Bone Marrow Biopsy to Diagnosis

The role of the pathologist

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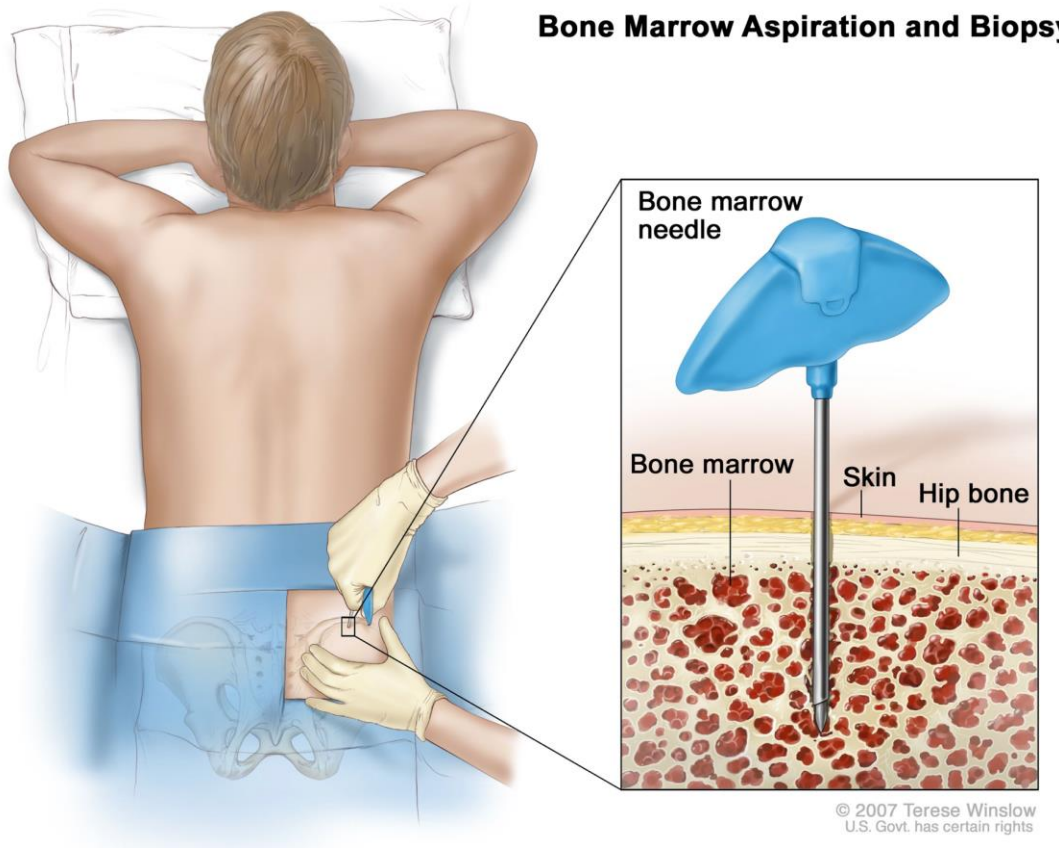
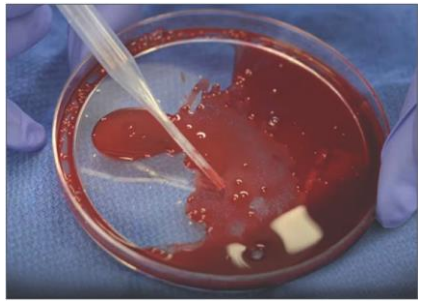
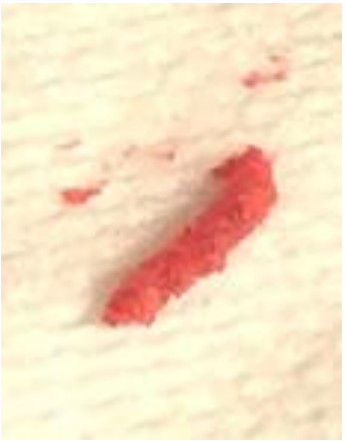
Bone Marrow Biopsy

- A bone marrow biopsy allows pathologists to evaluate the bone marrow and is required to diagnosis
- Bone marrow biopsies are performed on either the left or right the iliac crest (hip)
- The bone marrow biopsy consists of the two parts:
  - Aspirate (liquid)
  - Core (tissue)





