MPD - inclusions and nomenclature

1. Polycythemia (Rubra) Vera (PRV, PV)
2. Myelofibrosis (with Myeloid Metaplasia), Agnogenic Myeloid Metaplasia (MF,MMM, AMM)
3. Essential (Primary) Thrombocythemia

MPD - concepts

- Neoplastic (clonal) disorders of hemopoietic stem cells
- Over-production of all cell lines, with usually one line in particular
- Fibrosis is a secondary event

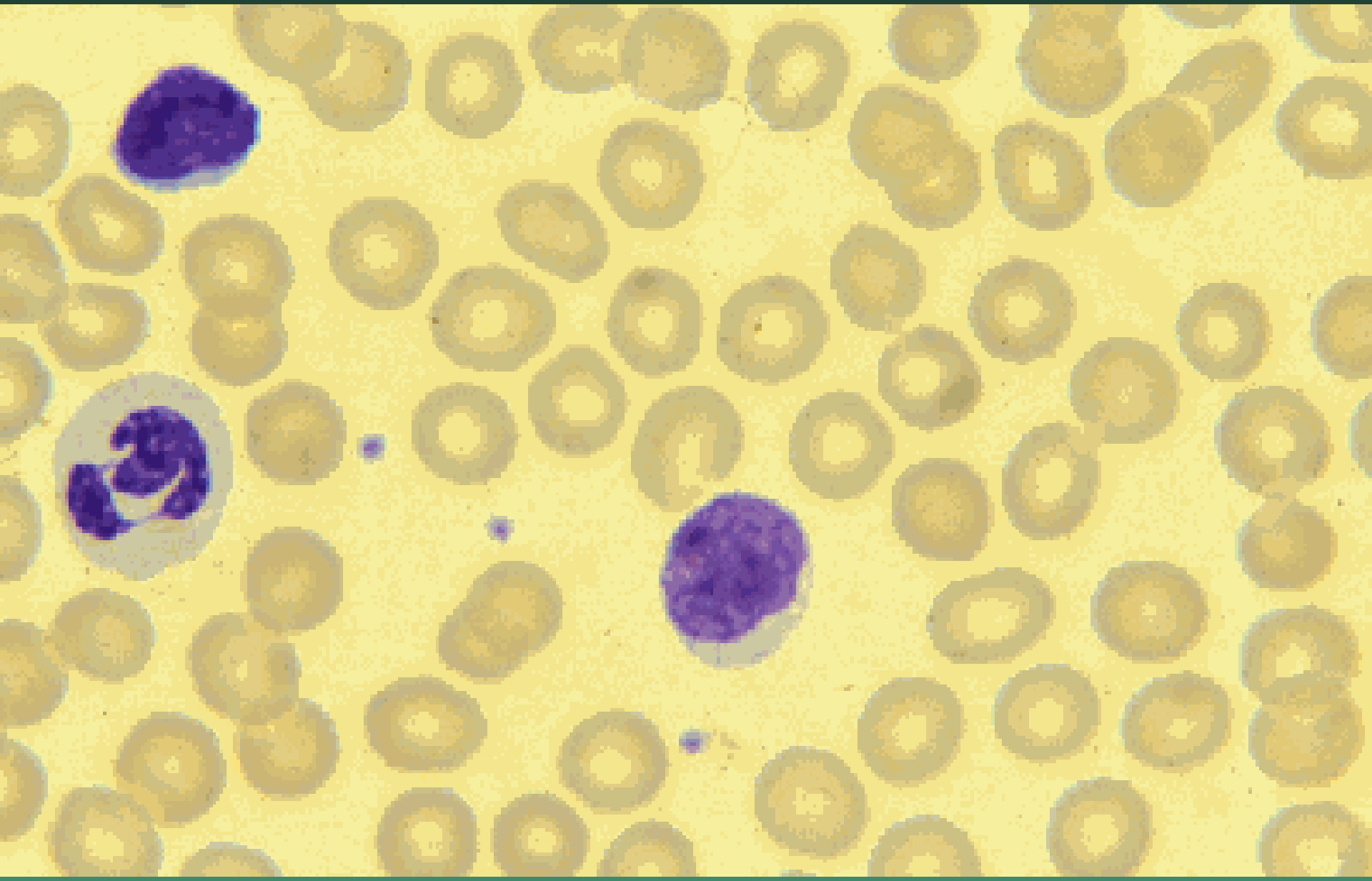
Essential Thrombocythemia (ET)

