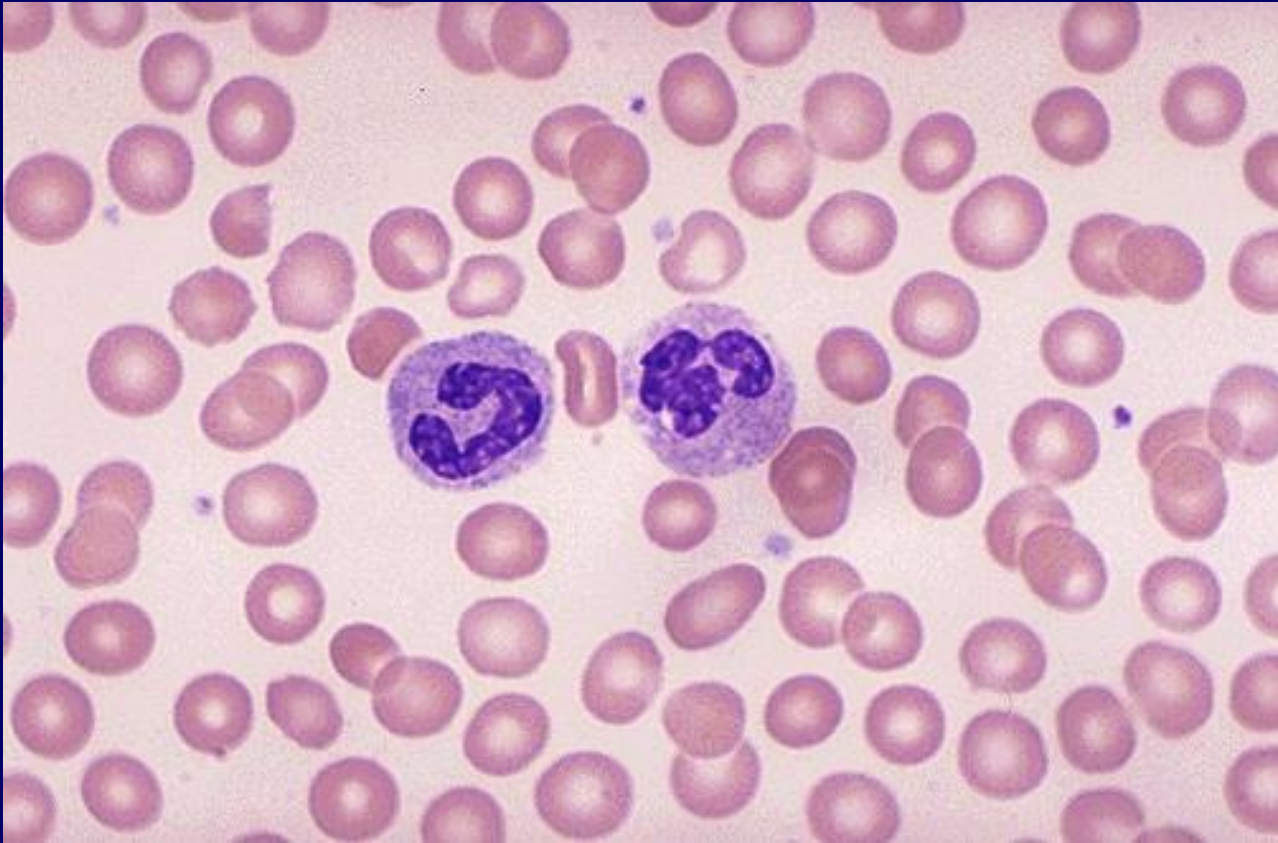


What is Myelodysplastic Syndrome?



