

# Myelodysplastic Syndrome



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- A 46 yrs old male patient presented with complaint of “ill—health”, weakness and occasional low grade fever.
- On examination, he was slightly pale, and did not manifest lumphadenopathy or hepatosplenomegaly.



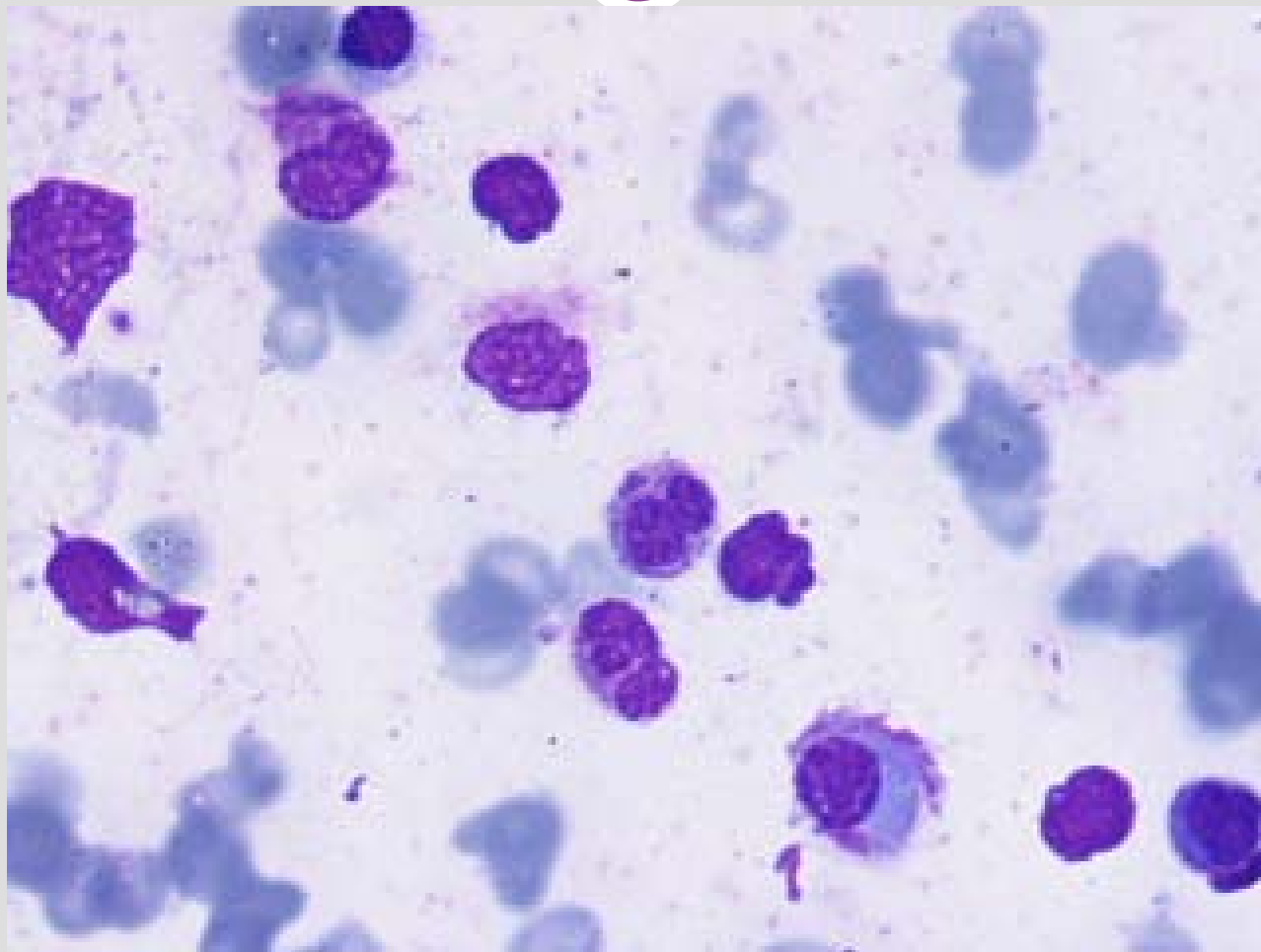
His CP showed:

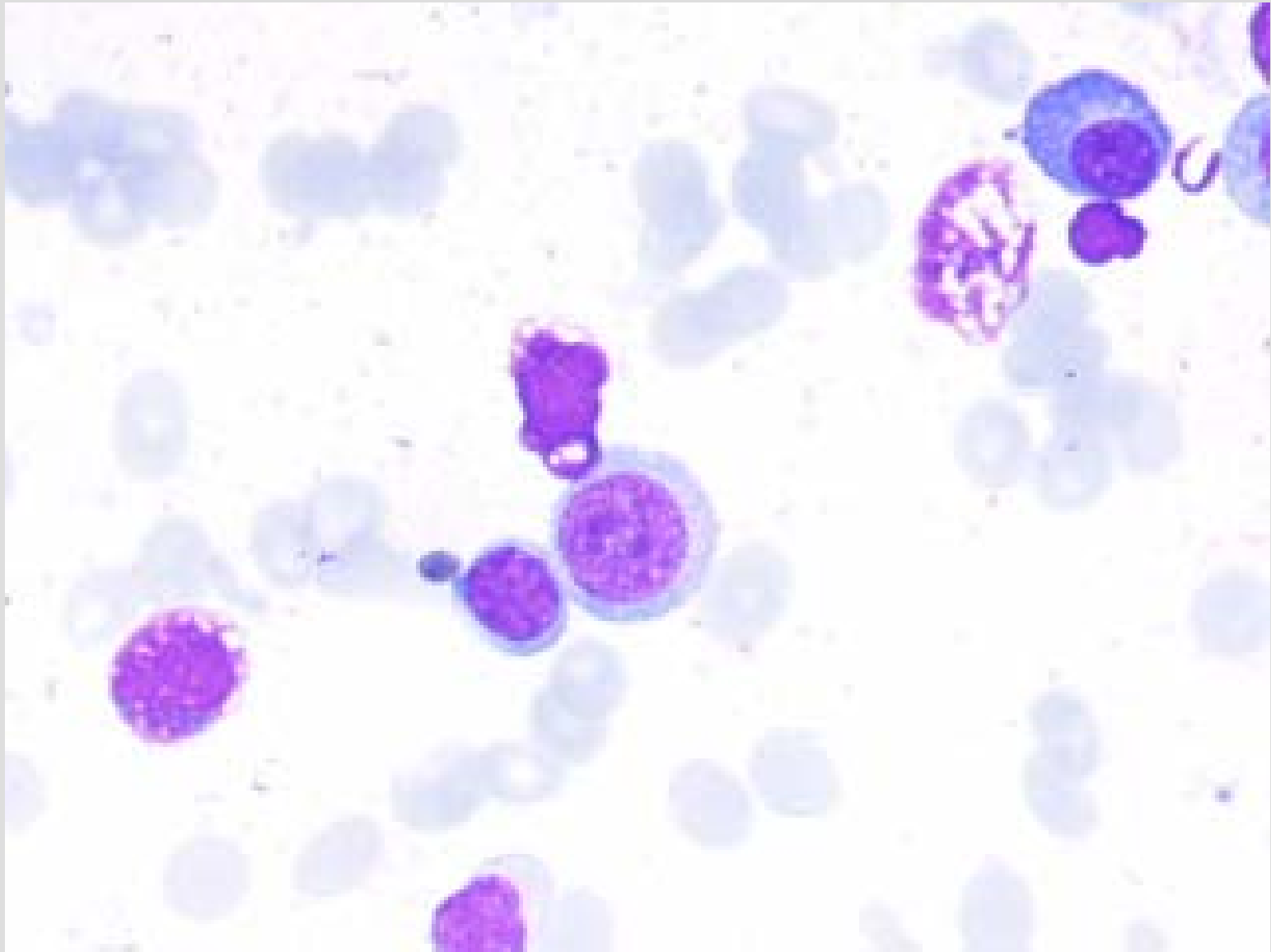
- pancytopenia
  - MCV 104 fl
  - MCH 32.2
  - Retics 0.4%
- 
- Possibilities!
  - Further work-up?

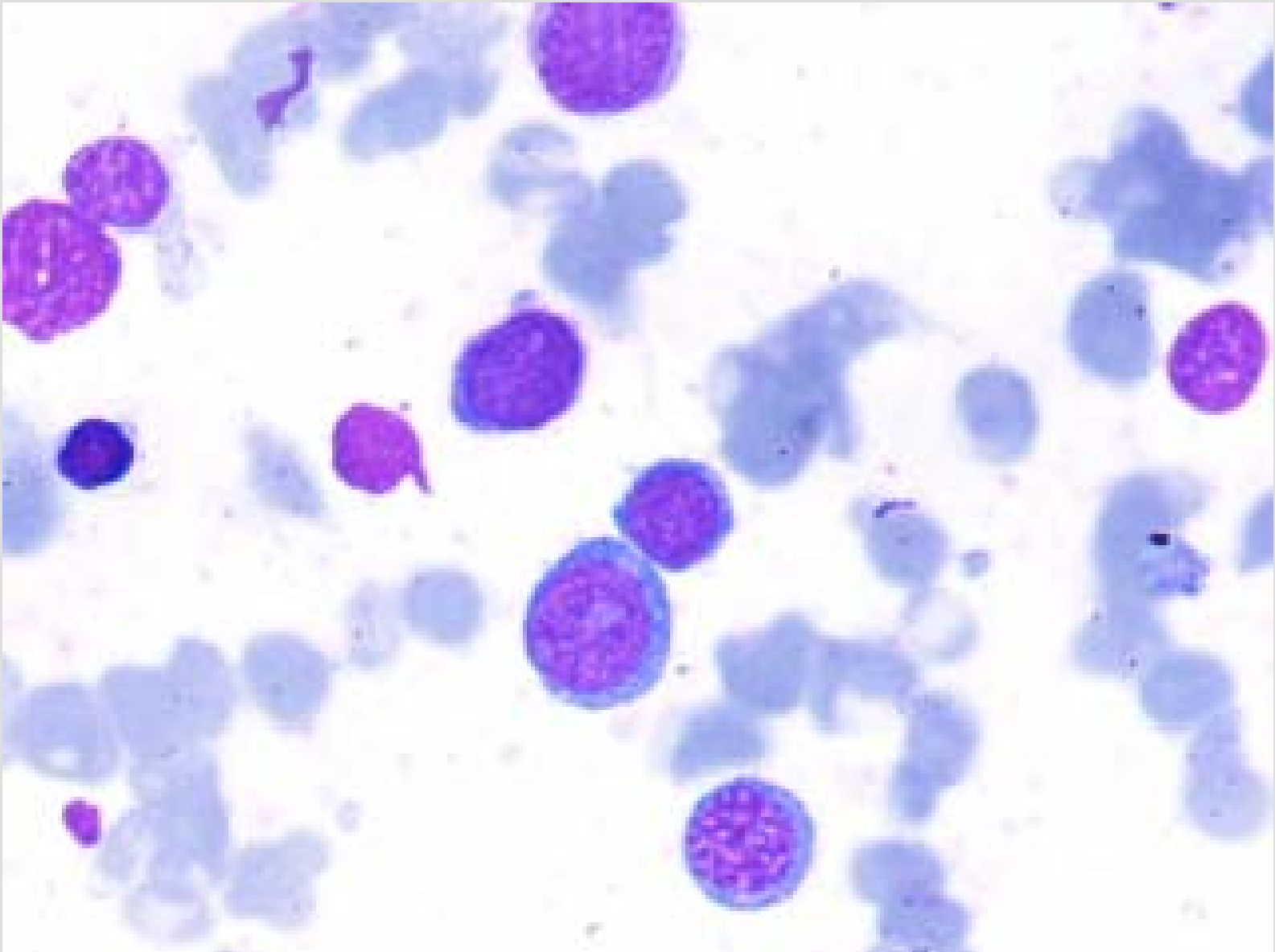


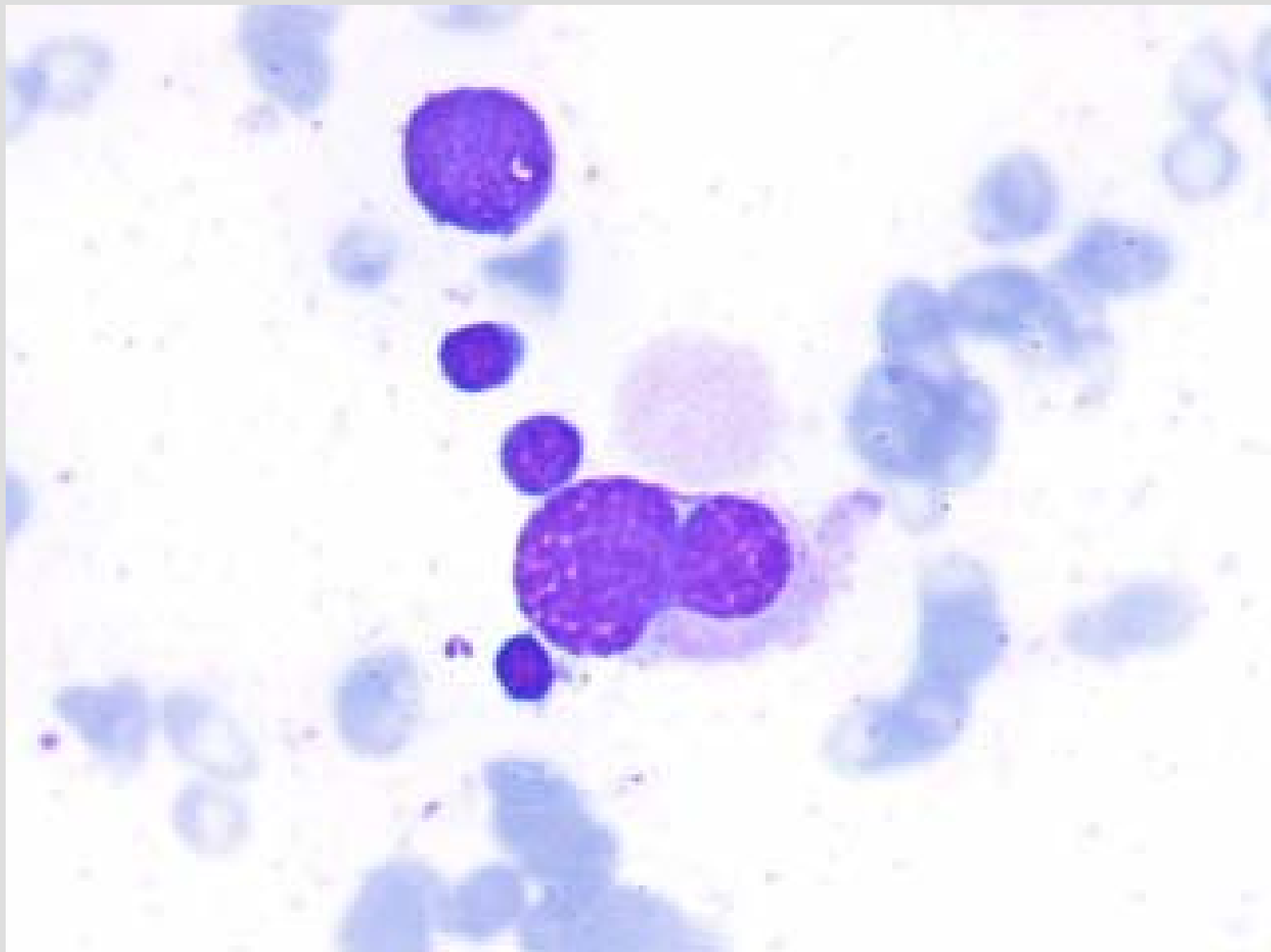
- Aplastic anemia
  - Megaloblastic anemia
  - Leukemia
  - MDS
  - Any other?
- 
- Bone marrow aspiration and trephine were done