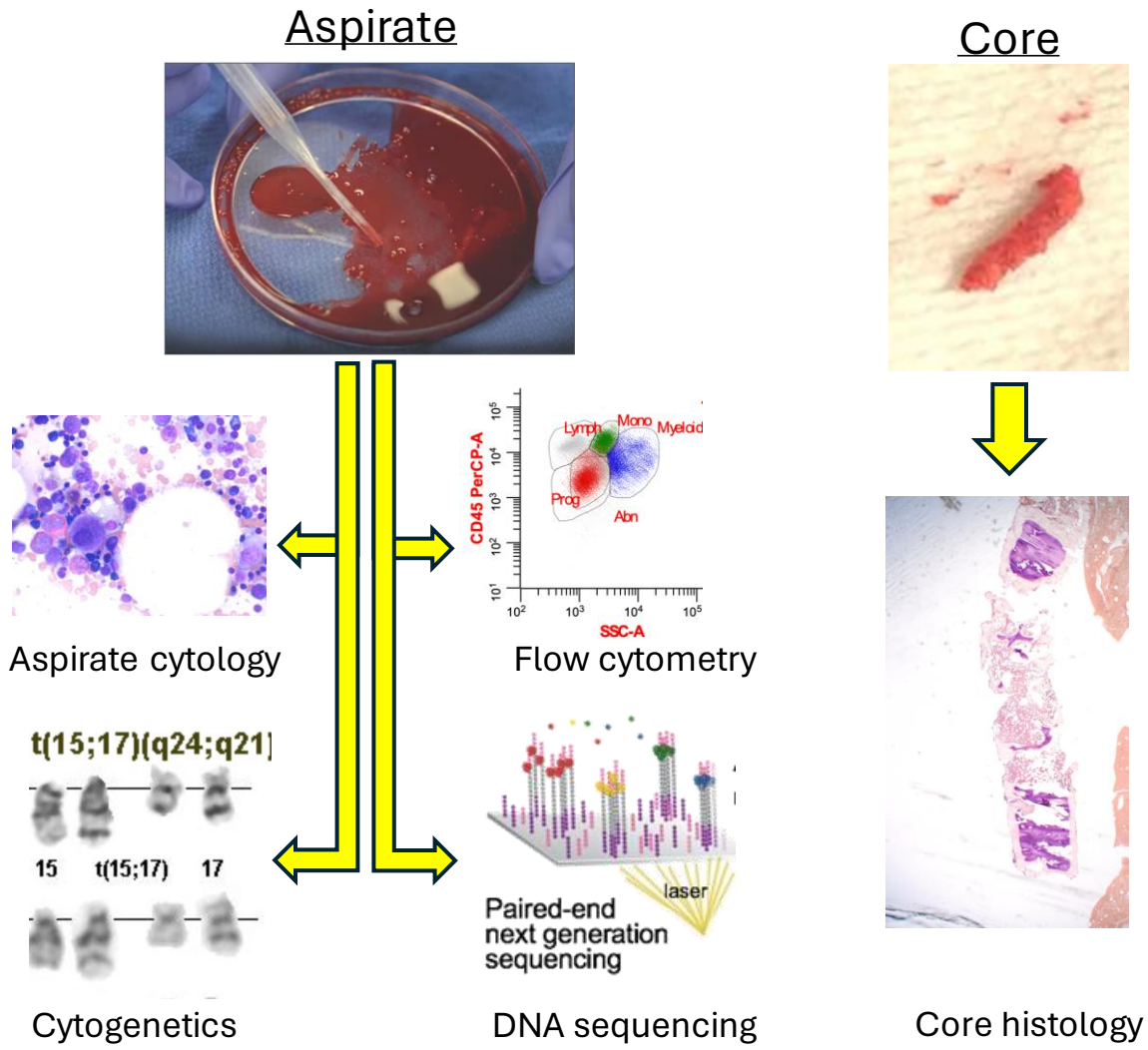
Bone Marrow Aspirate



Bone Marrow Core

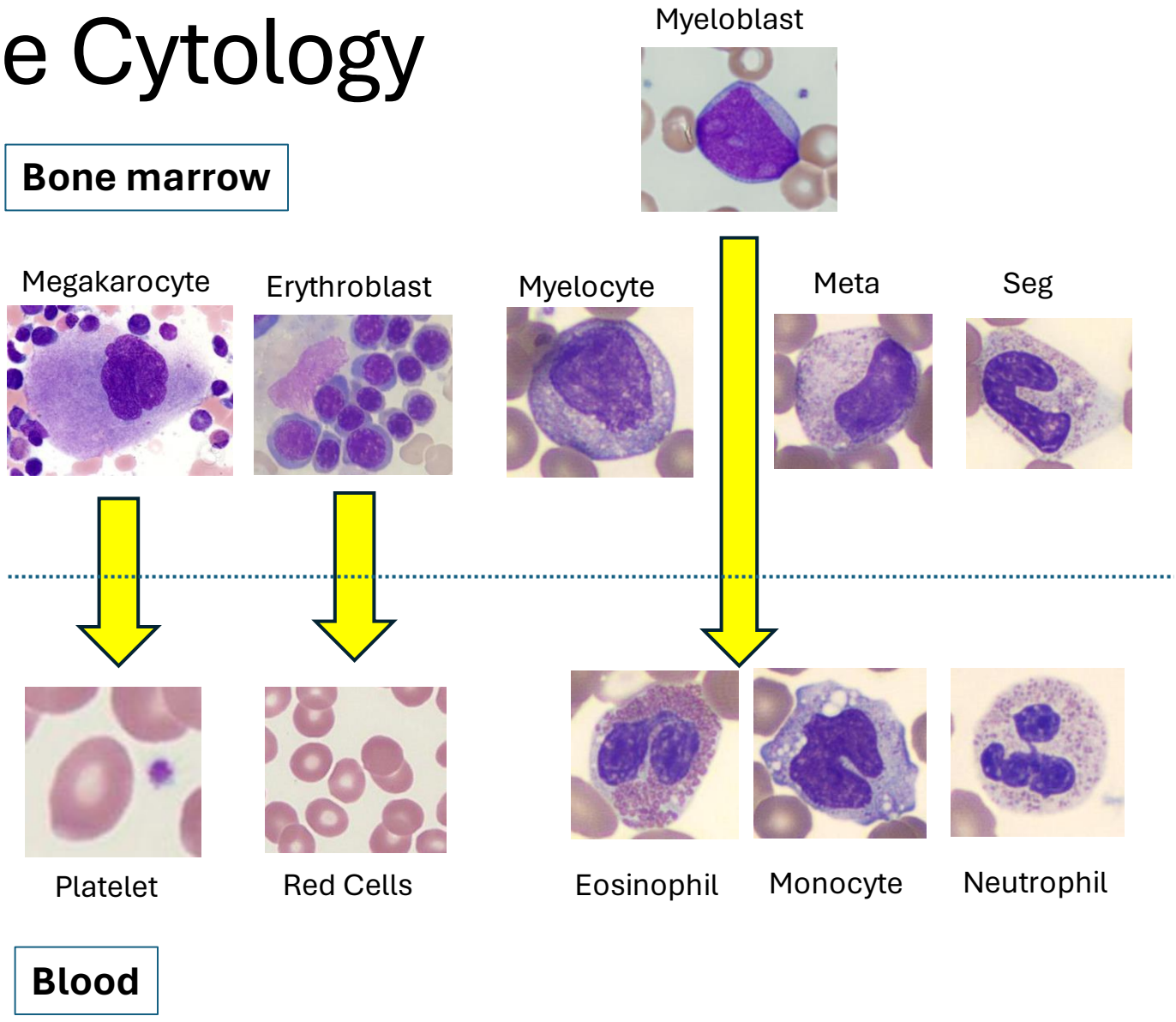
Bone Marrow Diagnostic Testing

- Multiple different tests are performed on the bone marrow biopsy material to make a diagnosis.
  - Core histology
  - Aspirate cytology
  - Flow cytometry
  - Cytogenetics
  - DNA mutation analysis



Bone Marrow Aspirate Cytology

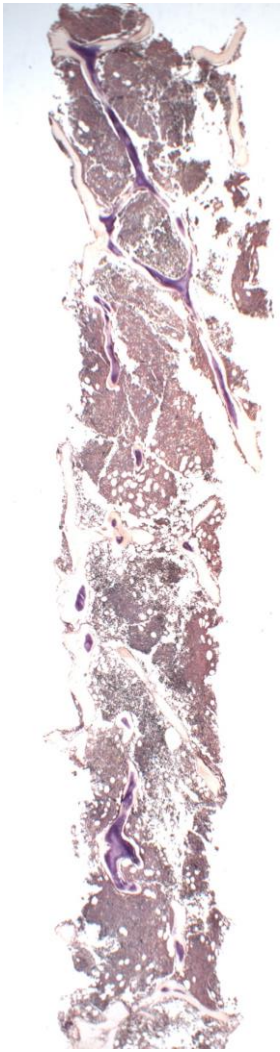
- Bone marrow aspirate is stained and evaluated by a pathologist under the microscope
- Typically 200-500 cells are counted to make a bone marrow differential
- Morphology of individual cells is evaluated

