

# Introduction to Bone Marrow Morphology: Normal and Dysplastic

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# Conflicts of Interest

- No relevant financial conflicts with regard to this lecture
- Consultant to Treeline Biosciences, Pure Marrow

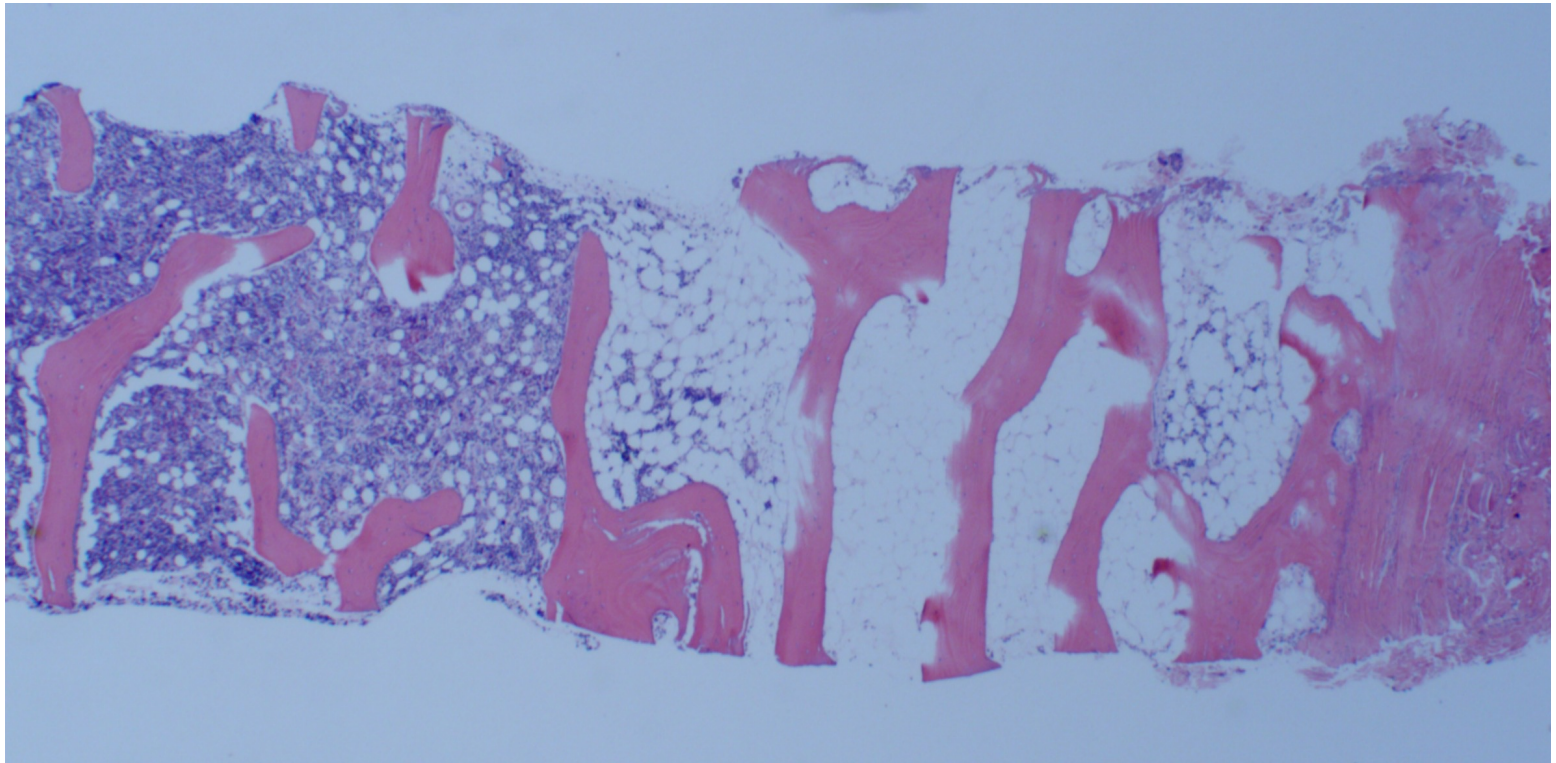
# Major Indication: Disease diagnosis

- Unexplained cytopenia
- Acute leukemia
- Chronic leukemia
- Myelodysplastic syndrome
- Myeloproliferative disease
- Plasma cell neoplasm
- Non-Hodgkin lymphoma
- Hodgkin lymphoma
- Aplastic anemia
- Fever of unknown origin
- Small cell tumors of childhood
- Mast cell disease
- Disseminated granulomatous disease
- Metastatic carcinoma

# Major Indication: Therapeutic Follow-up

- Chemotherapy/bone marrow transplantation
  - Minimal residual disease
- Treatment of isolated cytopenia
- Aplastic anemia

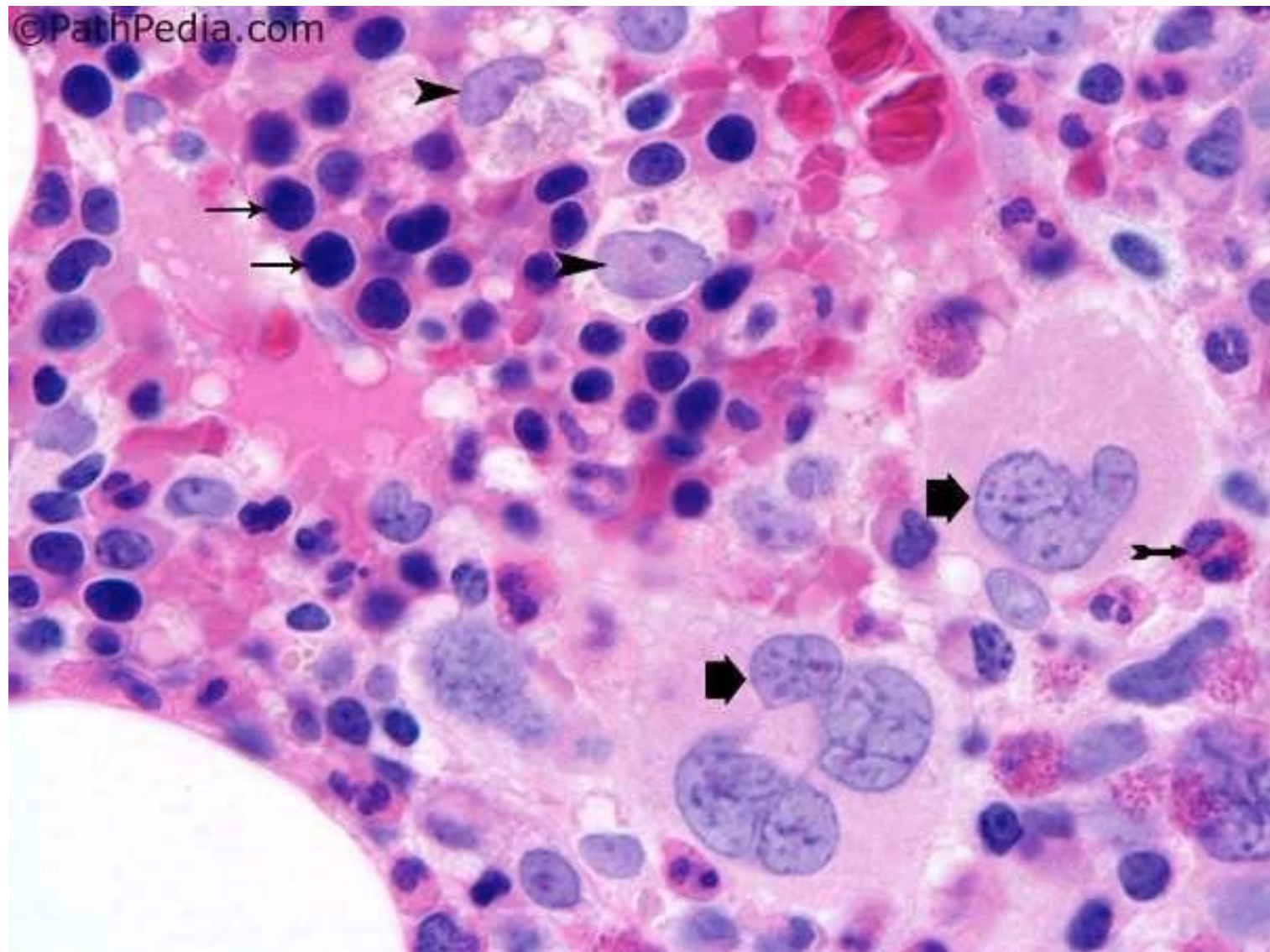




# Basic Components of BMBX evaluation

- Core biopsy
  - Cellularity
  - 3 lineages: quantity, quality of maturation
  - Lymphoid aggregates
  - Trabecular bone
- Aspirate
  - Cell differential count
  - 3 lineages: dysplasia, if any
- Flow cytometry
- Genetics/Molecular
  - Often referencing the prior since current sample is in process
  - Summative Interpretation

# Normal bone marrow





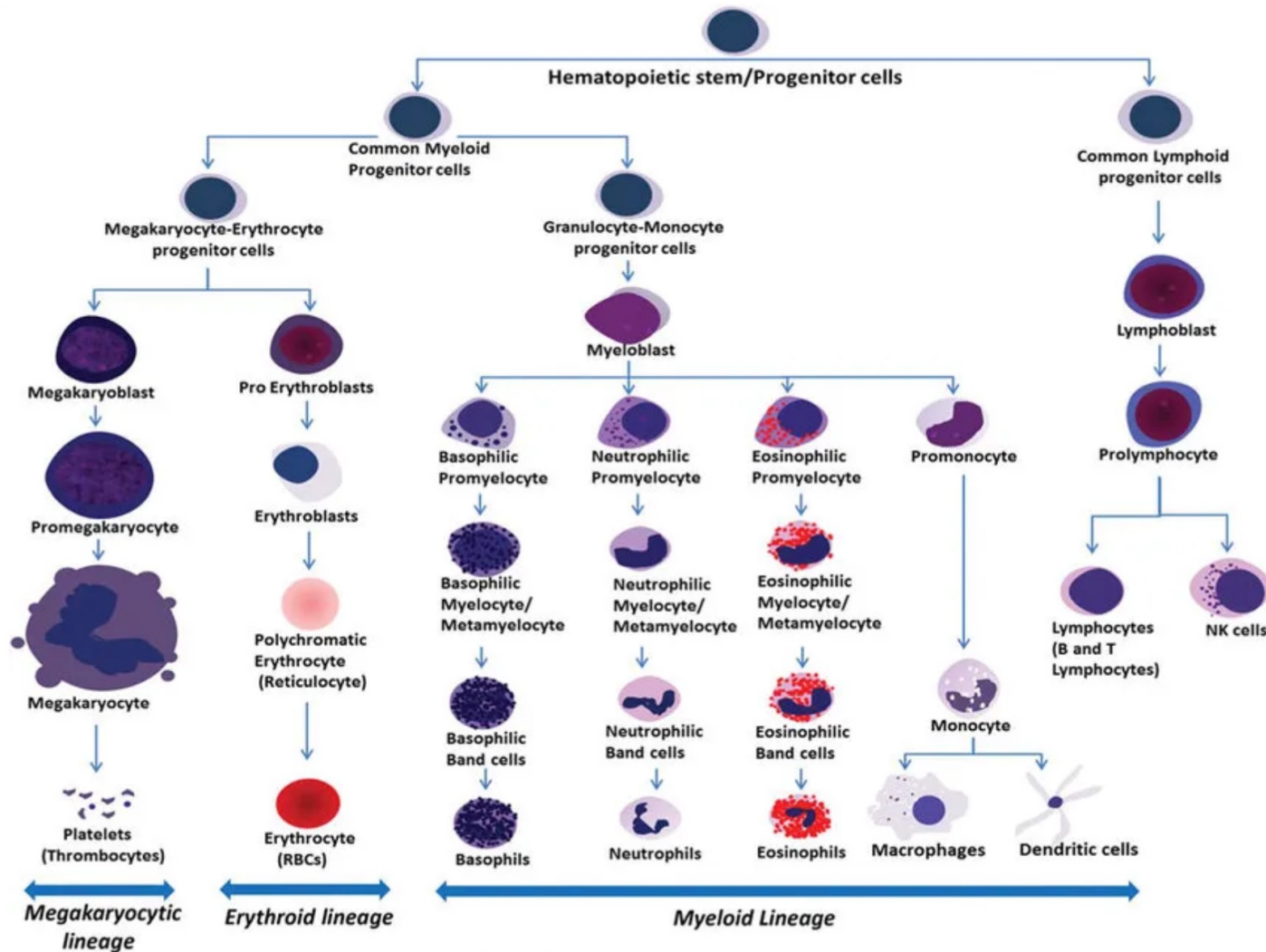
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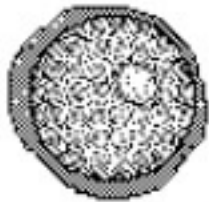


# Trilineage Hematopoiesis



# Myeloid maturation

myeloblast



promyelocyte



myelocyte



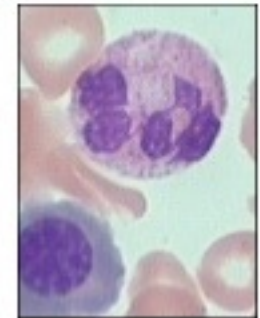
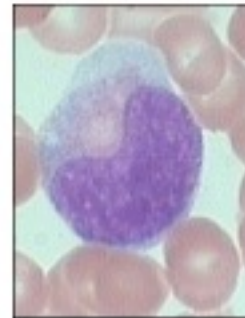
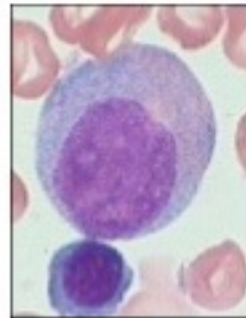
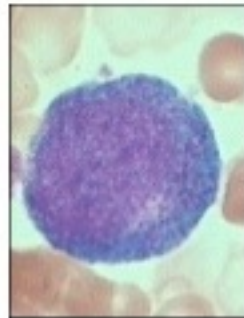
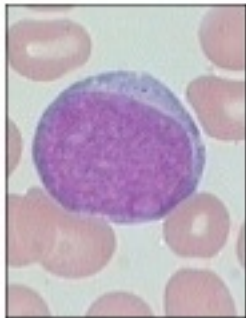
metamyelocyte



