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PEARLS OF LABORATORY MEDICINE

# Acute Myeloid Leukemia

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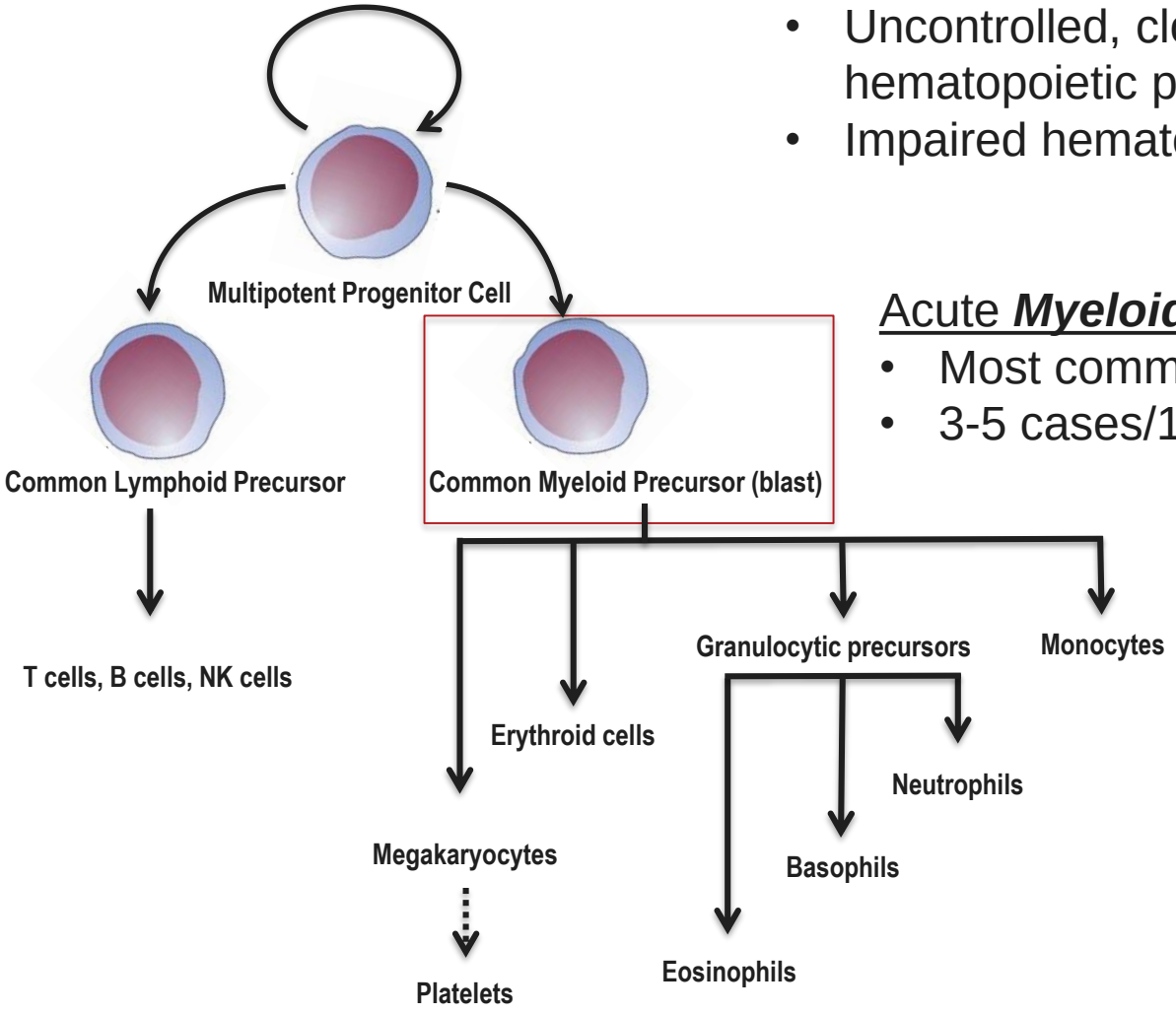
# Acute Leukemia