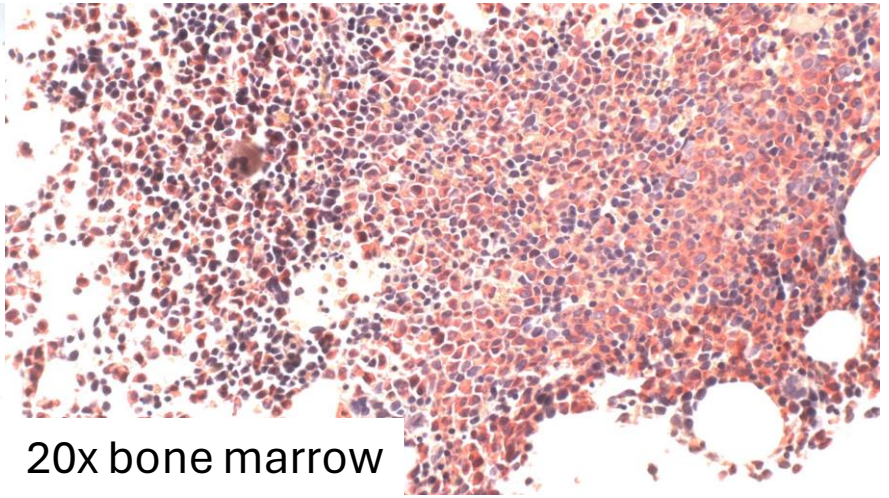


ASH Image Bank

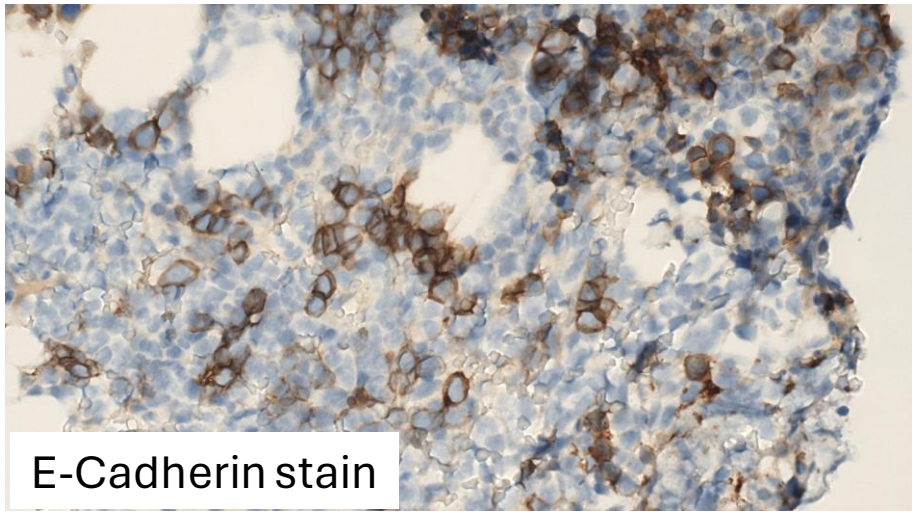
Bone Marrow Histology

- Sections of the bone marrow core are made in the lab and then stained to visualize cells.
- The pathologist will evaluate the bone marrow core under the microscope to determine cellularity and composition
- Different stains can be used to evaluate specific cell populations





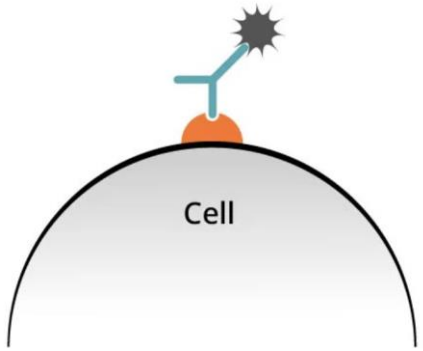
20x bone marrow

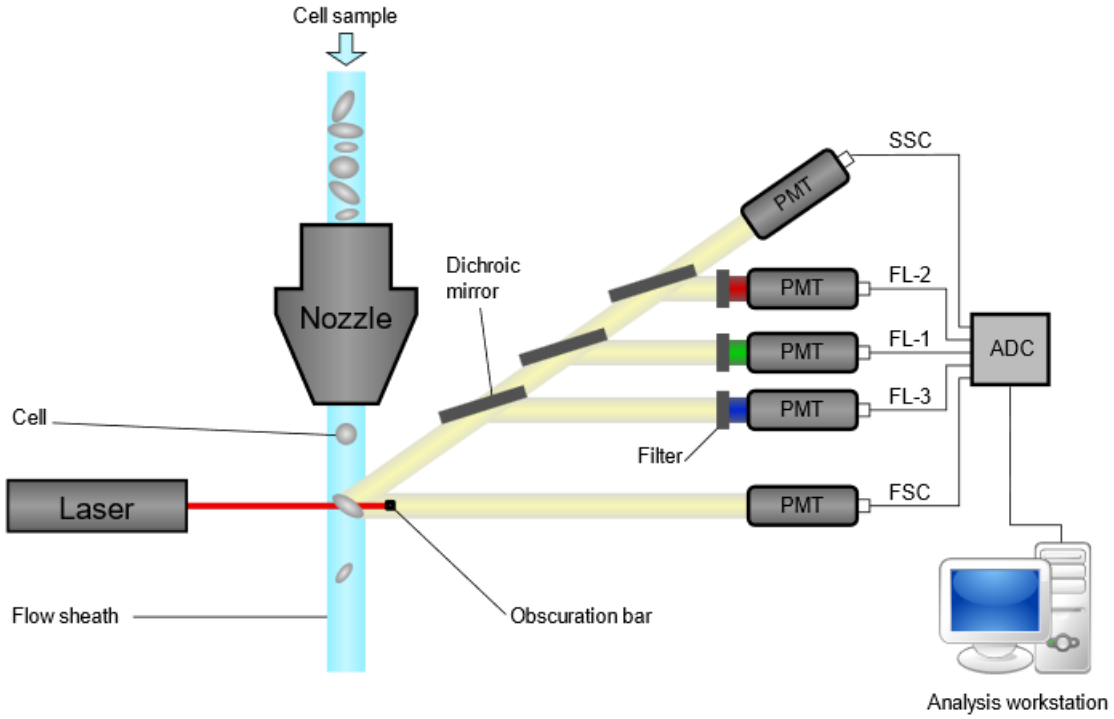


E-Cadherin stain

Flow Cytometry

- Flow cytometry measures antigen expression on individual cells.
- Flow can be used to quantitate specific populations (blasts, monocytes, B-cells, etc)
- Flow can be used to identify cells that have abnormal patterns of expression.