band

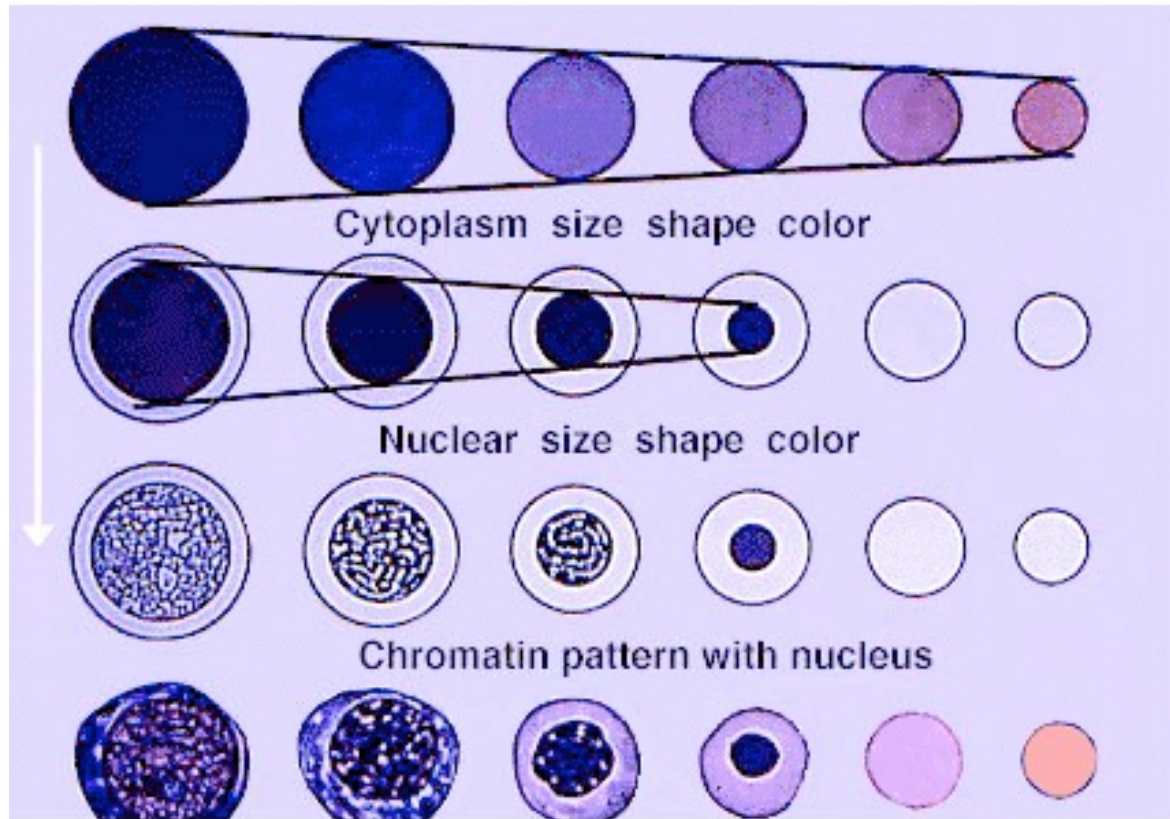


neutrophil



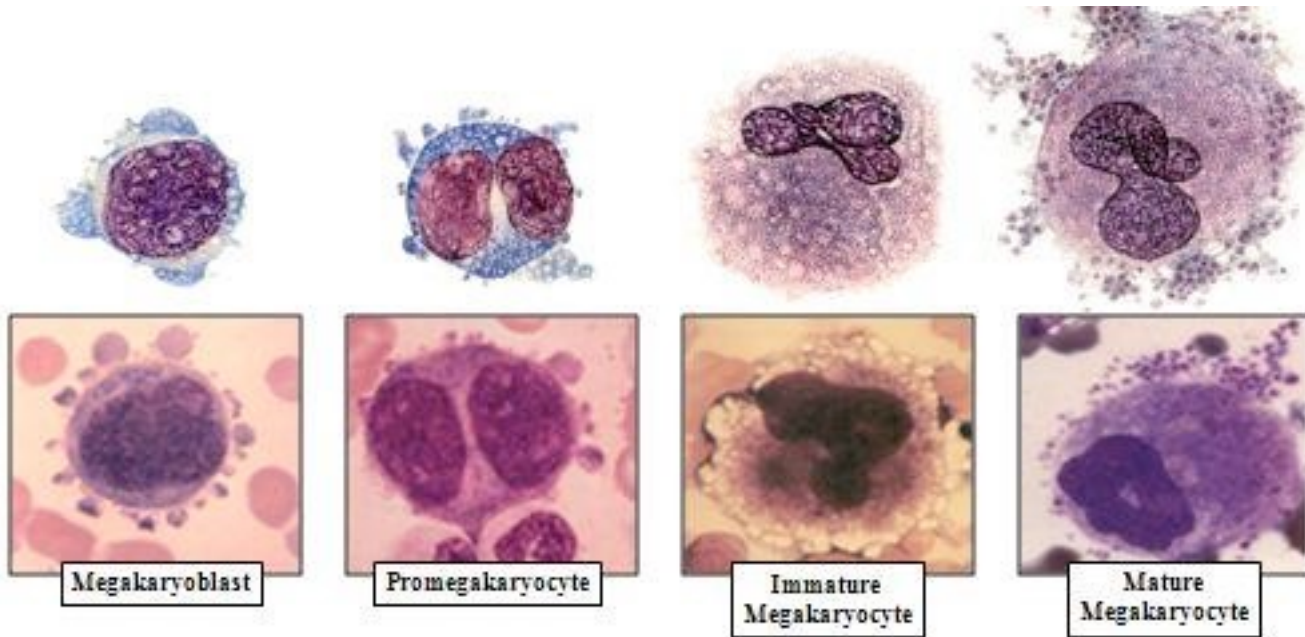
MATURATION

# Erythroid Maturation



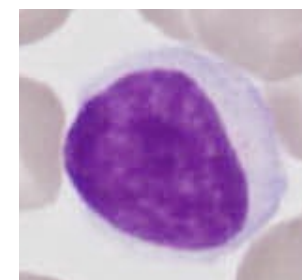
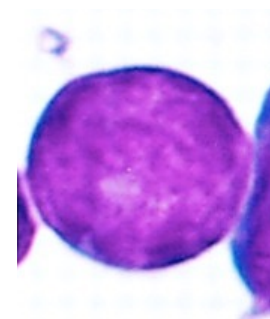
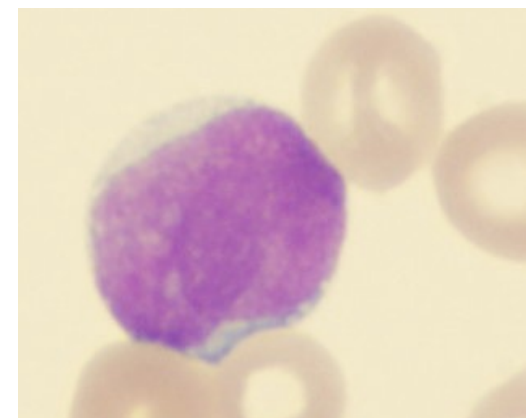
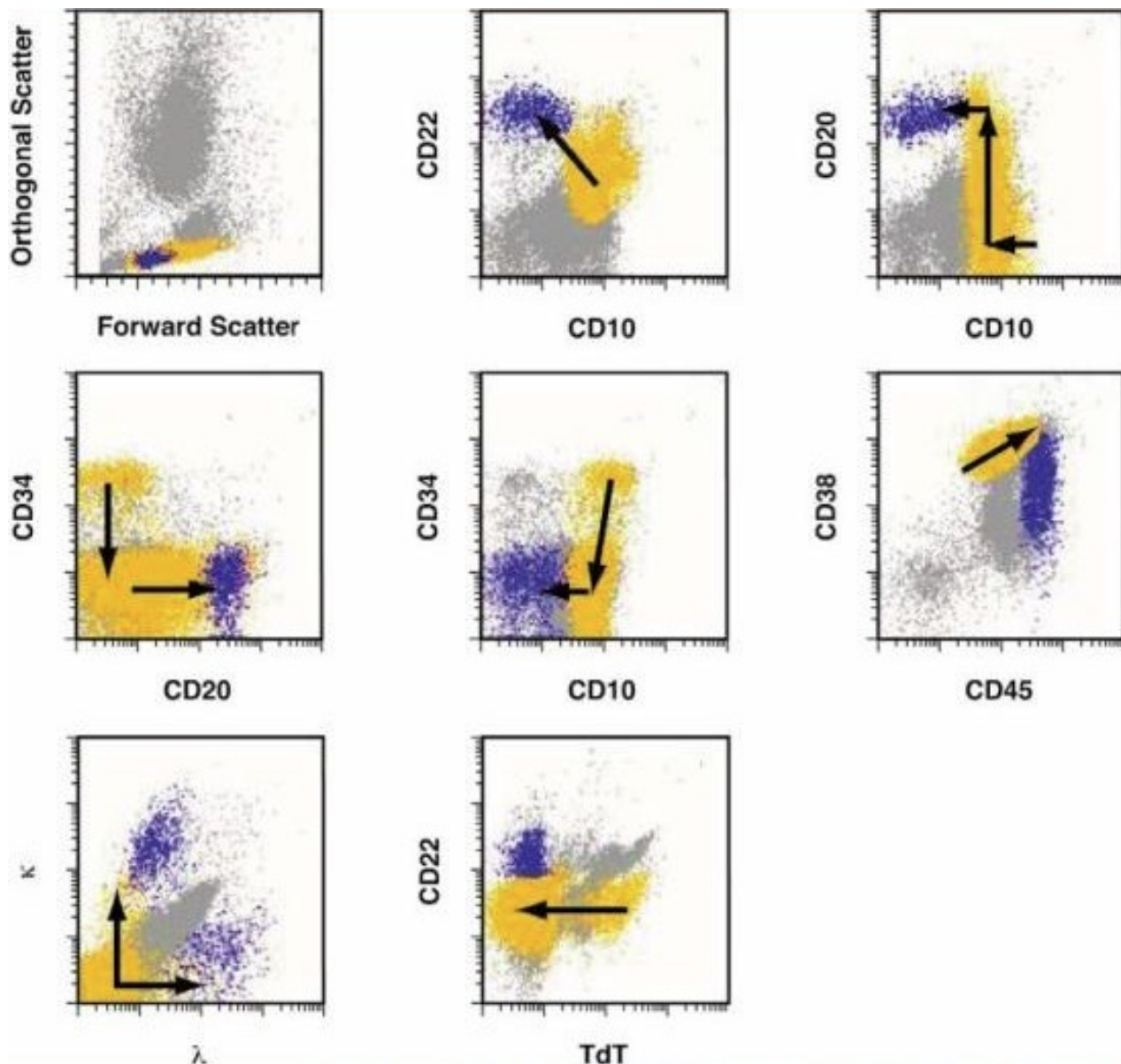


# Megakaryocytic Maturation





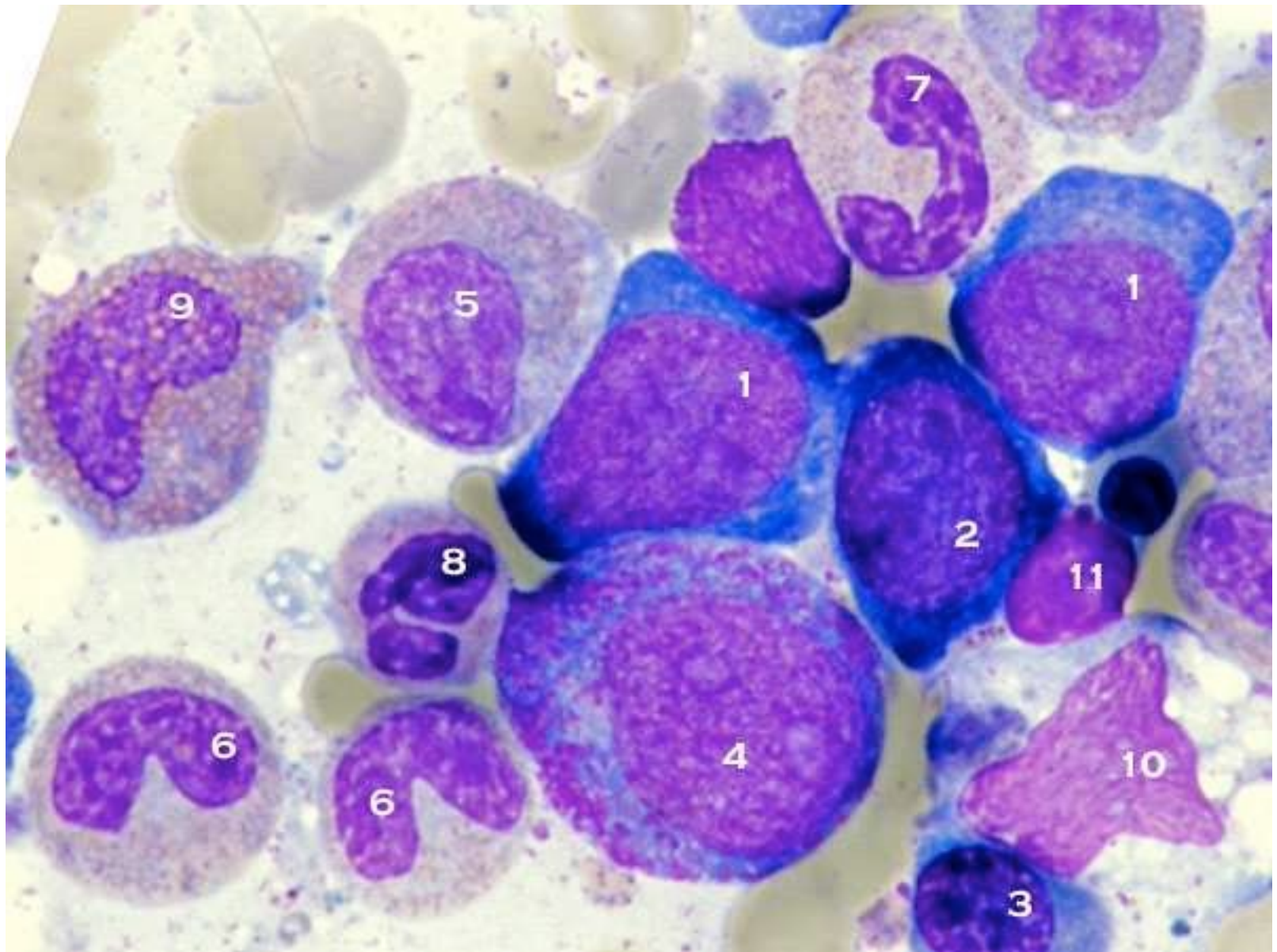
# Lymphoid Maturation (B cells)