## Acute leukemia

- Uncontrolled, clonal expansion of hematopoietic progenitors (blasts)
- Impaired hematopoiesis

## Acute ***Myeloid*** Leukemia (AML)

- Most common acute leukemia in adults
- 3-5 cases/100,000 population (USA)

## Pathogenesis

- *De novo*
- Hematological disorder
- Prior therapy
- Associated congenital disorder

**Chromosomal/Genetic abnormalities**

↓

**Chimeric proteins**

↓

**Alteration maturation of myeloid blasts**

# Diagnosis

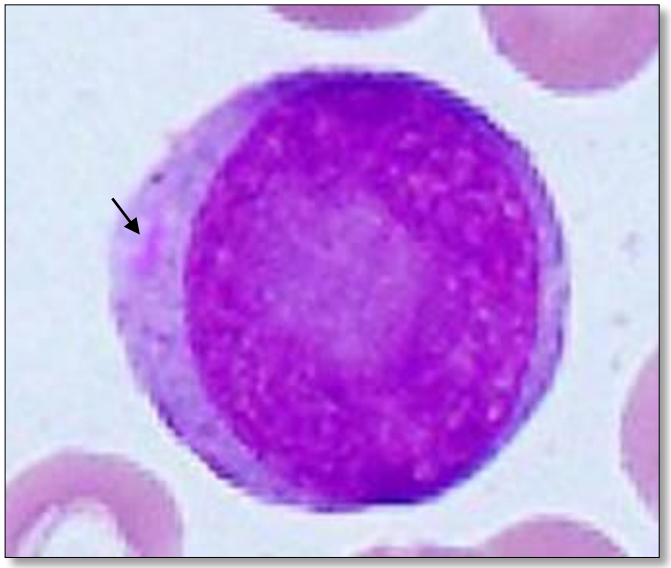
≥ 20% blasts in blood or bone marrow

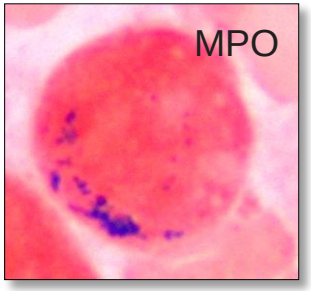
Considerations:

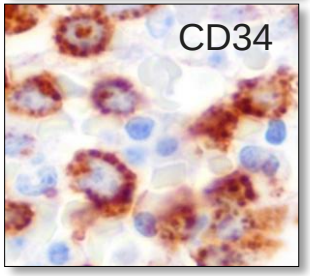
- Specific cytogenetic abnormalities, Pure Erythroid Leukemia, Acute Promyelocytic Leukemia and Myeloid Sarcoma (extramedullary leukemia)

To establish the diagnosis of AML the following questions need to be answered

- Are the cells counted truly myeloblasts (morphology, phenotyping, cytochemistry)
- Are they truly 20% (differential counts, ~~CD34 IHC?, Flow cytometry~~?)






Monocytic lineage: non-specific esterase, lysozyme, CD14, CD64, CD11c
Myeloid lineage: CD117, CD13, CD33, CD65, CD14, CD15, CD65

# Classification

**Classification schemes**

- 1976 French American British (FAB) classification
- 2001 World Health Organization (WHO) classification
  - Revised 2008 and 2016

AML with recurrent genetic abnormalities

- AML with t(8;21)(q22;q22.1); *RUNX1-RUNX1T1*
- AML with inv(16)(p13.1q22) or t(16;16)(p13.1;q22); *CBFB-MUH11*
- Acute promyelocytic leukemia with *PML-RARA*
- AML with t(9;11)(p21.3;q23.3); *KMT2A-MLLT3*
- AML with t(6;9)(p23;q34.1); *DEK-NUP214*
- AML with inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2); *GAT2, MECOM*
- AML (megakaryoblastic) with t(1;22)(p13.3;q13.1); *RBM15-MKL1*
- *AML with BCR-ABL1*
- AML with mutated NPM1
- AML with biallelic mutation of *CEBPA*
- *AML with mutated RUNX1*