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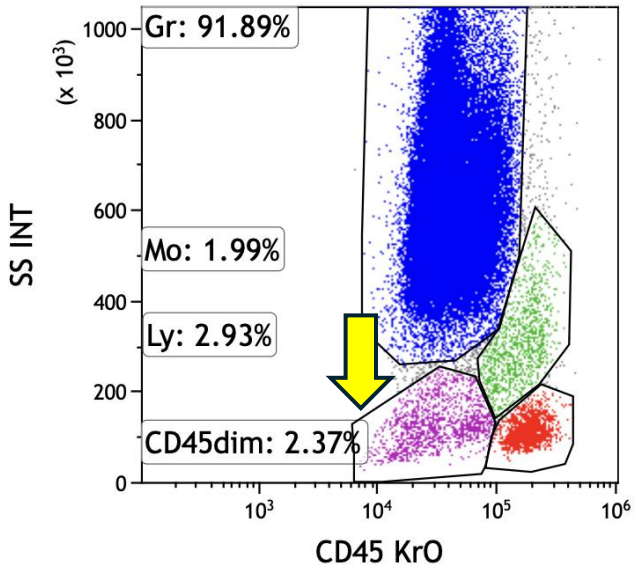
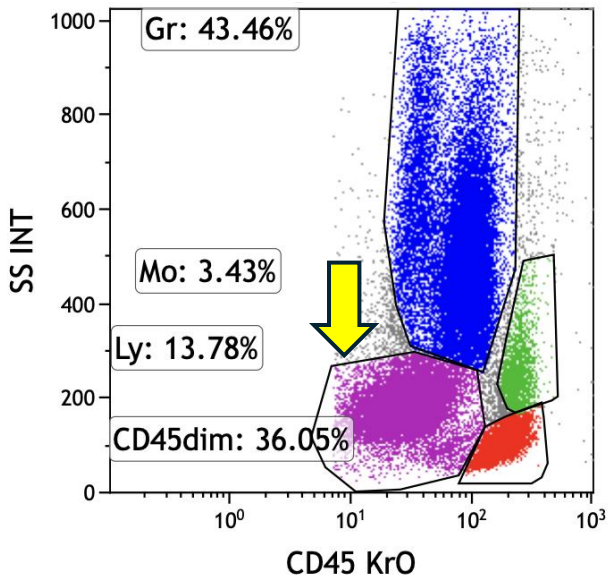


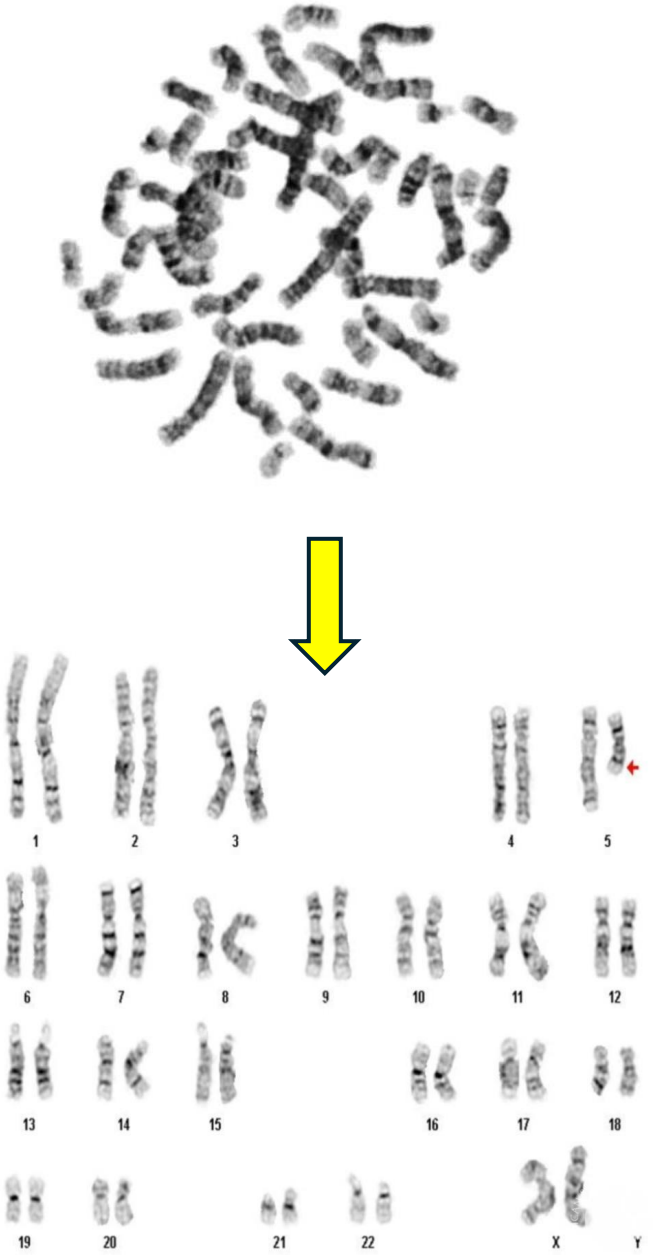
Normal Blast Number



Increased Blasts

Cytogenetics

- Cytogenetics identifies large changes in chromosomes
- Chromosomes (composed of DNA) are evaluated under the microscope to make a karyotype
- Can be used to identify MDS specific changes including del(5q) or -7.

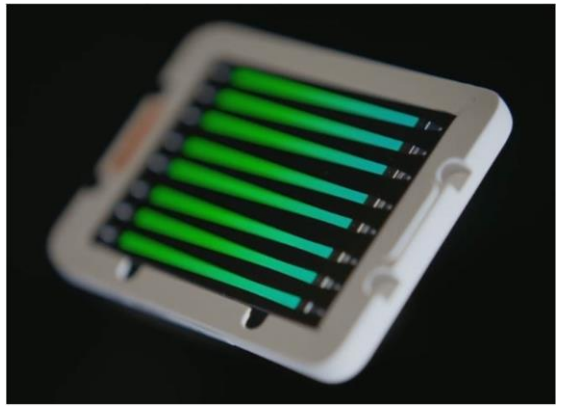


Del(5q)

ASH Image Bank

DNA Sequencing

- Identification of gene mutations can help diagnosis or risk stratify MDS
- Mutations can be inherited or more commonly acquired (somatic)
- Approximately 90% of MDS have an acquired gene mutation
- Sequencing can be targeted (a few genes) or the entire genome.