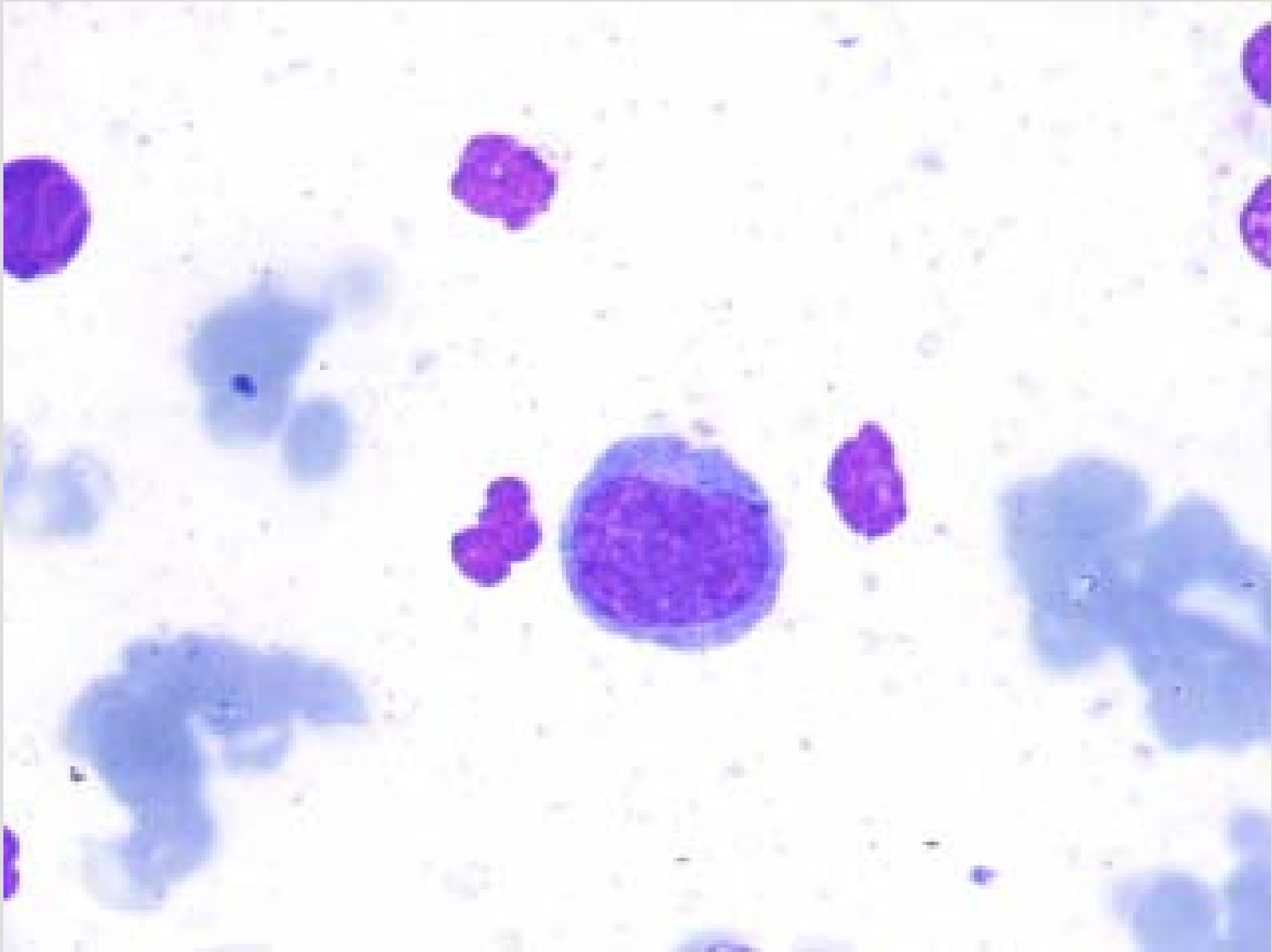
# Bone marrow aspirate

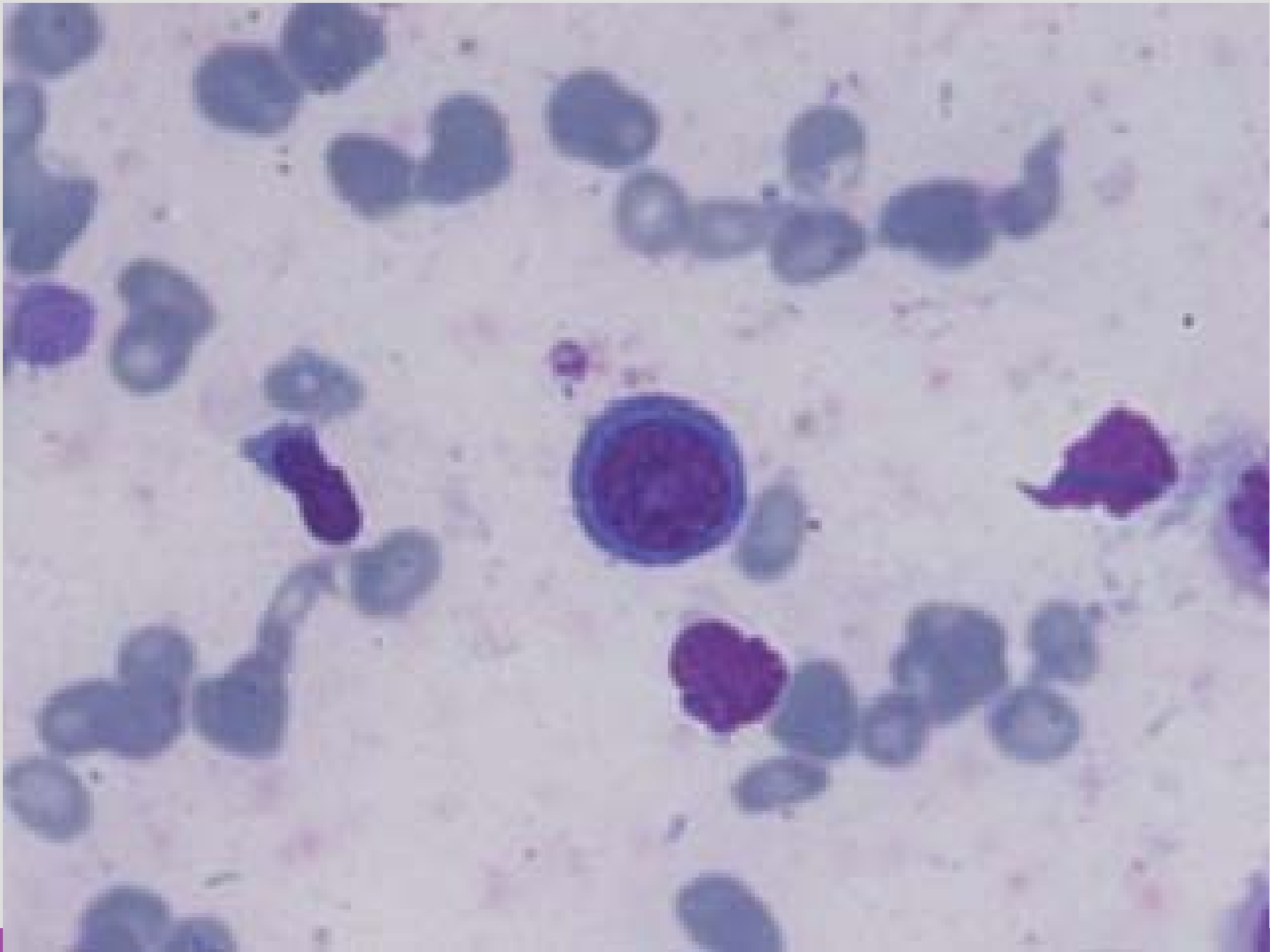


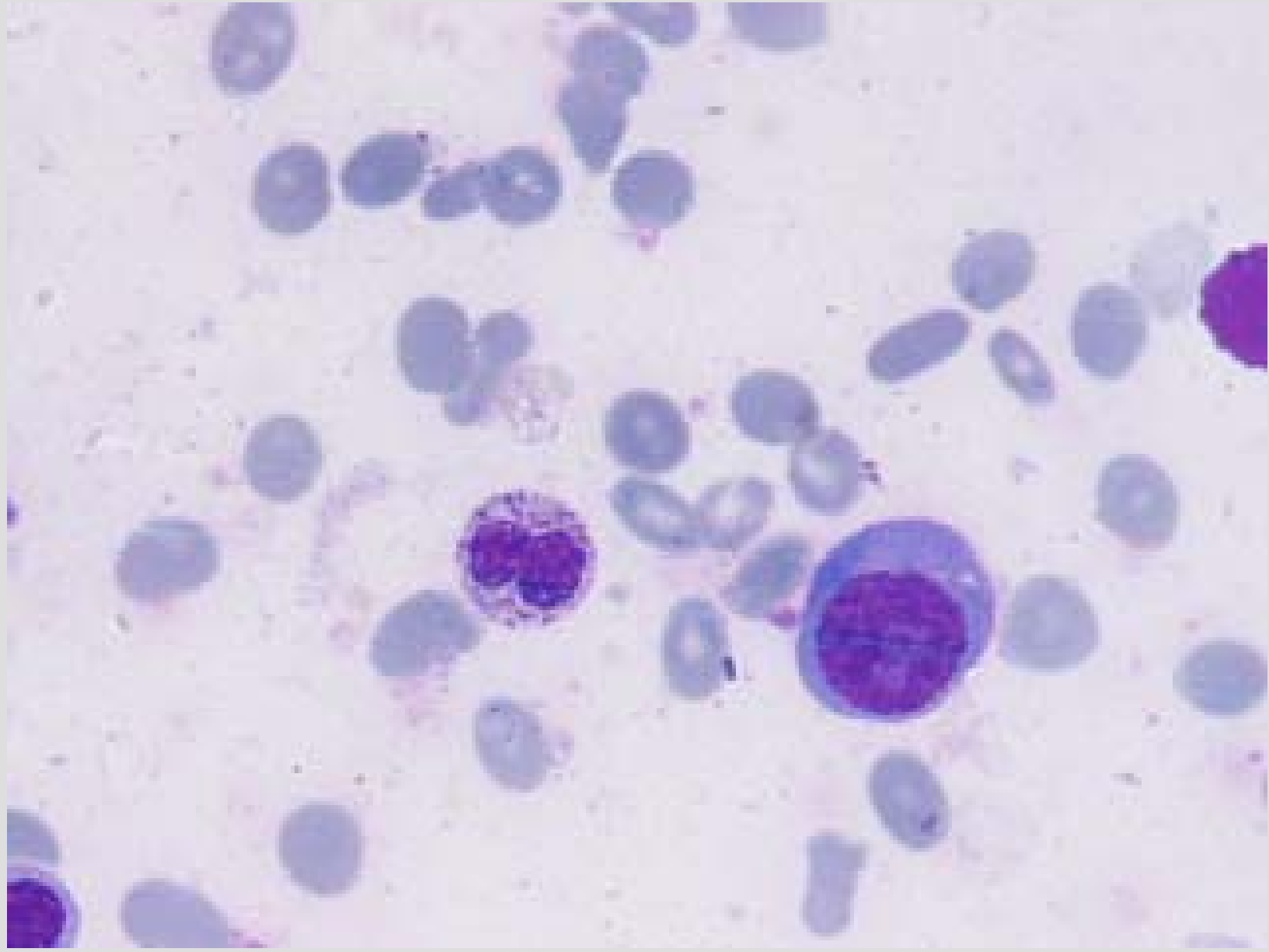


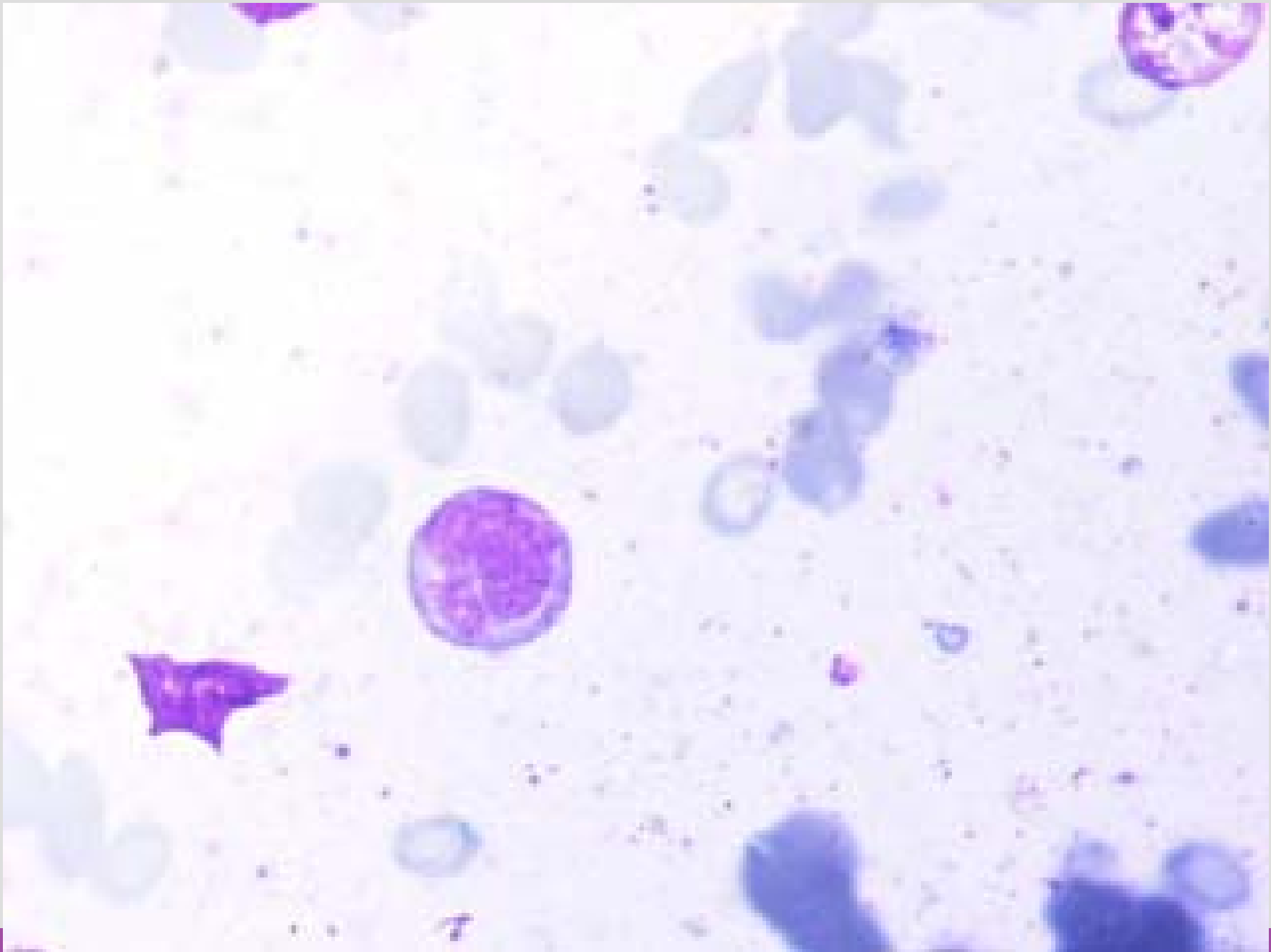


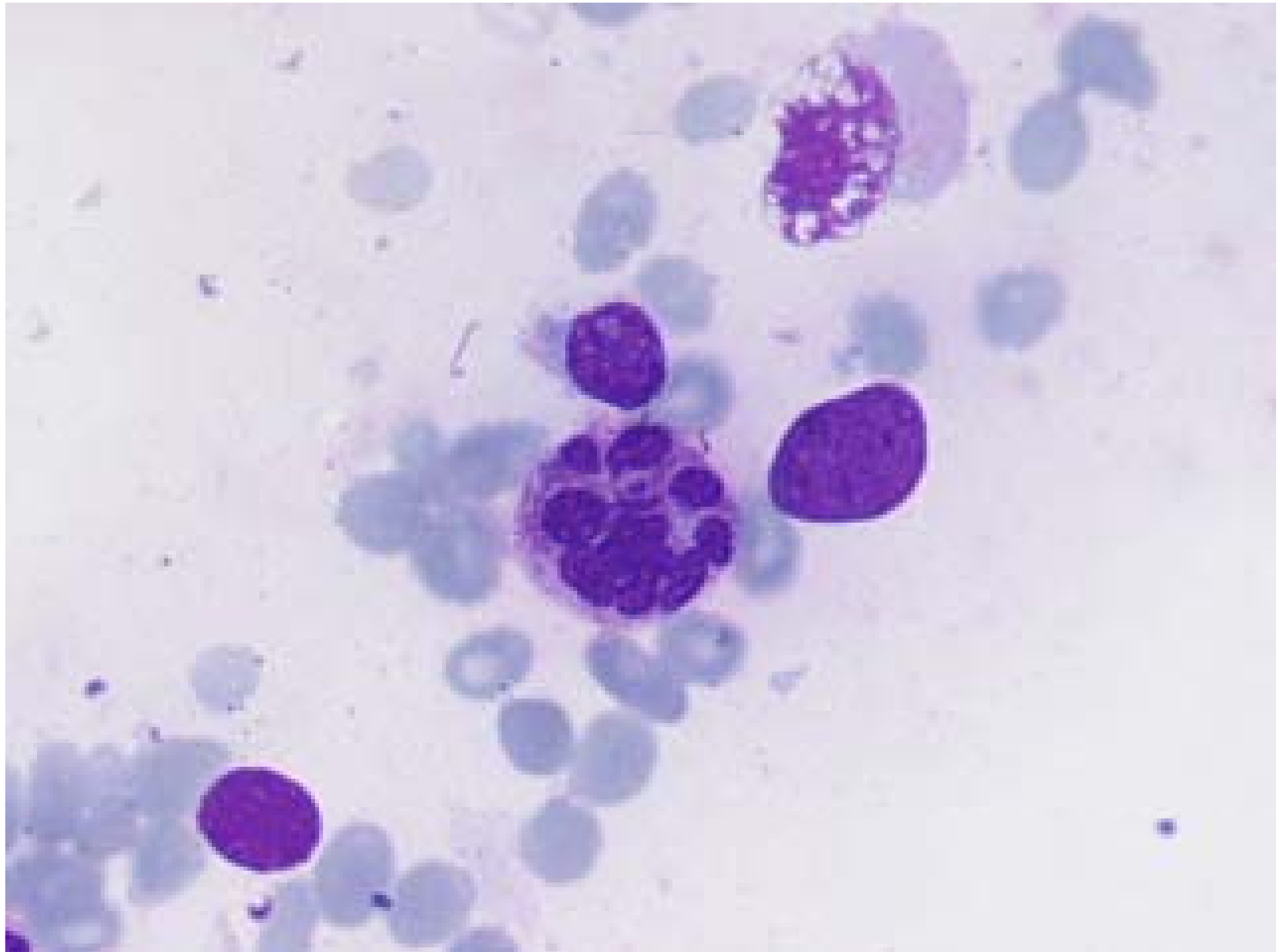


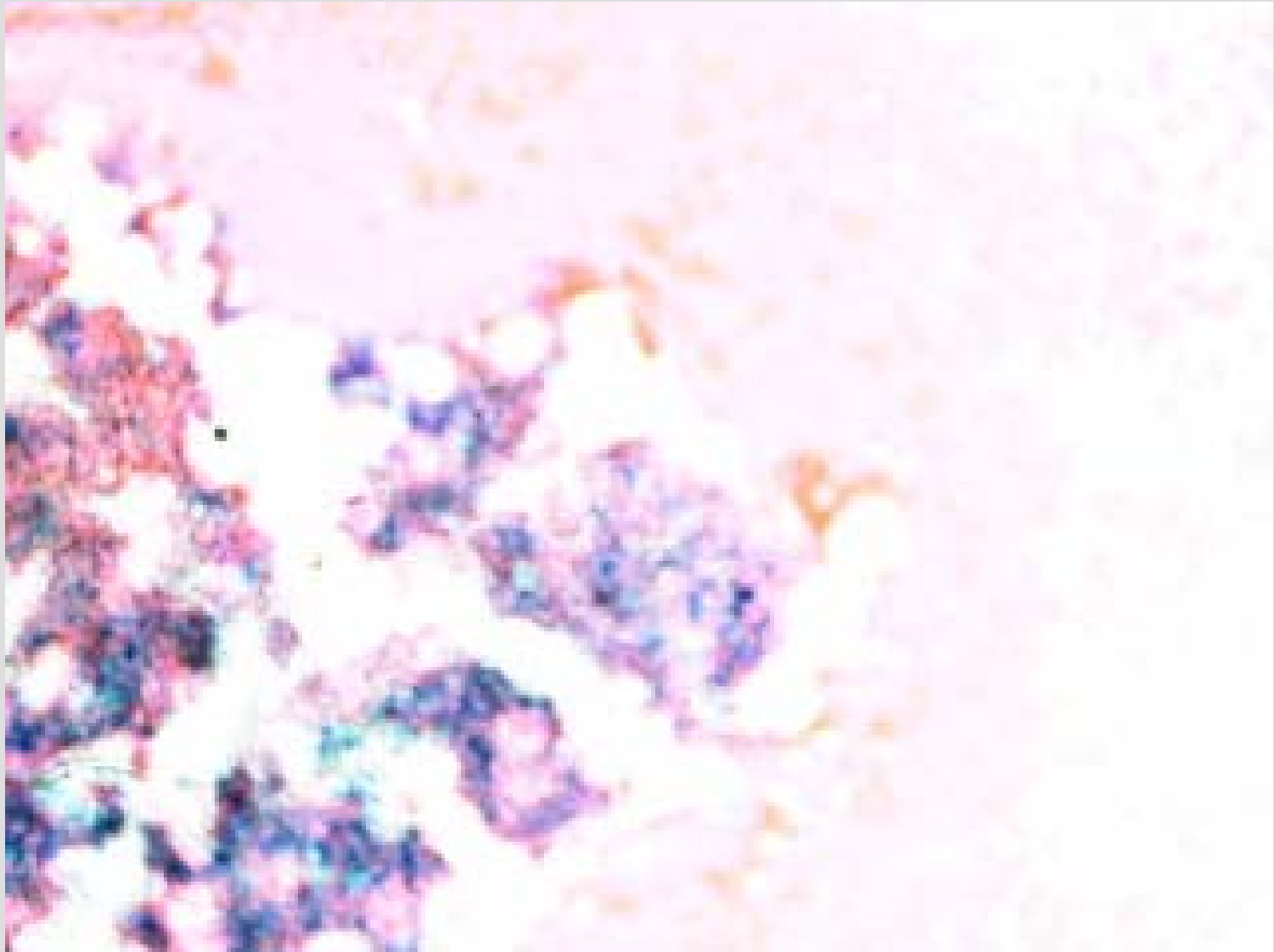


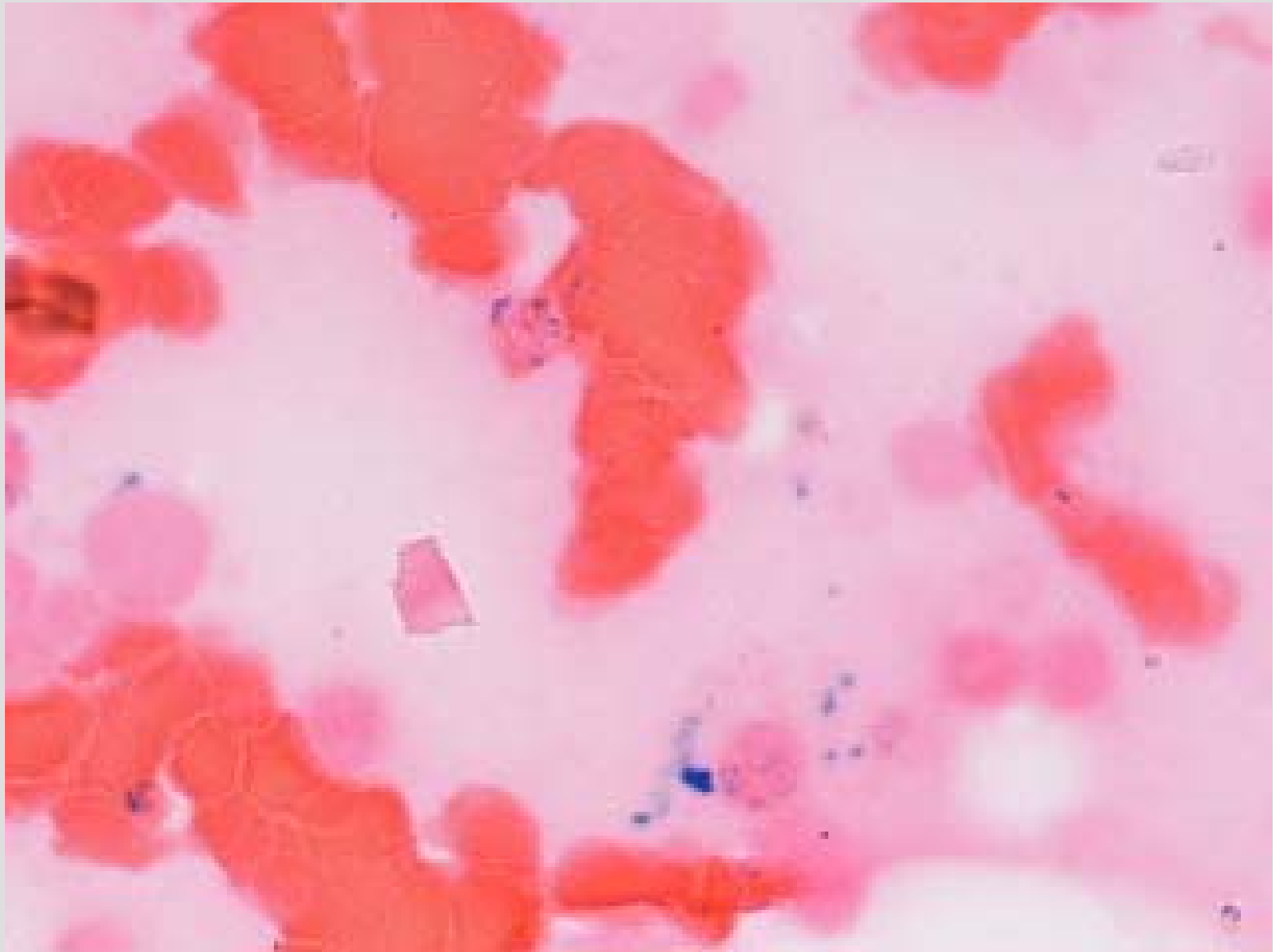


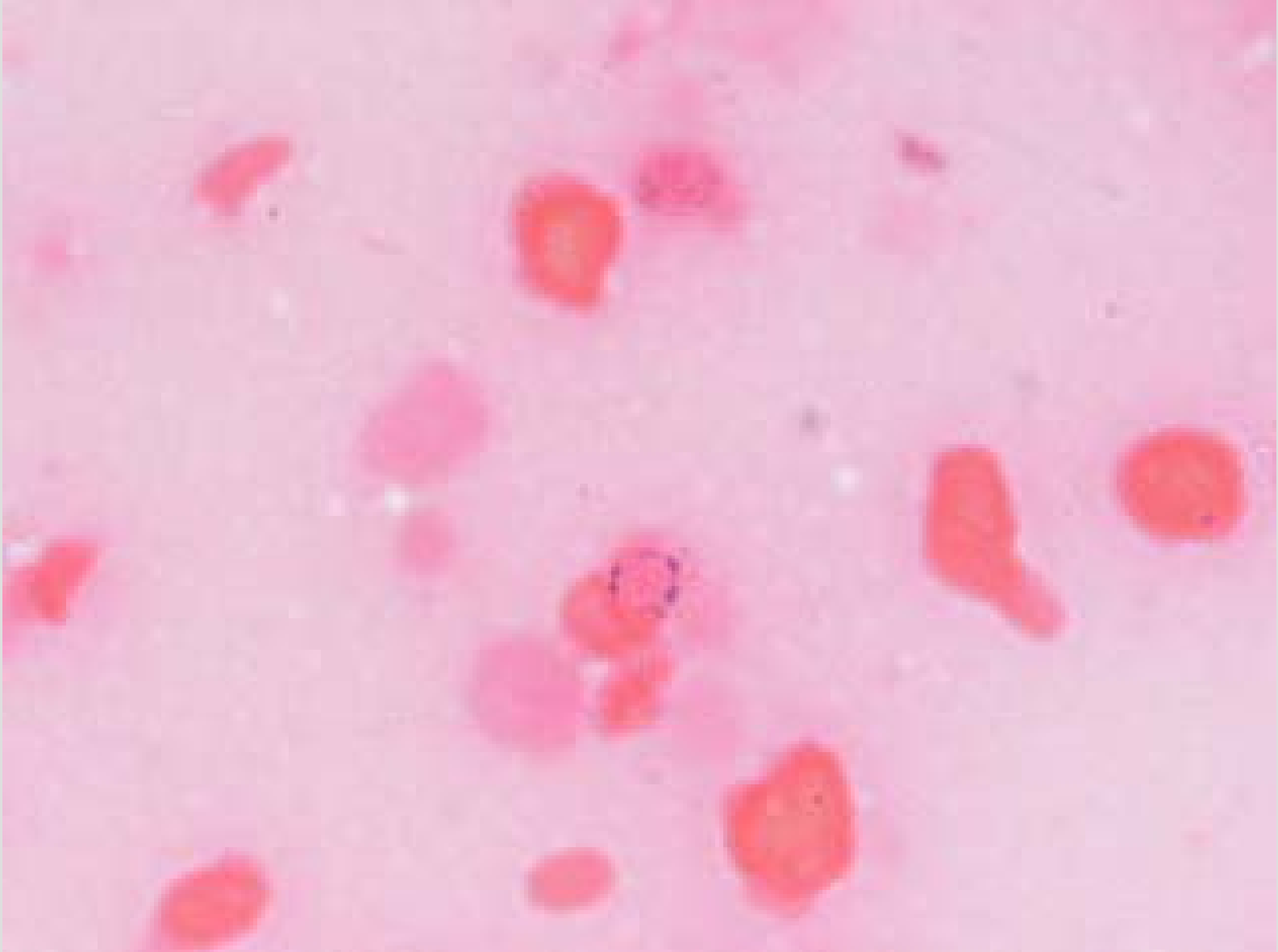












# Findings



- Slightly hypocellular bone marrow smear
- Megaloblastic change