AML with myelodysplasia related changes

Therapy-related myeloid neoplasms

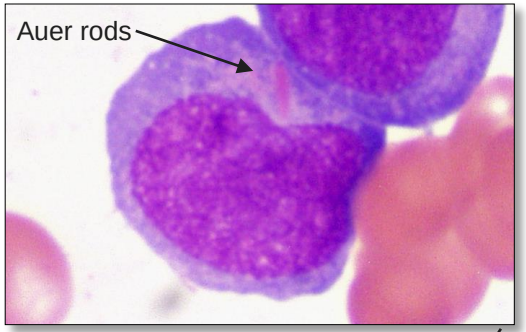
AML, not otherwise specified (NOS)

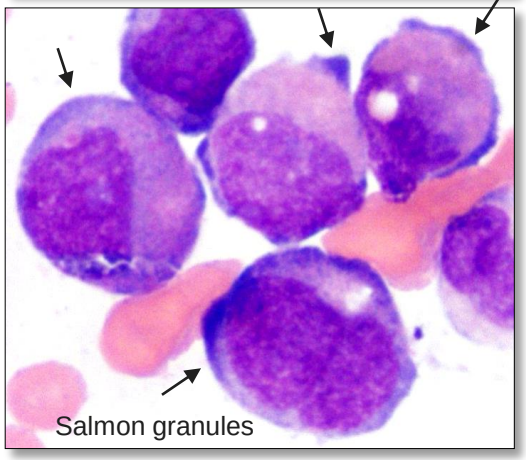
Myeloid sarcoma

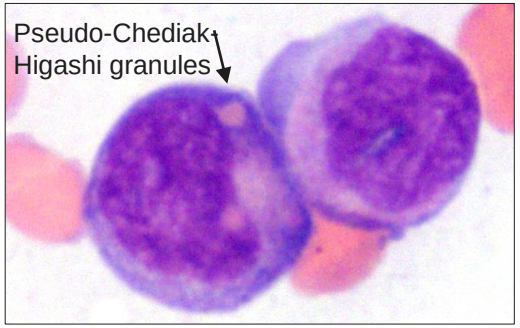
Myeloid proliferations associated with Down syndrome