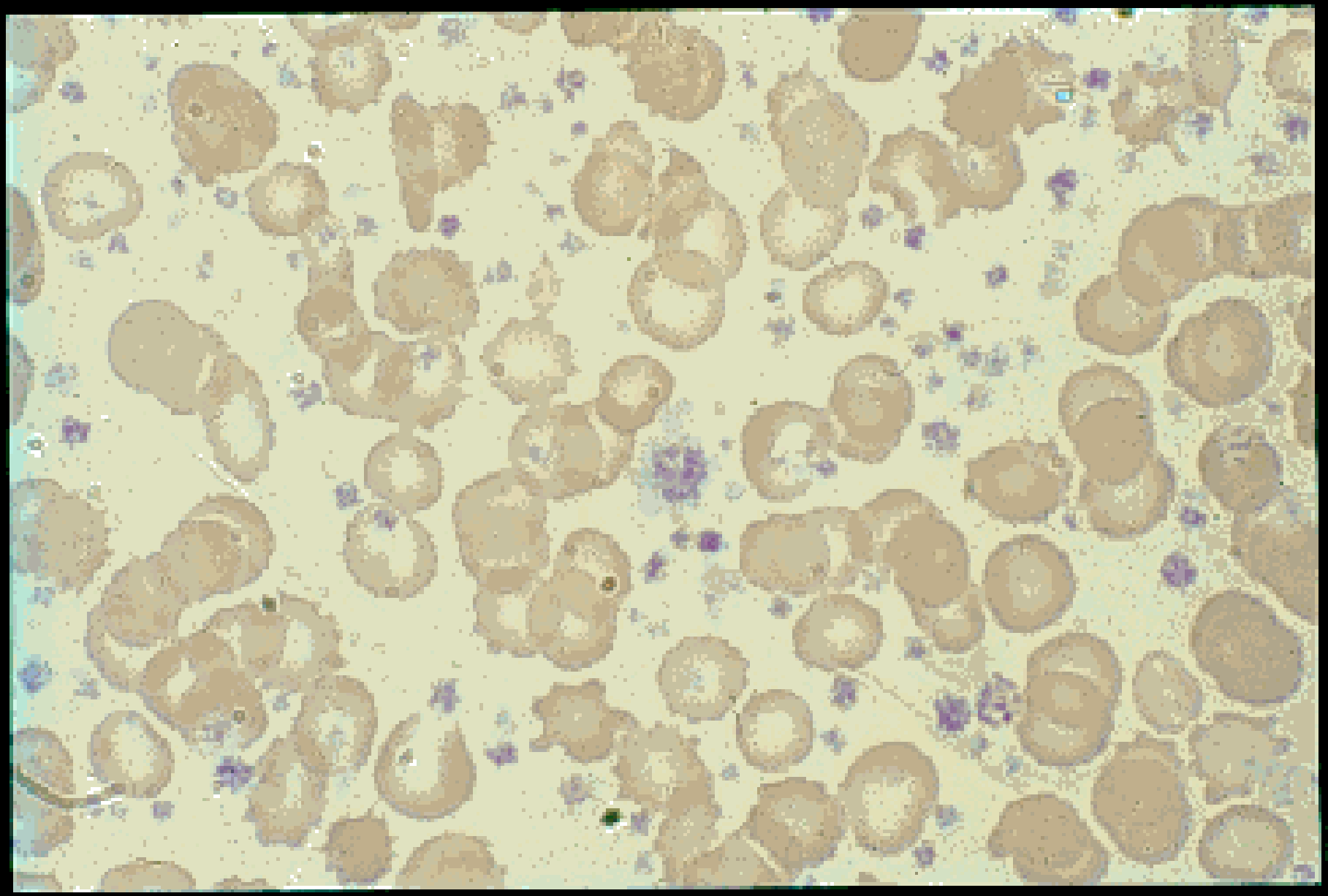
- Neoplastic stem cell disorder causing dysregulated production of large numbers of abnormal platelet
- Abnormal platelets aggregate in vivo, causing thrombosis
- Abnormal platelets also cause bleeding

ET-Typical Blood Count

WBC $\times 10^9$/L	10.0	[4-11]
Hb g/L	156	[140-180]
MCV fl	85	[80-100]
Platelets $\times 10^9$/L	1560	[150-450]
Neuts $\times 10^9$/L	7.0	[2-7.5]
Lymphs $\times 10^9$/L	2.0	[1.5-4]
Monos $\times 10^9$/L	0.8	[0.2-0.8]
Eos $\times 10^9$/L	0.1	[0-0.7]
Basos $\times 10^9$/L	0.1	[0-0.1]

Film Comment: many large and abnormal platelets present





ET - clinical

- None
- Stroke
- Transient Ischemic Attack (TIA)
- Peripheral Vascular Occlusion
- Erythromelalgia
- Bleeding (esp surgical)

ET - diagnosis

- Distinguish from reactive thrombocytosis, and Chronic Myeloid Leukemia
- Clinical setting, blood film, bone marrow, and cytogenetics help

ET- treatment

- None in low-risk cases
- Anti-platelet agents (aspirin)
- Anagrelide
- Chemotherapy (hydroxyurea)
- Special consideration pre-surgery

Polycythemia Rubra Vera (PRV)

- A neoplastic (clonal) stem cell disorder, which leads to excessive production of all myeloid cell lines, but predominantly red cells. The increase in whole blood viscosity causes vascular occlusion and ischemia, compounded by the increase in platelets.

