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Blood Disorders Day 2021

FOR Health Professionals

How I treat myelodysplastic syndrome (MDS) and acute leukemia in older adults

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University of Manitoba

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Presenter Disclosure

- **Faculty / Speaker's name:** Brett Houston

- **Relationships with commercial interests:**
  - **Grants/Research Support:** None
  - **Speakers Bureau/Honoraria:** None
  - **Consulting Fees:** None
  - **Other:** None

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Mitigating Potential Bias

- Not applicable

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Learning Objectives

1. Review the clinical presentation, diagnosis and treatment of myelodysplastic syndrome (MDS)
2. Summarize the clinical presentation, acute complications and management of acute leukemia in older adults

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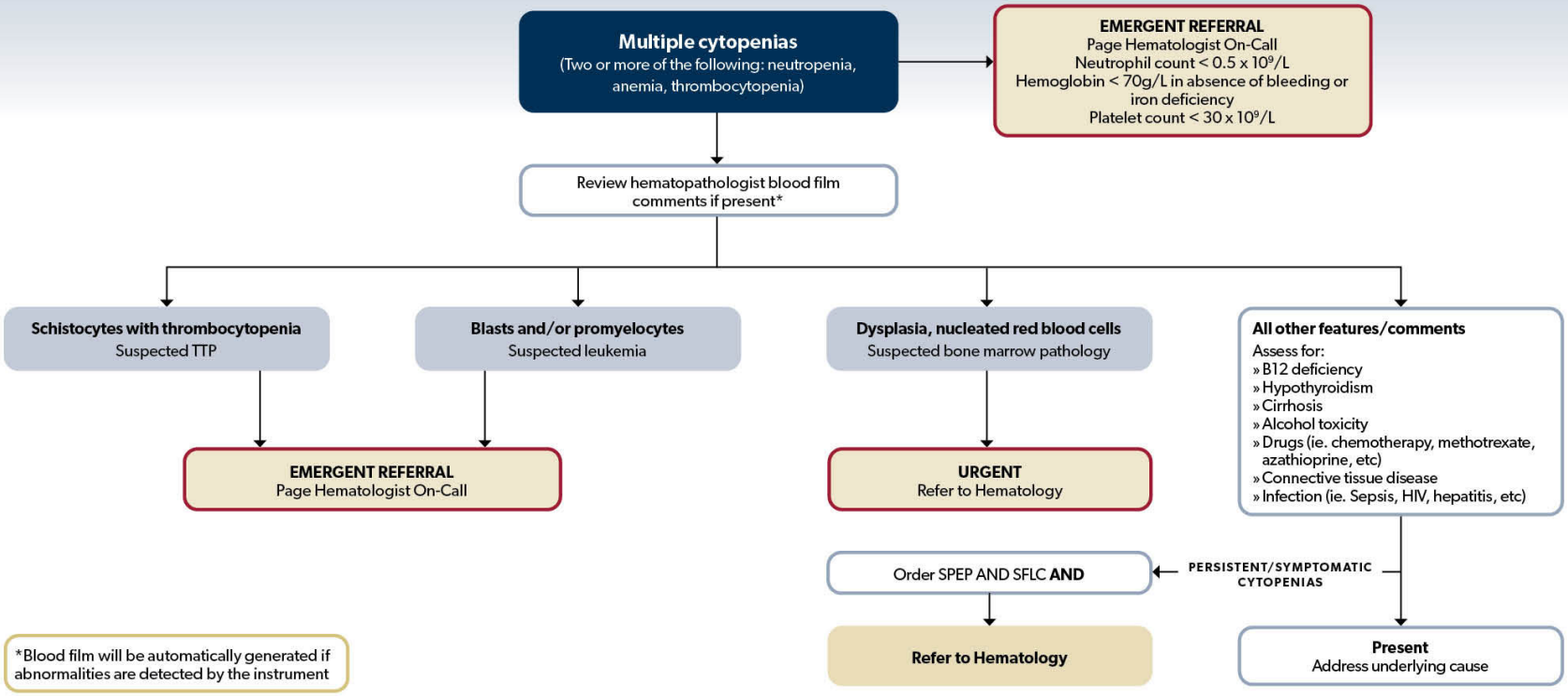
Case 1: Referral for pancytopenia