- Dyserythropoiesis
- Dysmegakaryopoiesis
- Iron: Stainable iron increase
- Ring sideroblasts 22%



## Diagnosis

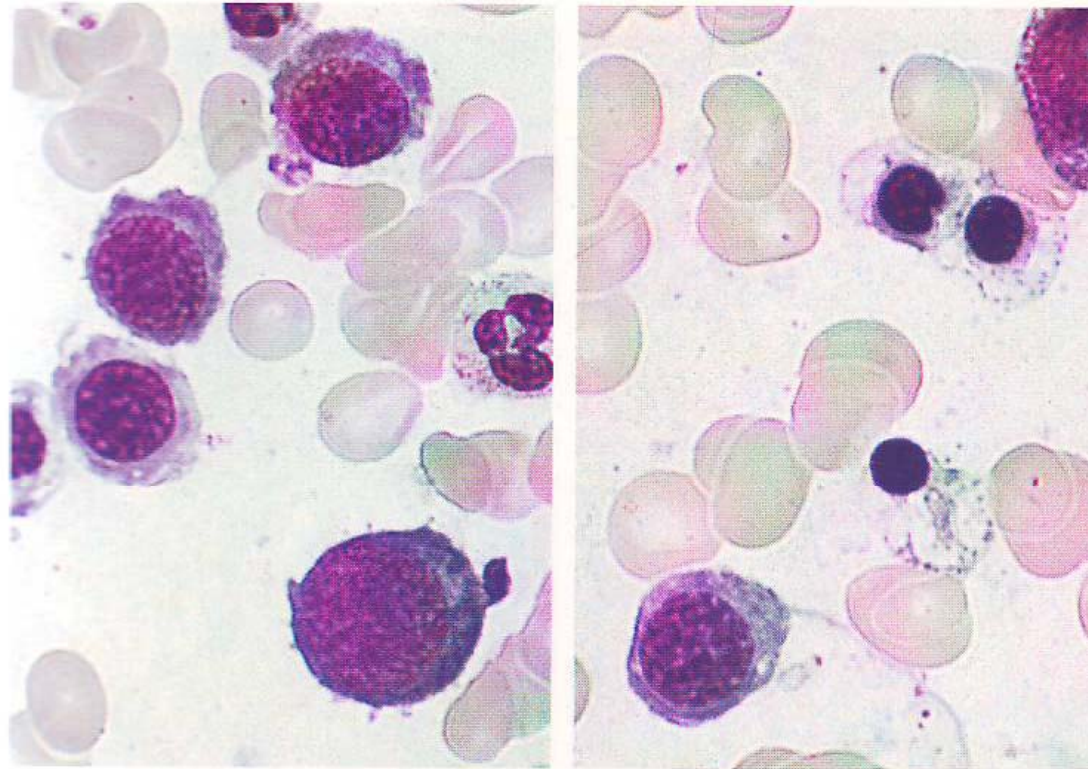
- RARS; RCMD

# Blood and marrow findings: FAB classification

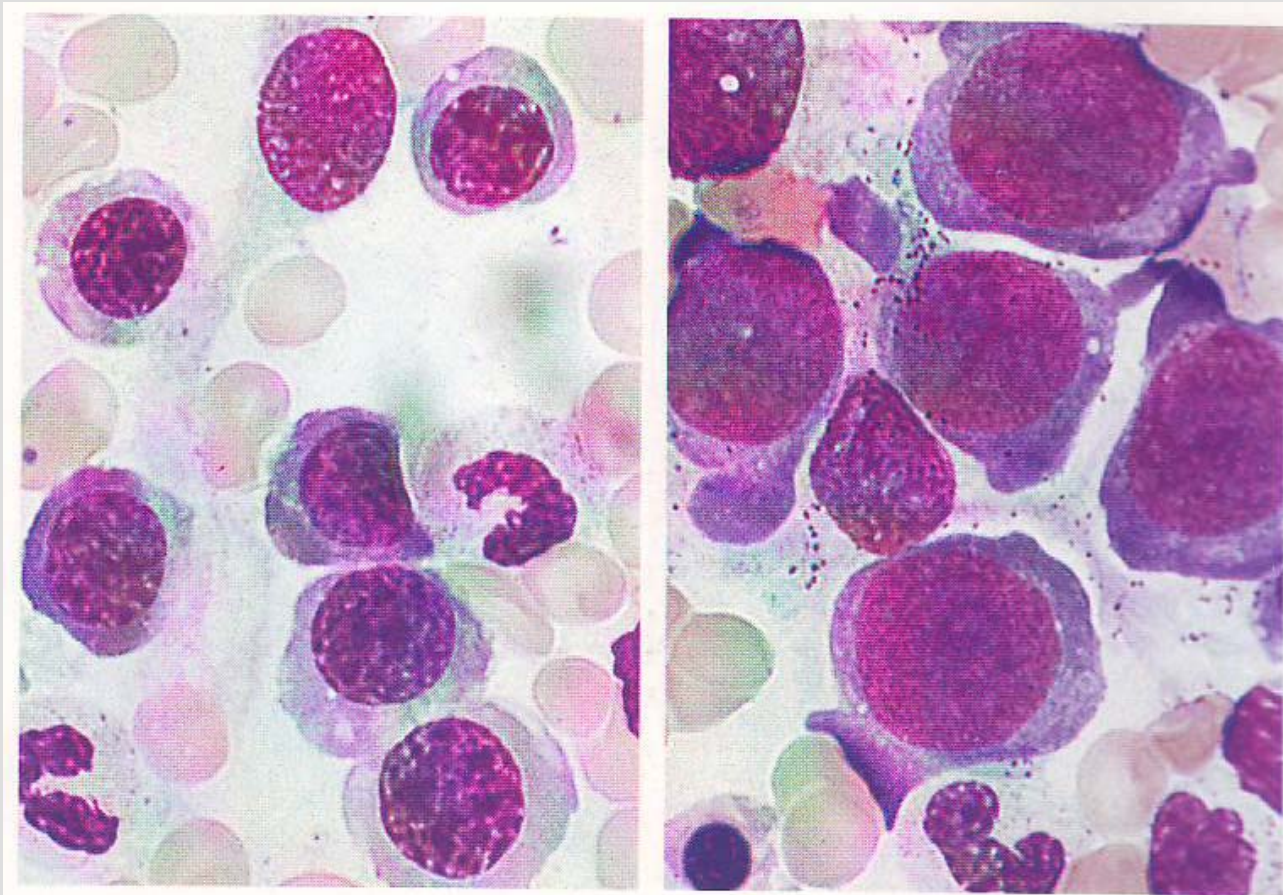


Blood & Marrow Findings in Myelodysplastic Syndromes					
	I (RA)	II (RASB)	III (RAEB)	IV (CMML)	V (RAEB-T)
<b>Blood:</b>					
haemoglobin	↓	↓	↓	↓	↓
total WBC	N or ↓	N or ↓	↓	↑	↓
monocytes	N	N	N	↑	↓ or N or ↑