Illumina Sequencing Flow Cell

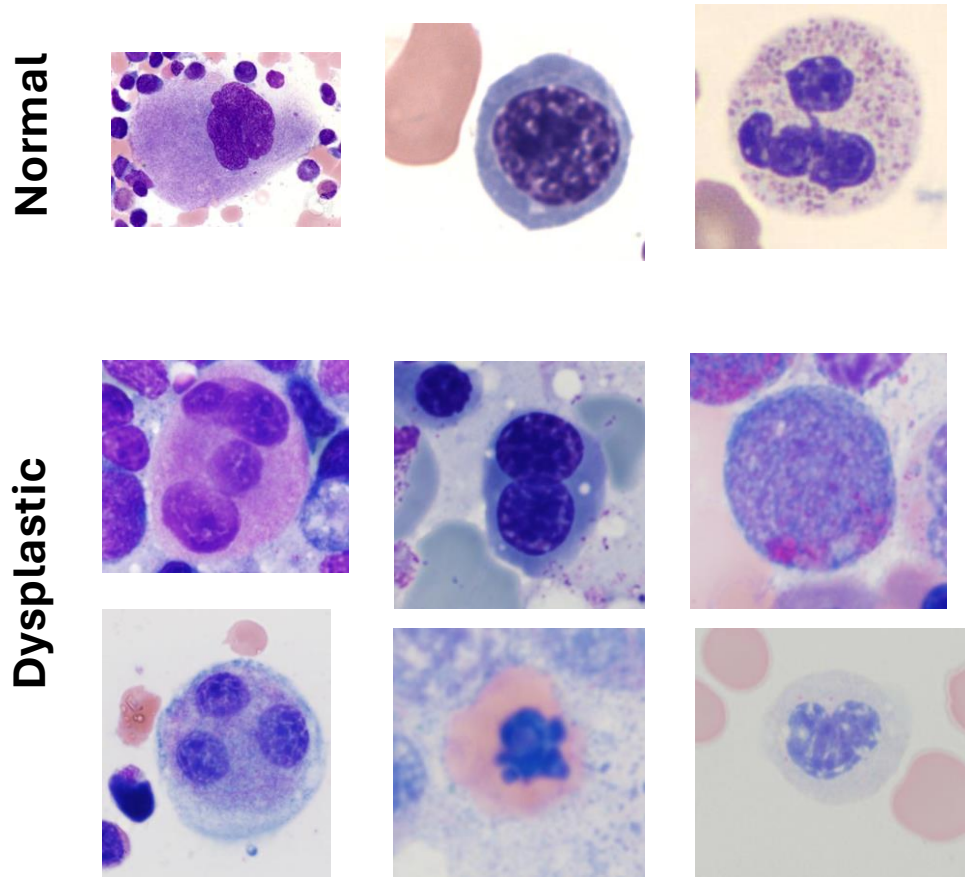
ChromoSeq

Illumina Inc

How is MDS Diagnosed?

- The diagnosis of MDS requires:
  - Unexplained cytopenia (low blood counts)
  - **Dysplasia** (cells look different)
  - ± Increased blasts (>5% of cells)
  - ± Cytogenetic findings (del(5q), -7, etc)
  - ± DNA mutations

Dysplasia can take many forms



MDS Classification

- MDS classification is designed to separate MDS sub-types based on risk
- High risk findings include increased blasts (>5%), TP53 gene mutations, or AML-like gene mutations
- Low risk findings include low blasts (<5%), del(5q), and SF3B1 gene mutations

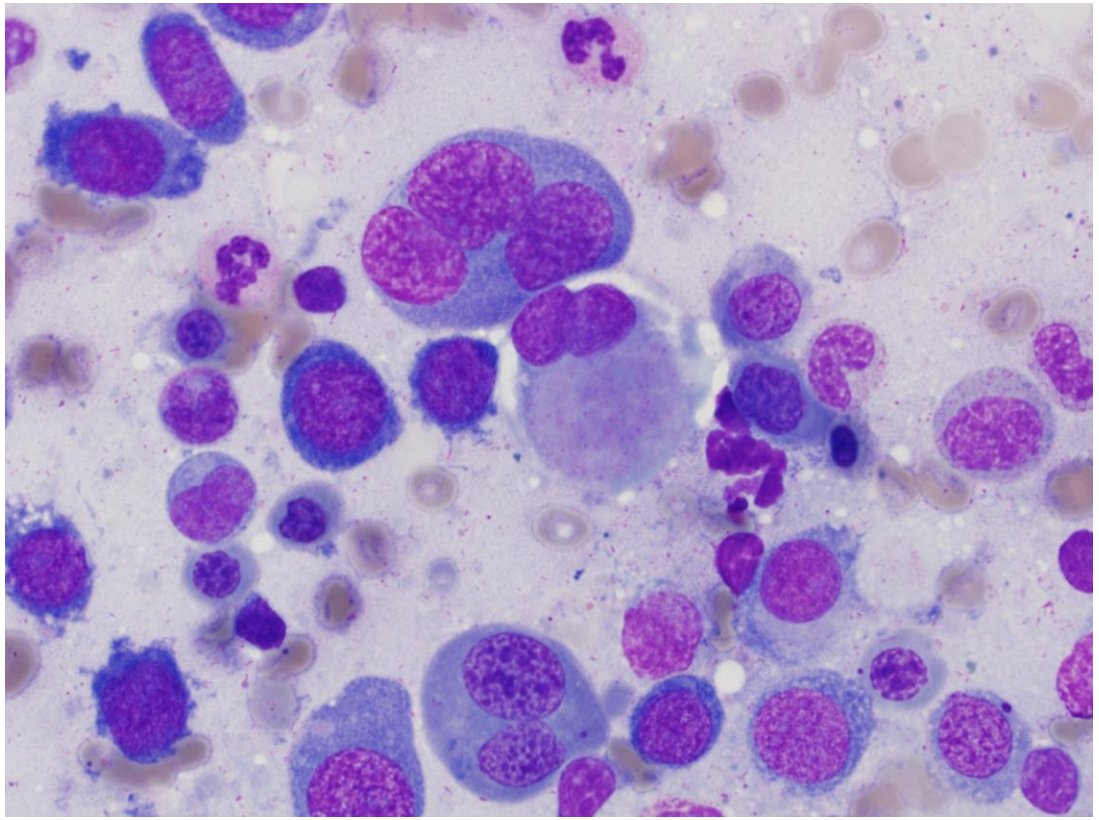
2022 World Health Organization Classification of MDS