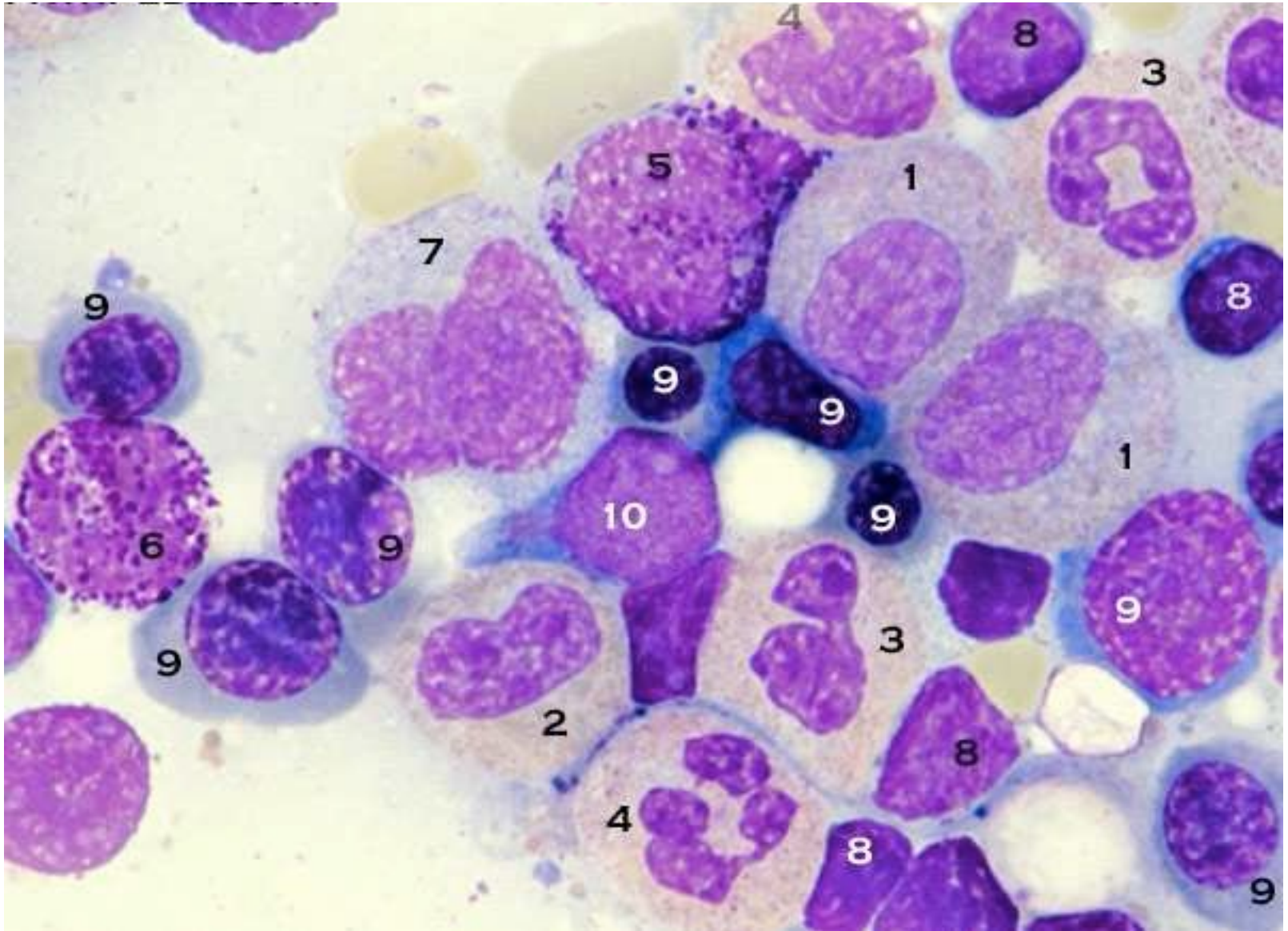
# Common IHC markers for marrow

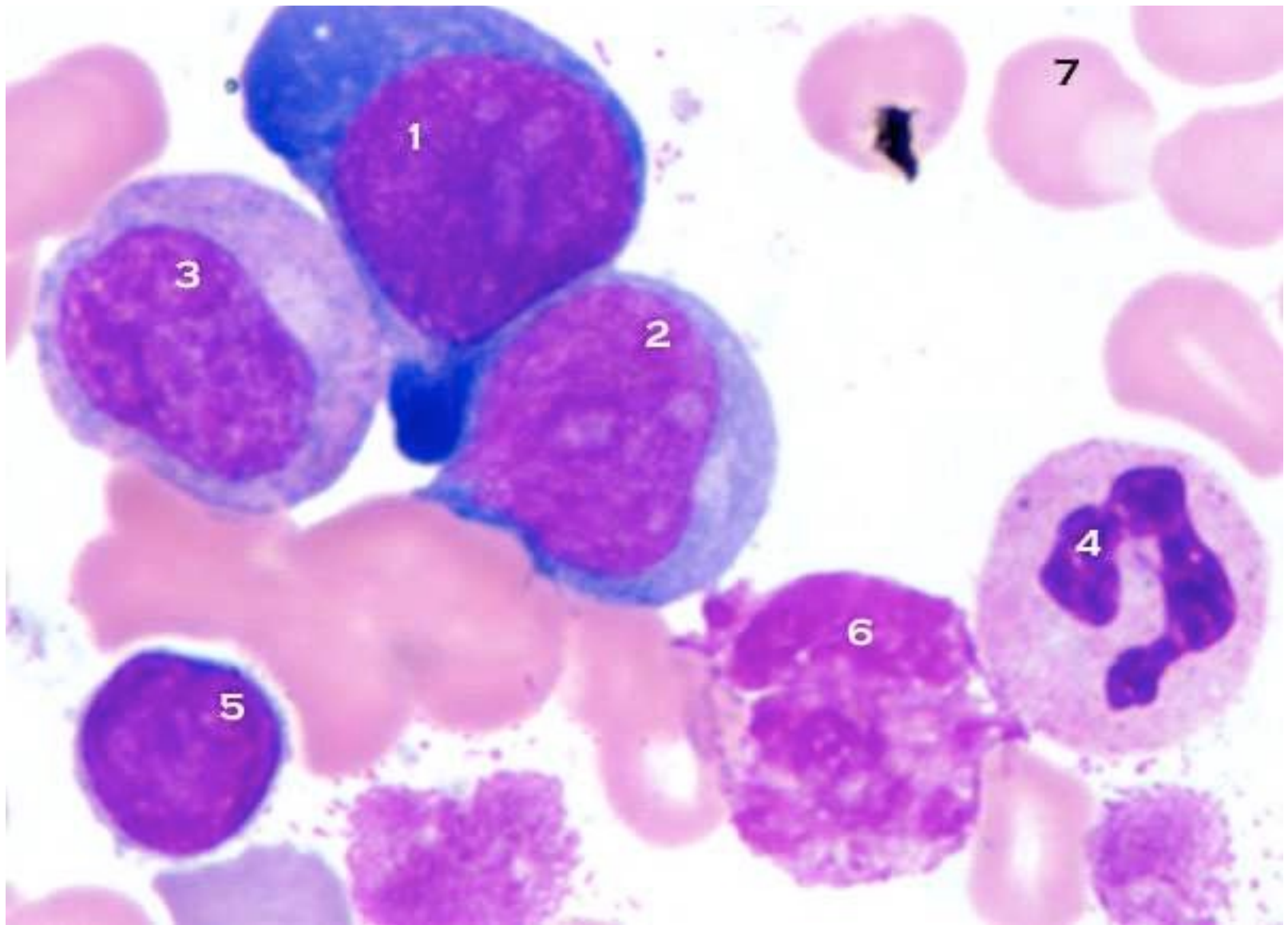
- CD34, CD117, TdT = immature markers
- CD138, kappa, lambda = plasma cell clonality
- CD20, CD3 = lymphoid infiltrates/aggregates

# Aspirate Cytology









# Cytochemical stains

- MPO, Sudan black, CAE – granulocytic lineage
- NSE – monocytic lineage
- PAS – lymphoblasts, pure erythroid leukemia
- Iron

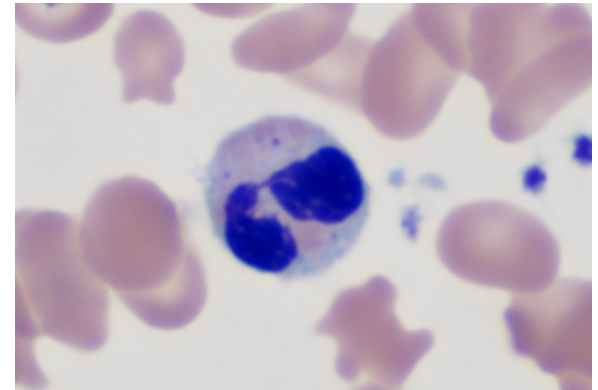
# Myelodysplasia

- 4 components:
  - Unexplained & persistent cytopenia(s)
  - Dysplasia in at least 1 lineage
  - Ineffective hematopoiesis with bm hypercellularity
  - Risk of transformation to AML
- Dysplasia of erythroid and myeloid is best assessed on aspirate
  - At least 10% of any lineage
- Architectural disorganization (core biopsy)
  - Usually, myeloid progenitors paratrabecular
    - In dysplasia, Atypical Localization of Immature Precursors
  - Usually, erythroid “islands” nonparatrabecular, surrounding a macrophage
    - In dysplasia, loss of colony formation



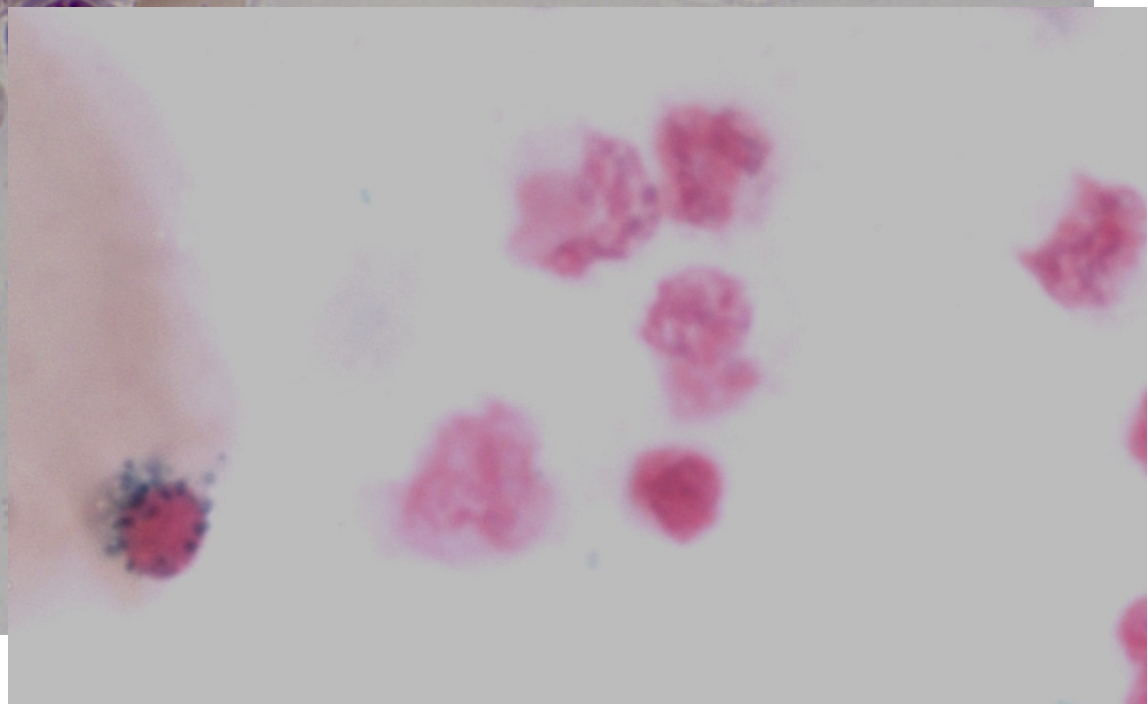
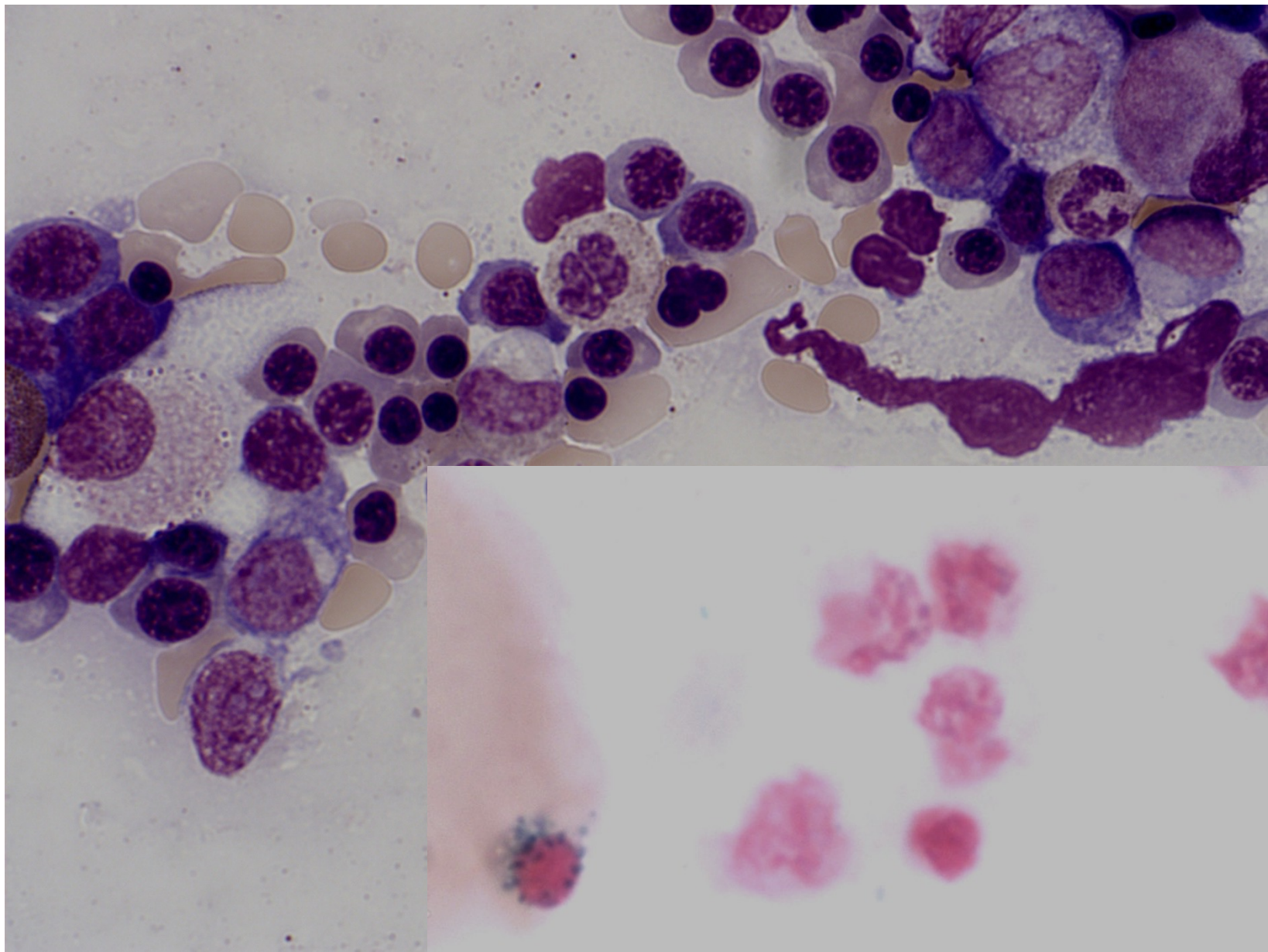
# Myeloid Lineage

- Maturation pyramid
- Proportion of myeloblasts
- Nuclear morphology
  - Pseudo-Pelger Huet
  - Hyper/hypo-segmentation
- Localization on biopsy
- Cytoplasmic
  - Granulation