blasts (%)	<1	<1	<5	<5	>5
platelets	N or ↓	N or ↓	↓	↓ or N or ↑	↓
<b>Marrow:</b>					
sideroblasts (%)	<15	>15	<15	<15	<15
myeloblasts (%)	<5	<5	5-20	0-20	20-30

# Dysplastic features

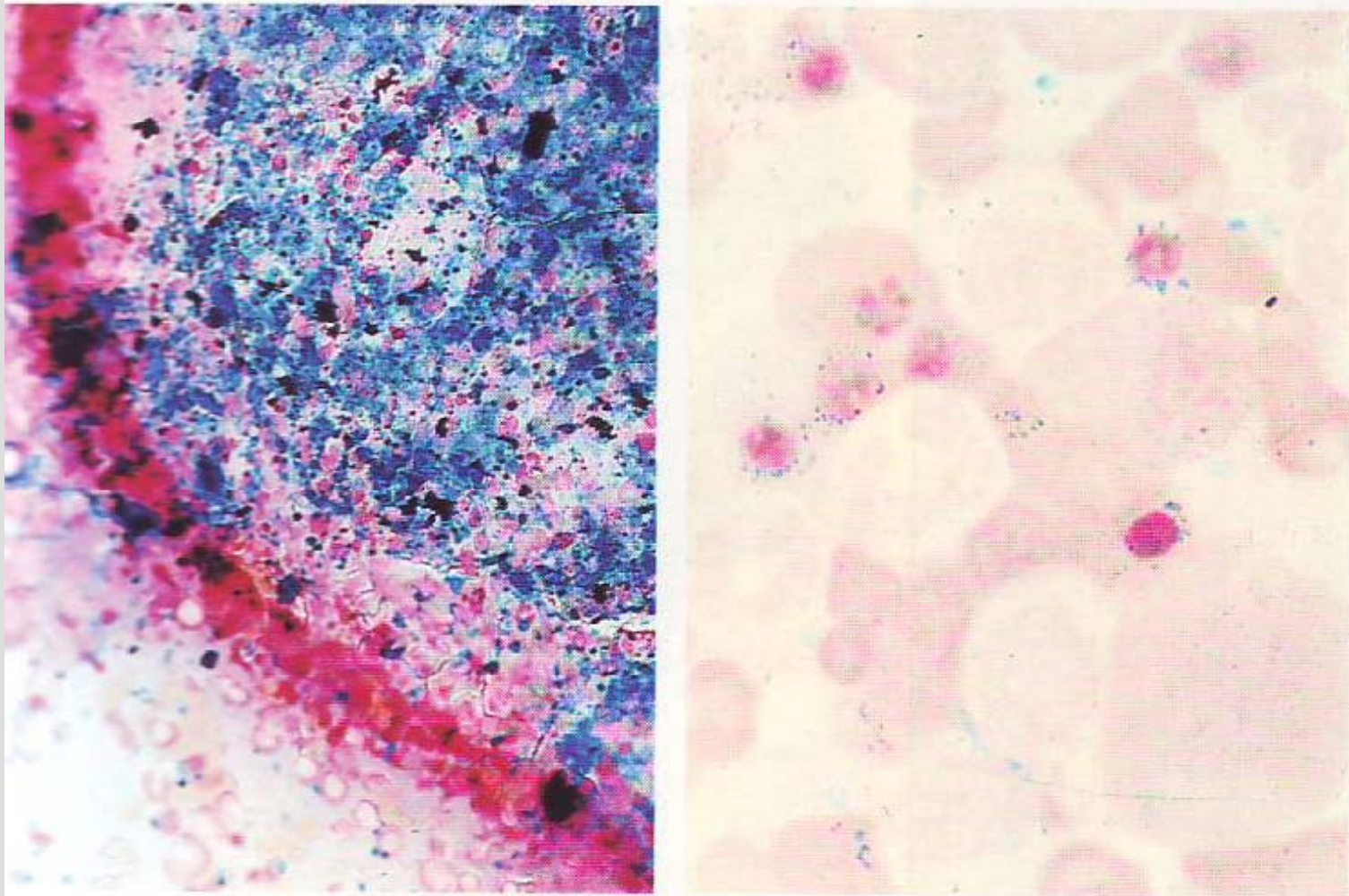


*Fig. 9.60  
Myelodysplastic syndrome: bone marrow cell trails in acquired sideroblastic anaemia (Type II), showing marked defective haemoglobinization and vacuolation in later-stage polychromatic and pyknotic erythroblasts.*