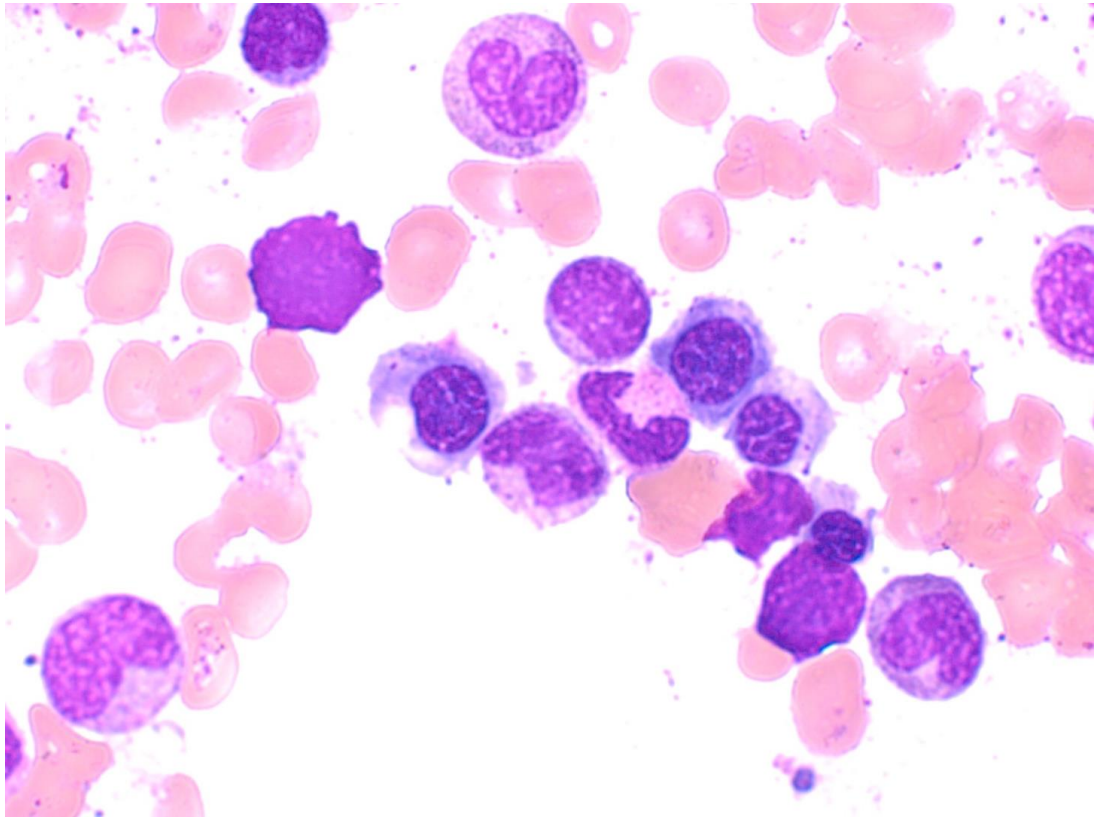
	Blasts	Cytogenetics	Mutations
MDS with defining genetic abnormalities			
MDS with low blasts and isolated 5q deletion (MDS-5q)	<5% BM and <2% PB	5q deletion alone, or with 1 other abnormality other than monosomy 7 or 7q deletion	
MDS with low blasts and *SF3B1* mutation[a] (MDS-*SF3B1*)		Absence of 5q deletion, monosomy 7, or complex karyotype	*SF3B1*
MDS with biallelic *TP53* inactivation (MDS-bi*TP53*)	<20% BM and PB	Usually complex	Two or more *TP53* mutations, or 1 mutation with evidence of *TP53* copy number loss or cnLOH
MDS, morphologically defined			
MDS with low blasts (MDS-LB)	<5% BM and <2% PB		
MDS, hypoplastic[b] (MDS-h)			
MDS with increased blasts (MDS-IB)			
MDS-IB1	5–9% BM or 2–4% PB		
MDS-IB2	10-19% BM or 5–19% PB or Auer rods		
MDS with fibrosis (MDS-f)	5–19% BM; 2–19% PB		

[a]Detection of ≥15% ring sideroblasts may substitute for *SF3B1* mutation. Acceptable related terminology: MDS with low blasts and ring sideroblasts.
[b]By definition, ≤25% bone marrow cellularity, age adjusted.
BM bone marrow, *PB* peripheral blood, *cnLOH* copy neutral loss of heterozygosity.

Test Time

Dysplastic or Not?