# Erythroid Lineage

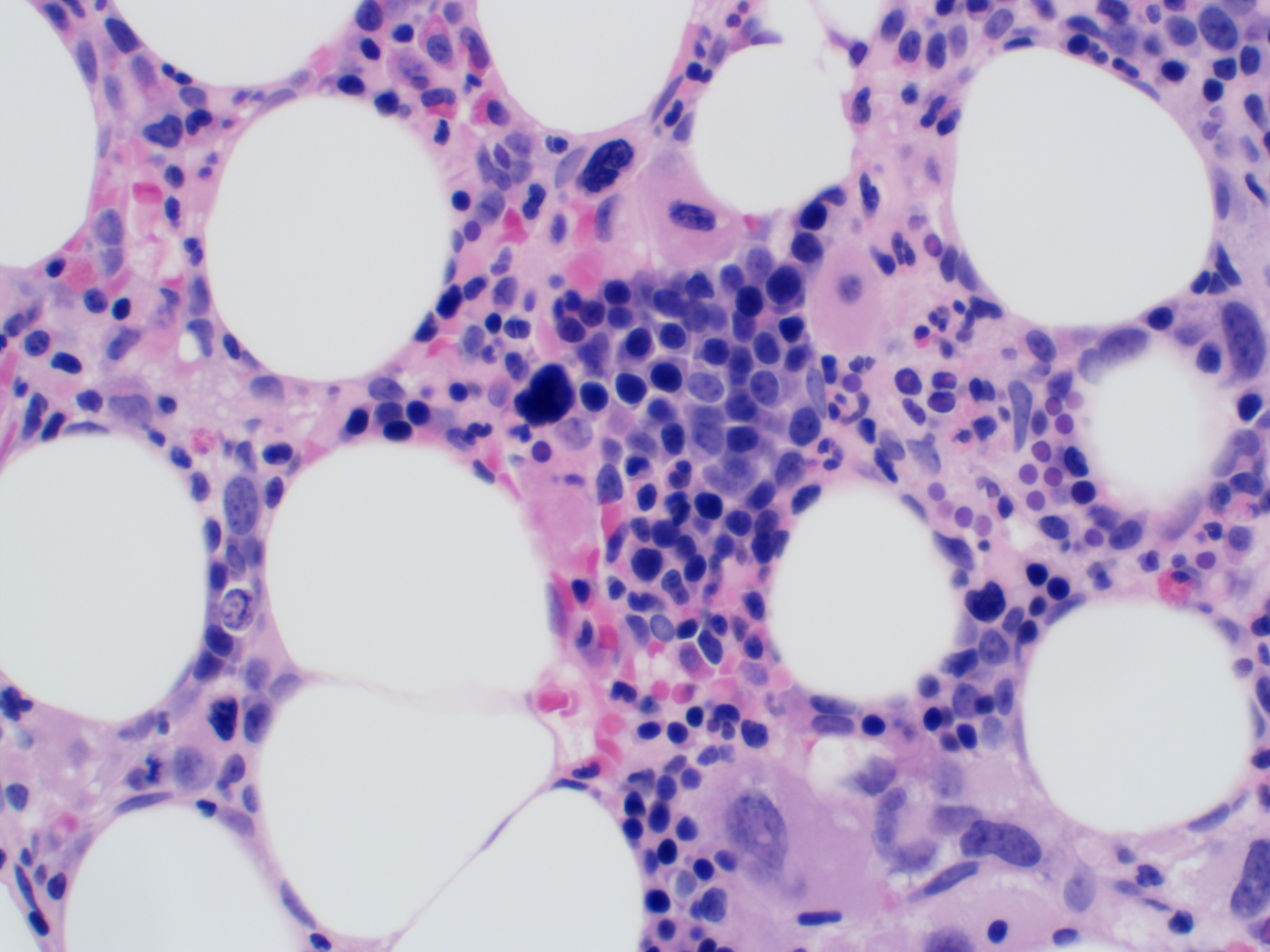
- Nuclear morphology
  - Budding
  - Nuclear irregularities; bridging
  - Karyorrhexis
  - Megaloblastic changes
- Vacuolization of cytoplasm
- Ring sideroblasts



# Megakaryocyte Lineage

- Number and distribution (on core bx)
- Overall size, range of sizes
- Nuclear morphology
  - Hypo/hyperlobation
  - Pyknotic nuclei
- Mega clustering, intrasinusoidal localization (core bx)
- Associated fibrosis and abnl bony trabeculae



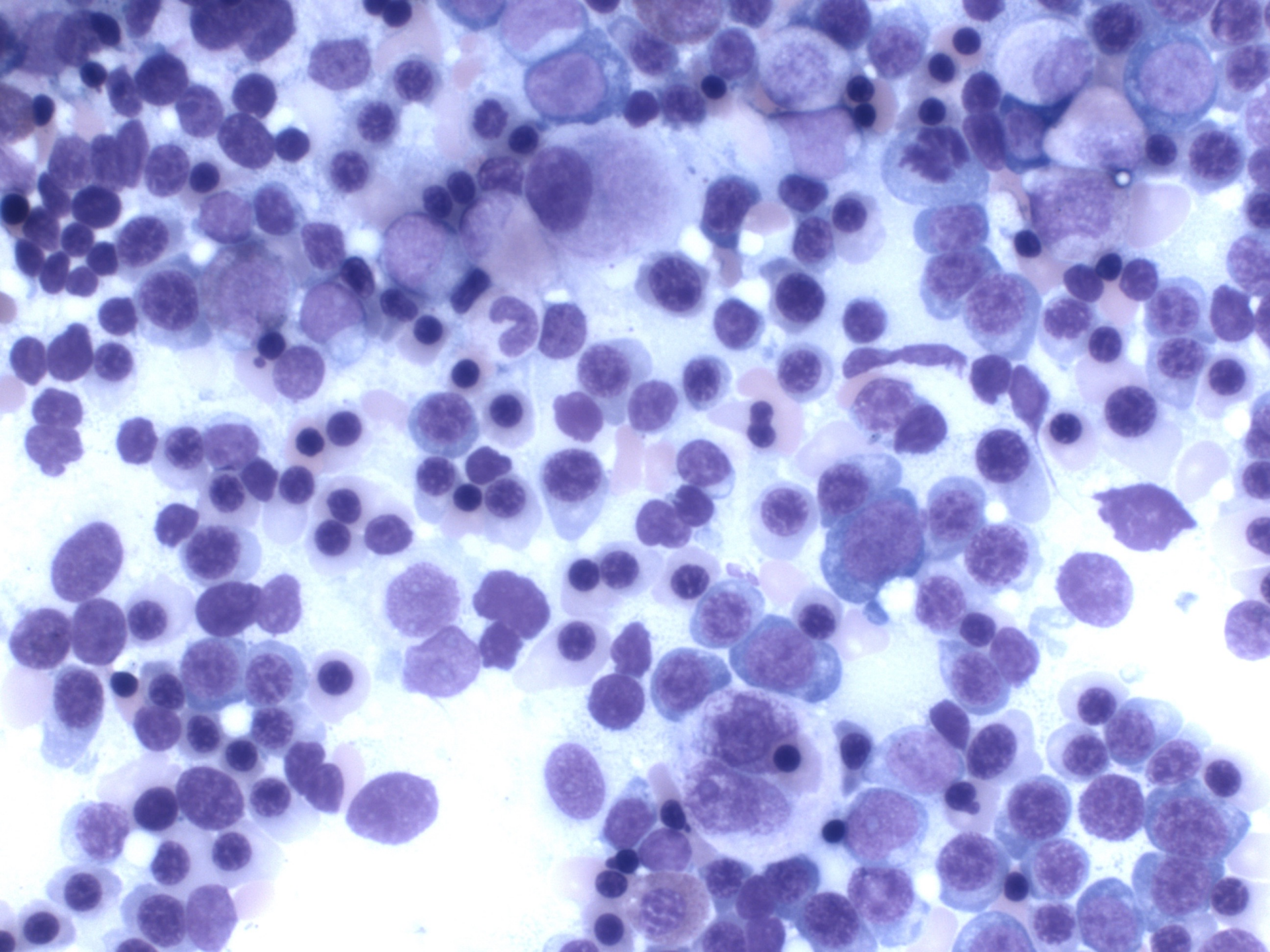


On to the slide set...