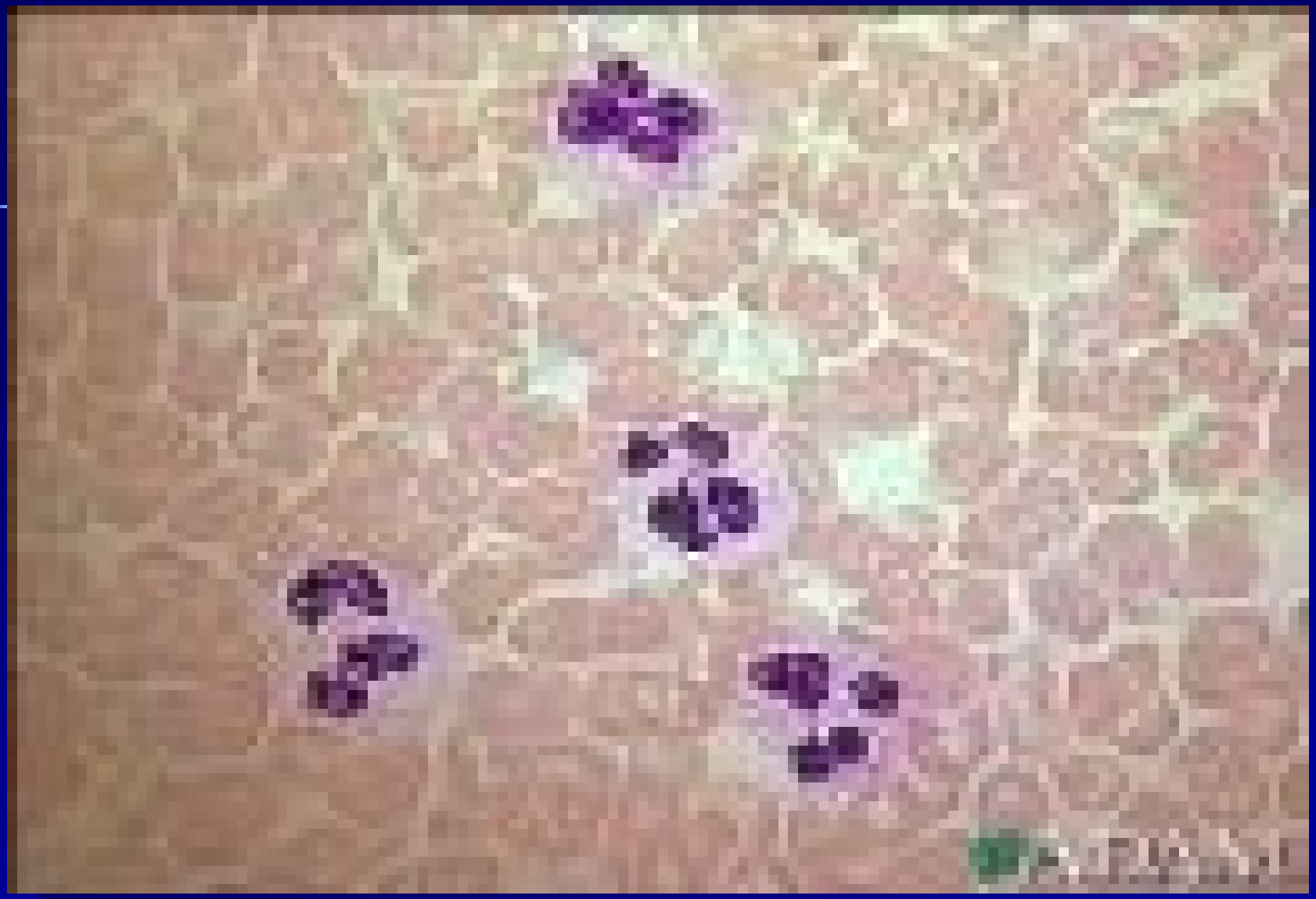
PRV - clinical features

- Headaches
- Itch
- Vascular occlusion
- Thrombosis
- TIA, stroke
- Splenomegaly

PRV - typical blood count

WBC x 10^9/L	18.0	[4-11]
Hb g/L	200	[140-180]
HCt	0.62	[.42-.51]
MCV fl	75	[80-100]
Platelets x 10^9/L	850	[150-450]
Neuts x 10^9/L	14.6	[2-7.5]
Lymphs x 10^9/L	2.0	[1.5-4]
Monos x 10^9/L	0.8	[0.2-0.8]
Eos x 10^9/L	0.1	[0-0.7]
Basos x 10^9/L	0.5	[0-0.1]

Film: microcytosis: large and abnormal platelets present



PRV - diagnosis

- red cell mass
- exclude secondary causes of true polycythemia
- look for features of primary polycythemia

PRV - treatment

- phlebotomy to hematocrit less than 0.45
- low-dose aspirin (controversial) - 325 mg/day or less
- hydroxyurea if necessary
- do not treat with iron

Myelofibrosis (MF)

- neoplastic (clonal) hemopoietic stem cell disorder
- secondary marrow fibrosis
- bone marrow failure
- myeloid metaplasia (extra-medullary hemopoiesis)

MF - typical blood count

WBC $\times 10^9$/L	2.4	[4-11]
Hb g/L	88	[140-180]
MCV fl	85	[80-100]
Platelets $\times 10^9$/L	60	[150-450]
Neuts $\times 10^9$/L	1.0	[2-7.5]
Lymphs $\times 10^9$/L	1.0	[1.5-4]
Monos $\times 10^9$/L	0.2	[0.2-0.8]
Eos $\times 10^9$/L	0.1	[0-0.7]
Basos $\times 10^9$/L	0.1	[0-0.1]