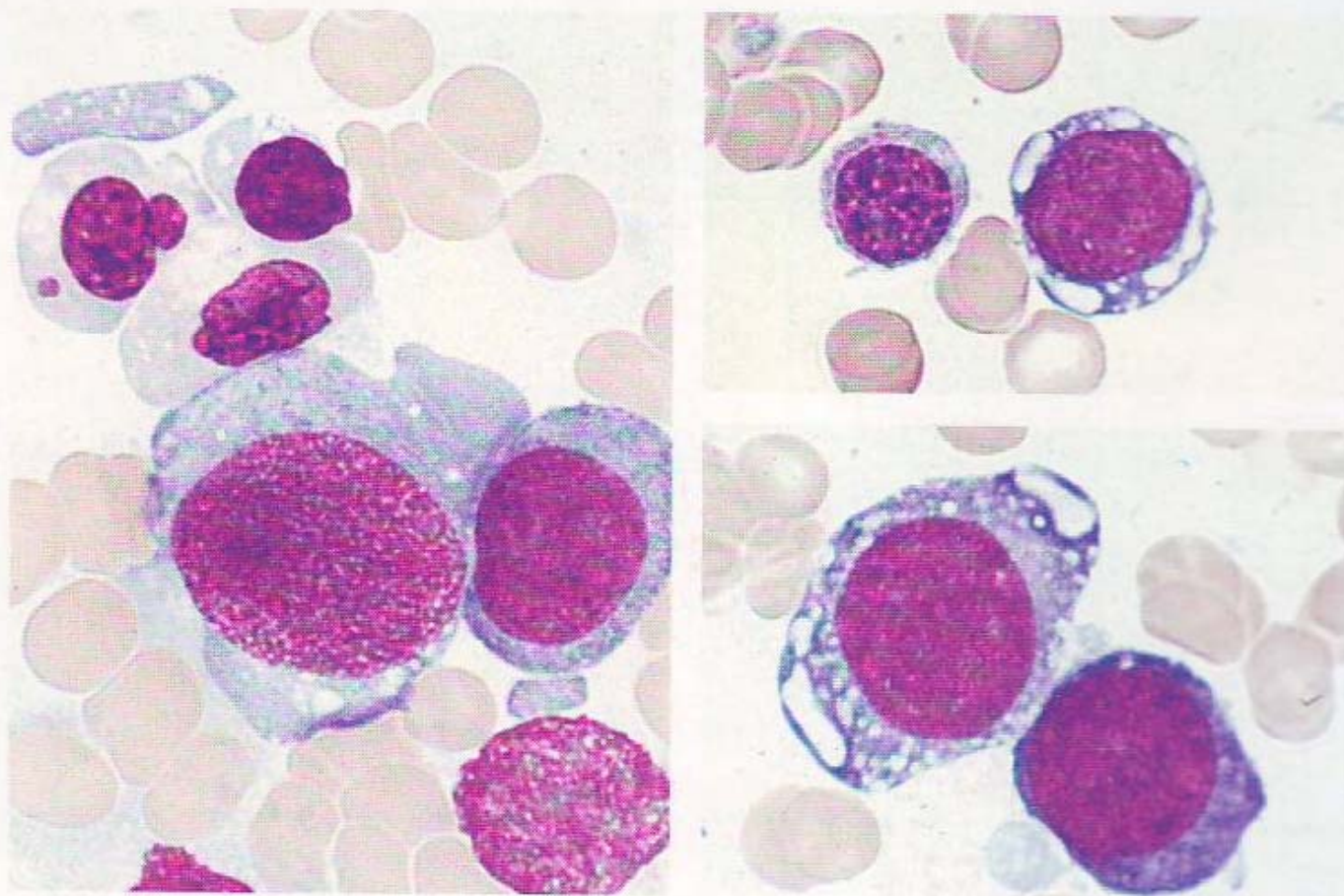
*Fig. 9.61*

*Myelodysplastic syndrome: bone marrow cell trails in Type II, showing (left) erythroblasts with vacuolation of cytoplasm in later cells and mild megaloblastic features; (right) a prominent group of proerythroblasts.*

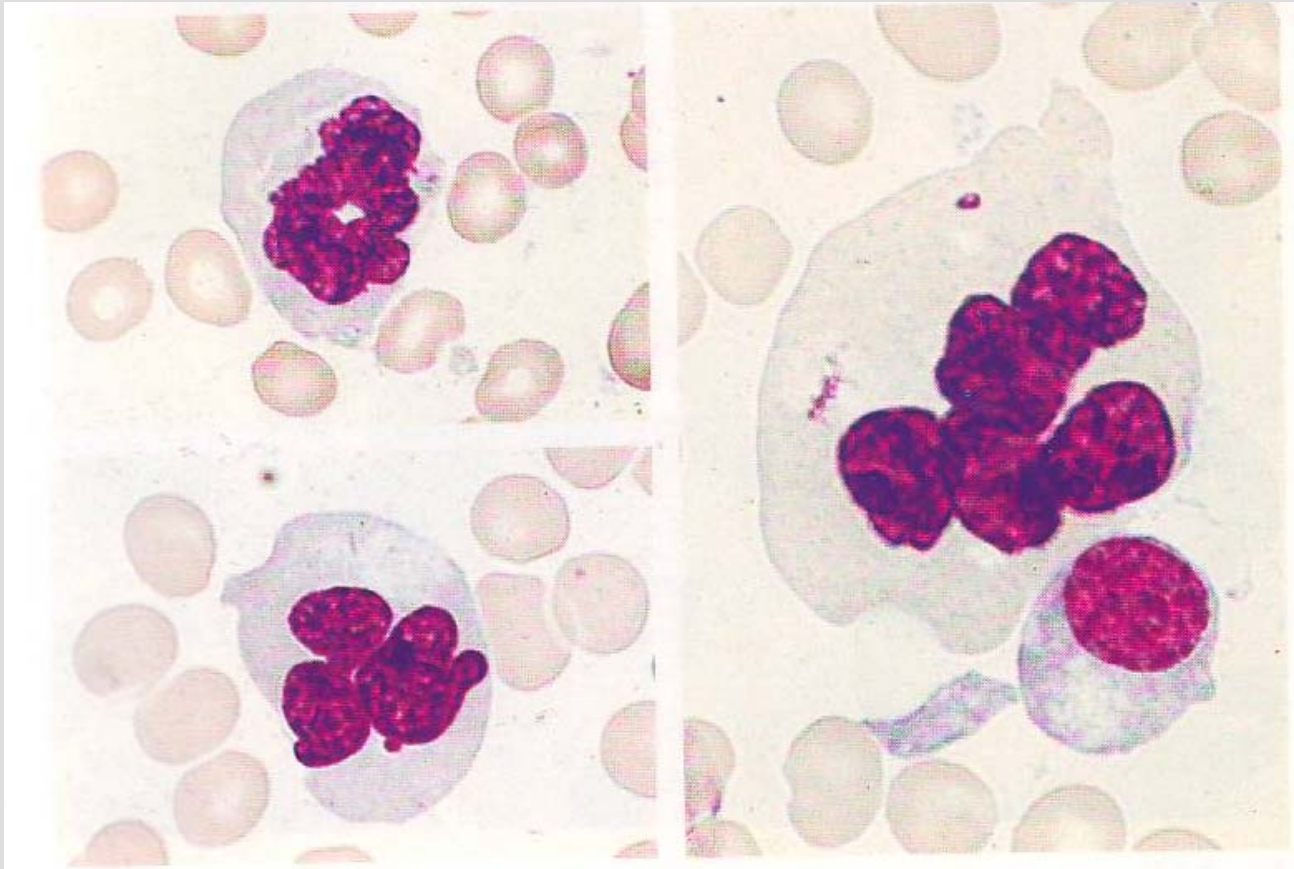


*Fig. 9.62*

*Myelodysplastic syndrome: bone marrow fragment in Type II, showing (left) increased iron stores and (right) pathological ring sideroblasts at higher magnification. Perls' stain.*

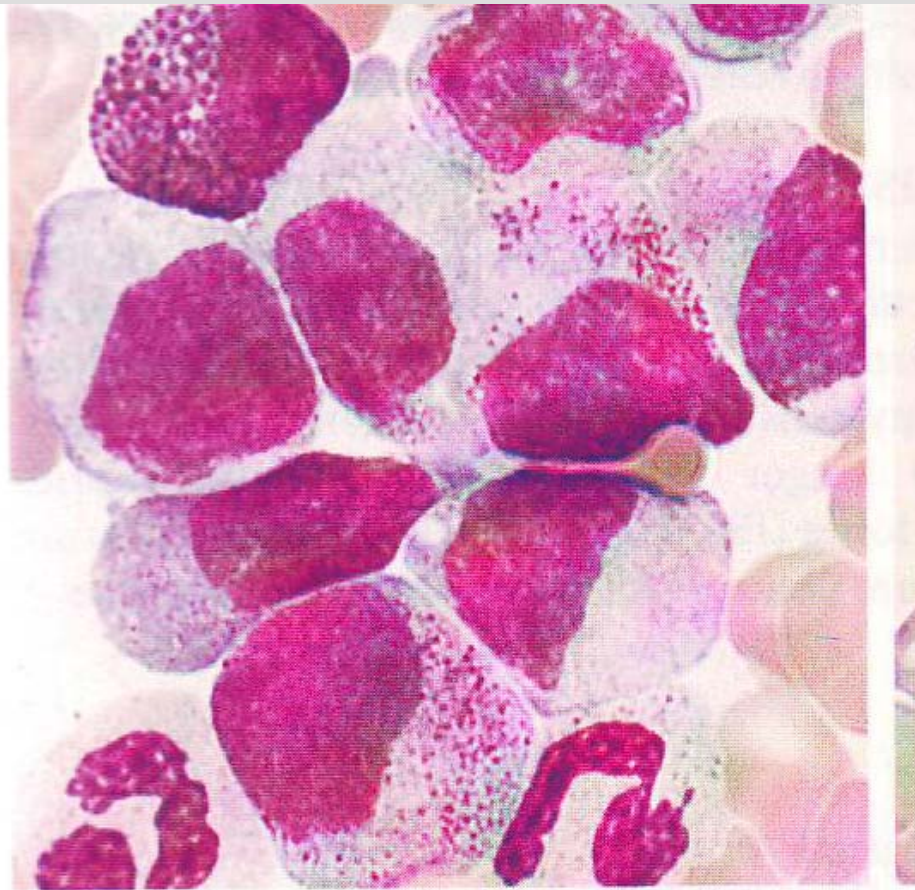


*Fig. 9.63  
Myelodysplastic syndrome: bone marrow aspirates in Type III, showing (left) abnormal proerythroblasts and megaloblast-like changes and (right) prominent cytoplasmic vacuolation in the basophilic erythroblasts, evidence of dyserythropoiesis.*