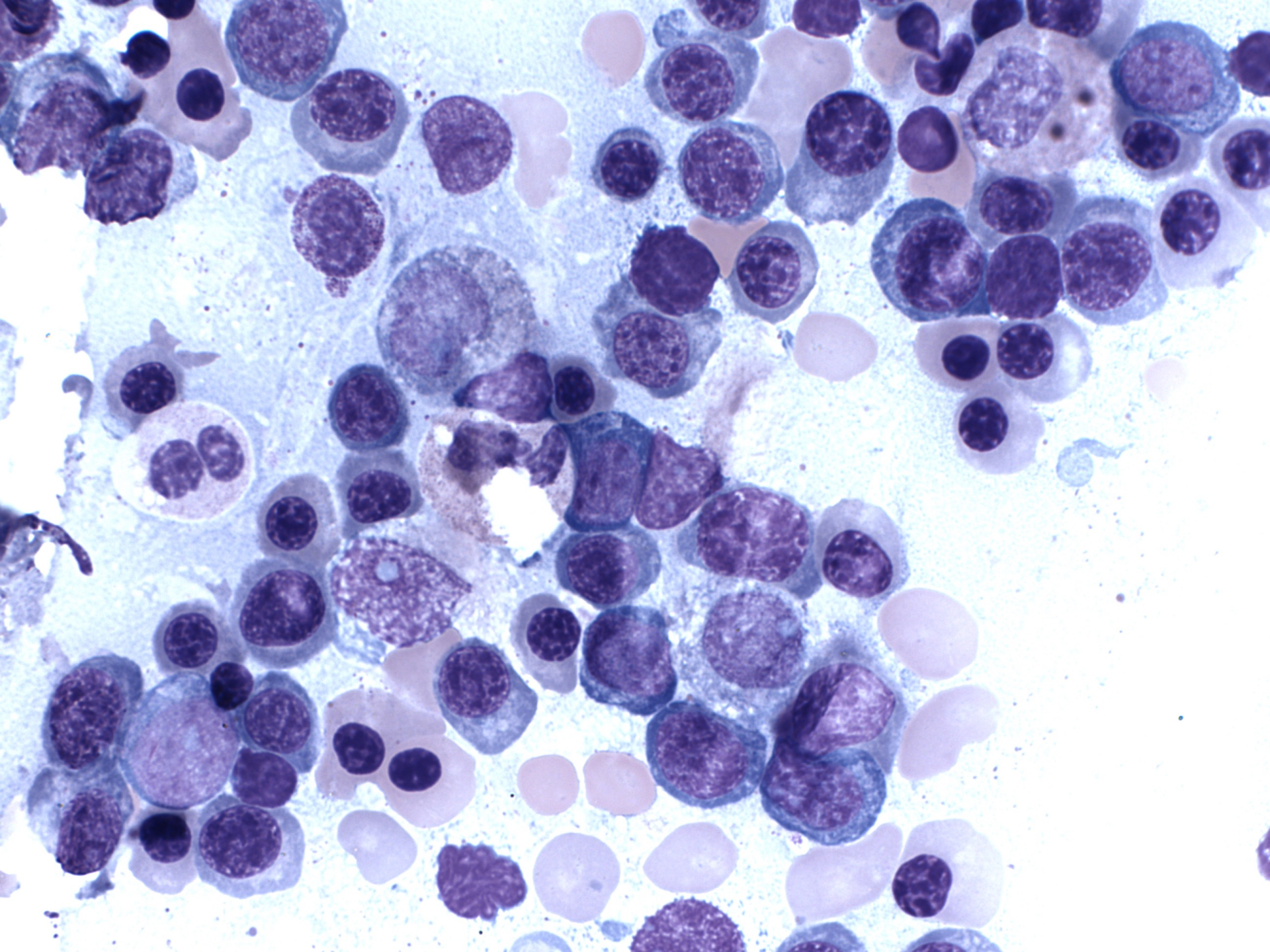
# Example 1

- 61 yo man with pancytopenia

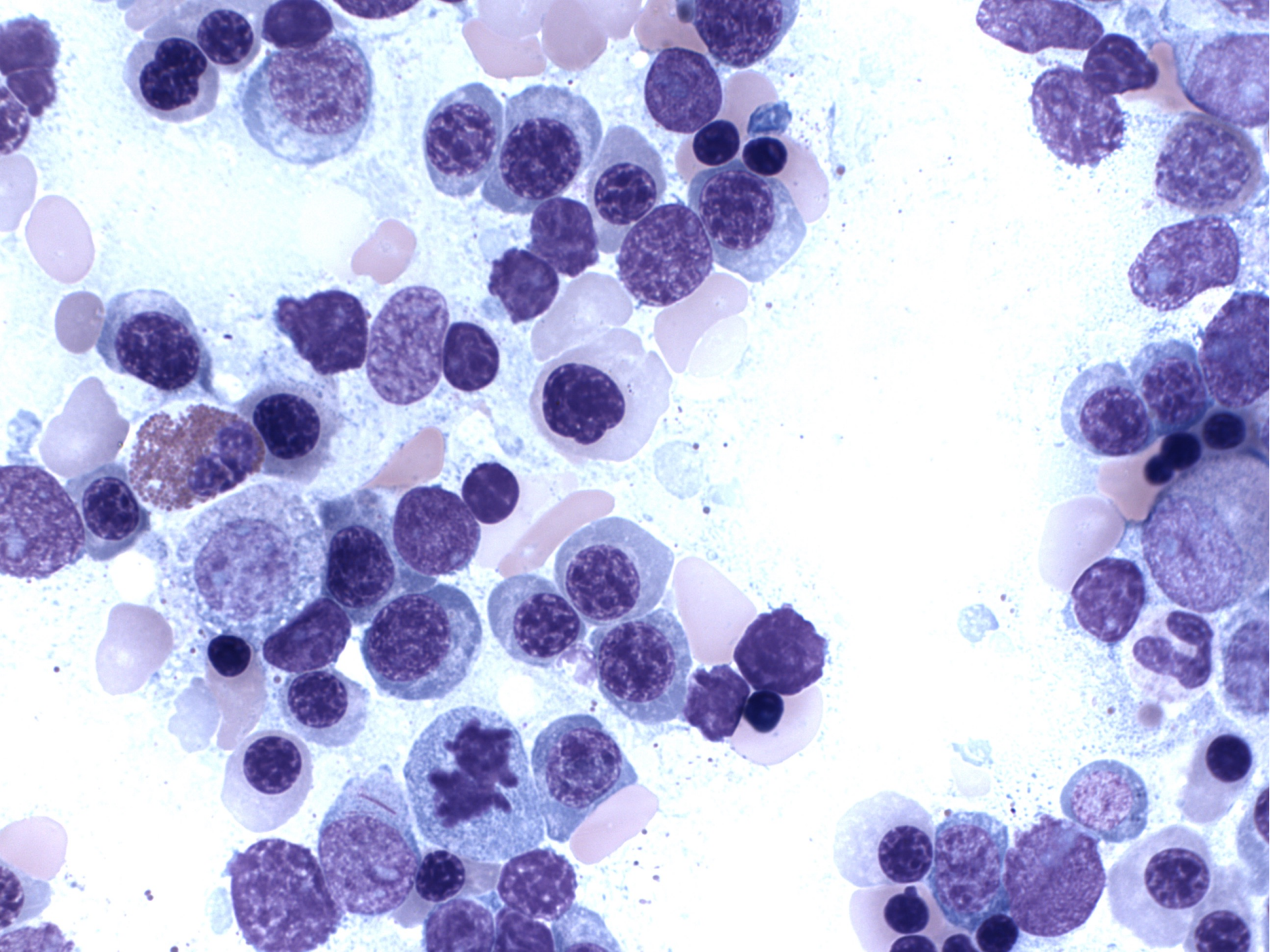








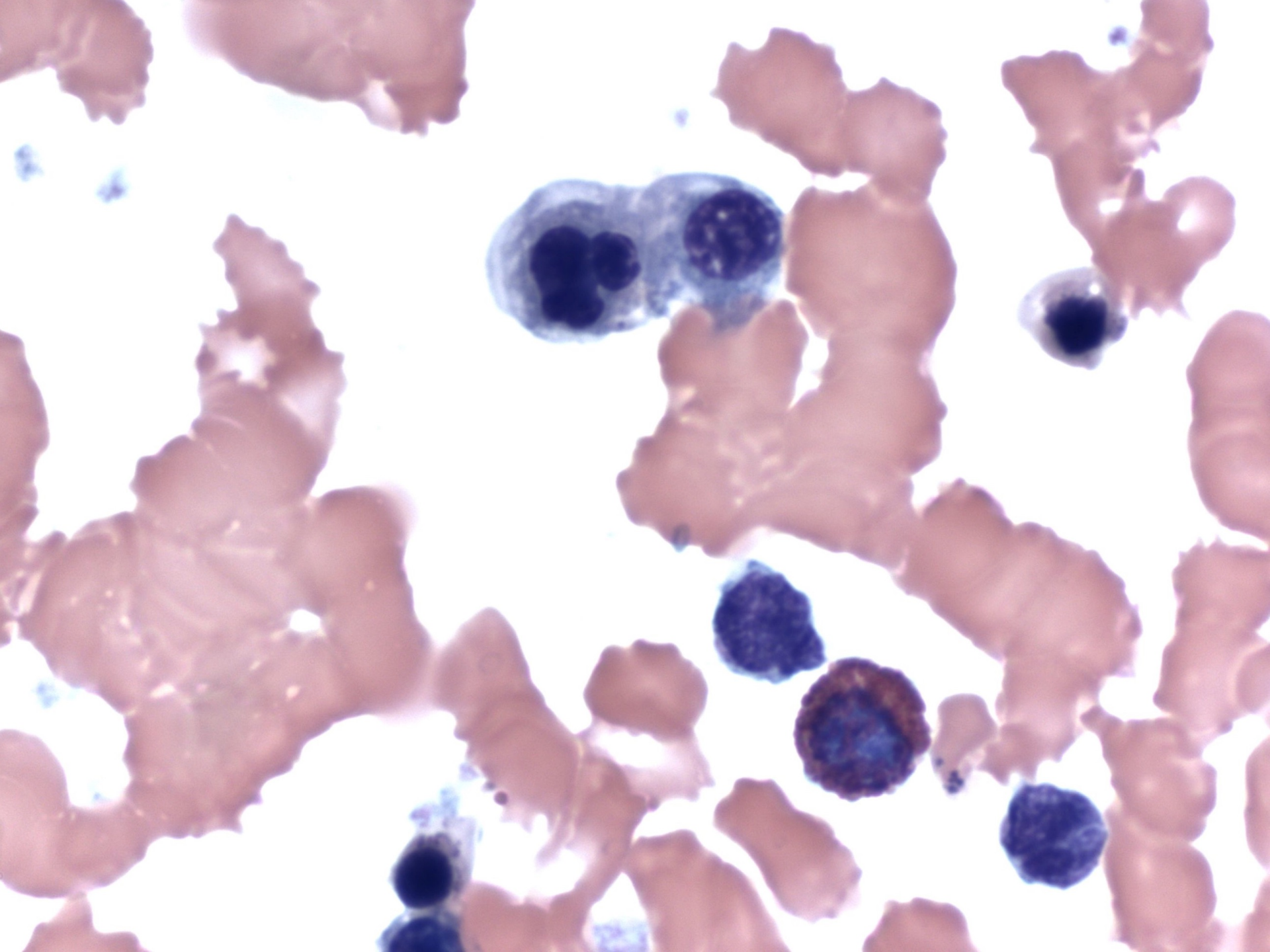


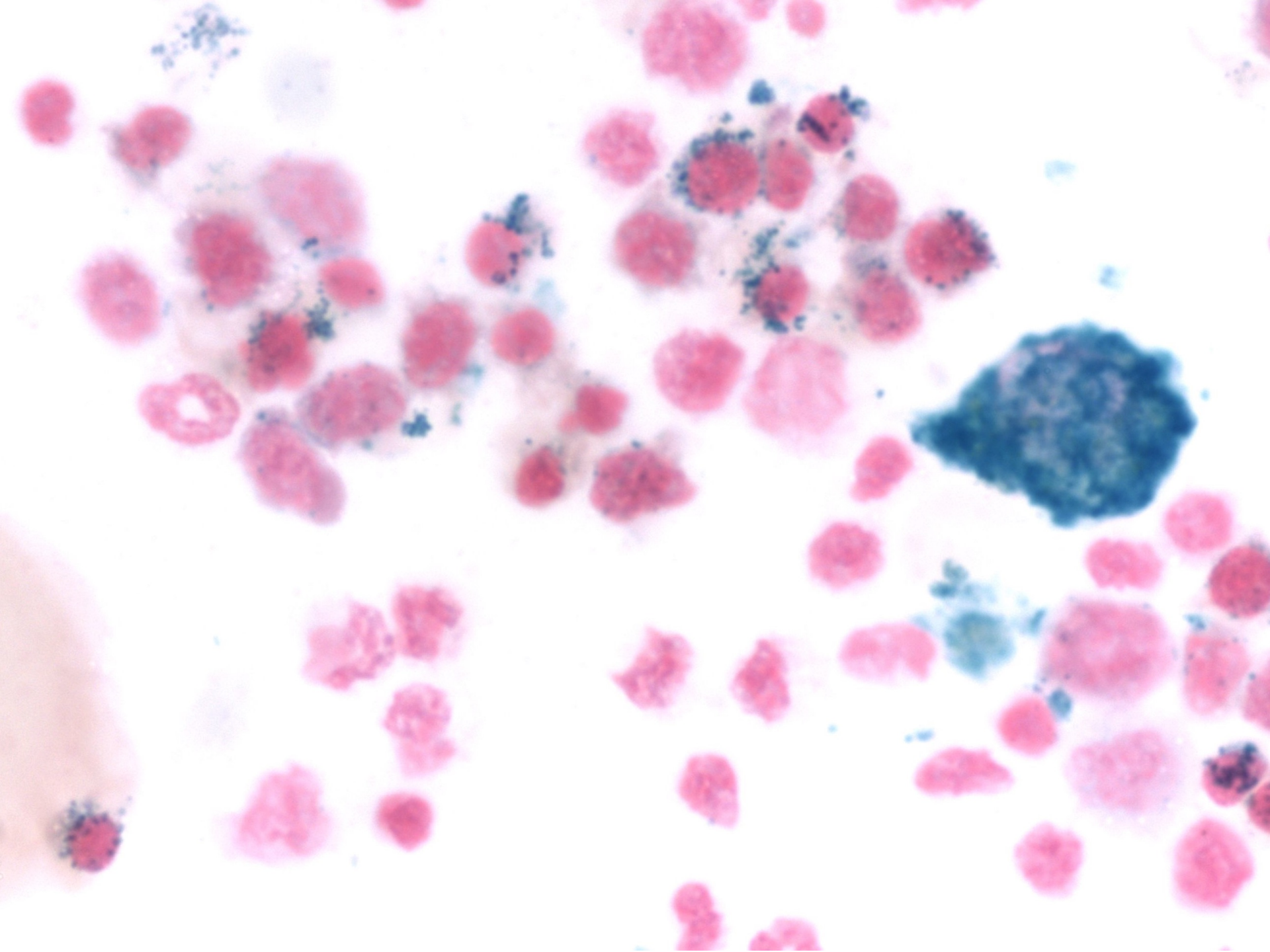


# Example 2

- 83 yo man with macrocytic anemia



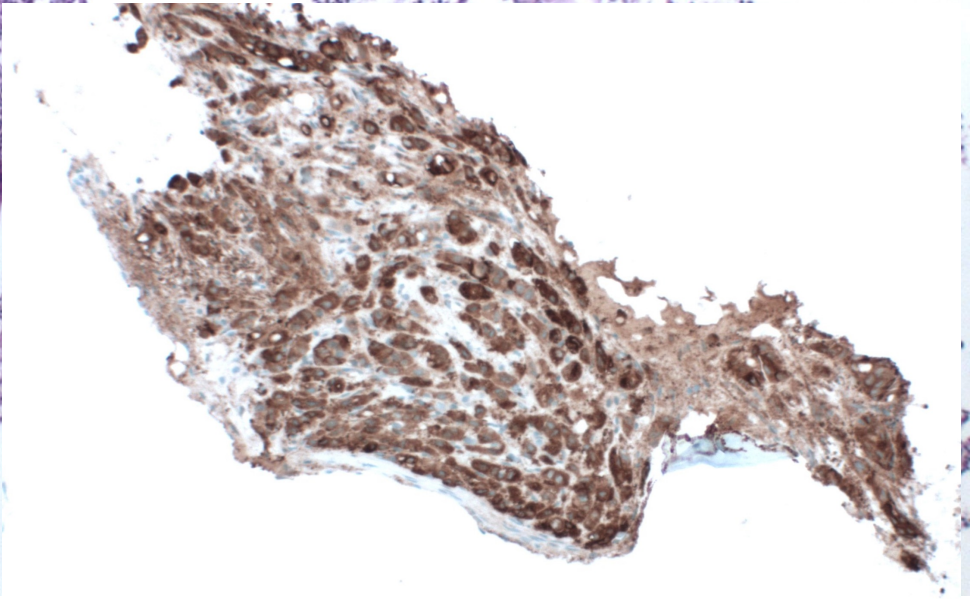
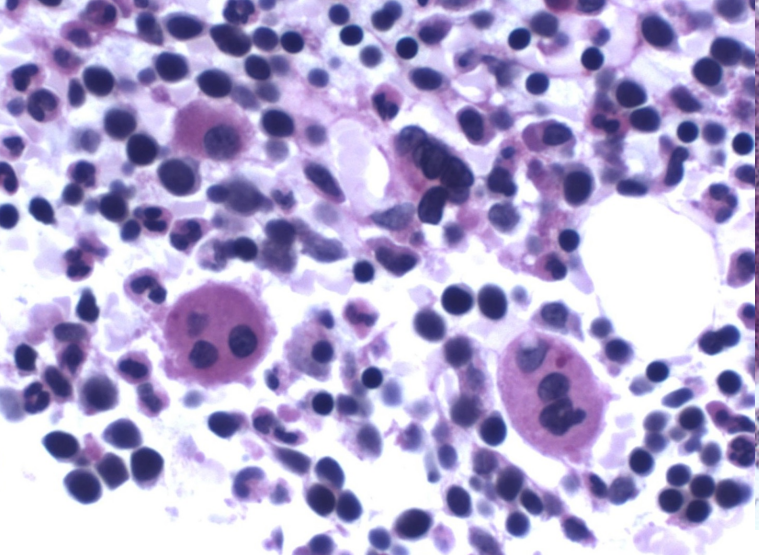
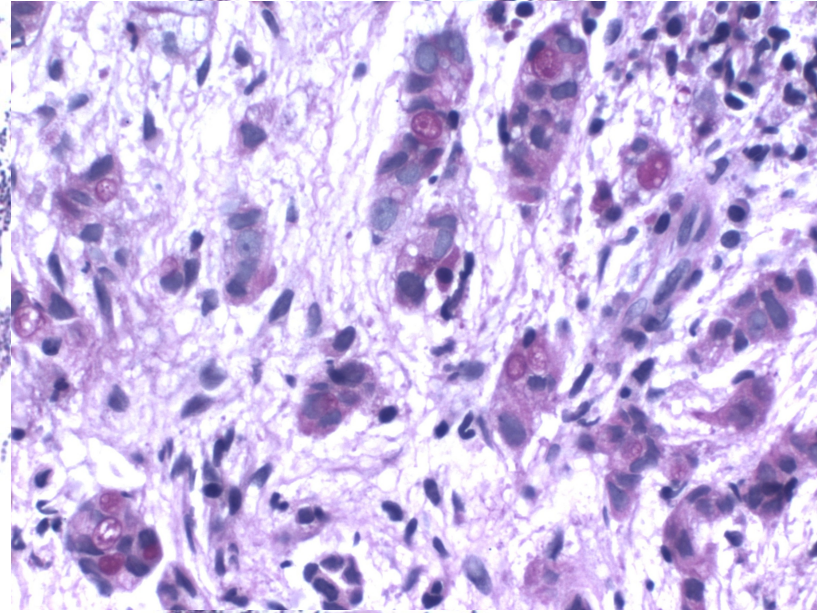
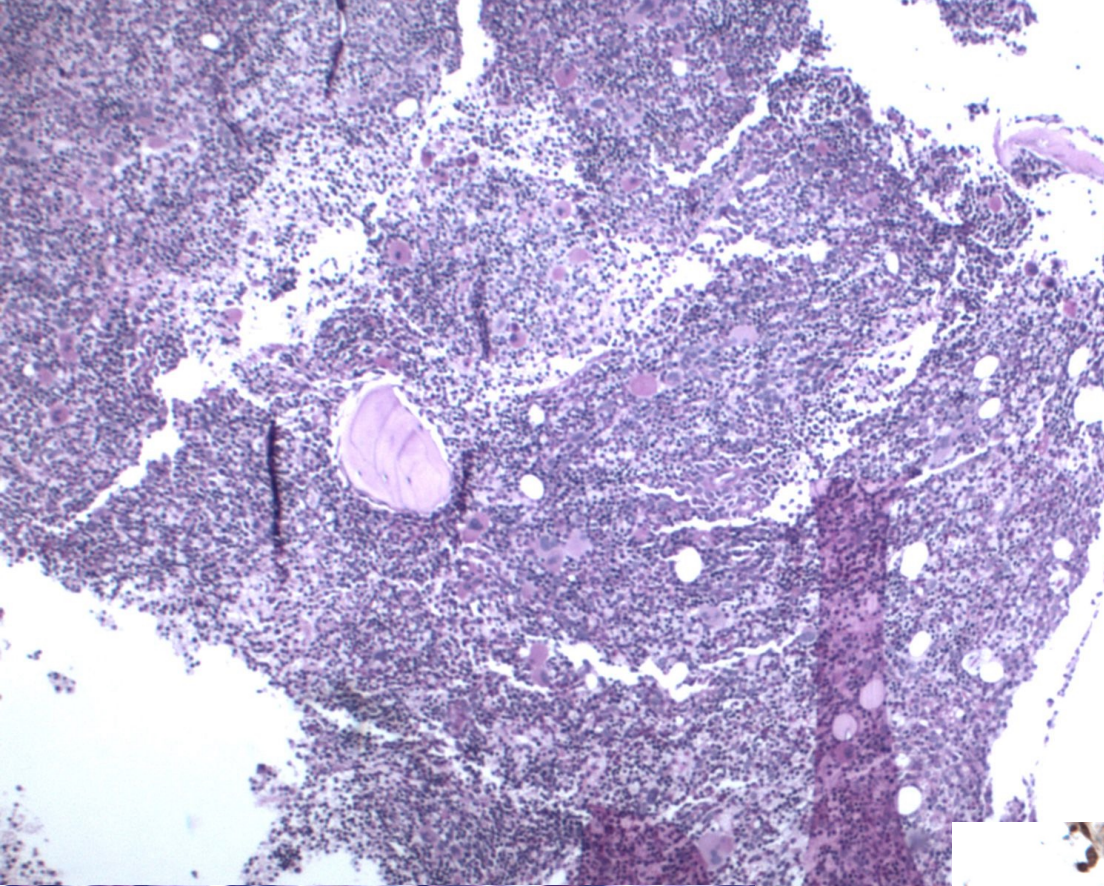