**AML without regard to blast count**

## AML with t(8;21)

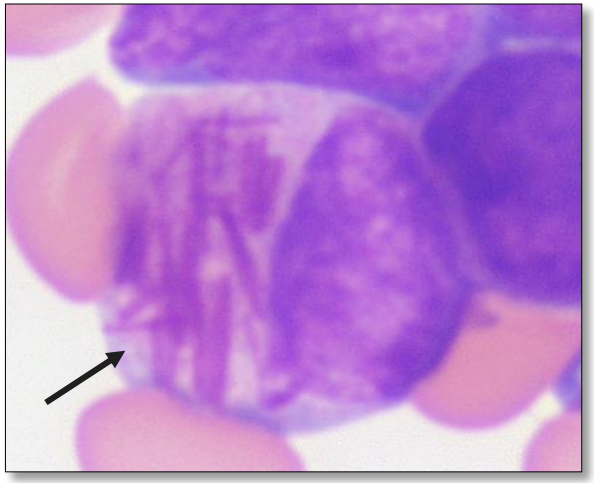


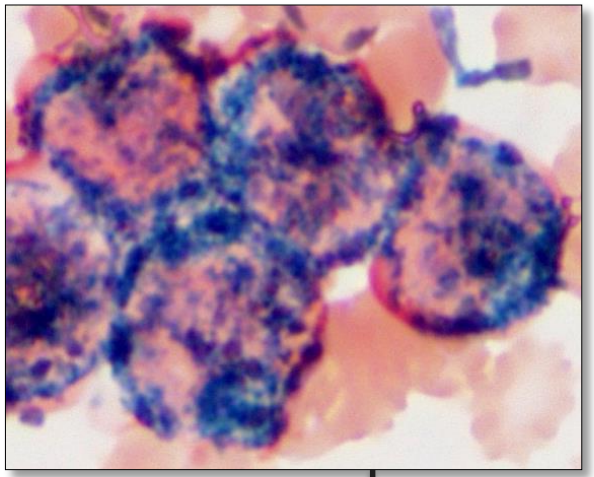



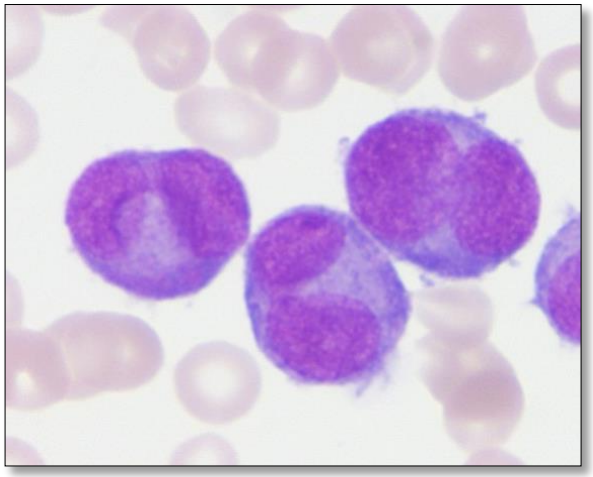

## APL with *PML-RARA*

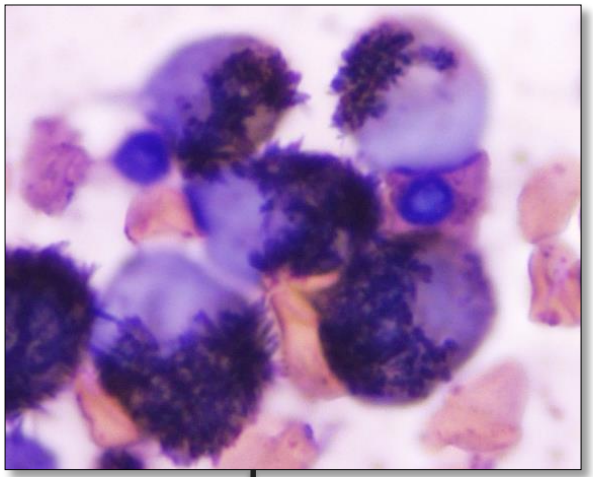
### Hypergranular





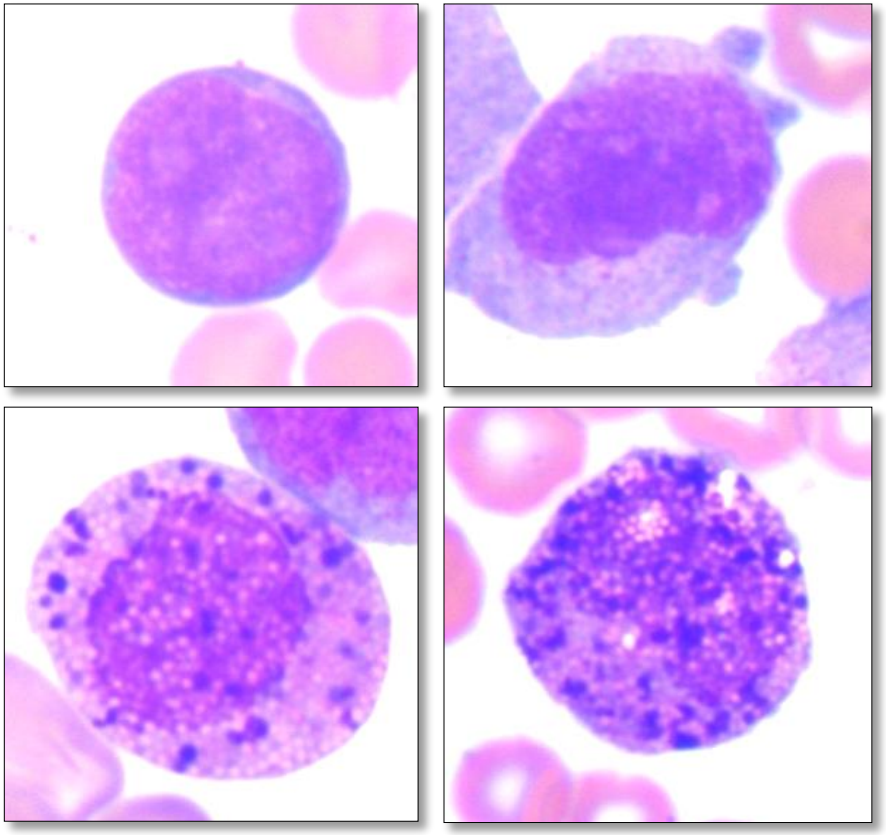
### Microgranular



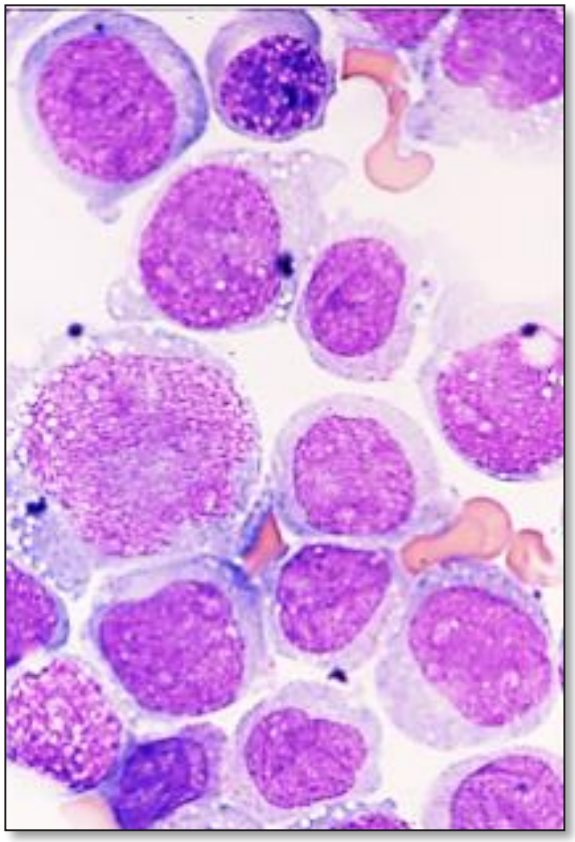


**MPO cytochemistry**

## AML with inv(16)



## AML with t(9;11) – monocytic features



# Other AMLs with recurrent genetic abnormalities (≥20% blasts required)



## AML with t(6;9)

- Monocytic features
- Basophilia
- Multilineage dysplasia
- Poor prognosis

## AML with inv(3)

- Thrombocytosis
- Dysplastic megakaryocytes
- Multilineage dysplasia
- Aggressive – short survival

## AML with t(1;22)

- Megakaryoblastic
- Rare
- Down syndrome patients
  - Female preponderance
- Long disease-free survival

## AML with *BCR-ABL1* (provisional entity)

- *De novo* AML
- Leukocytosis
- Aggressive
- No previous history of Chronic Myeloid Leukemia (CML)

## AML with mutated *NPM1*

- Exon 12
- Monocytic, myelomonocytic
- Good response
  - Absence of *FLT3*-ITD favorable