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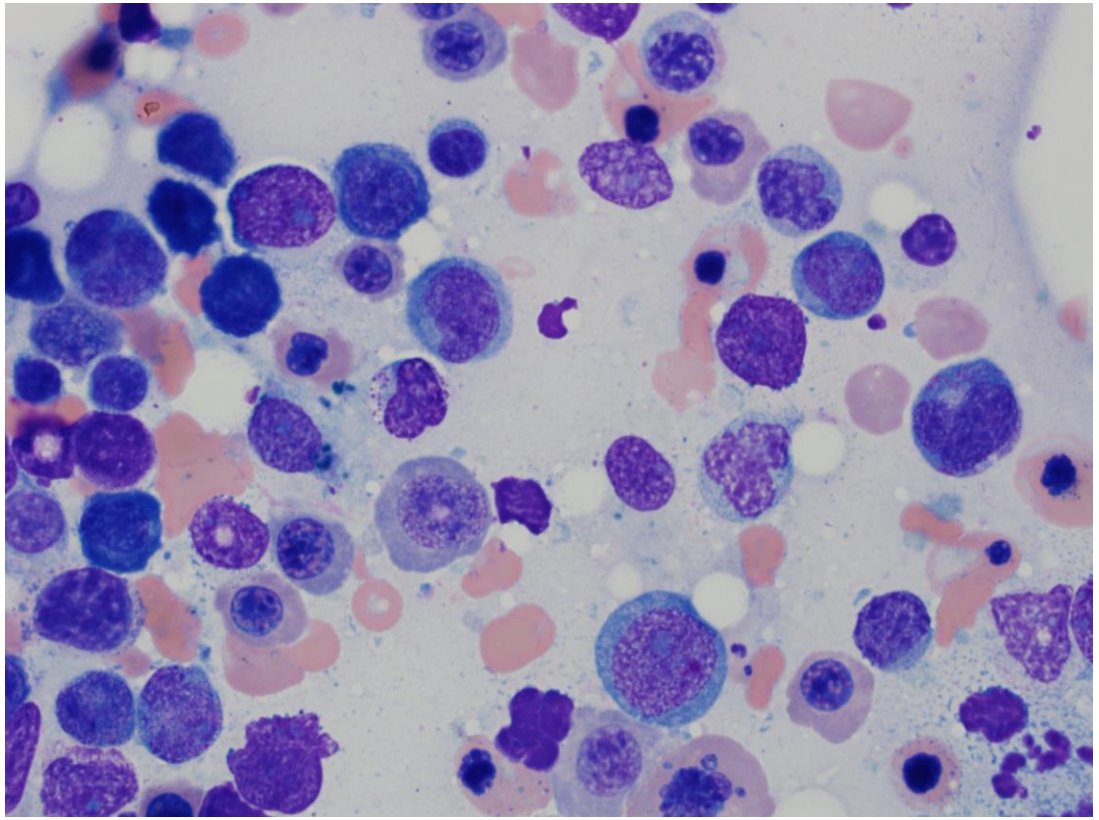
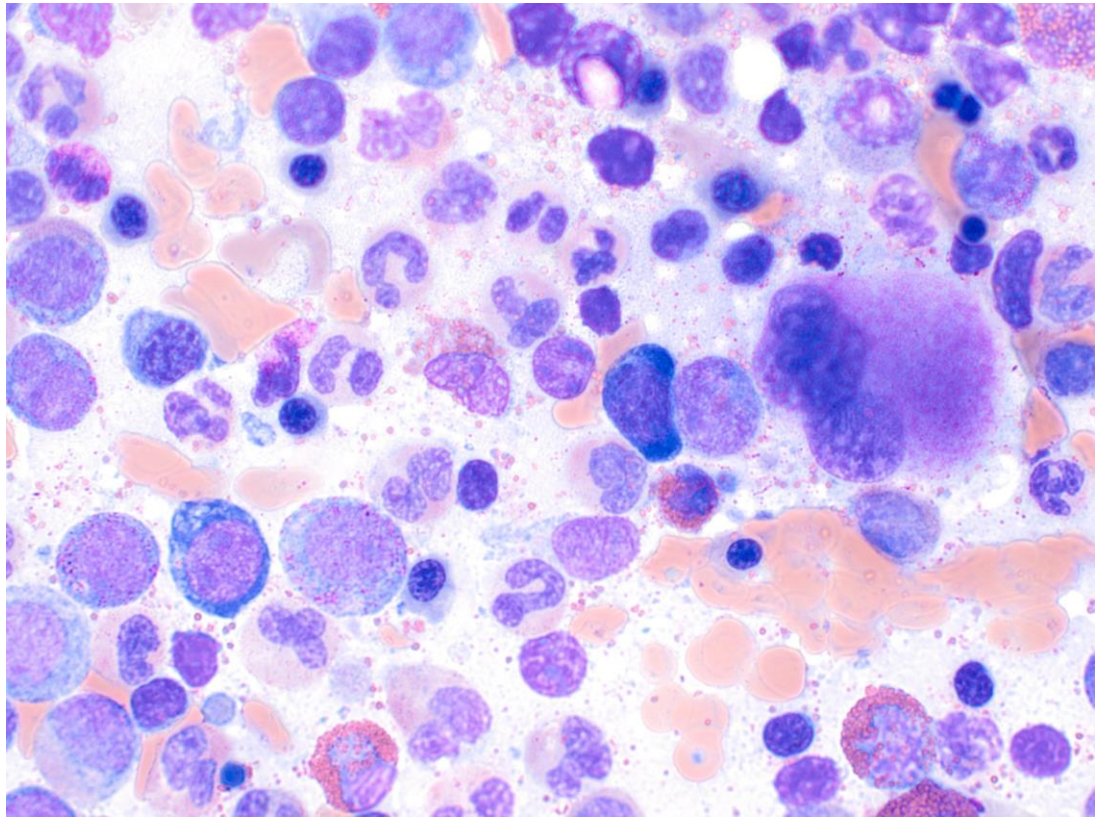
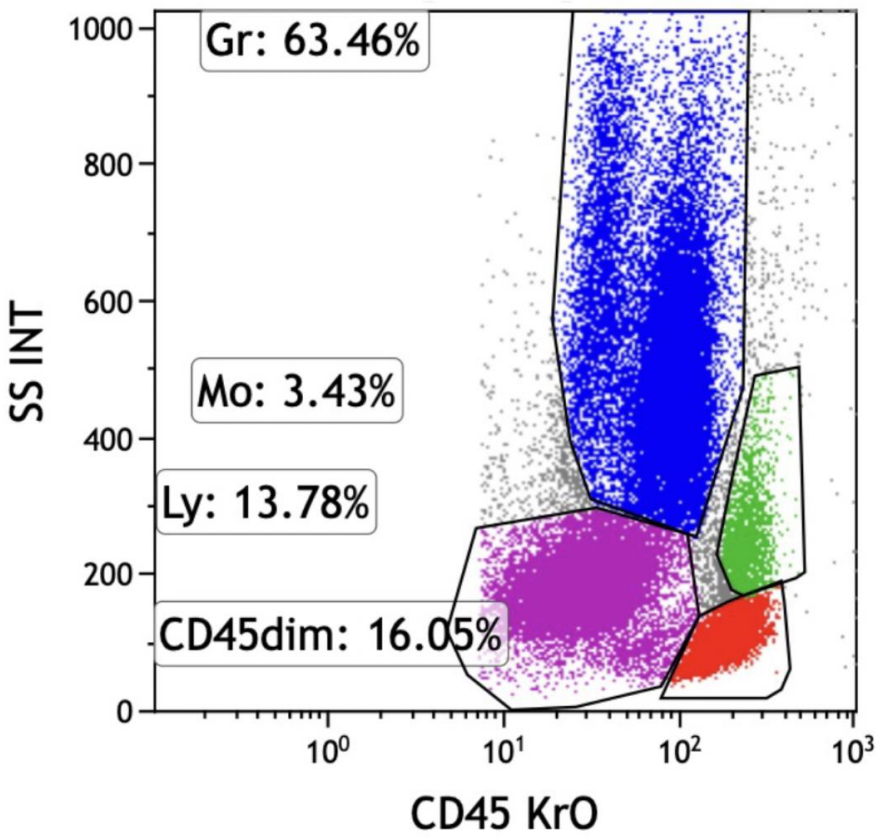