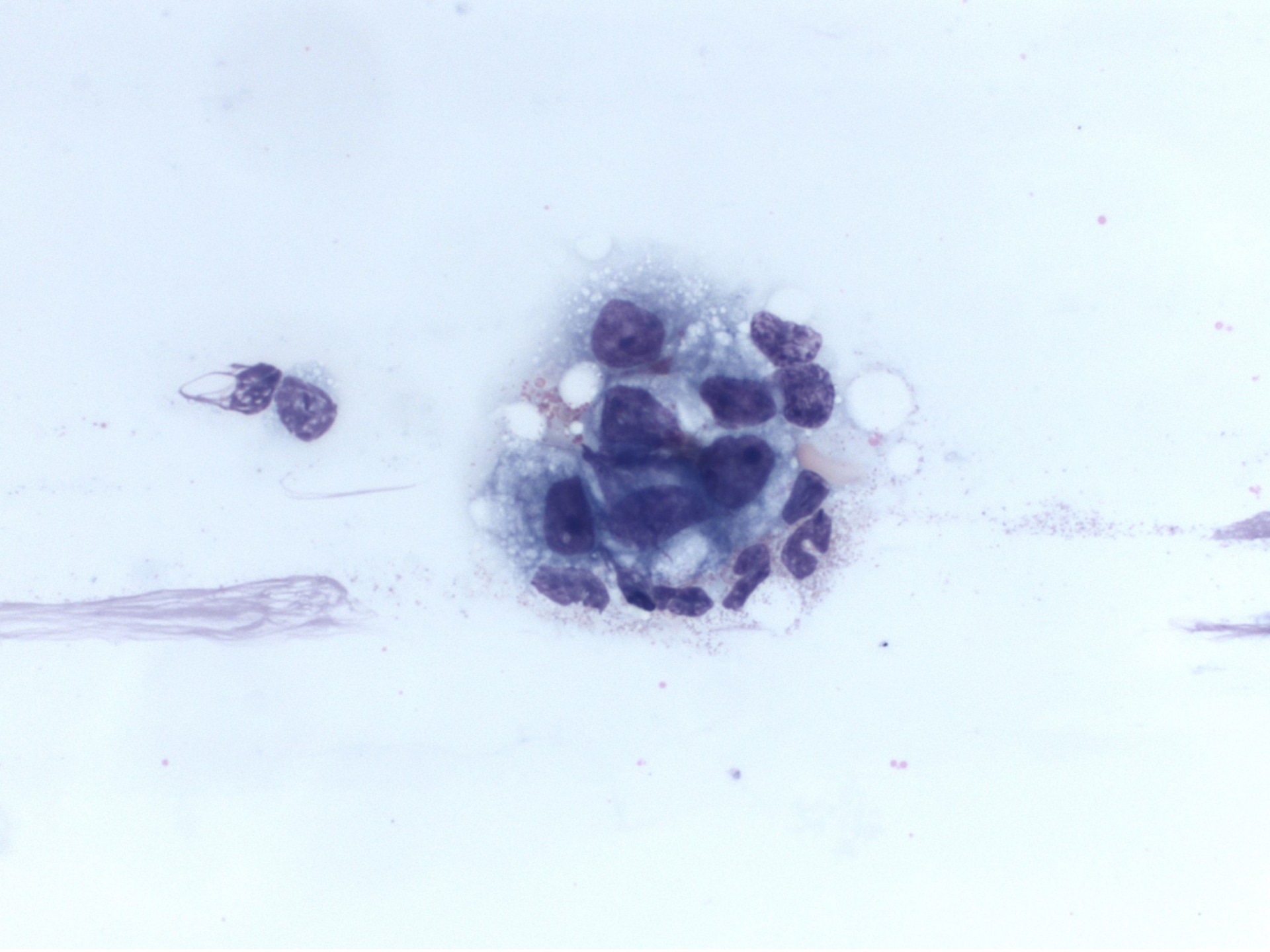
# Example 3

- 45 year old woman w/pancytopenia





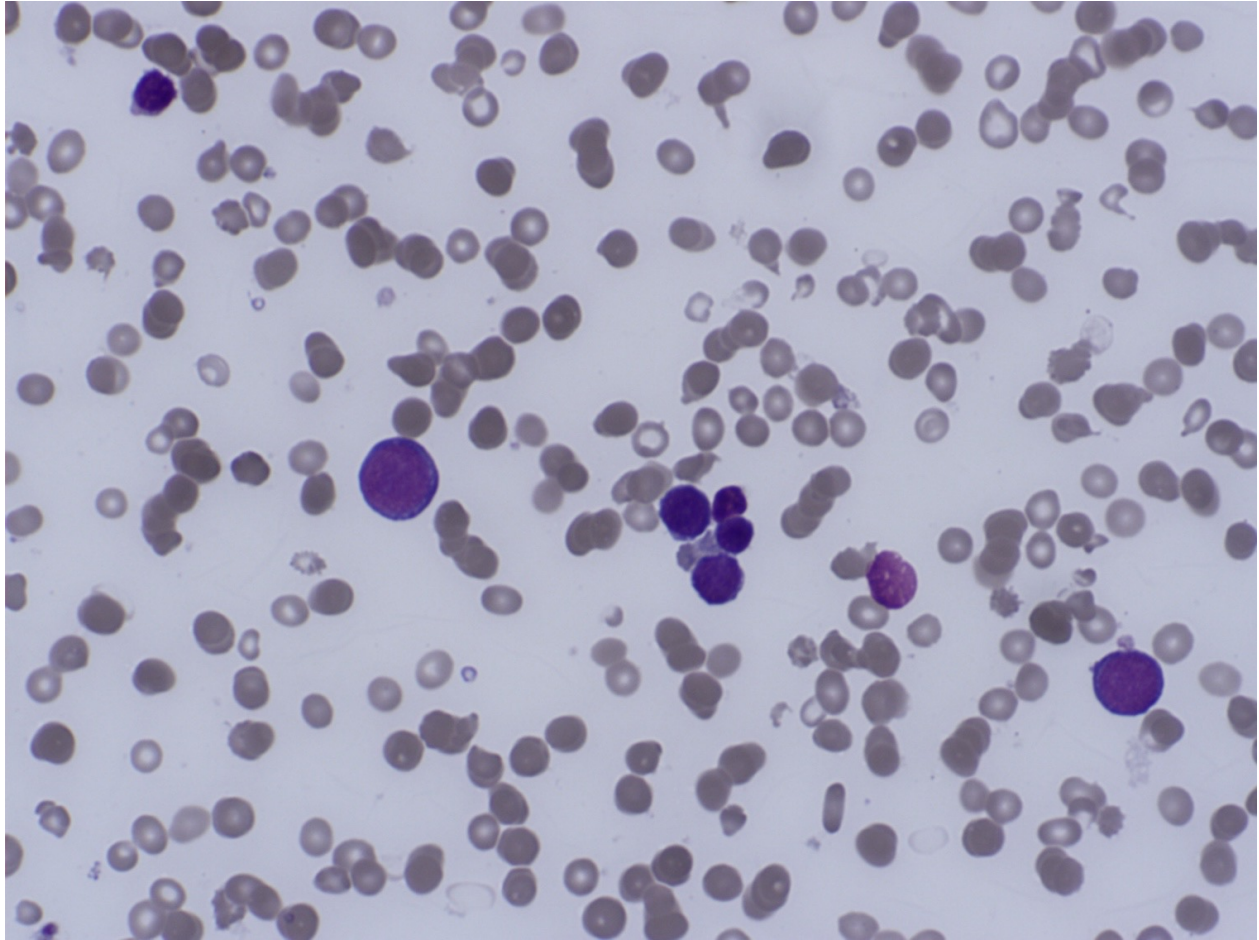


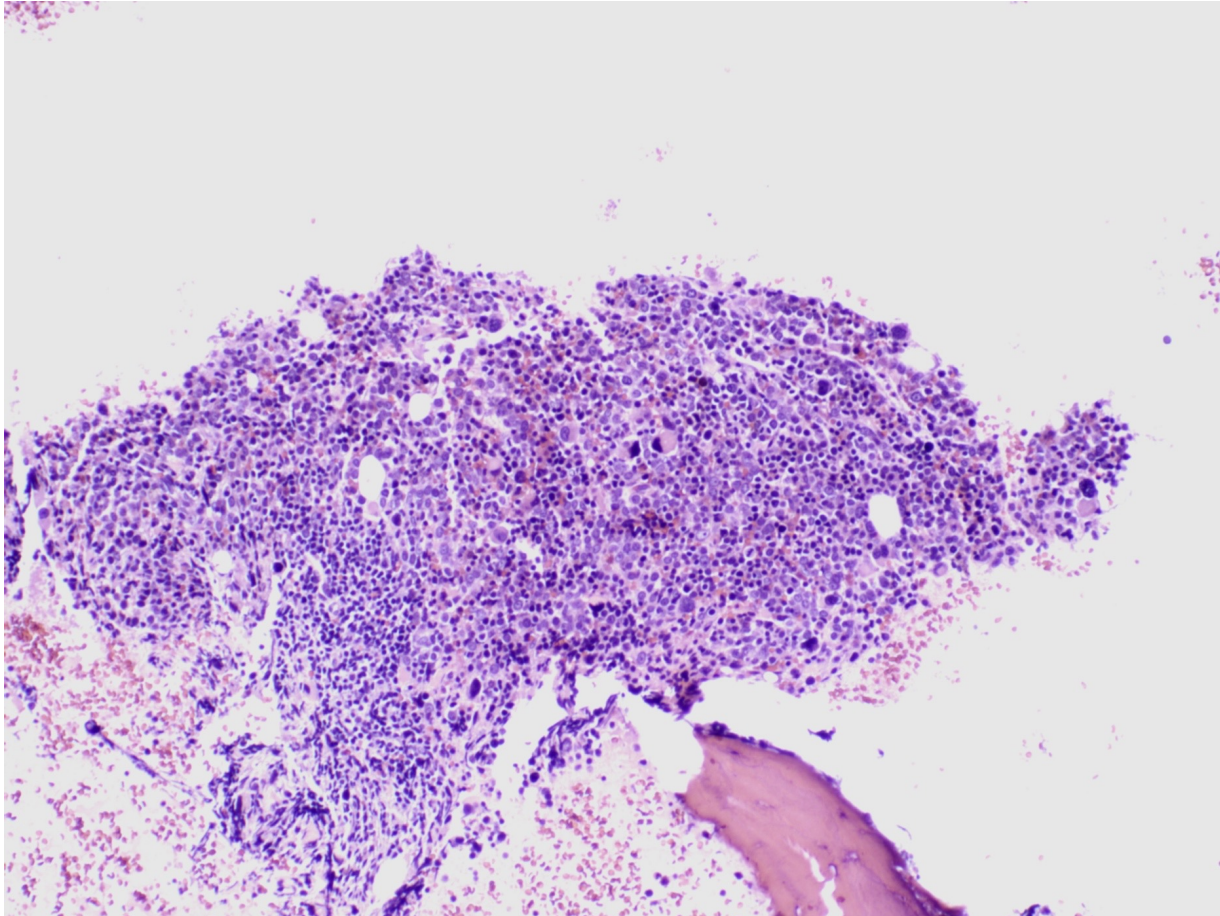




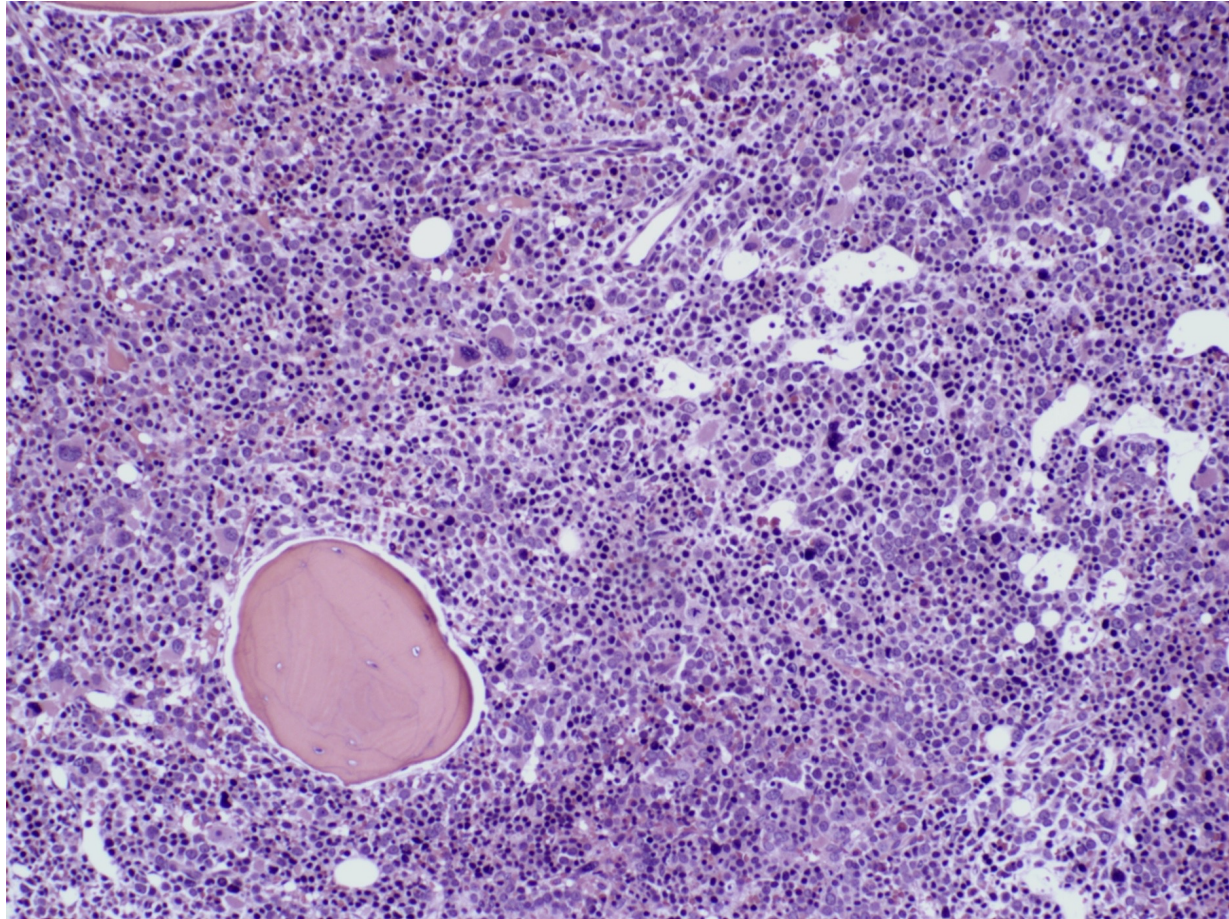
# Example 4

- 56 year old woman with history of chemotherapy for ovarian cancer now w/pancytopenia