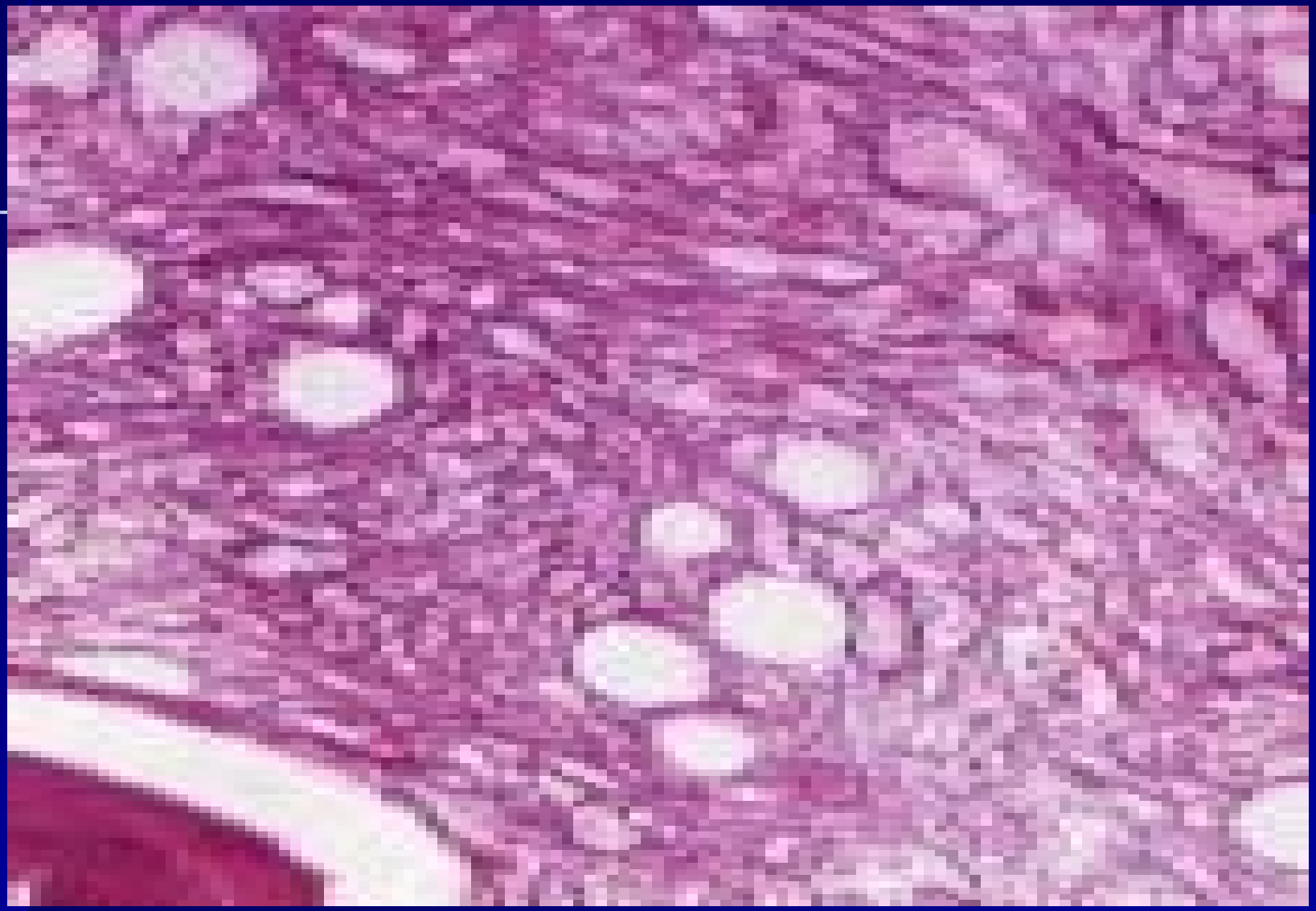
Film Comment: a few nucleated red cells and myelocytes (leukoerythroblastic). Tear-drop poikilocytes