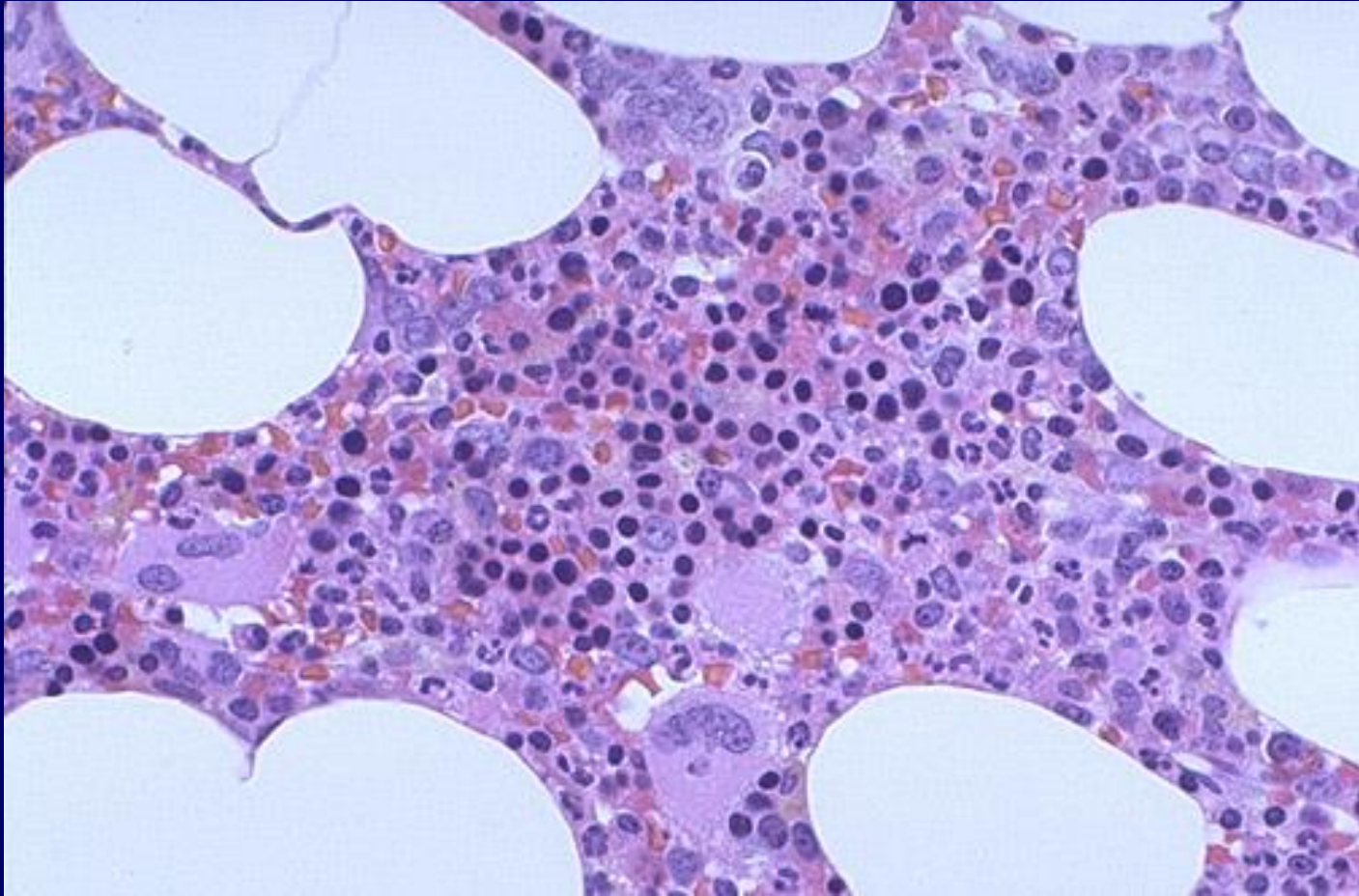
Maria R. Baer, M.D.
University of Maryland
Greenebaum Comprehensive Cancer Center

Normal blood cells



- Red blood cells
- White blood cells
- Platelets

Normal bone marrow



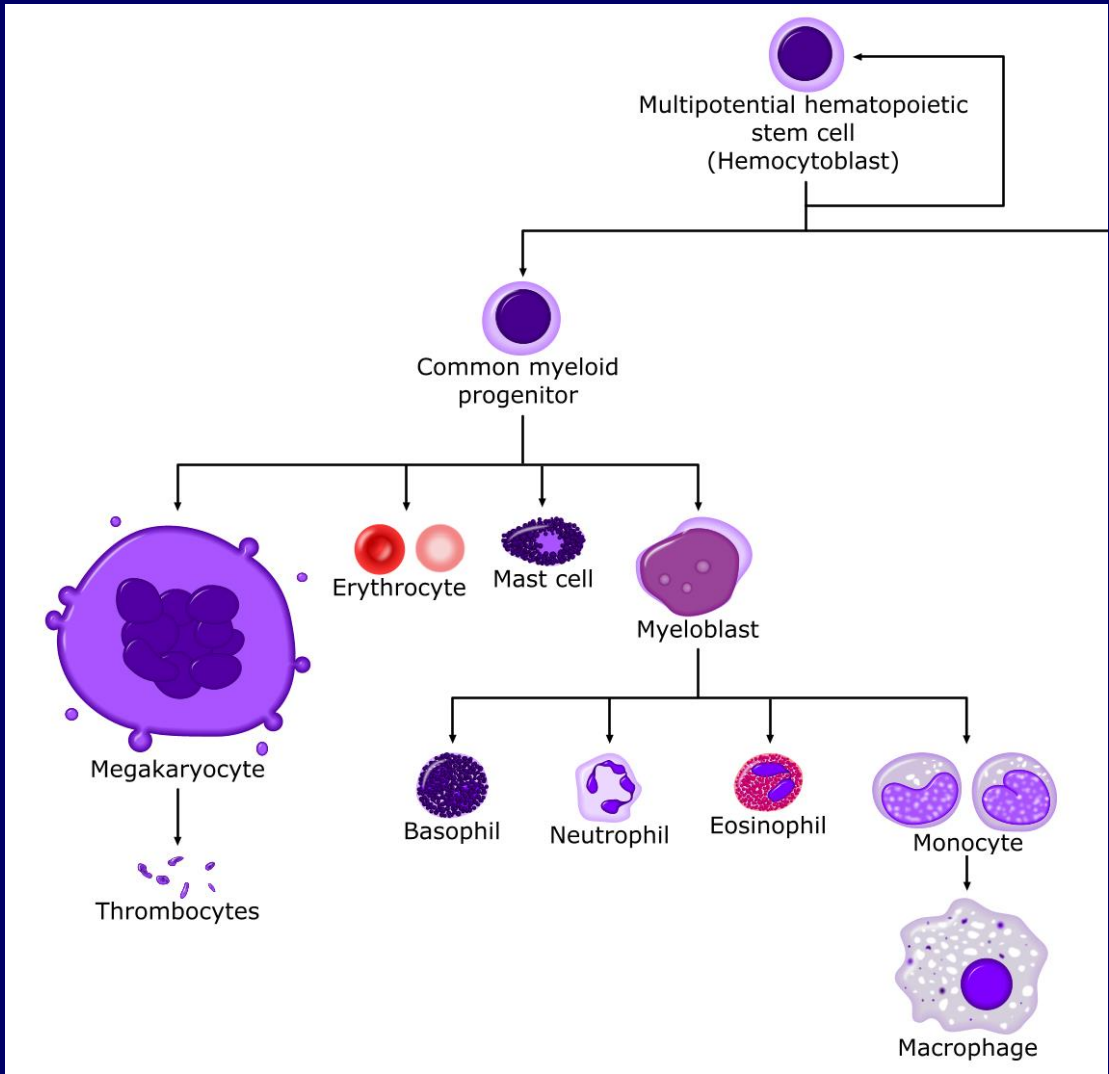
- Red cell precursors
- White cell precursors
- Platelet precursors (megakaryocytes)