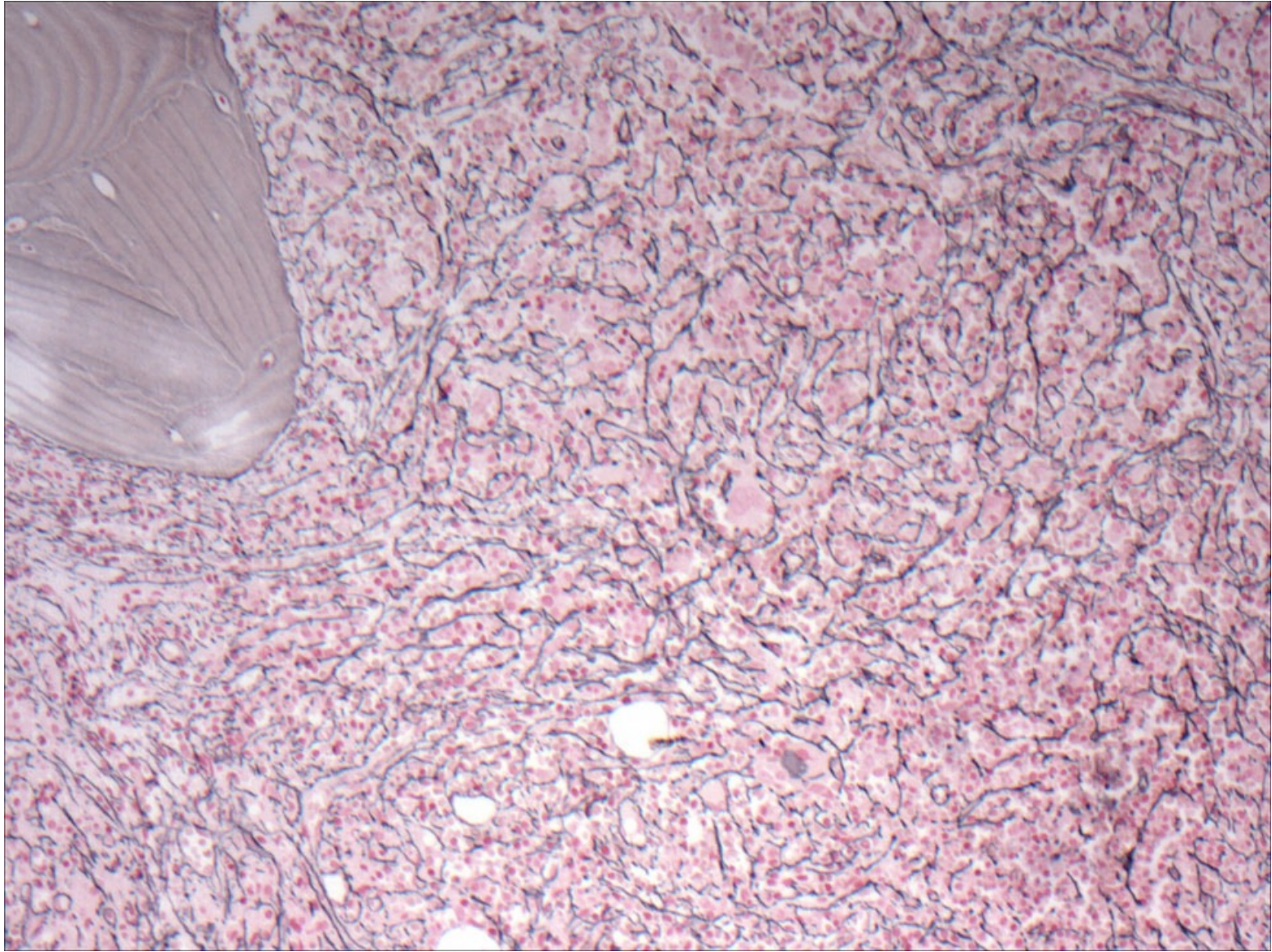




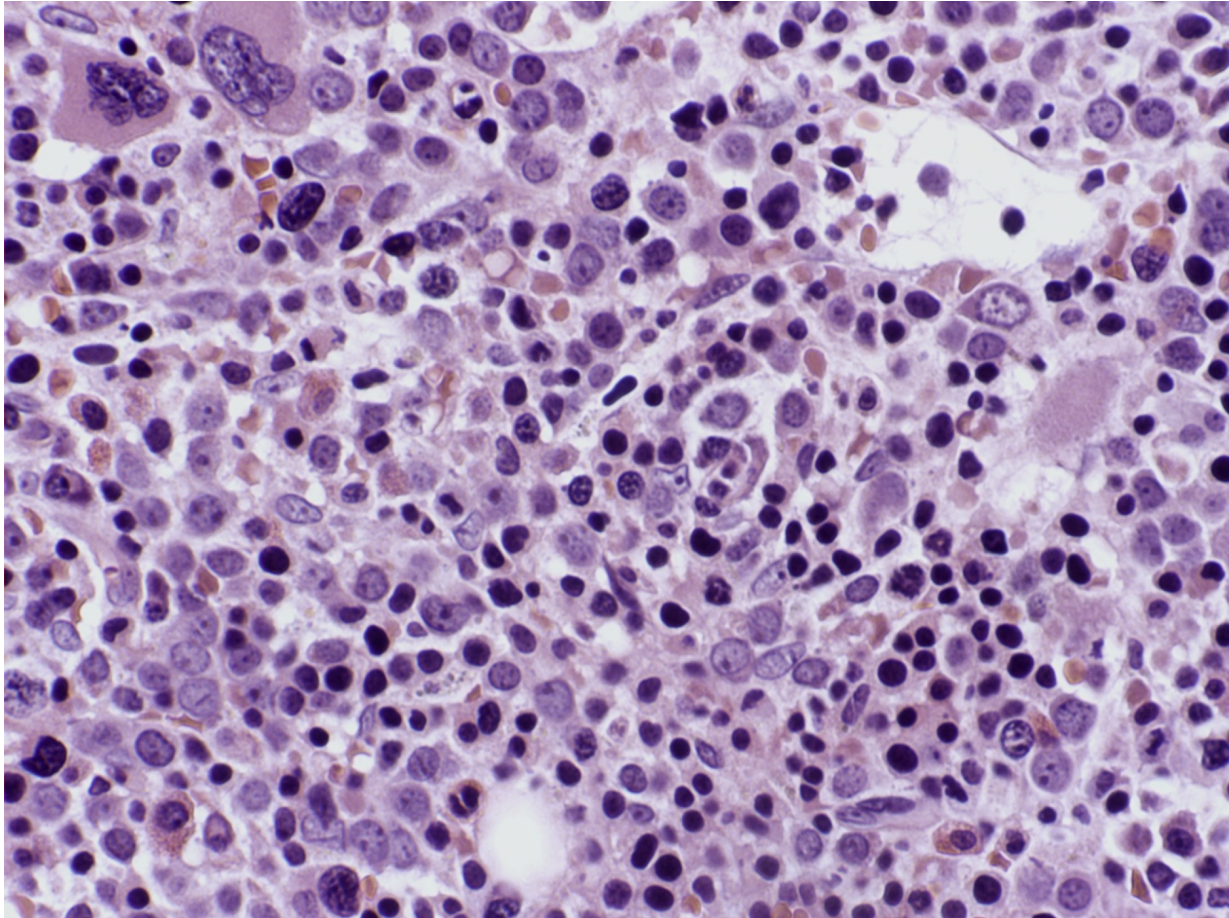




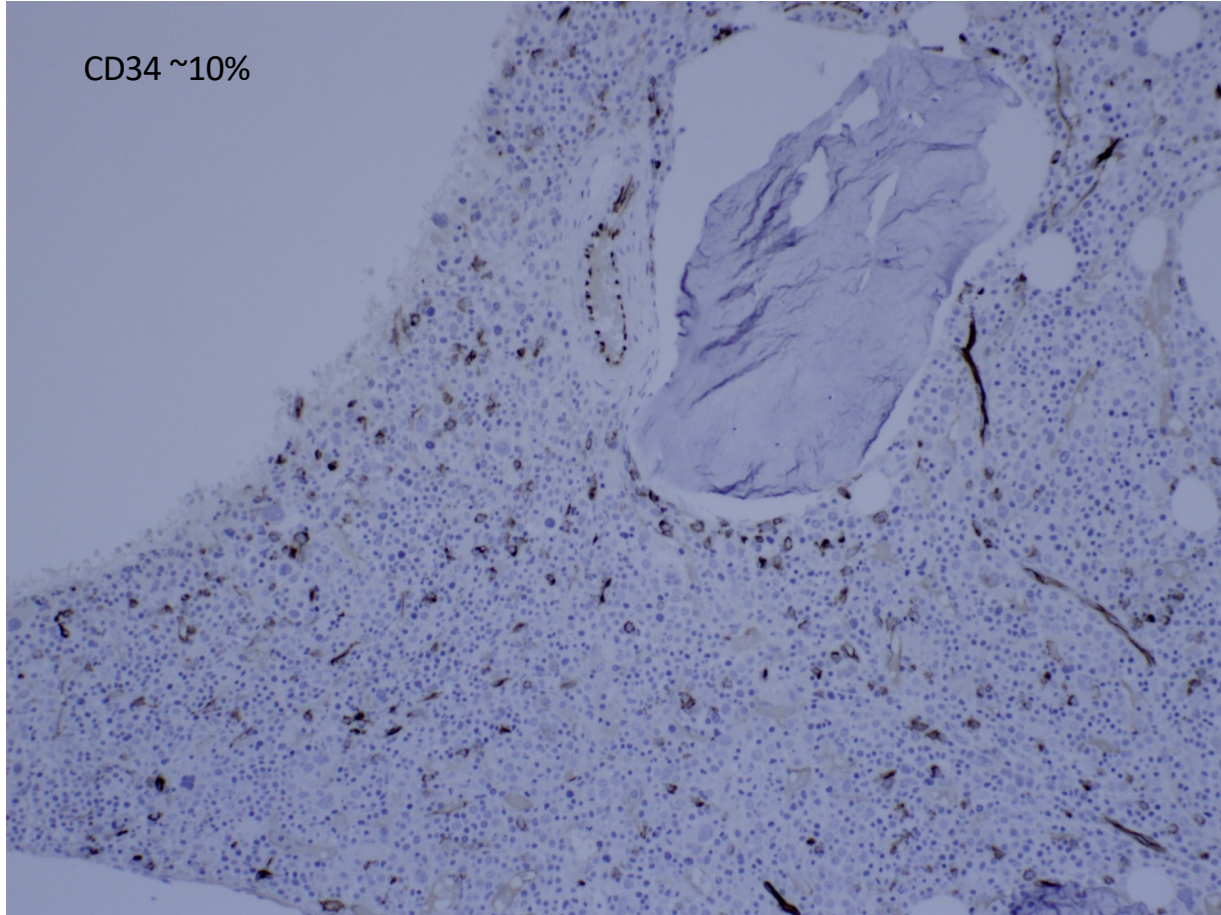






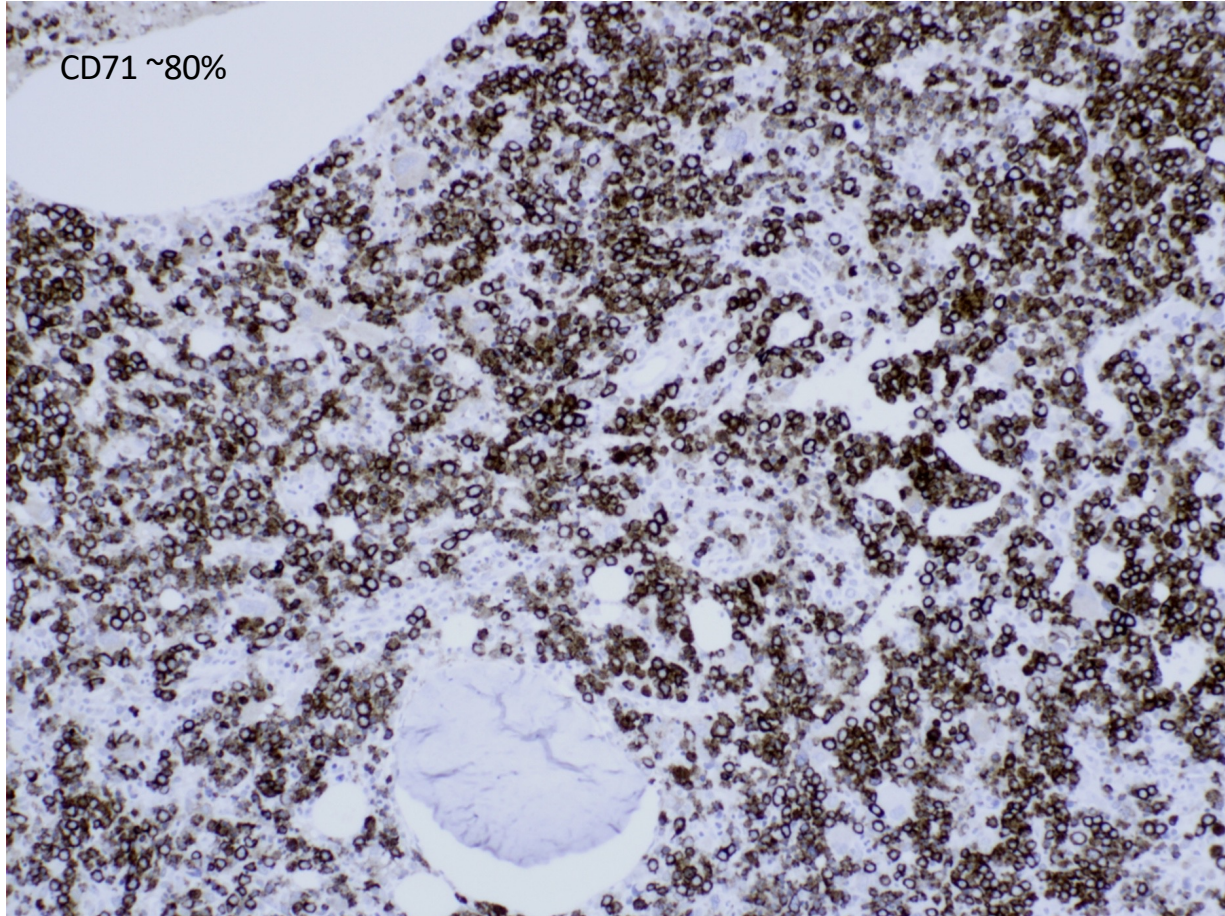


CD34 ~10%

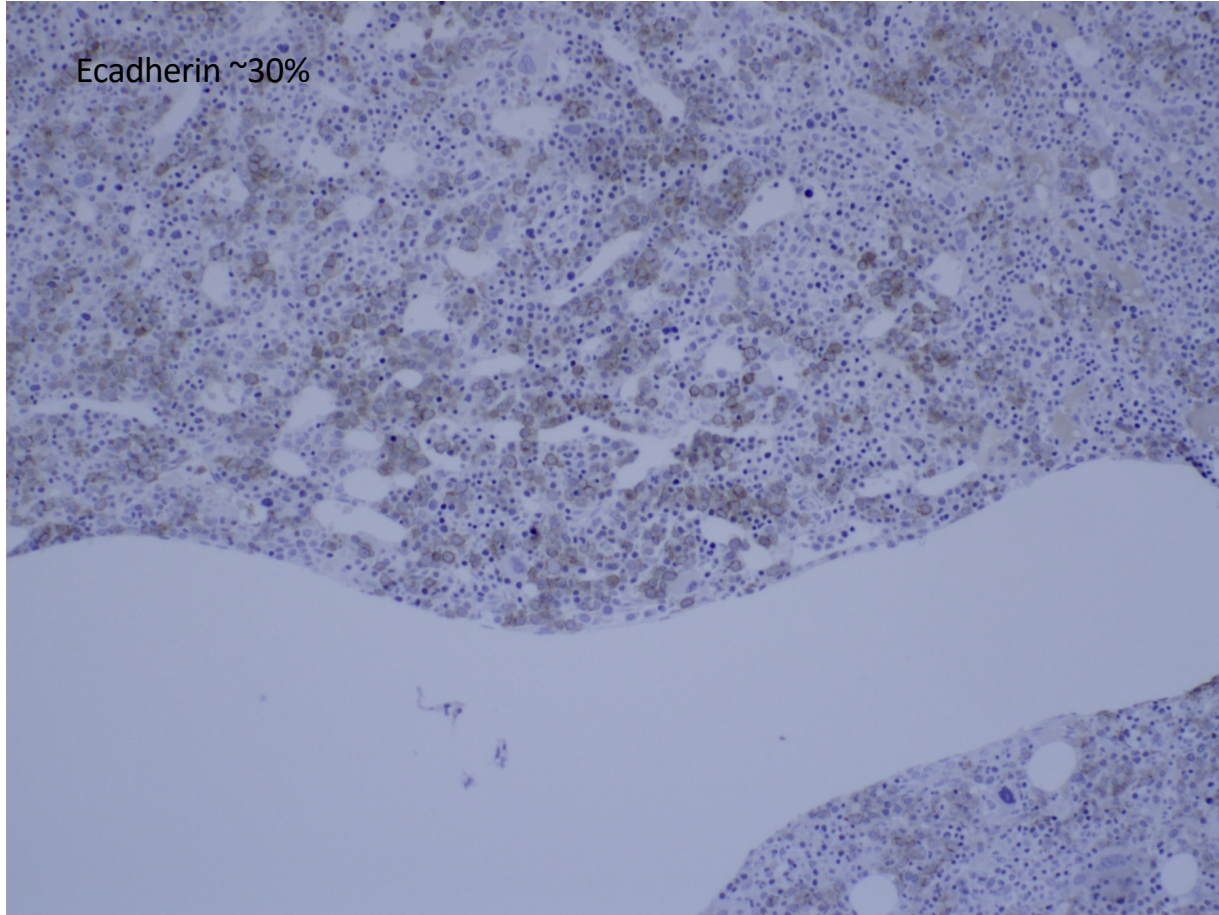




CD71 ~80%

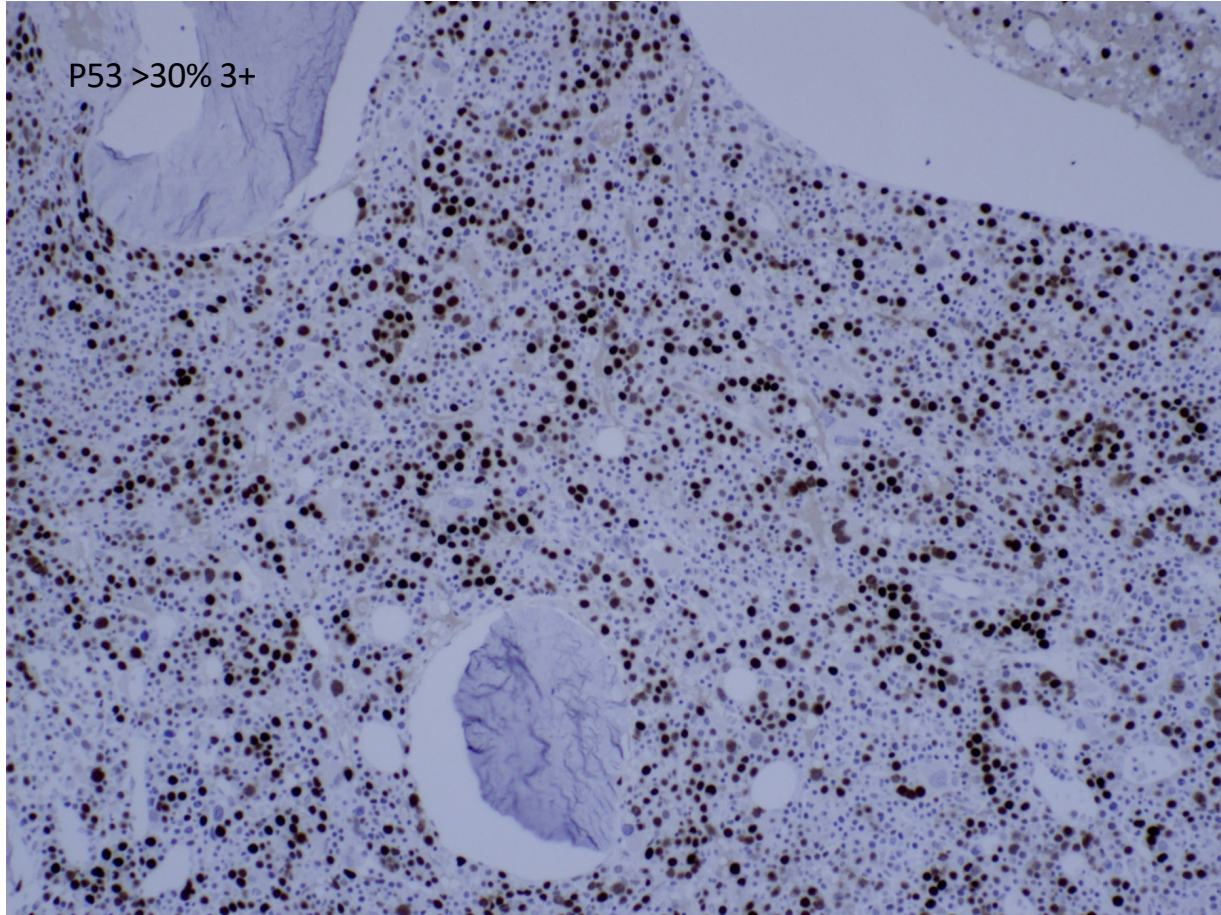


Ecadherin ~30%





P53 >30% 3+





# What would you call this?

- MDS-IB? MDS/AML? Therapy-related? AEL (old PEL)? MDS-f? Where does *TP53* fit in?

# Morphologic diagnosis

- Erythroid dominant marrow showing increased blasts, see note

NOTE: In light of increased blasts of both myeloid and erythroid lineages as well as elevated p53 staining, features are worrisome for acute erythroid leukemia or AML with mutated *TP53*. Correlation with pending cytogenetic and molecular studies are recommended. Given the patient's history of therapy for prior carcinoma, findings in this marrow are most compatible with myeloid neoplasm post cytotoxic therapy.

# Cytogenetic and Molecular findings

- Del 7q, Del 5q by FISH (karyotype failed)