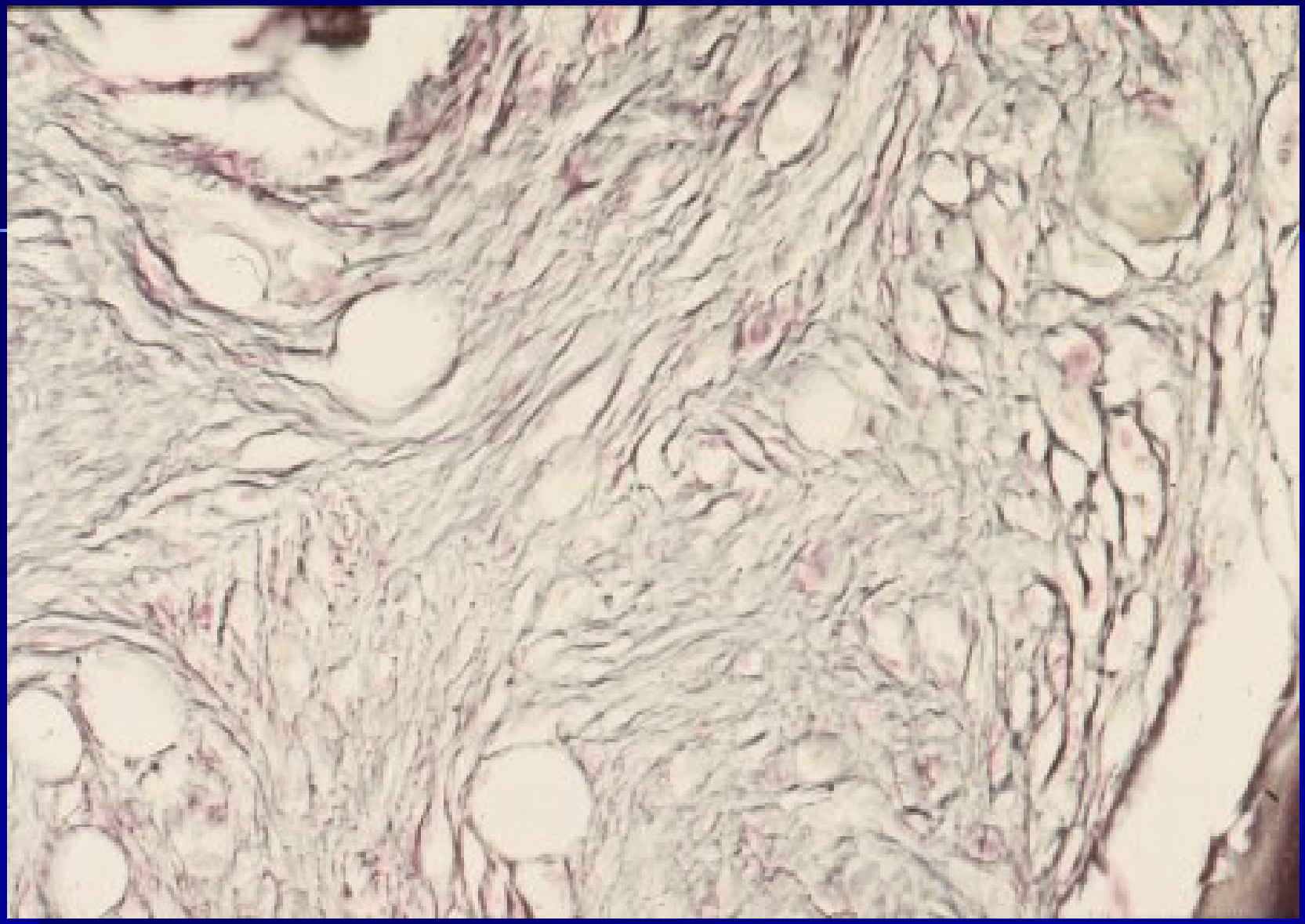
MF - diagnosis

- typical blood picture
- splenomegaly
- dry aspirate
- fibrosis on trephine biopsy
- absence of other cause

MF - clinical

- Marrow failure
- splenomegaly etc





MF - treatment

- supportive care
- splenectomy if necessary

Chronic Meloid Leukemia

- Chronic myeloproliferative disease are clonal haemopoietic stem cell disorders characterized by proliferation in the bone marrow of one or more of the myeloid lineages

Pathogenesis

- Activation of tyrosine kinase signal transduction pathway

Constantly associated with Ph chromosome

- Biphasic or triphasic disease

Chronic myeloid leukemia

- Chronic phase
  - increased pool of clonal precursors committed to become myeloid cells
  - most of the clonal precursors differentiate into mature cells