Myelodysplastic syndrome definition

“Clonal bone marrow stem cell disorder characterized by ineffective blood cell production”

- Clonal - Arises in a single stem cell in the bone marrow.
- Ineffective blood cell production – Blood precursor cells are present in the bone marrow, but do not produce normal numbers of blood cells.
- Myelodysplastic - Bone marrow cells have an abnormal appearance.

Bone marrow stem cells



Myelodysplastic syndrome findings

One or more low blood count(s)

- Low red blood cell count/hemoglobin/hematocrit (anemia) in 85%
- Low white count cell count (neutropenia) in 50%
- Low platelet count (thrombocytopenia) in 60%

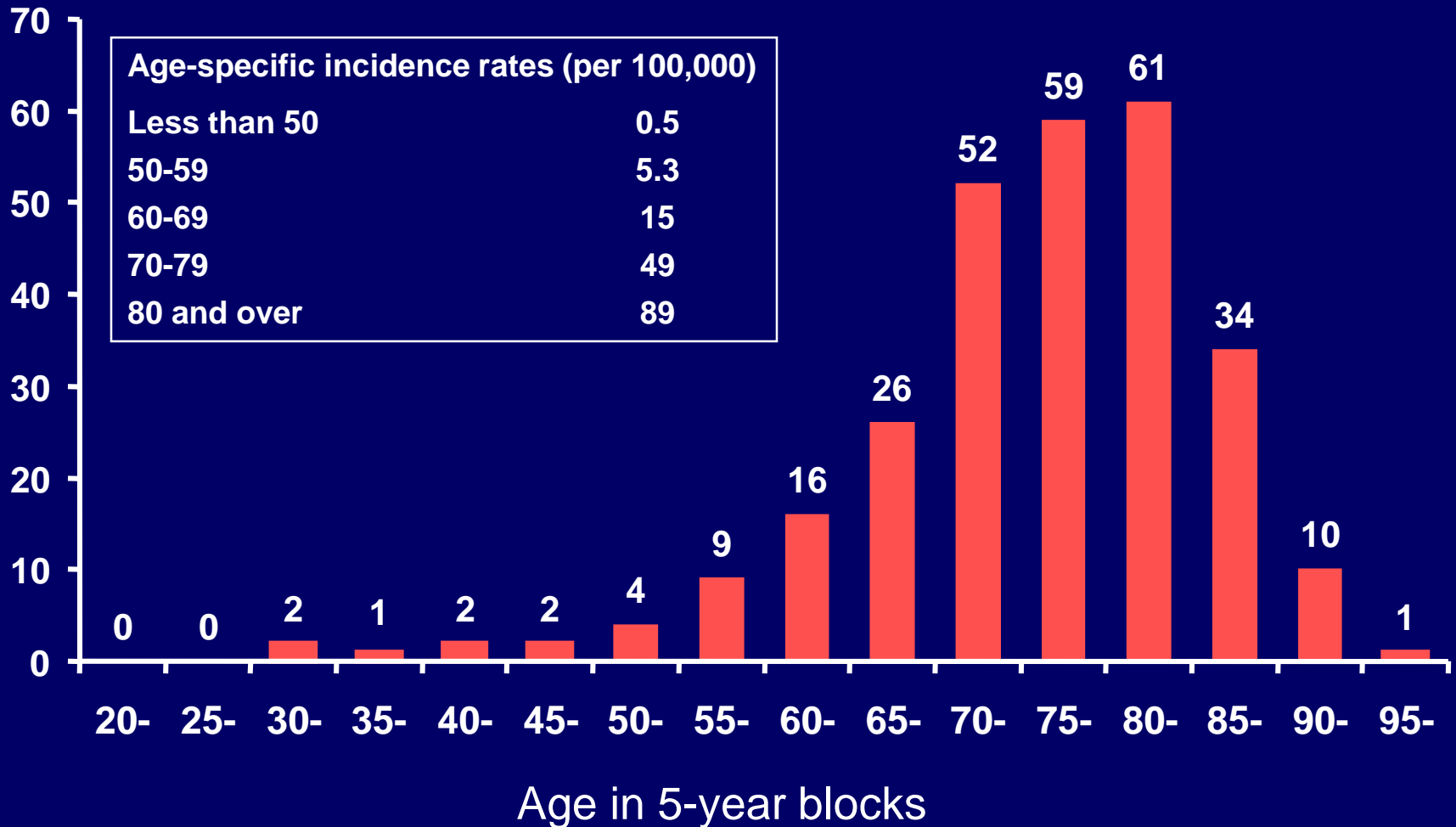
Myelodysplastic syndrome presentation

- Discovered after a blood count is drawn due to symptoms, including:
 - Fatigue, weakness, shortness of breath (anemia)
 - Infections (neutropenia)
 - Bleeding, petechiae, bruising (thrombocytopenia)
- Discovered incidentally