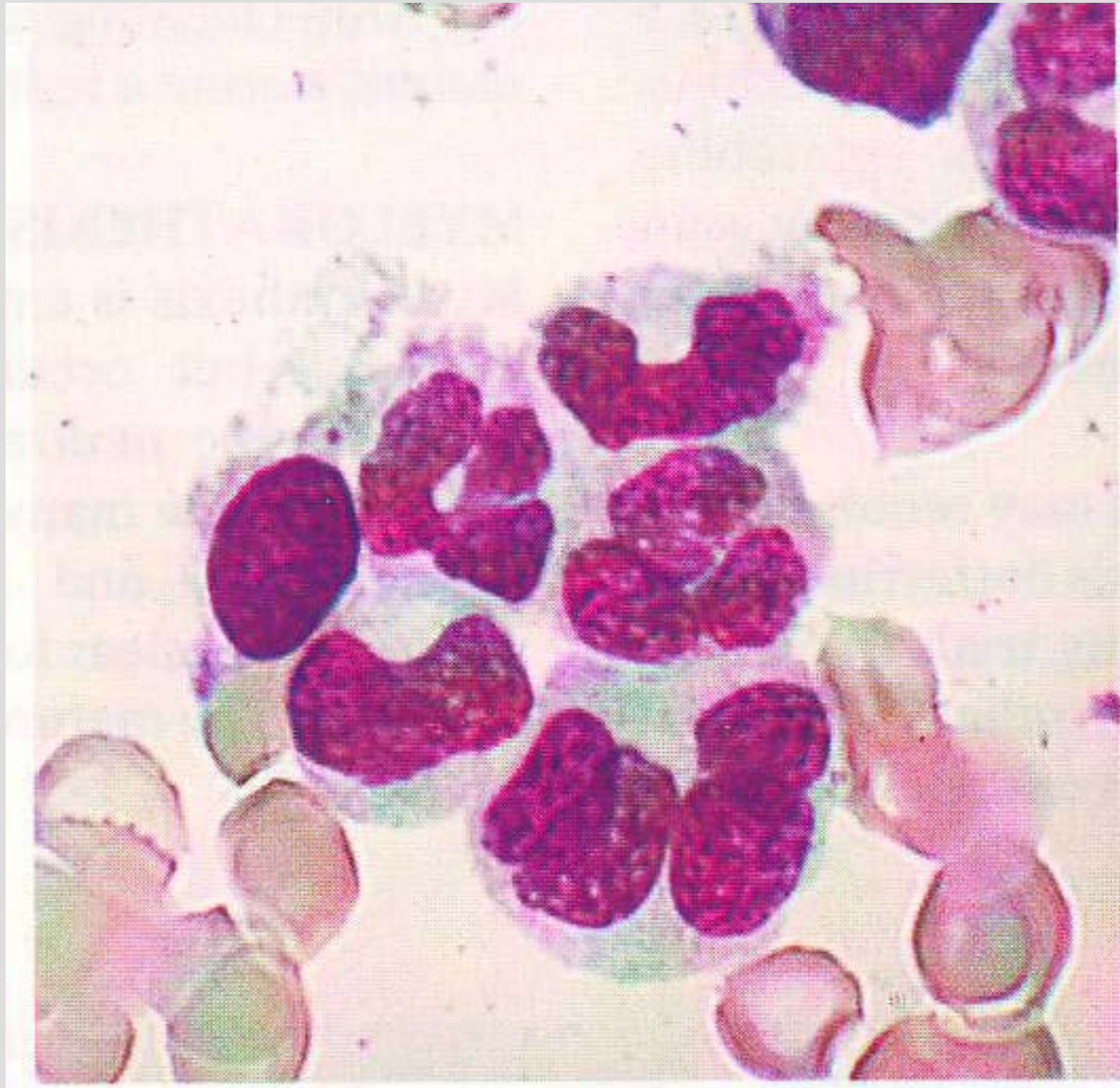


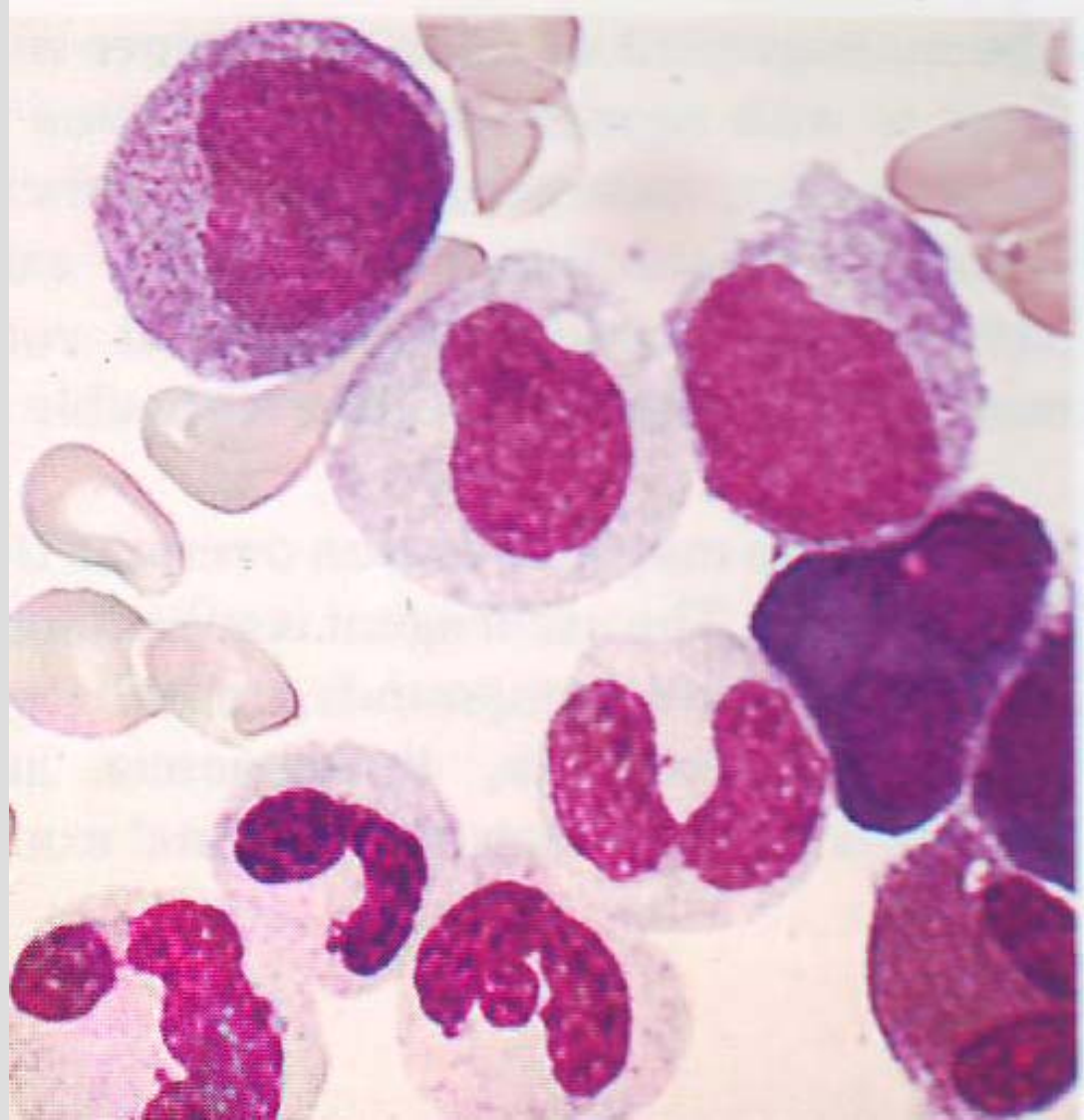
*Fig. 9.64*

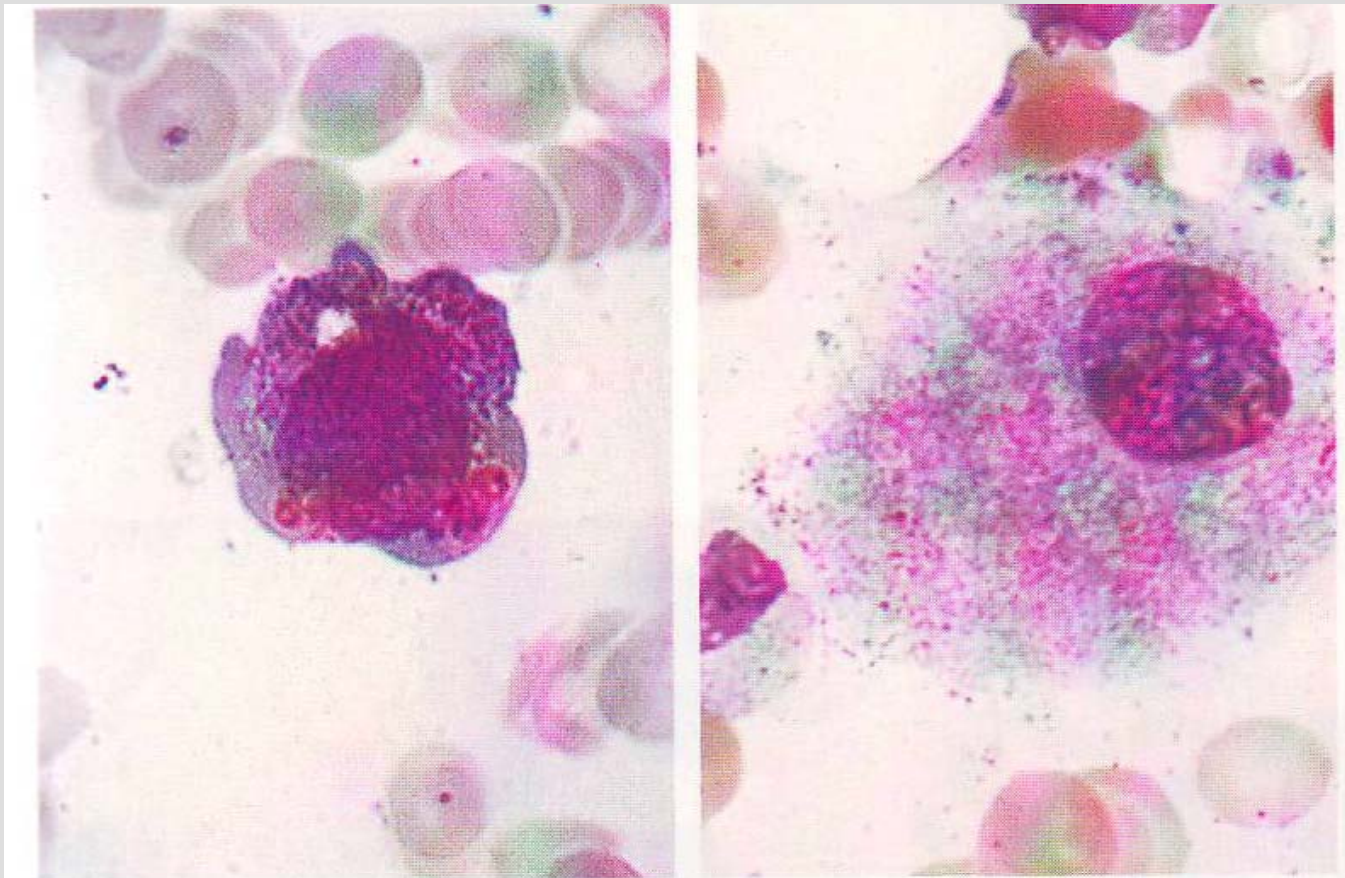
*Myelodysplastic syndrome: bone marrow aspirates in Type III, showing three examples of polyploid multinucleate polychromatic erythroblasts, further evidence of gross dyserythropoiesis.*



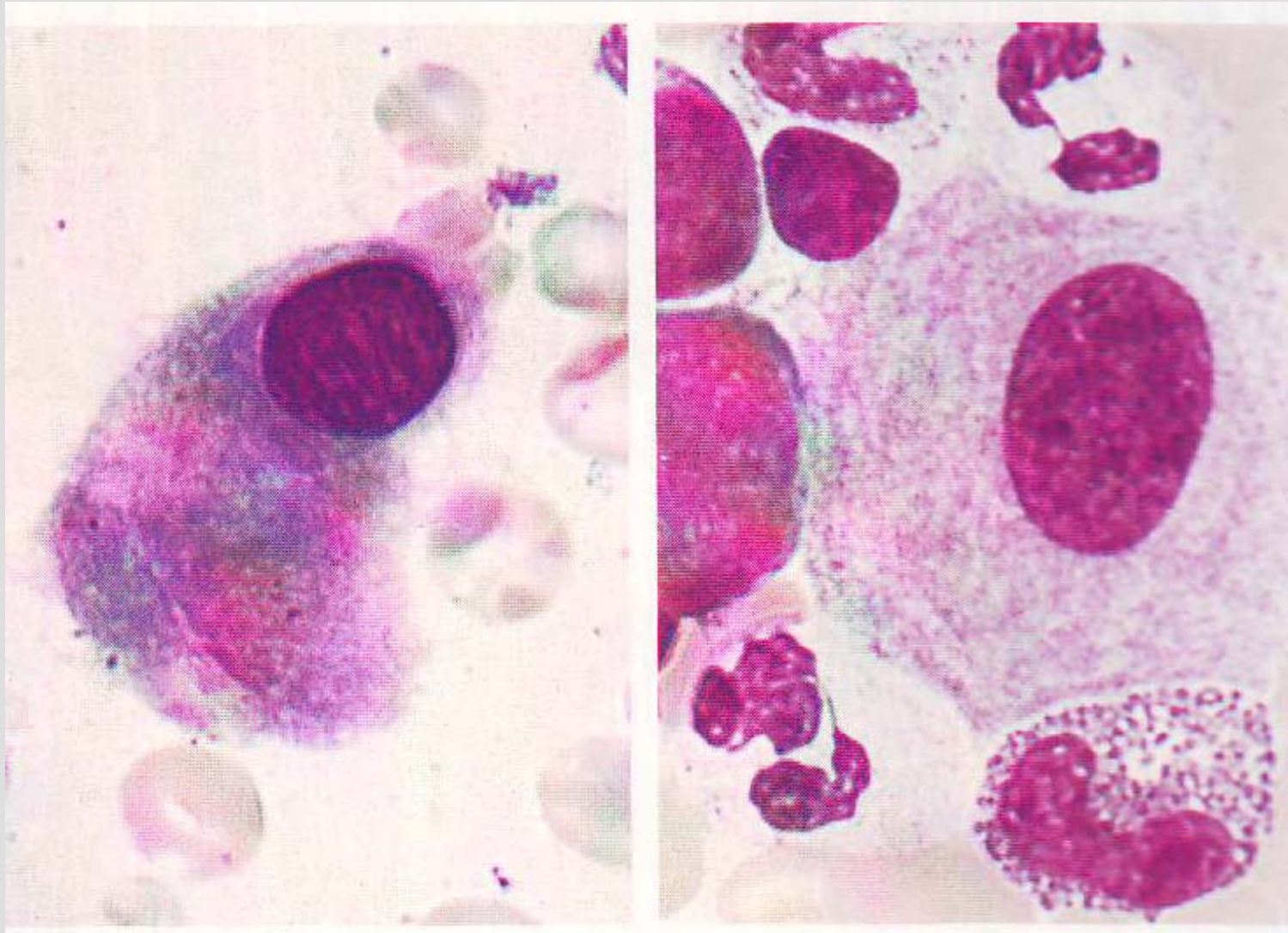
*Fig. 9.67*  
*Myelodysplastic syndrome: bone marrow aspirates in Tj*  
*agranular neutrophils and abnormal myelomonocytic ce*