- *TP53* level 1 mutation at 79% VAF
- Diagnosis?



# WHO5

- Acute Erythroid Leukemia (PEL is acceptable term)
- Usually 80% or more erythroid, of which 30% or more are proerythroblasts
- Central role of biallelic *TP53* mutations
- Dx of AEL supercedes AML-MR
- This subtype critical in treatment resistance and poor prognosis
- Given the prior therapy:  
Myeloid neoplasm post-cytotoxic therapy, Acute Erythroid Leukemia

# ICC

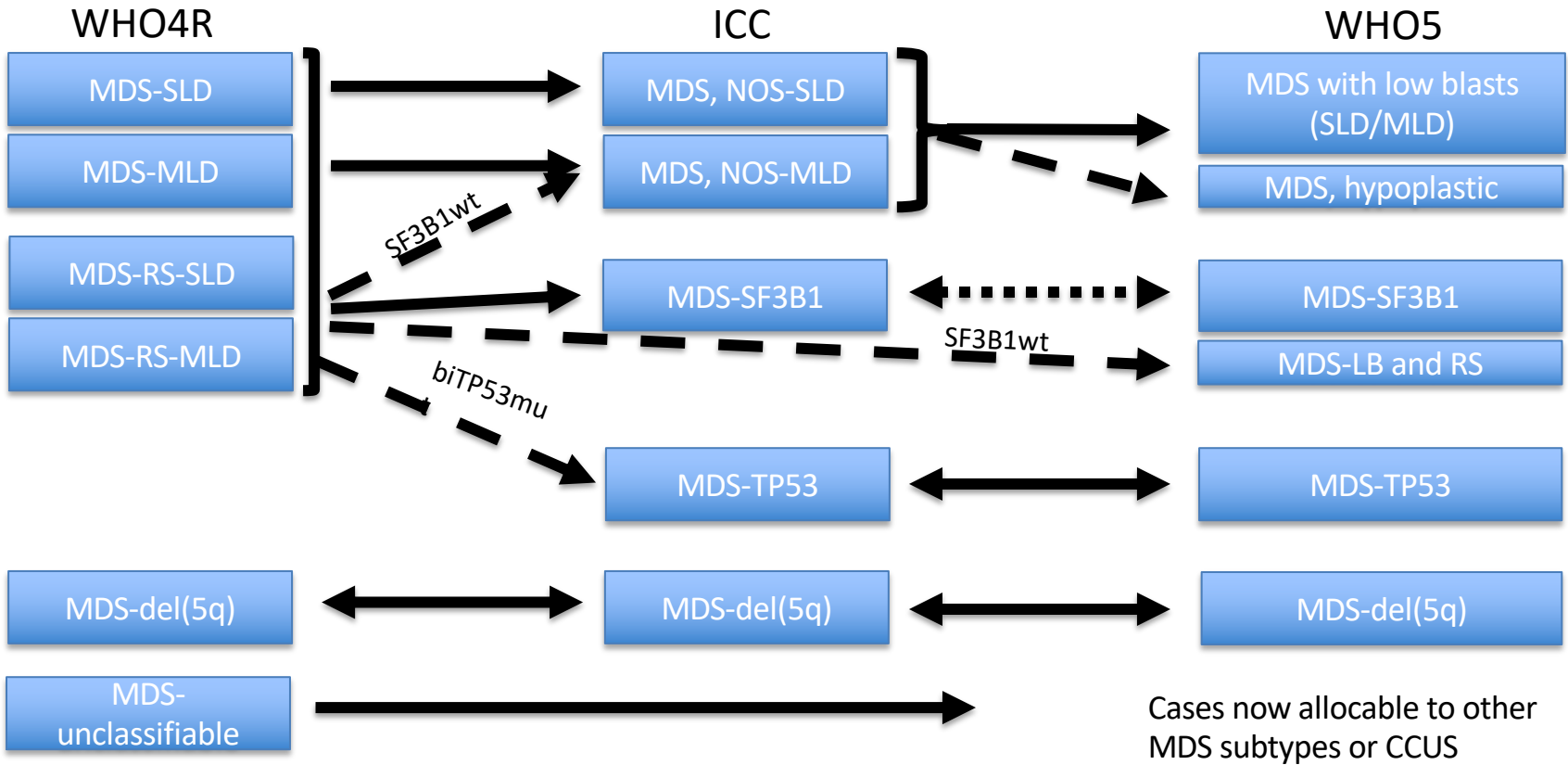
- AML with mutated *TP53*, therapy-related
  - Could consider MDS/AML w mutated *TP53* due to myeloblast criteria but can be AML due to meeting prior criteria for PEL.

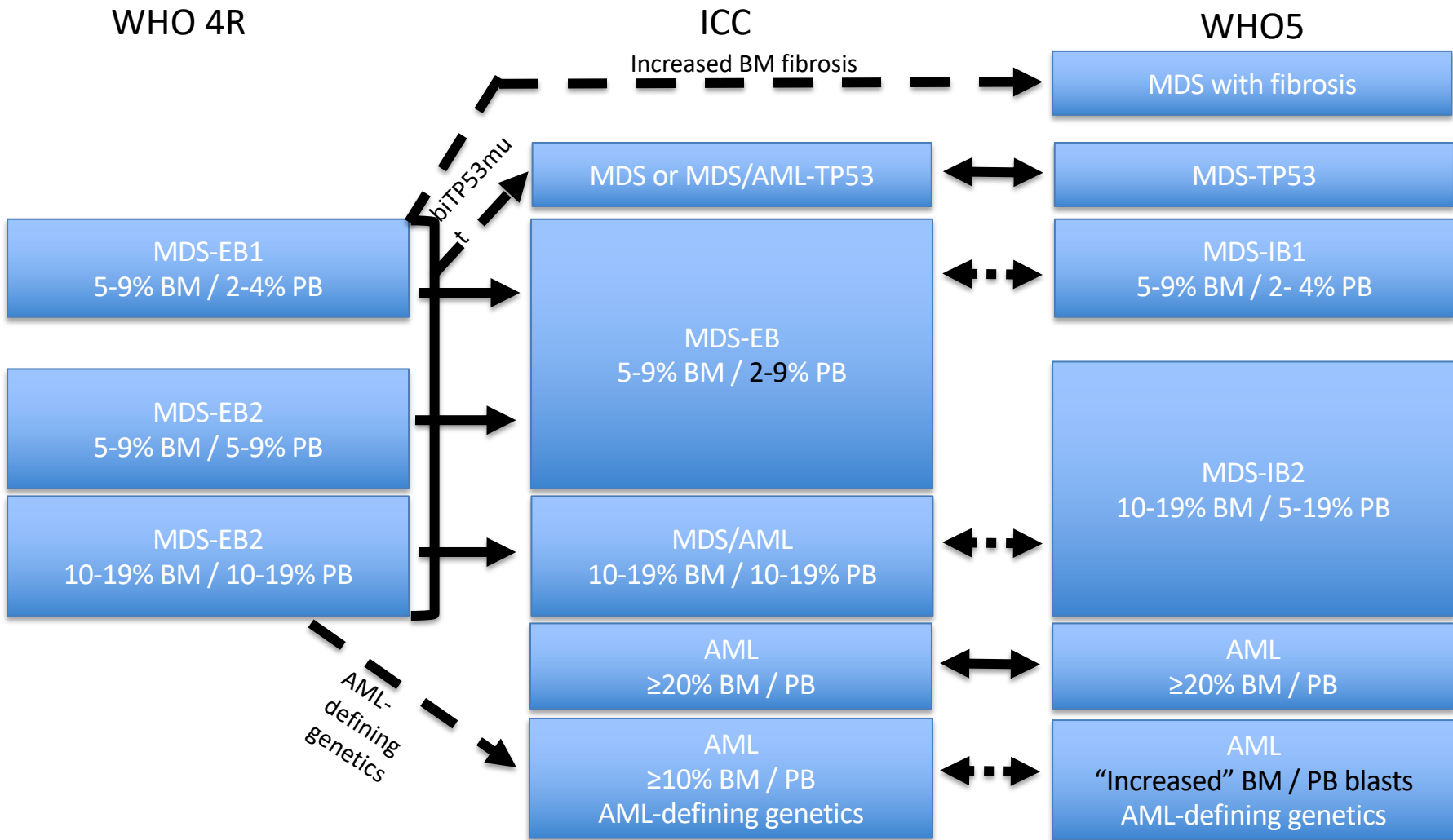
# Summative Interpretation

- Erythroid-dominant myeloid neoplasm with increased blasts, see note

NOTE: Given the clinical history of prior chemotherapy, features are compatible with WHO5 diagnosis “Acute Erythroid Leukemia, post cytotoxic therapy” and ICC diagnosis “AML with mutated TP53, therapy-related.”

# Relationship of ICC/WHO5 to WHO4R







**Thank You!**