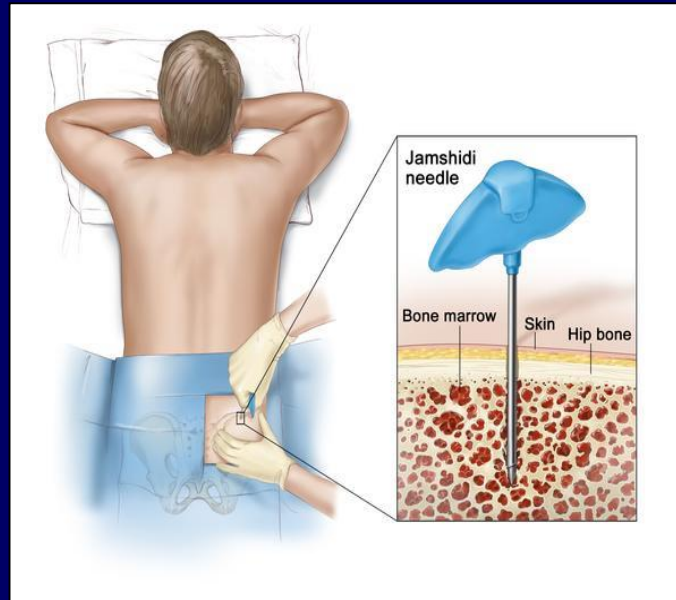
Myelodysplastic syndrome statistics

- 20,000 - 30,000 estimated new cases each year in the United States
- Average age 76 years
- Male > female: 4.5 vs. 2.7/100,000/year
- Acute leukemia ($\geq 20\%$ blasts in the bone marrow) develops in 25%
- Risk factors: age, chemicals, chemotherapy, radiation, tobacco, genetic abnormalities

Age-related incidence of MDS



Bone marrow aspirate and biopsy



Aspirate

- Morphology (appearance of cells under the microscope)
- Cytogenetics (chromosome analysis)
- Molecular (mutation analysis)

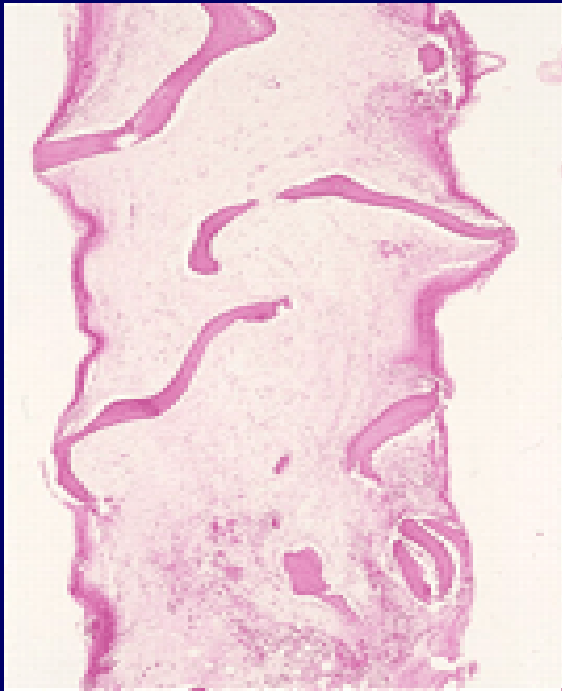
Biopsy

- Cellularity (amount of cells in the bone marrow)

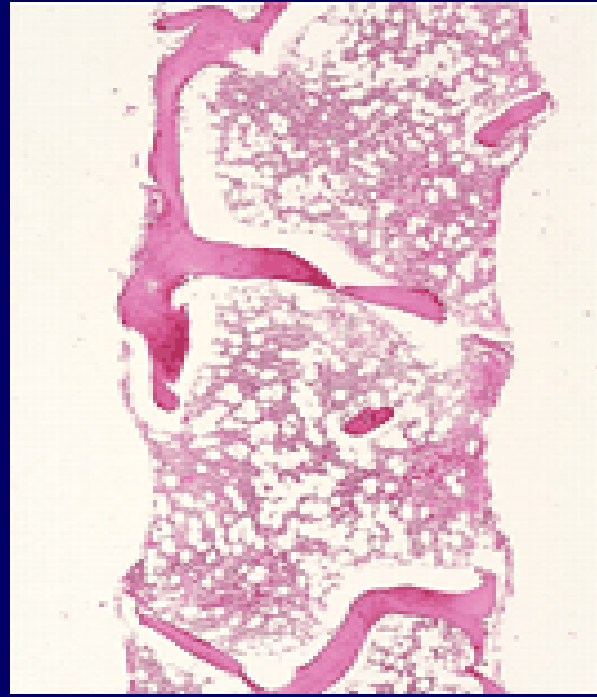
Myelodysplastic syndrome diagnosis

- Adequate numbers of cells (“cellularity”) are present in the bone marrow.
- Red cell, white cell and platelet precursors (megakaryocytes) are present in the bone marrow.
- Bone marrow cells have an abnormal appearance (“dysplasia”).