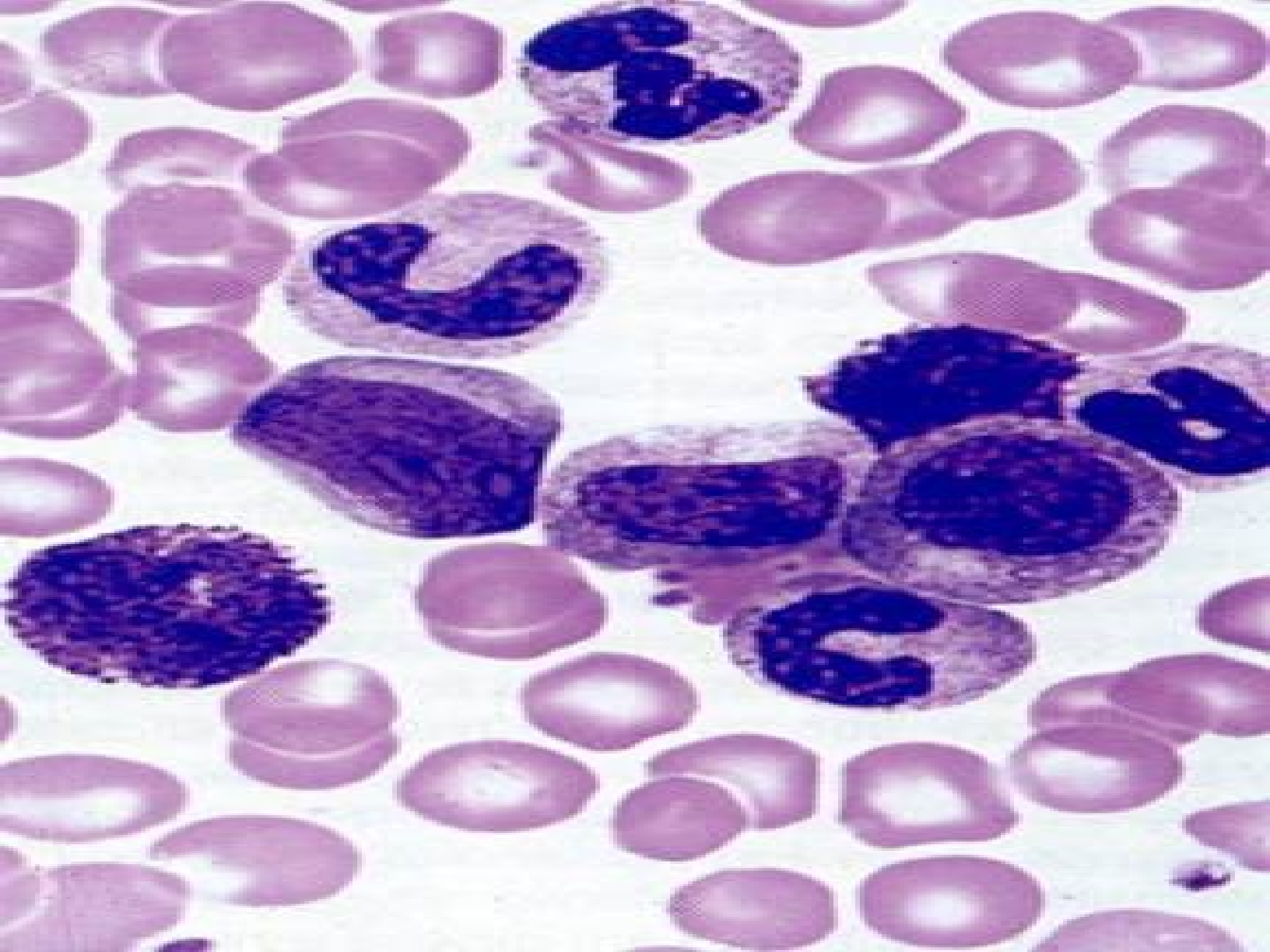
CML - chronic phase

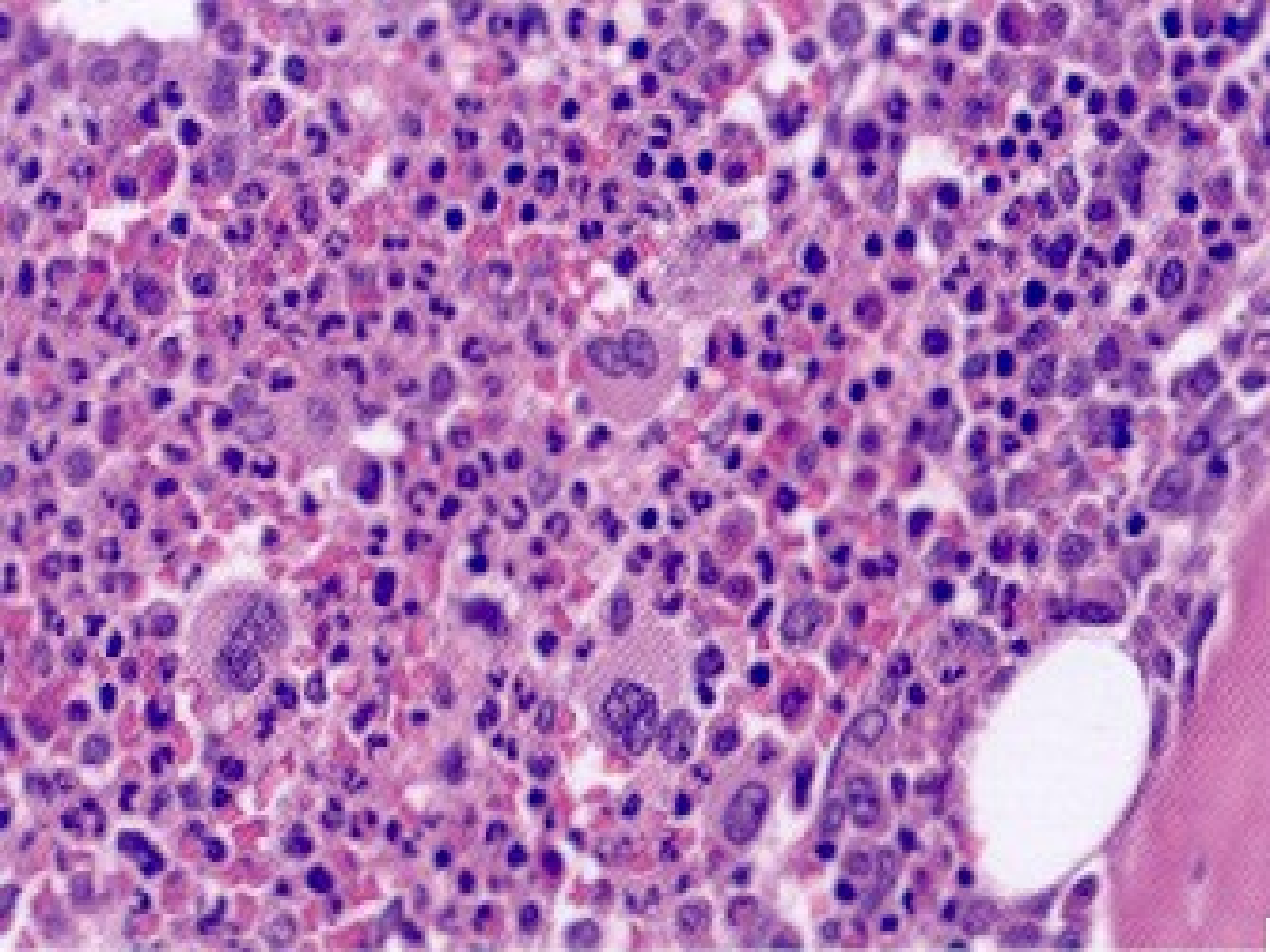
- weakness, weight loss, purpura
- thrombocytosis
- anemia - normal MCV
- splenomegaly
- priapism