MDS Diagnosis

Bone Marrow Flow Cytometry



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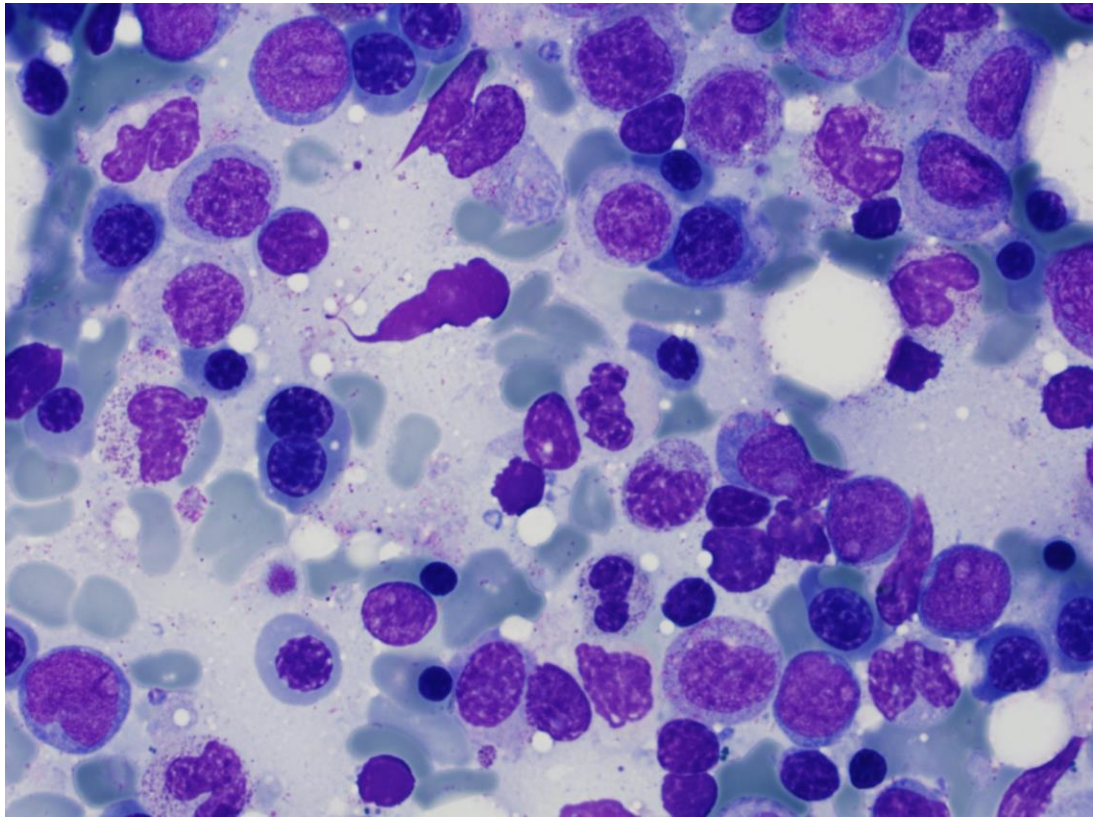
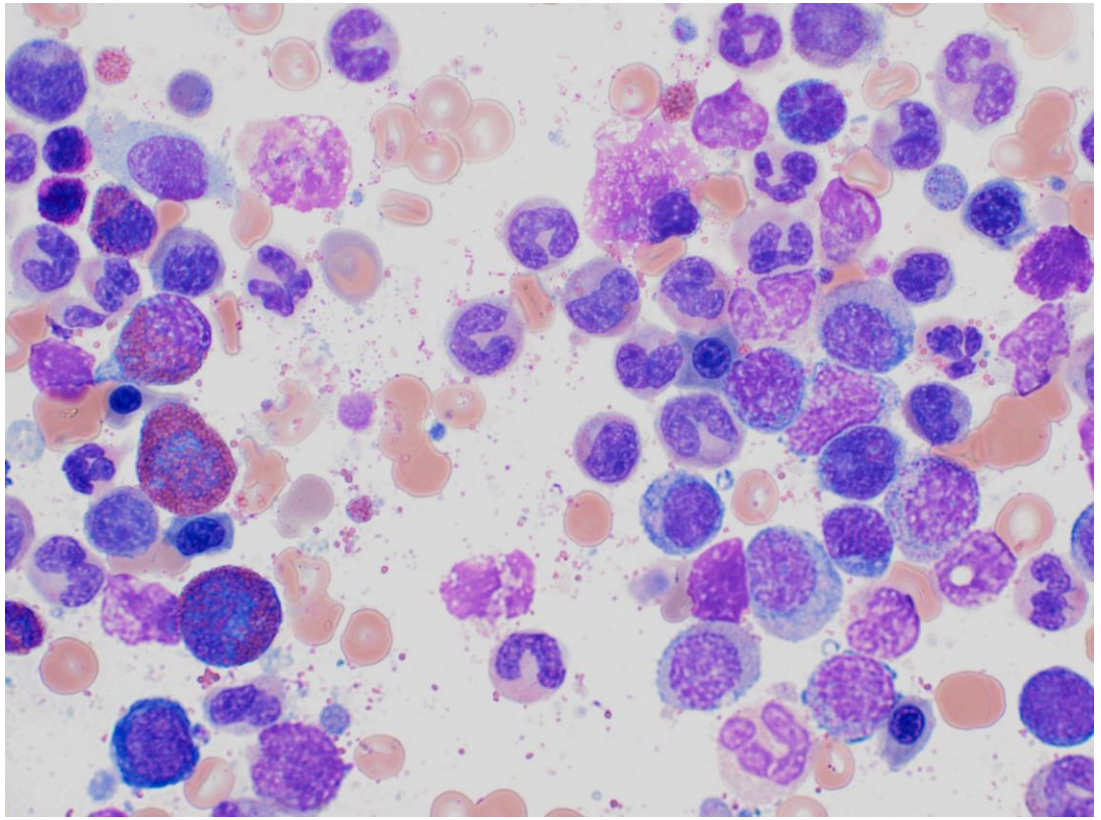
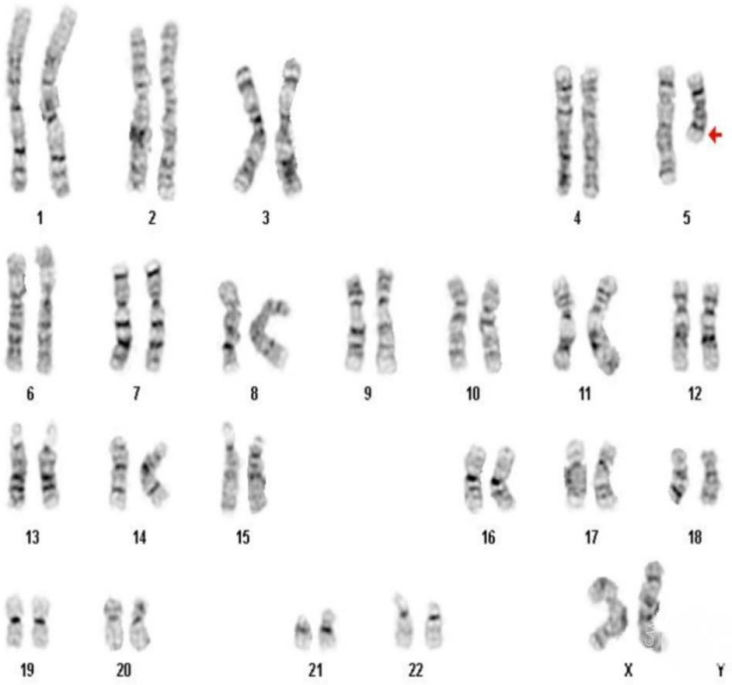




MDS Diagnosis

Bone Marrow Cytogenetics



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