## AML with biallelic mutation of *CEBPA*

- No distinctive morphologic features
- Favorable prognosis

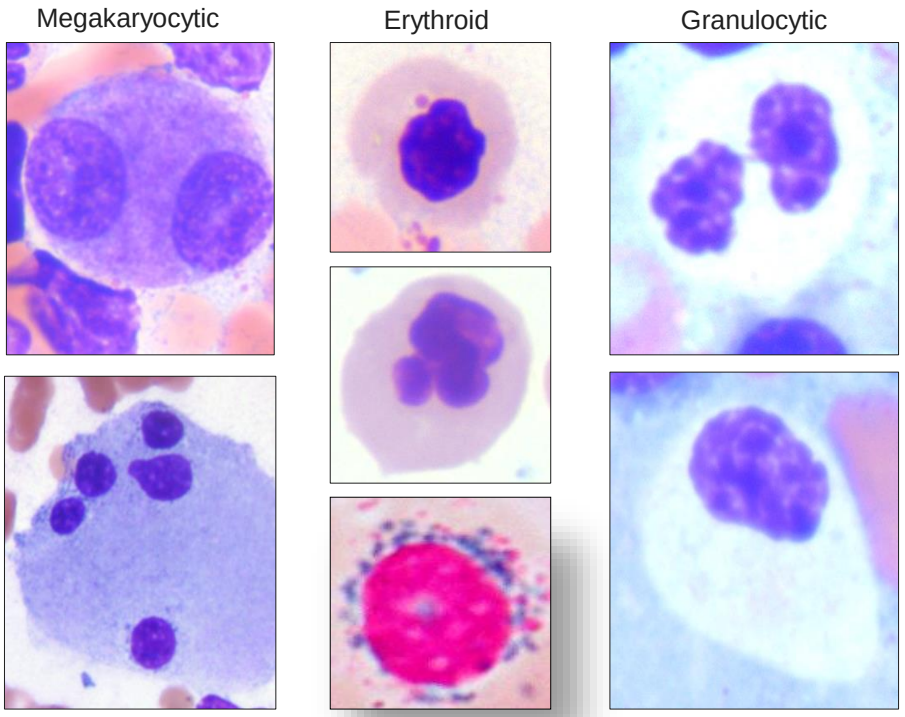
## AML with mutated *RUNX1* (provisional entity)

- Worse overall survival

# AML with myelodysplasia-related changes

- ≥20% blasts
- History of MDS, or MDS/MPN
- MDS-related cytogenetic abnormality
- Multilineage dysplasia
- No prior cytotoxic therapy
- No recurrent genetic abnormality

**Complex karyotype (≥ 3 abnormalities)**
**Unbalanced abnormalities**
-7/del(7q)
del(5q)/t(5q)
i(17q)/t(17p)
-13/del(13q)
del(11q)
del(12p)/t(12p)
idic(X)(q13)
**Balanced abnormalities**
t(11;16)(q23.3;p13.3)
t(3;21)(q26.2;q22.1)
t(1;3)(p36.3;q21.2)
t(2;11)(p21;q23.3)
t(5;12)(q32;p13.2)
t(5;7)(q32;q11.2)
t(5;17)(q32;p13.2)
t(5;10)(q32;q21.2)
t(3;5)(q25.3;q35.1)



# Therapy-related myeloid neoplasms

Cytotoxic chemotherapy and/or radiation therapy

- Alkylating agents
- Ionizing radiation

**5-10 years after exposure**
**Unbalanced loss of genetic material (chr 5/7)**

- Topoisomerase II inhibitors
- Antimetabolites
- Antitubulin agents

**1-5 years after exposure**
**Balanced chromosomal translocation**

t-AML (≥ 20% blasts)
t-MDS
t-MDS/MPN

t-MN

**POOR PROGNOSIS**

# Acute Myeloid Leukemia, NOS

AML with minimal differentiation (FAB M0)

AML without maturation (FAB M1)

AML with maturation (FAB M2)

Acute myelomonocytic leukemia (FAB M4)

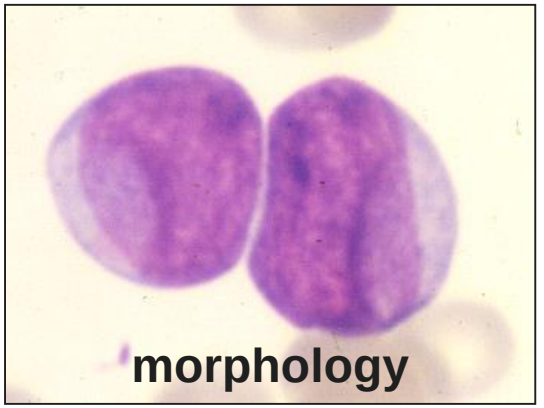
Acute monoblastic and monocytic leukemia (FAB M5)