- median duration 3-4 yrs

CML - chronic phase

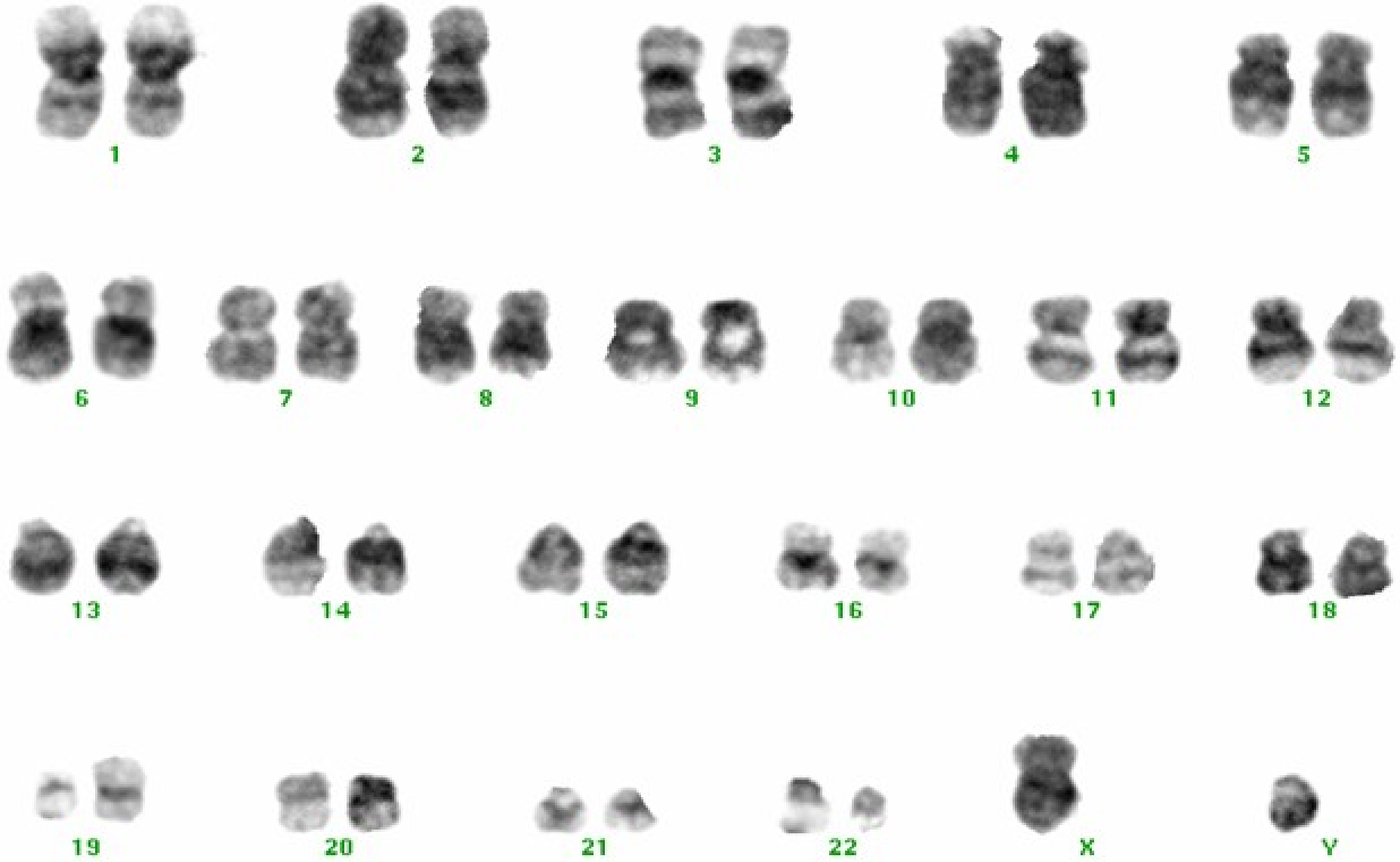
- WBC increased
- Entire granulocytic spectrum on blood film
- Marrow hyperplasia
  - expanded myeloid series
  - eo and basophil precursors
  - megakaryocytes
- Low neutrophil alkaline phosphatase
- Ph chromosome [t(9;22)] present