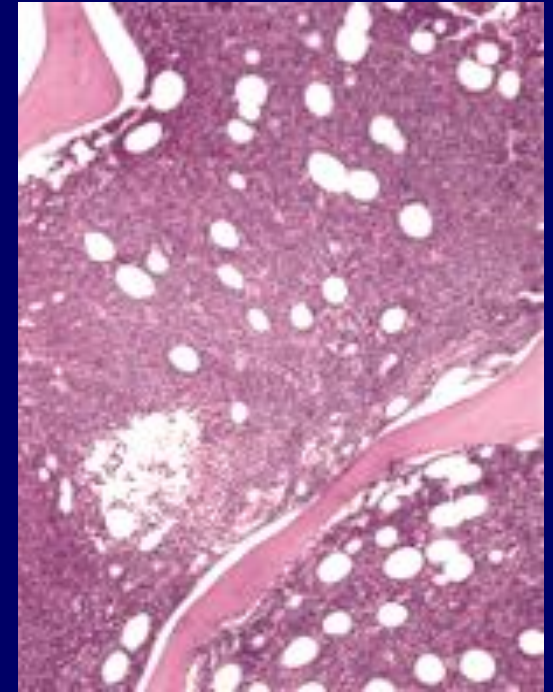
Bone marrow cellularity



Decreased

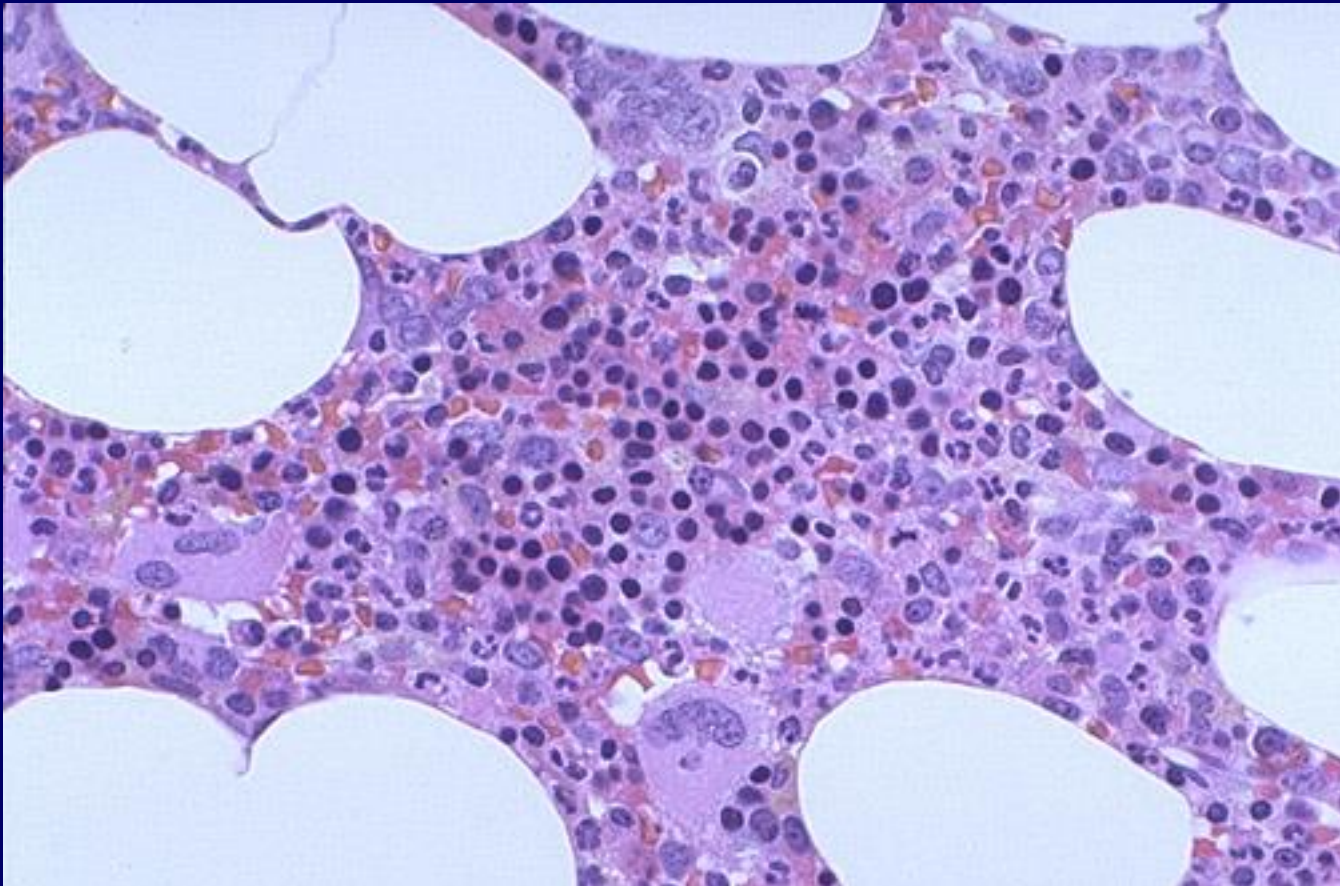


Normal