- 70-year-old man, otherwise healthy
- Normal CBC in 2018
- WBC 2.7 (ANC 1.1), Hb 110, MCV 108, Reticulocyte count 35, Platelets 131
- Blood film: no blasts or schistocytes

IMPRESSION: pancytopenia

Pancytopenia



SPEP = Serum protein electrophoresis
SFLC = Serum free light chain

TTP = Thrombotic thrombocytopenic purpura

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Pancytopenia

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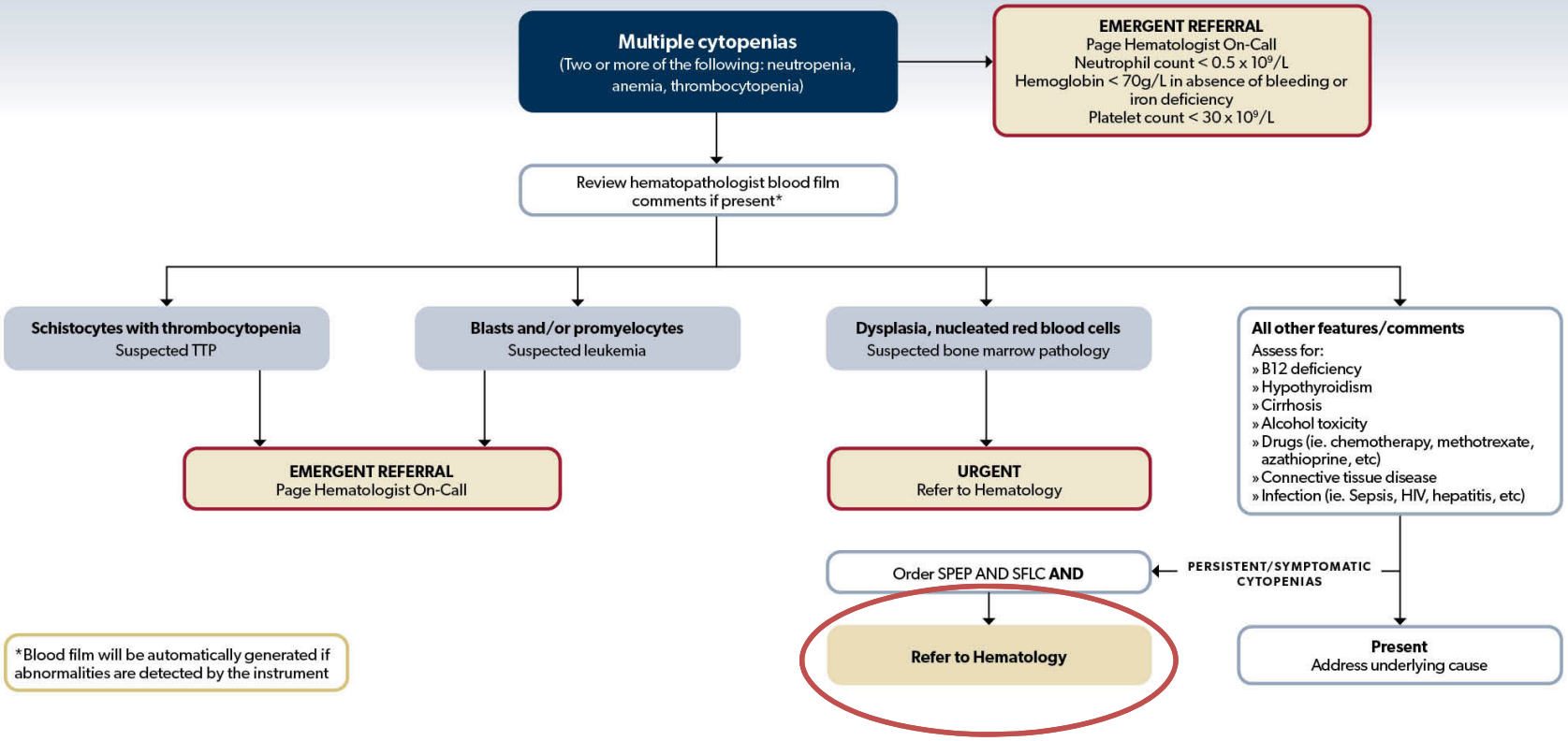