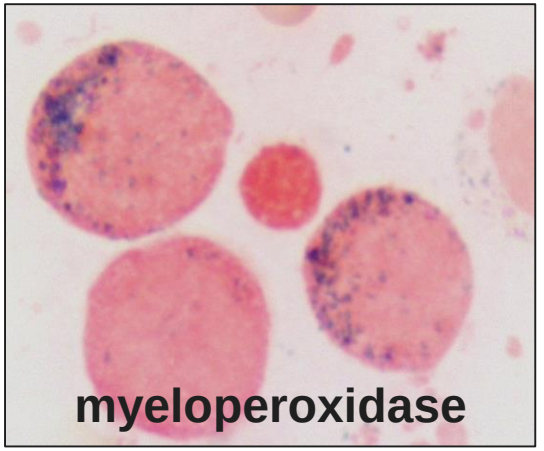
Pure erythroid leukemia (FAB M6)

Acute megakaryoblastic leukemia (FAB M7)

Acute basophilic leukemia

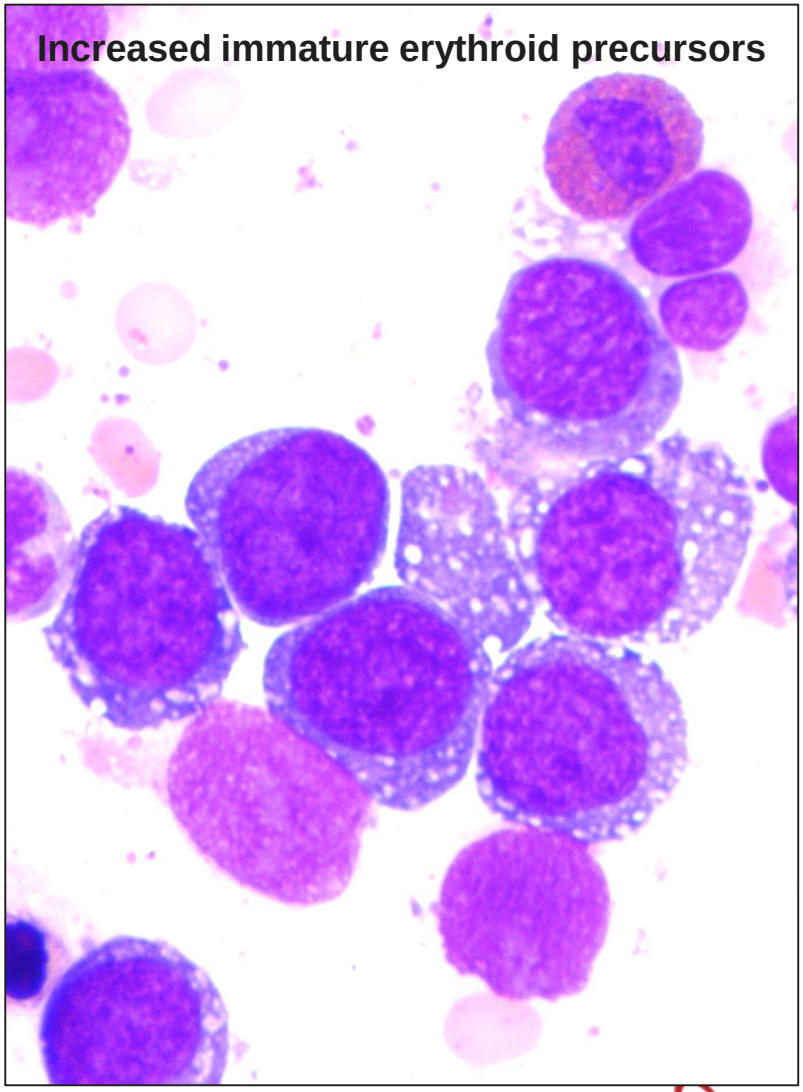
Acute panmyelosis with myelofibrosis



# Pure erythroid leukemia

- >80% erythroid cells
- ≥ 30% pro-erythroblasts
- No significant myeloblastic component
- Extremely rare
- Median survival 3 months