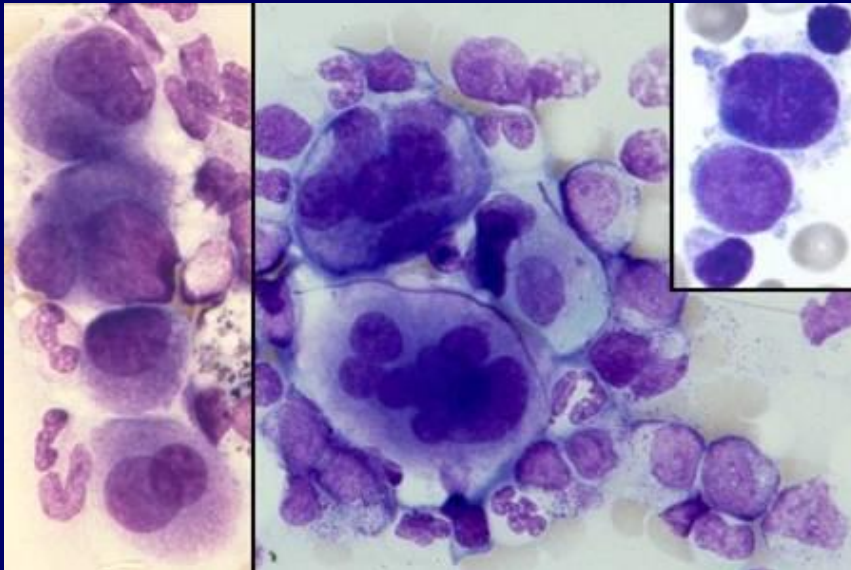
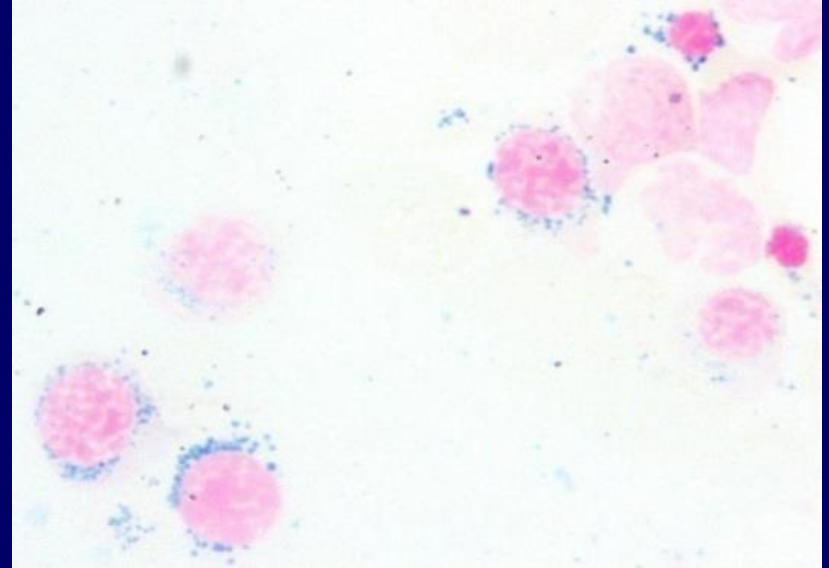
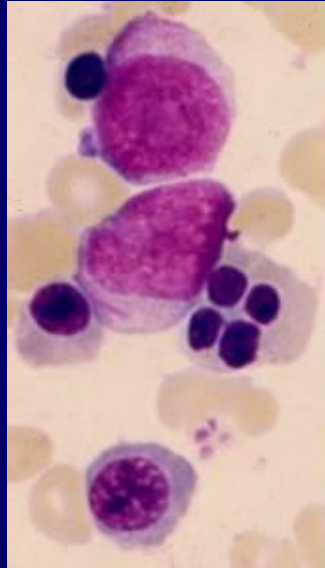
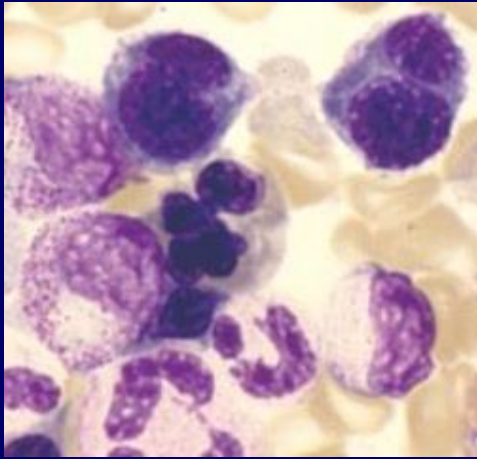


