (RAEB-1)	Cytopenias <5% blasts No Auer rods <1x10^9/L monocytes	Unilineage or multilineage dysplasia 5-9% blasts No Auer rods
Refractory anaemia with excess blasts –2 (RAEB-2)	Cytopenias 5-19% blasts Auer rods ± <1x10^9/L monocytes	Unilineage or multilineage dysplasia 10%-19% blasts Auer rods ±
Myelodysplastic syndrome – unclassified (MDS-U)	Cytopenias No or rare blasts No Auer rods	Unilineage dysplasia: one myeloid cell line <5% blasts No Auer Rods
MDS associated with isolated del(5q)	Anaemia Usually normal or increased platelet count <5% blasts	Normal to increased megakaryocytes with hypolobated nuclei <5% blasts Isolated del(5q) cytogenetic abnormality No Auer rods

ALIP

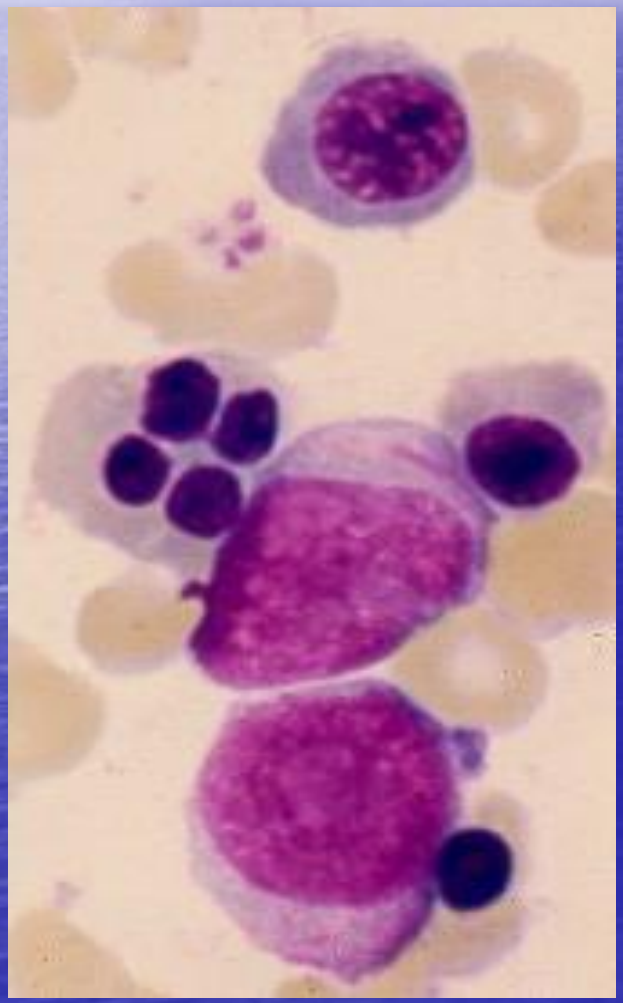


Abnormal localization of immature precursors (ALIP):
Immature myeloid cell clusters (5-8 cells) present in central portion of marrow away from usual locations (paratrabecular or perivascular); three or more foci is significant