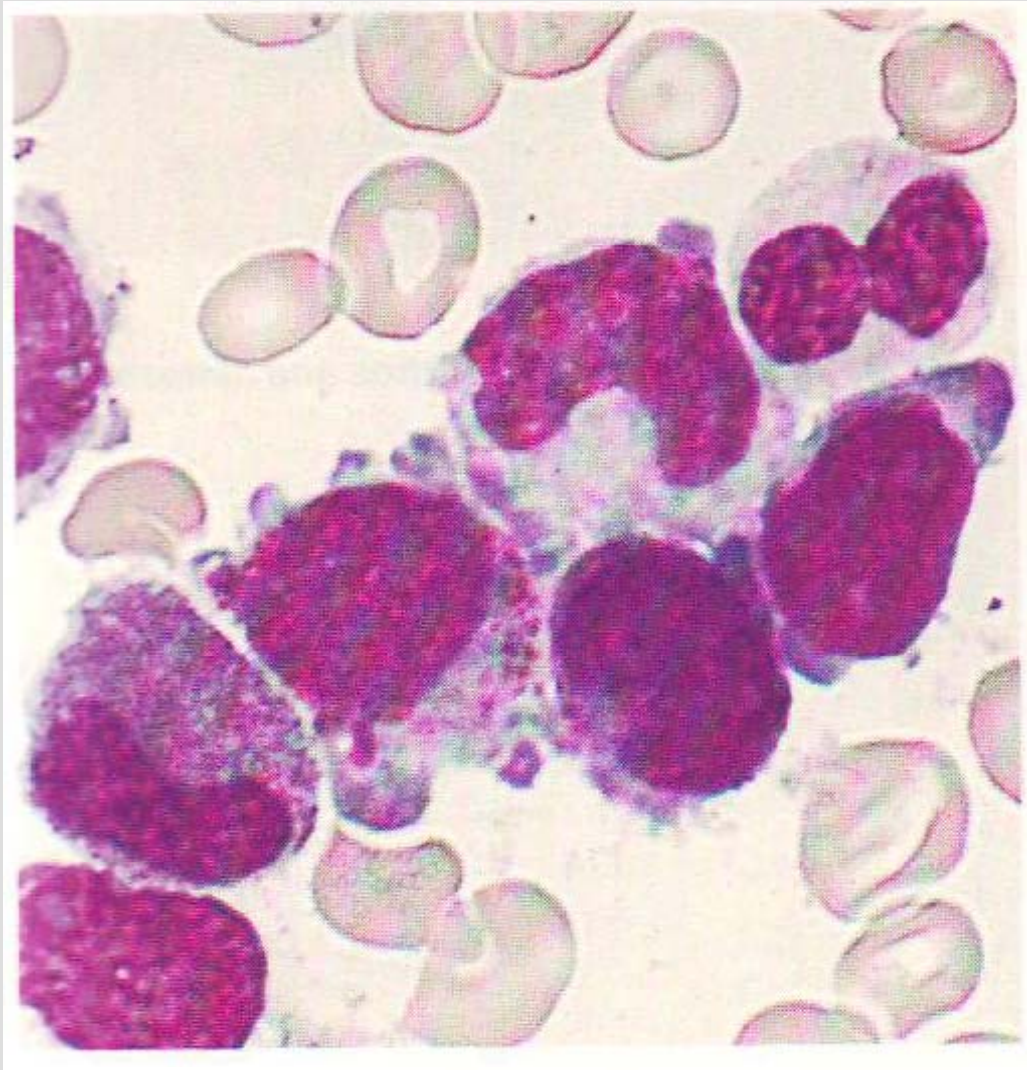


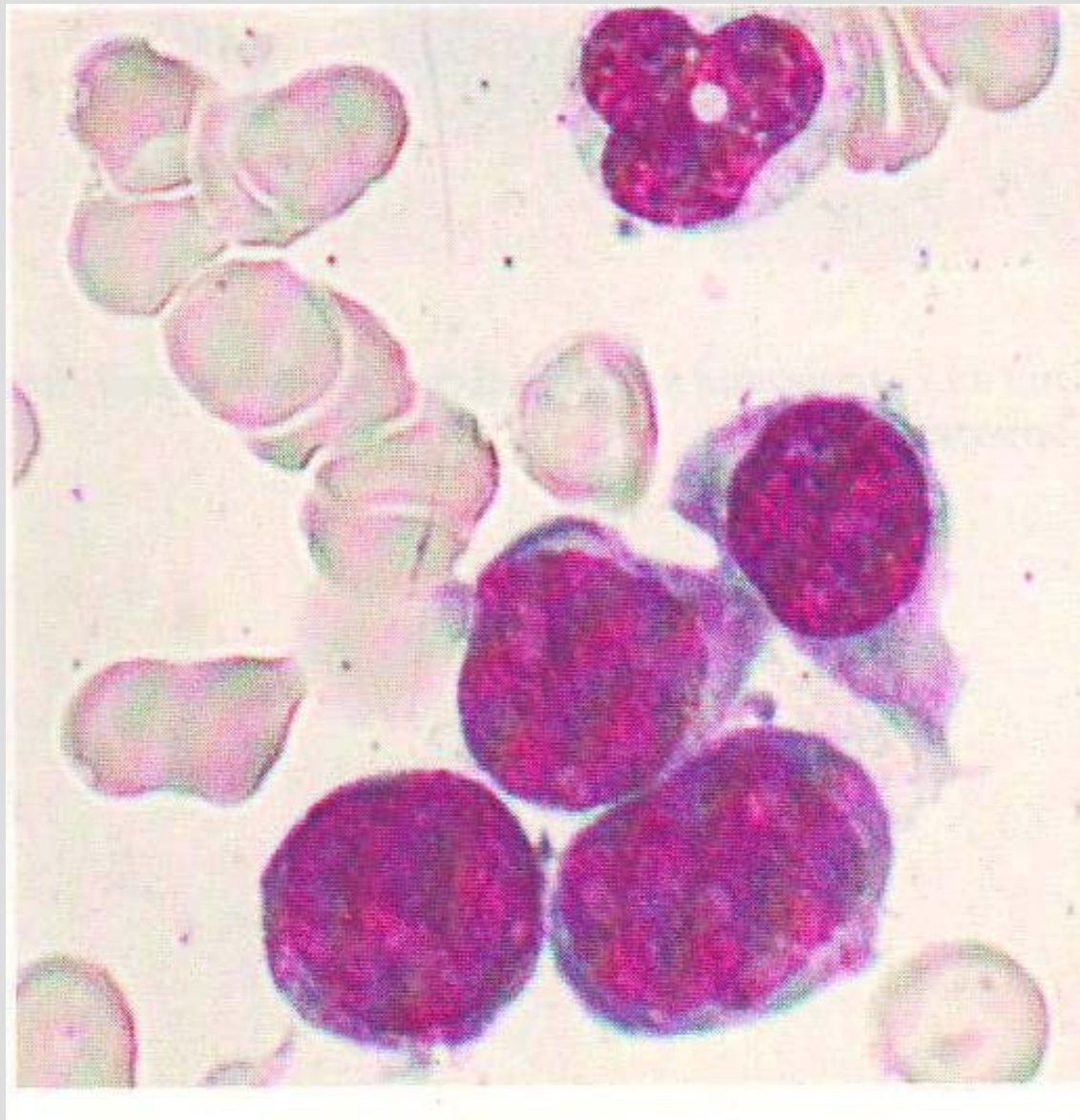


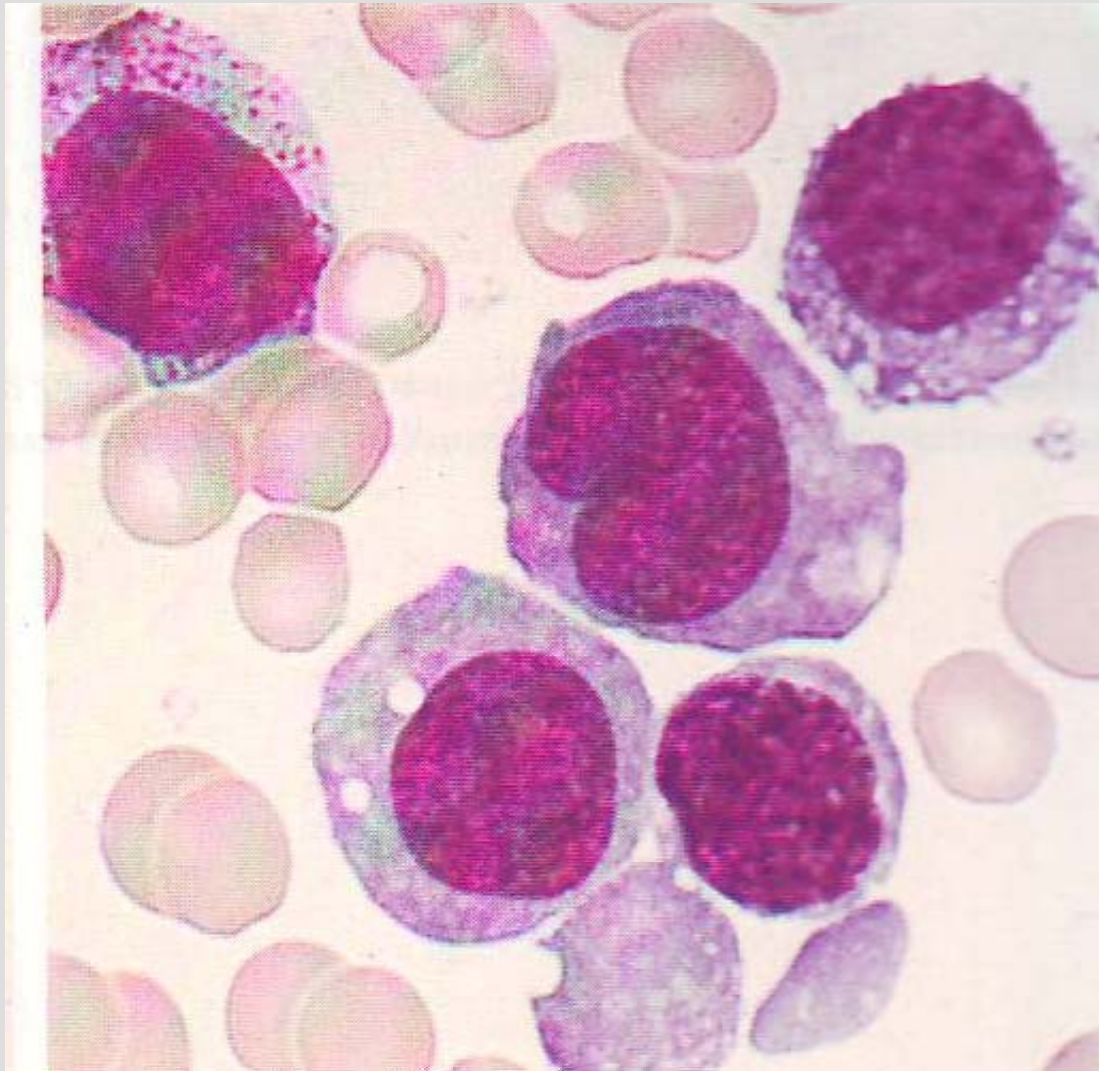


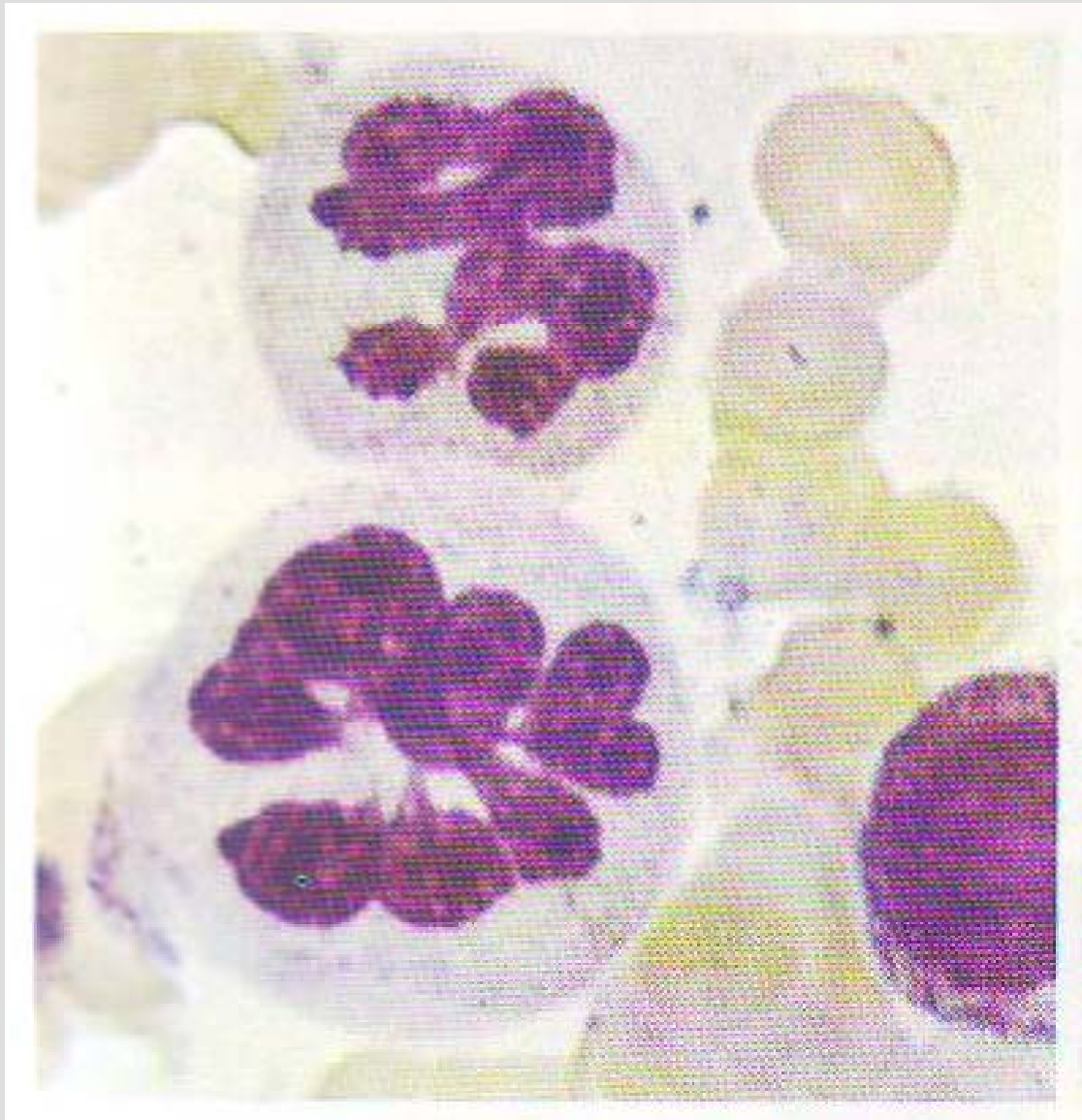
*Fig. 9.68  
Myelodysplastic syndrome: bone marrow aspirates showing an atypical megakaryocyte with evidence of cytoplasmic maturation and granulation.*