Increased

Red cell, white cell and platelet precursors (megakaryocytes) are present

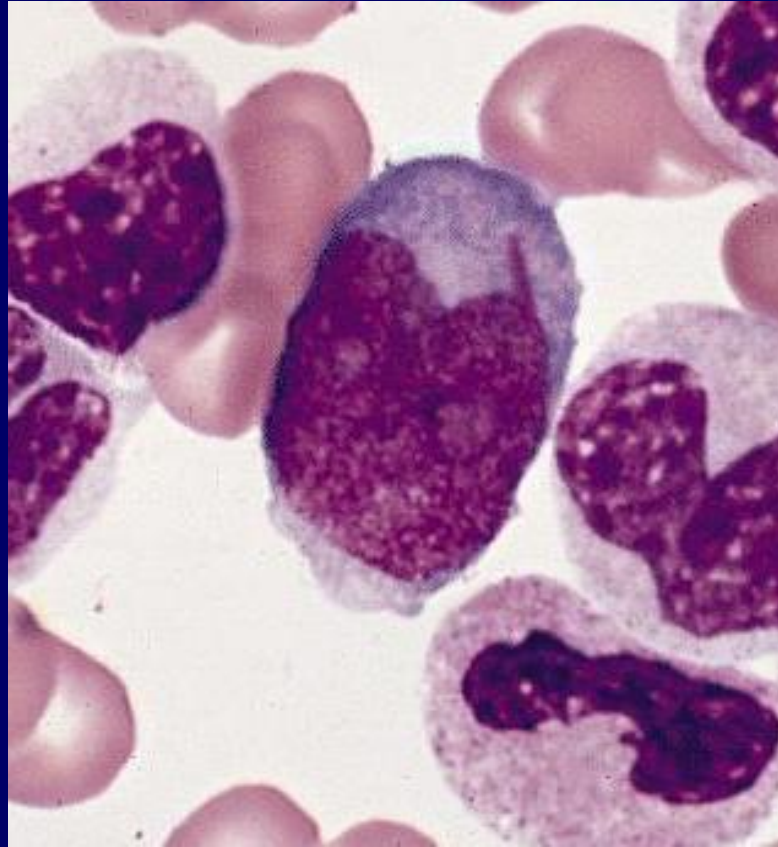


Dysplasia



- Red cell precursors
- White cell precursors
- Megakaryocytes

Myeloblasts



Normal bone marrow - <5%

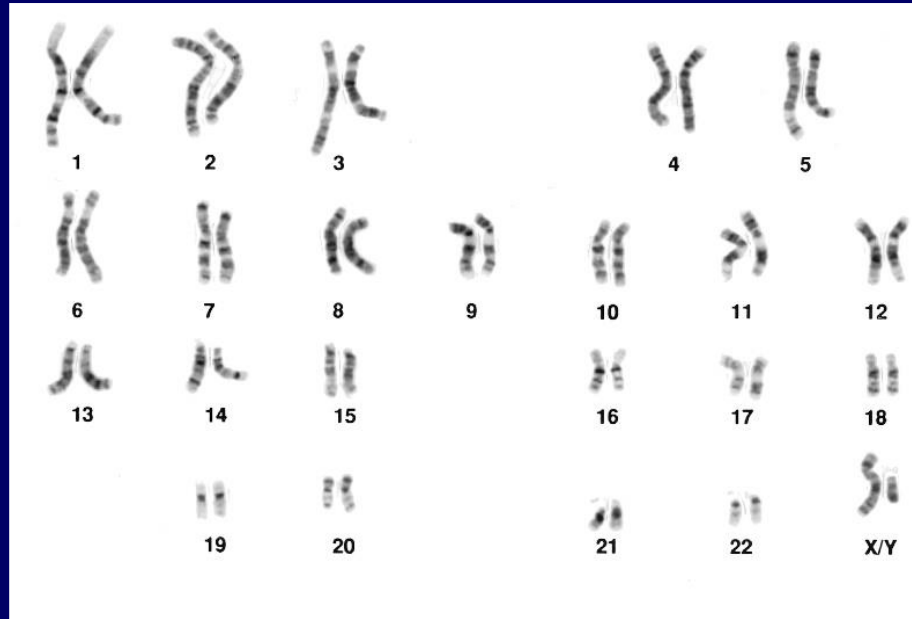
MDS - <20%

Acute myeloid leukemia (AML) - \geq 20%

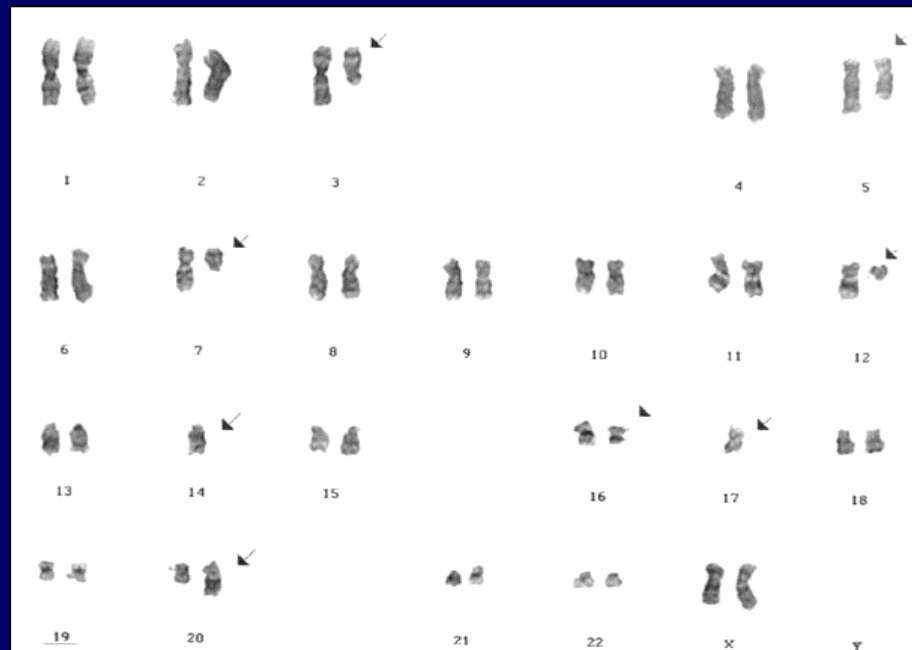
Evaluate for other causes of low blood counts and/or dysplasia

- Medications
- Vitamin B12 deficiency
- Nutrition
- Autoimmune
- Infections
- Enlarged spleen
- Alcohol
- Chemotherapy
- etc... etc... etc...