Ph chromosome: t(9;22)

- reciprocal translocation between long arms of chromosomes 9 and 22
- Ph-negative CML: 9;22 translocation present but not visible
- ABL sequences from 9 translocated into BCR gene on 22 → FUSION GENE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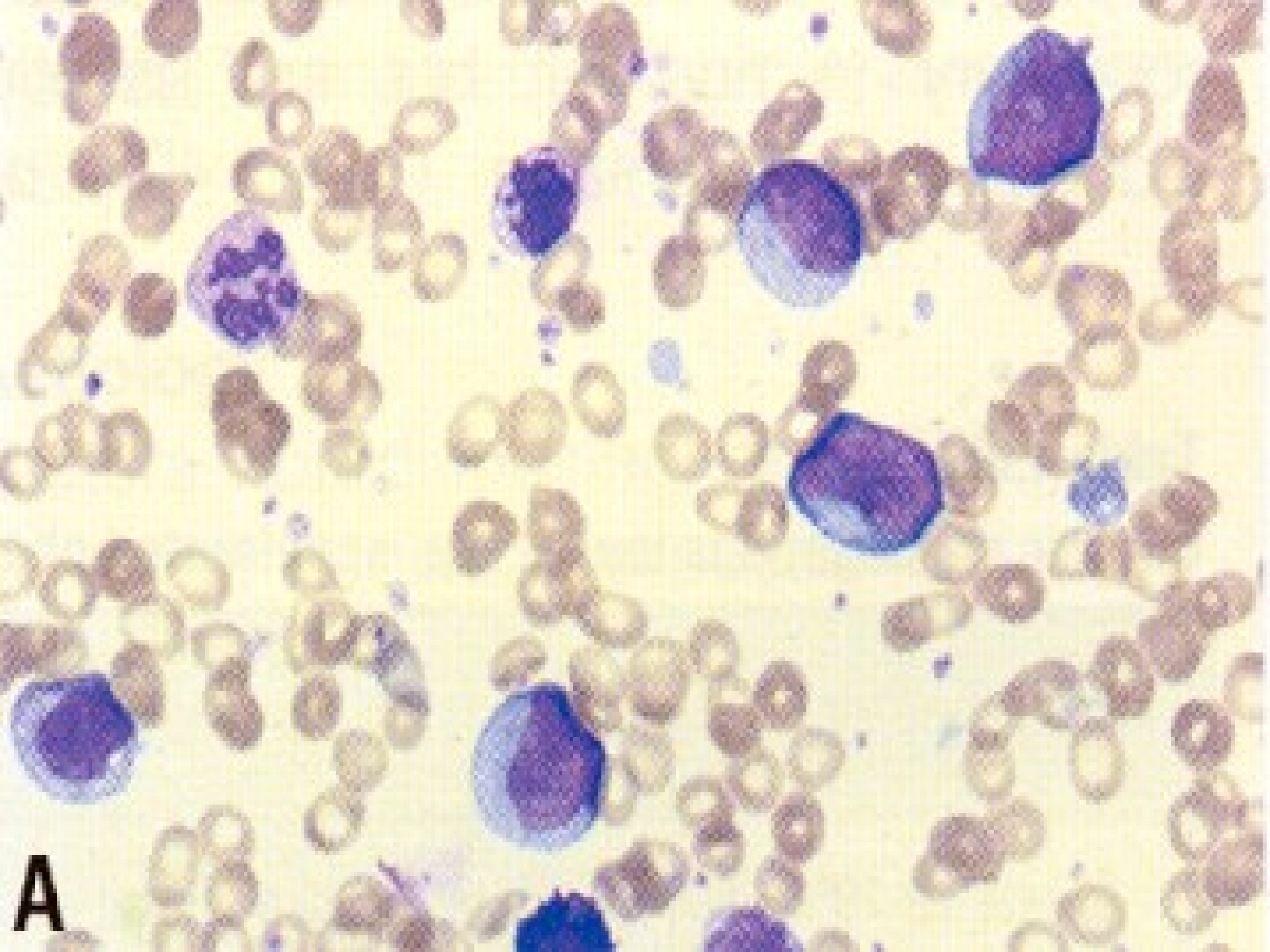
CML in blastic transformation

- unstable disease
- weight loss, fever, sweats, bone pain
- worsening
  - splenomegaly
  - anemia
  - platelet counts
  - blast and promyelocyte counts
  - basophilia and eosinophilia
- resistance to therapy
- ‘blastic crisis’ develops in most
- death in weeks or months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