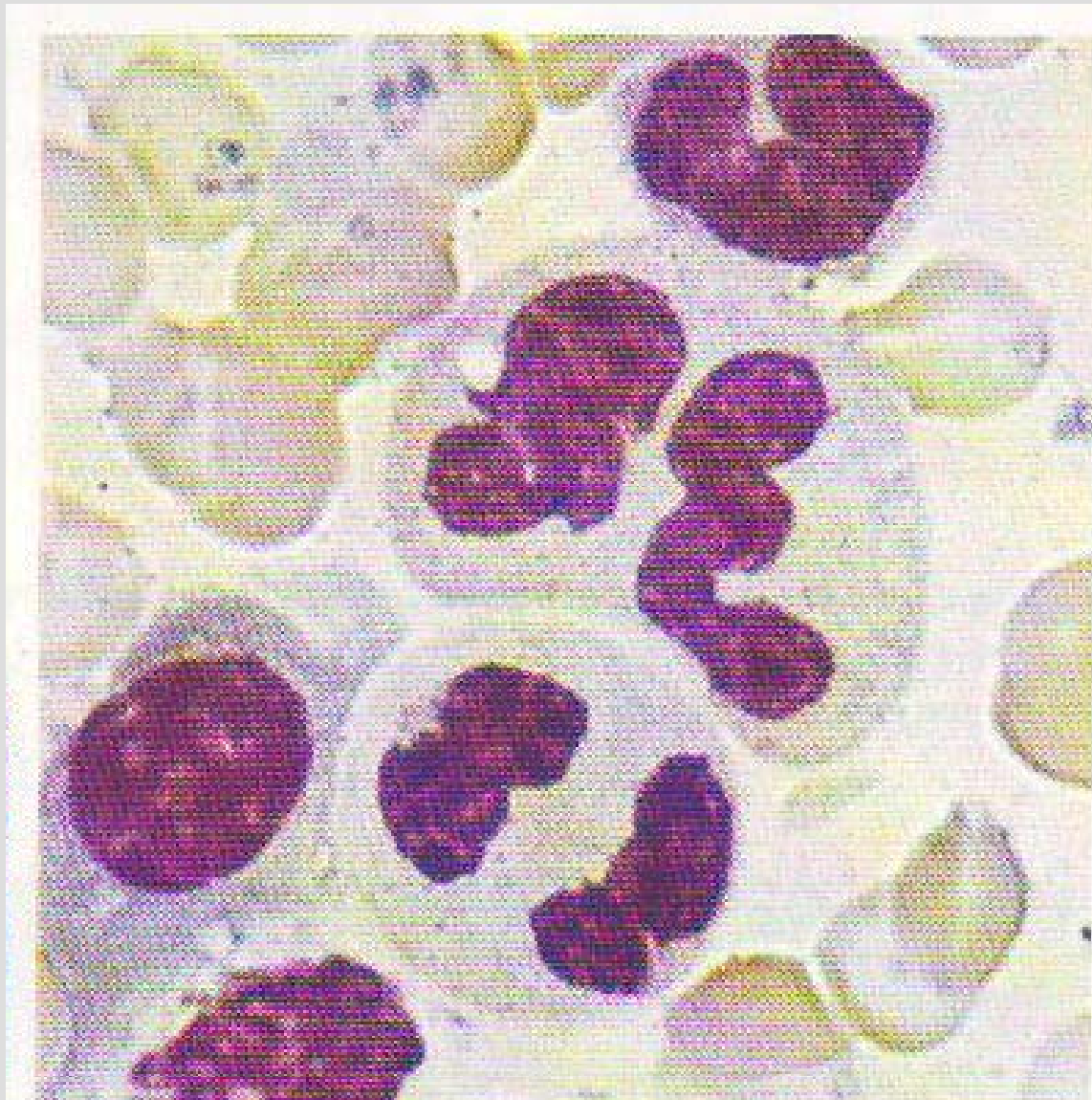


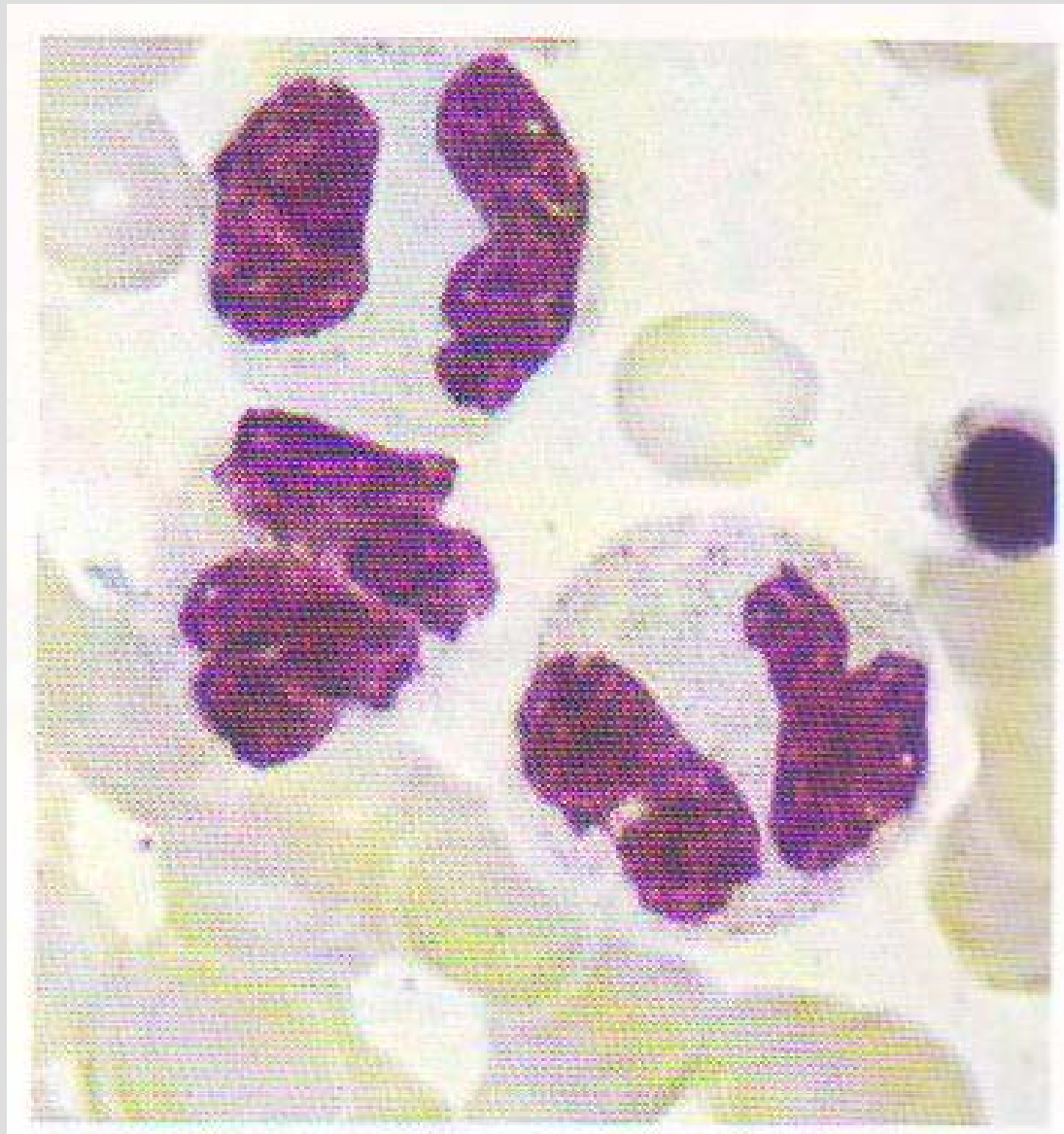


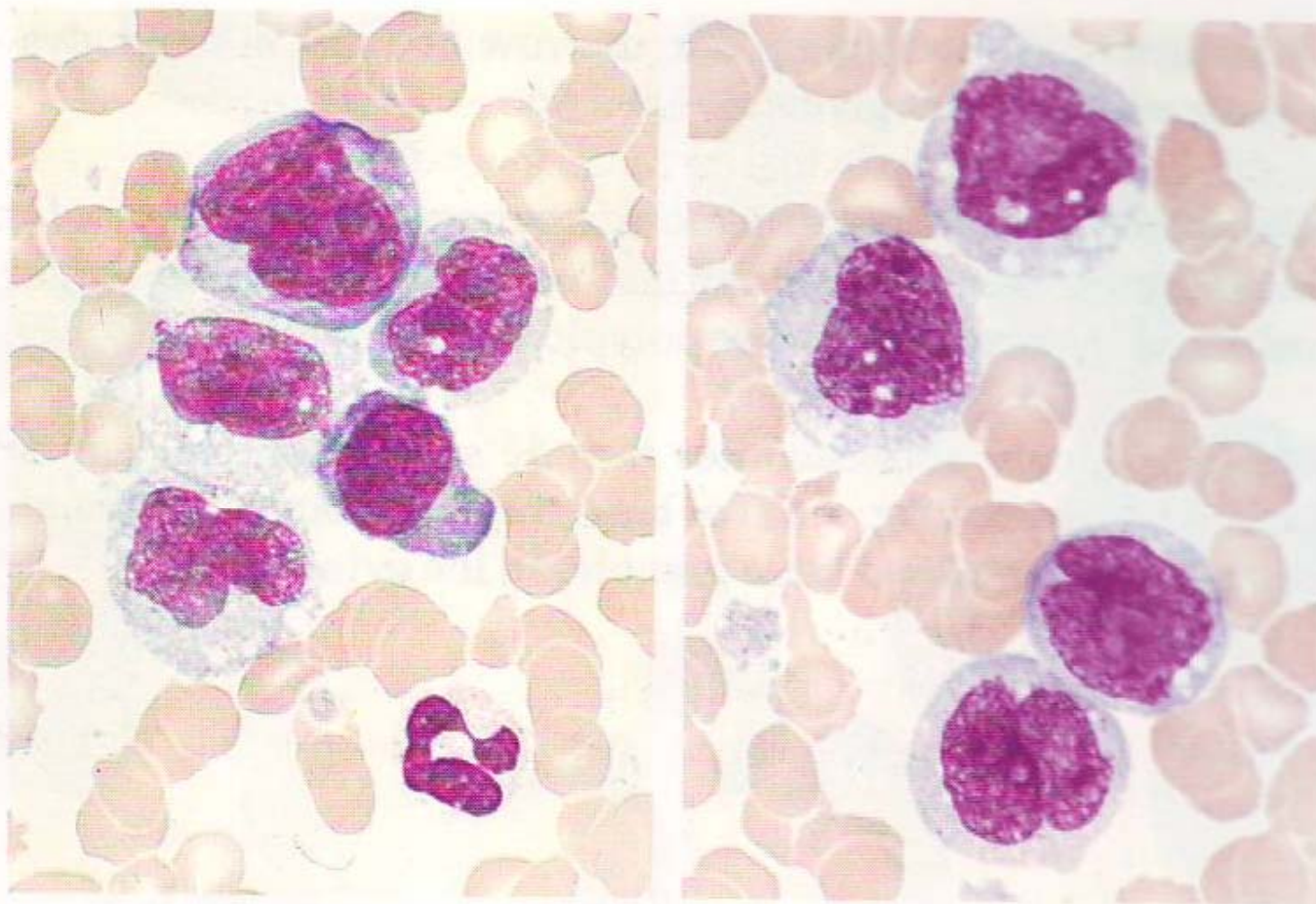






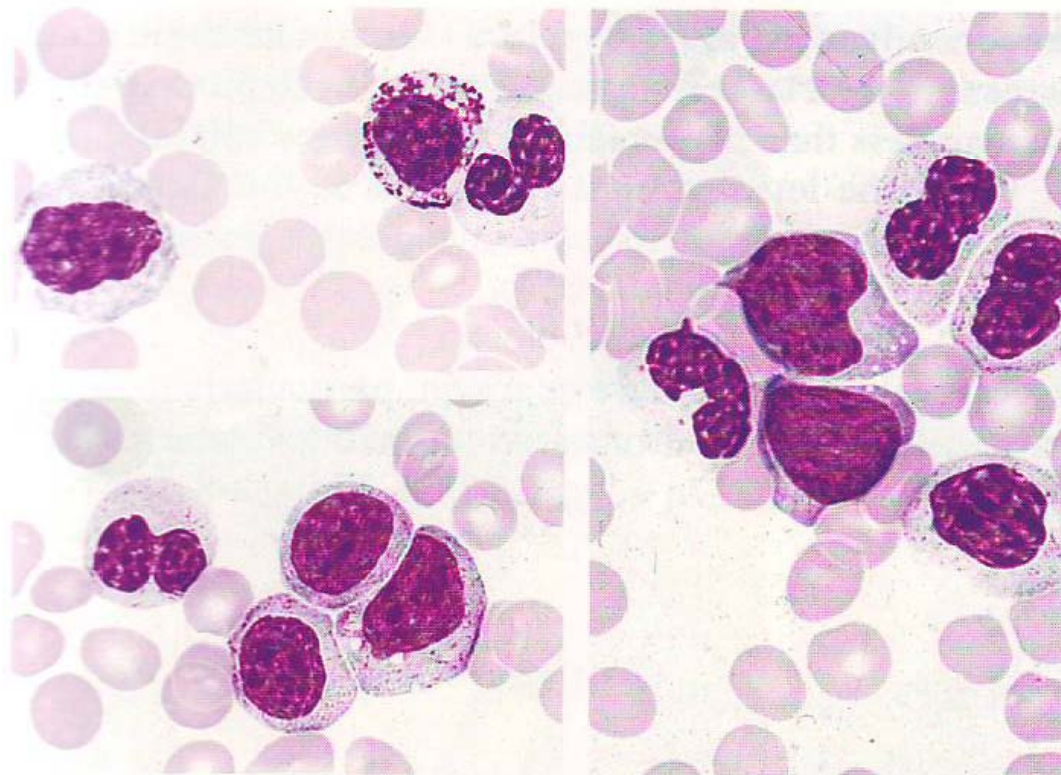






*Fig. 9.59*

*Myelodysplastic syndrome: peripheral blood films showing white cells in chronic myelomonocytic leukaemia (Type IV). The majority of cells are more monocytoid than in Fig. 9.58 and the neutrophil shown is agranular.*



*Fig. 9.58*

*Myelodysplastic syndrome: peripheral blood films showing white cells in chronic myelomonocytic leukaemia (Type IV). There are many atypical myelomonocytic cells and pseudo-Pelger neutrophils, some of which are agranular.*

# Myelodysplastic syndromes (MDS)



- A group of clonal hematopoietic disorders characterized by bone marrow failure, dysplasia, and an increased likelihood of evolution to acute myeloid leukemia (AML).
- Generally classified as “primary” (or *de novo*)
- and “treatment-related” (secondary to prior cytotoxic
- chemotherapy).

Kouides PA, Bennett JM. Et al (1997)



- Thought to arise due to abnormalities in hematopoietic stem cell self renewal and differentiation.
- The incidence of MDS increases with age, perhaps as a result of ongoing acquisition of DNA damage, natural depletion of stem cells, and/or accumulated exposure of the bone marrow to environmental stresses or toxins.

(Cazzola and Malcovati , 2005)



- Many different conditions are grouped together under the “MDS” umbrella based on common clinical characteristics, thus accounting for the wide heterogeneity observed.
- Diagnosis of patients with this disease can be difficult at times.



- Similarly, the assigning of prognosis and the selection of appropriate therapy require careful application of prognostic scoring systems taking into account:
  - Clinical characteristics (e.g., cytopenias age, performance status), and
  - Cytological parameters (e.g., blast count, morphology, karyotype).

**[Catenacci and Schiller, 2005; Komrokji and Bennett; 2007]**

**Table 1. — Common Cytogenetic Alterations in MDS**

<b>MDS Subtype</b>	<b>Frequency</b>	<b>Chromosomal Aberrations</b>
RA	25%	del(5q), del(20q), -Y, -7, +8
RARS	10%	del(5q), del(20q), -Y, -7, +8, idic(X)(q13)
RCMD	50%	del(5q), -7, +8
RCMD-RS	50%	del(5q), -7, +8
RAEB-1	50%	del(5q), -7, +8, del(20q)
RAEB-2	50%–75%	del(5q), -7, +8, -17p, del(11q), t(11q23), -13, del(13q)
MDS del(5q)	100%	del(5q)

Data from Mufti<sup>20</sup> and Fenaux.<sup>22</sup>

## 5q– Syndrome



Characterized by

- < 5% blasts in the bone marrow (with no Auer rods)
- Thrombocytosis
- typical dysmegakaryopoiesis, macrocytic anemia, and an isolated 5q– abnormality.
- predominantly female
- Typically have a low frequency of progression to AML (10%) and
- favorable survival
- Cytogenetic and FISH analyses have shown that this deletion is present in the pluripotent hematopoietic progenitor cells (CD34+, CD38–) of MDS patients.



- Patients with 5q– and no other karyotypic changes had a median survival of 76 months compared to 42 months for MDS patients with a normal karyotype.
- The presence of additional (complex) chromosomal changes or an increased bone marrow blast count significantly reduces median survival in patients with a 5q– deletion.

# FAB Classification For MDS



- RA  
Cytopenia of 1 PB lineage; normo- or hypercellular marrow with dysplasias; < 1% blasts in PB and < 5% bone marrow blasts
- RARS  
Cytopenia and dysplasia, with same percentage blast as RA; > 15% ringed sideroblasts in BM
- RAEB  
Cytopenia of  $\geq 2$  PB lineages; dysplasia involving all 3 lineages; < 5% PB blasts and 5%–20BM blasts
- RAEB-t  
Same hematologic features as RAEB; > 5% blasts in PB or 21%–30% blasts in BM or presence of Auer rods in blasts
- CMML  
Monocytosis in PB; < 5% blasts in PB and up to 20% BM blasts

# WHO Classification



- WHO scheme is based on the FAB system but better defines each class by use of specific criteria for assigning dysplasia to one or more lineages in the bone marrow cells.
- RA and RARS are considered as **erythroid dysplasia** with < 10% dysplasia in the myeloid or megakaryocytic lineages.
- Refractory anemia with excess blasts (RAEB) is considered as **RAEB-1** (5% to 9% blasts) or **RAEB-2** (10% to 19% blasts).
- A new category, refractory cytopenia with multilineage dysplasia, was added. **RCMD**



- CMML, atypical chronic myelogenous leukemia (CML), and JMML are classified under MDS/MPD disorders.
- The **5q- syndrome** is considered as a separate subgroup
- In addition, AML was defined based on a lower minimum criterion for percentage of bone marrow blasts compared to FAB (20% vs30%).