Chromosome analysis

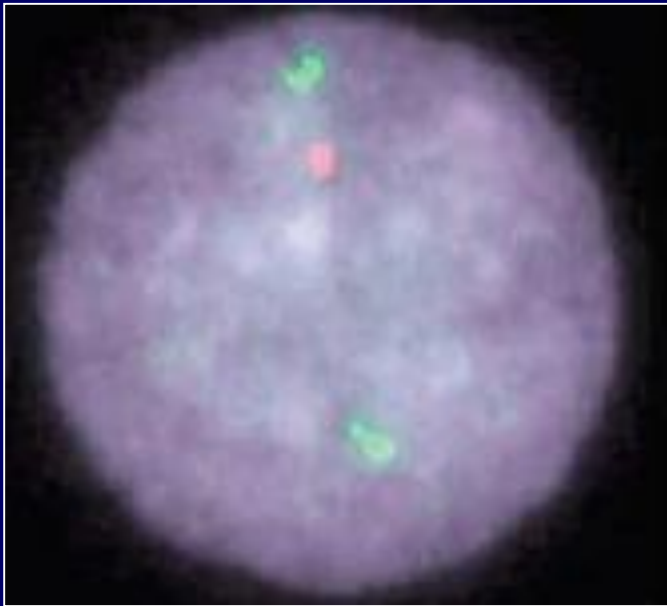


Normal

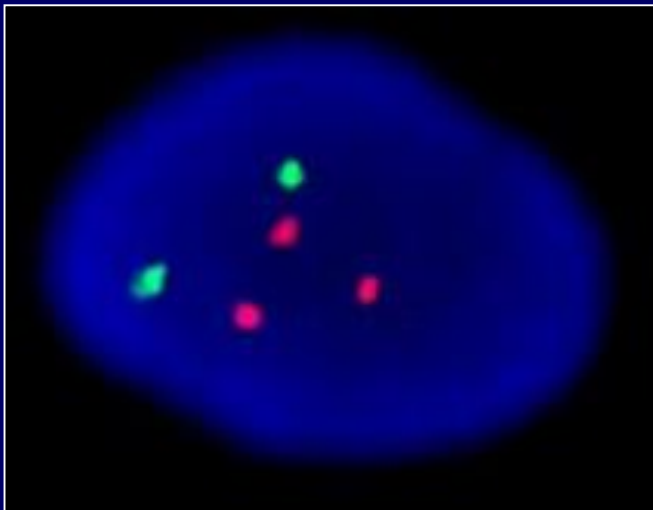


Abnormal

Fluorescence in situ hybridization (MDS FISH)

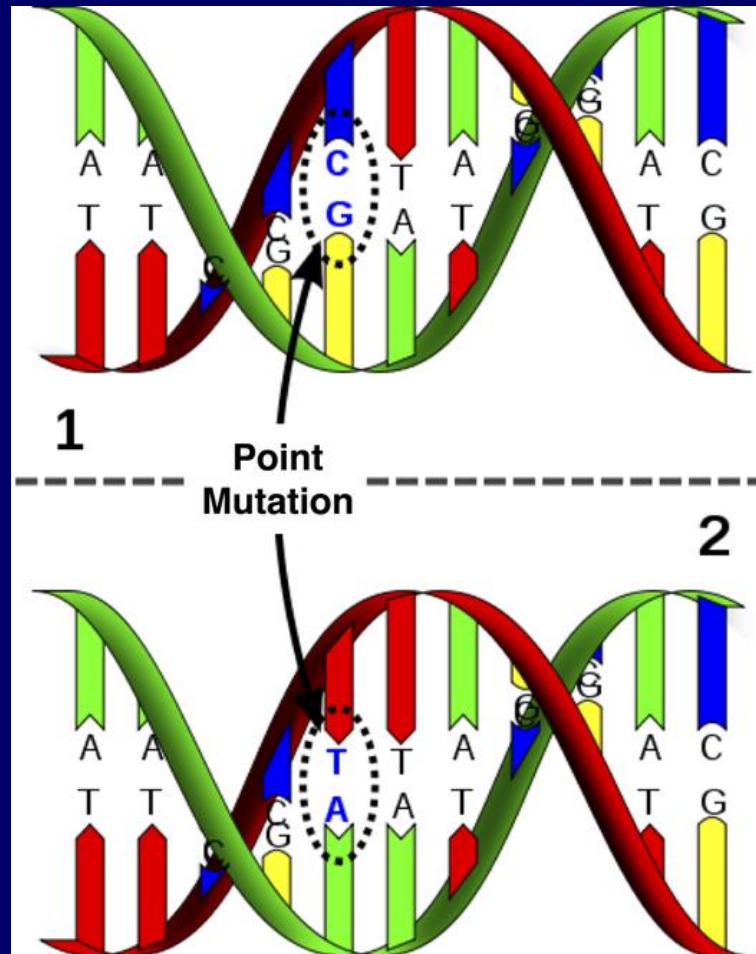


del(5q)



+8

Mutations



Myelodysplastic syndrome mutations

Chromatin modification

ASXL1	14-29%
EZH2	6-8%

Transcription regulation

RUNX1	9-16%
BcoR	4%
ETV6	1.3-3%

DNA methylation

TET2	12-23%
DNMT3A	13-18%
IDH2	2-9%
IDH1	2-4%

RNA splicing

SF3B1	9-75%
U2AF1/U2AF35	12-16%
SRSF2	12-15%
ZRSR2	3-11%

DNA repair

TP53	2-21%
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Signal transduction

NRAS	3-4%
JAK2	3%
CBL	2%

Cohesin complex

STAG2	6-8%
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MDS Prognosis

- Number of low blood counts (hemoglobin <10 , neutrophils <1800 , platelets $<100,000$)
- Percentage of bone marrow blasts
- Chromosome abnormalities
- (Mutations)