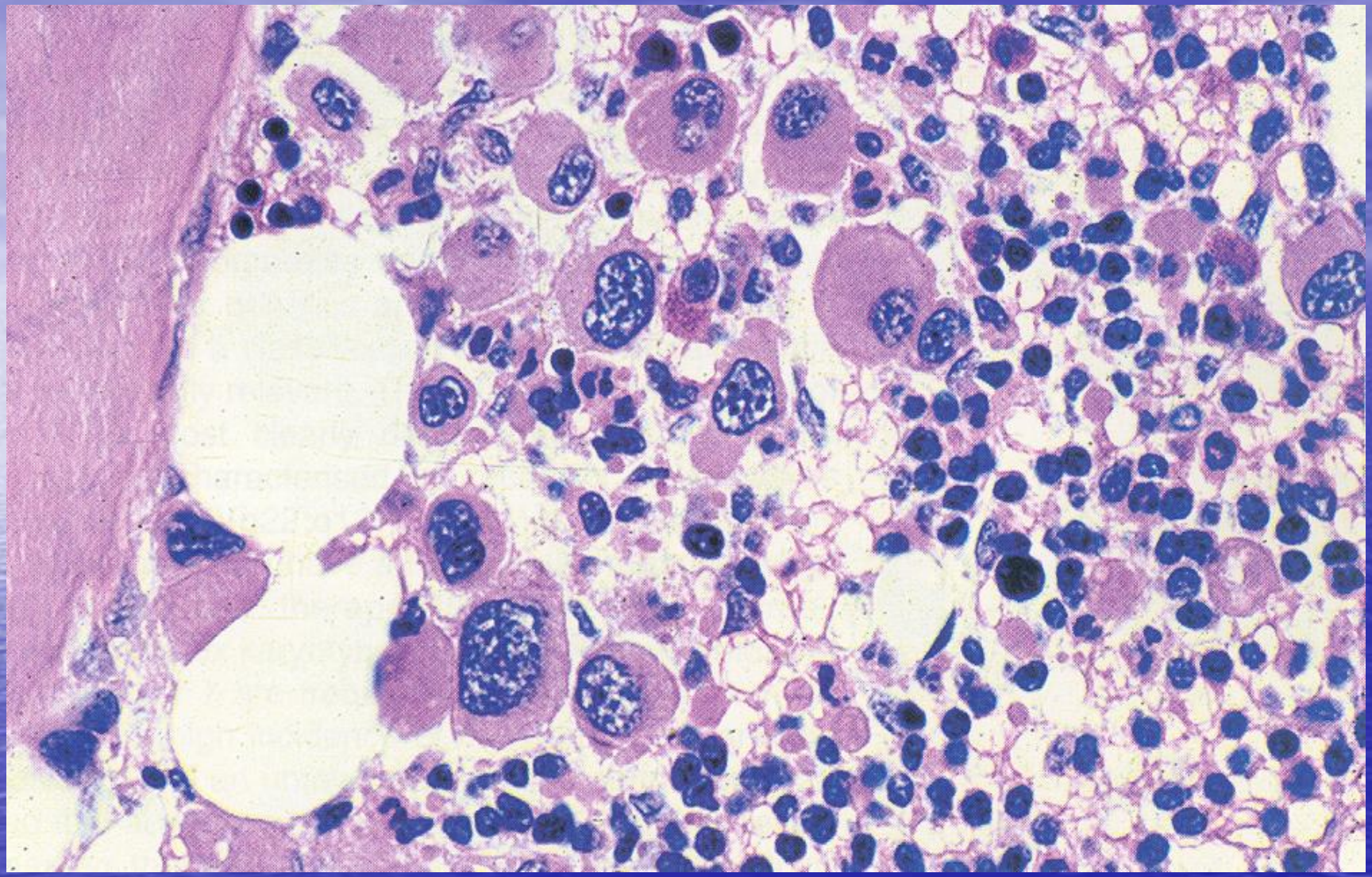
ALIP

- Frequently present in RAEB
- Associated with rapid evolution to AML
- If found in other subtype
  - Re-evaluate
    - Peripheral blood smear
    - Bone marrow aspirate smear

RAEB-2



Two myeloblasts,
one with an Auer rod,
and a quadrinucleate normoblast



Numerous megakaryocytes
varying sizes with hypolobulated nuclei

Cytogenetics

- Primary or "de novo"
  - 30% cytogenetic abnormalities
- Secondary MDS
  - More than 80% cytogenetic abnormalities
- Abnormalities more common in
  - RAEB, RCMD vs. RA, RARS

Refractory Cytopenia with Multilineage Dysplasia (RCMD)

Refractory cytopenia with multilineage dysplasia (RCMD)	Cytopenias (bicytopenia or pancytopenia) No or rare blasts (<1%) No Auer rods <1x10^9/L monocytes	Dysplasia in ≥10% of the cells of two or more myeloid cell lines <5% blasts in marrow No Auer rods <15% ringed sideroblasts
Refractory cytopenia with multilineage dysplasia and ringed sideroblasts (RCMD-RS)	Cytopenias (bicytopenia or pancytopenia) No or rare blasts (<1%) No Auer rods <1x10^9/L monocytes	Dysplasia in ≥10% of the cells in two or more myeloid cell lines ≥15% ringed sideroblasts <5% blasts No Auer rods

- Evidence of bone marrow failure
- Cytogenetic abnormalities in up to 50%