WHO 2008 Erythroleukemia

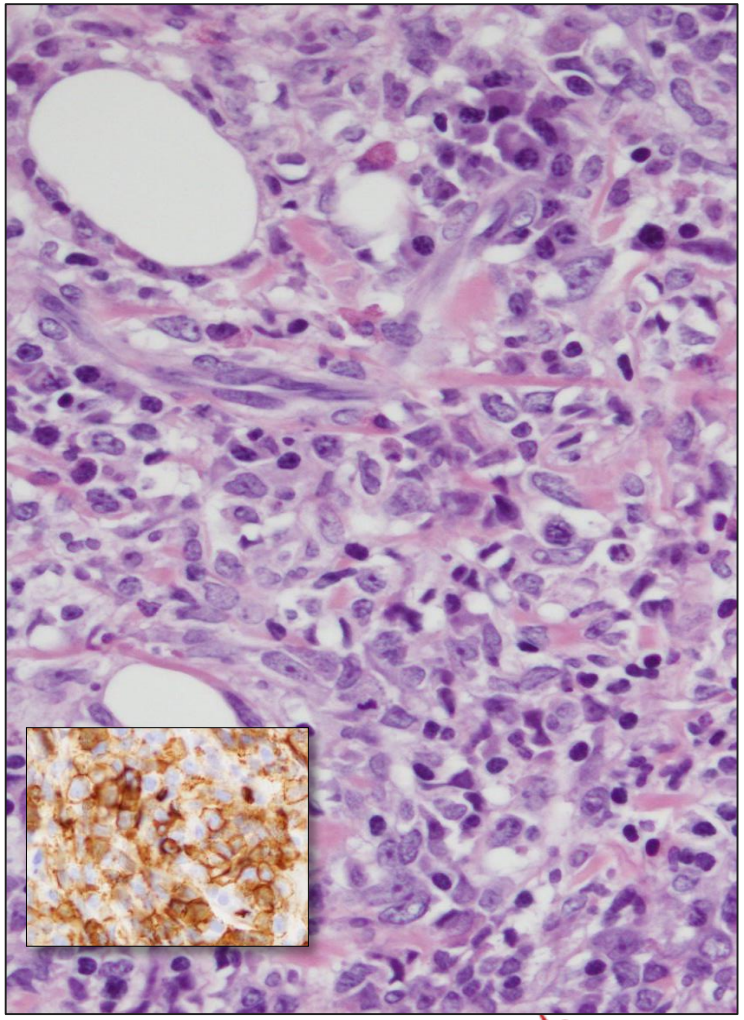
- Erythroid/Myeloid
- MDS <20% blasts
- AML-MRC ≥20%

Now classified as MDS

# Myeloid sarcoma

- Extramedullary presentation of AML as a tumor mass
- *De novo* leukemia
- Skin most commonly involved
  - lymph nodes, GI tract, bone, soft tissues, testes
- 25% of cases of myeloid sarcoma do not have an underlying ‘conventional’ AML
- Age, gender, anatomic site – no difference in clinical behavior
- Bone marrow transplantation increases probability of prolonged survival/cure

**CD34 positive (inset) blasts infiltrating the GI tract**



# Myeloid Neoplasms with Germline Predisposition

These category includes 3 main groups:

Myeloid neoplasms with germline predisposition…

- *…without a pre-existing disorder or organ dysfunction*
- *… and pre-existing platelet disorders*
- *… and other organ dysfunction*

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# Disclosures/Potential Conflicts of Interest

*Upon Pearl submission, the presenter completed the Clinical Chemistry disclosure form. Disclosures and/or potential conflicts of interest:*

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