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Additional information

- Bone marrow biopsy: hypercellular marrow, significant dyserythropoiesis and megakaryopoiesis. Blasts 1%. Normal cytogenetics

- Diagnosis: myelodysplastic syndrome with multilineage dysplasia

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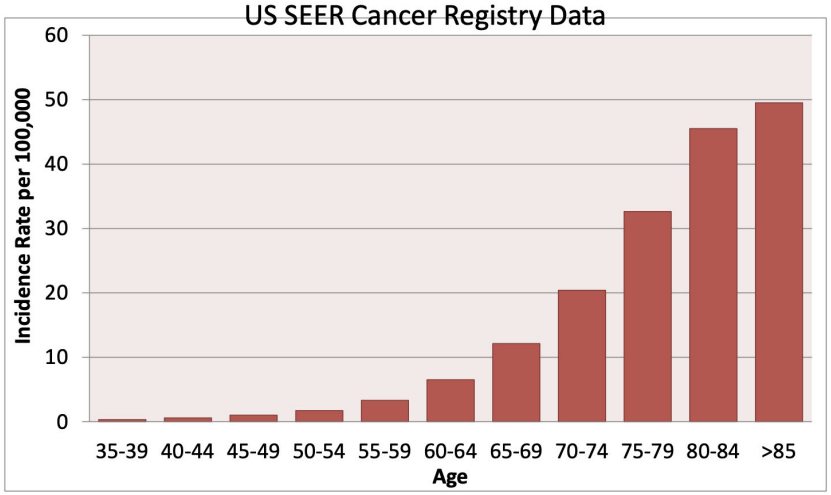
What is MDS?

- Blood cancer
- Predominantly affects older adults
- Results in cytopenias and increased risk of progression to acute leukemia

Epidemiology of MDS



- Affects ~ 5 / 100,000
- Median age 71 years
- Idiopathic in 80%

http://seer.cancer.gov. Accessed May 1, 2013
Fazal, MDS Foundation, 2019

Pathophysiology of MDS

- Clonal expansion of hematopoietic stem cells
- Ineffective hematopoiesis
  - Hypercellular marrow
  - Cytopenias
- Multi-step process involving cytogenetic changes (50%) / genetic mutations (90%)

Clinical manifestations

- **Anemia (90%)**
- Neutropenia
- Thrombocytopenia (severe in <20%)
- Autoimmune manifestations (15%)

- Dysplasia / nucleated red blood cells or blasts (<20%) on peripheral blood film

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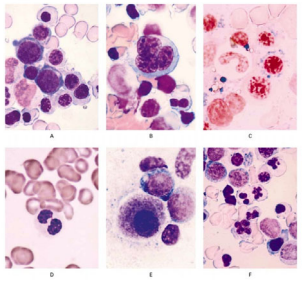
Diagnosis of MDS

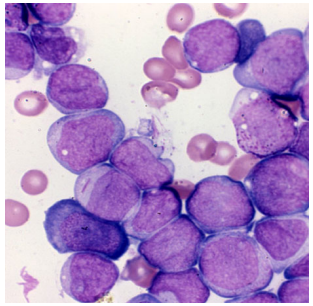
Cytopenias

+



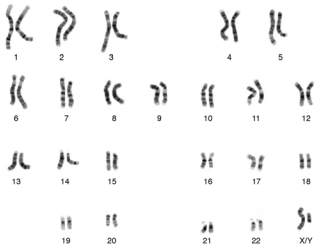
Dysplasia

OR



Increase in blasts
(<20%)

OR



Cytogenetic abnormalities
(Excluding +8, del(20q) or -Y)

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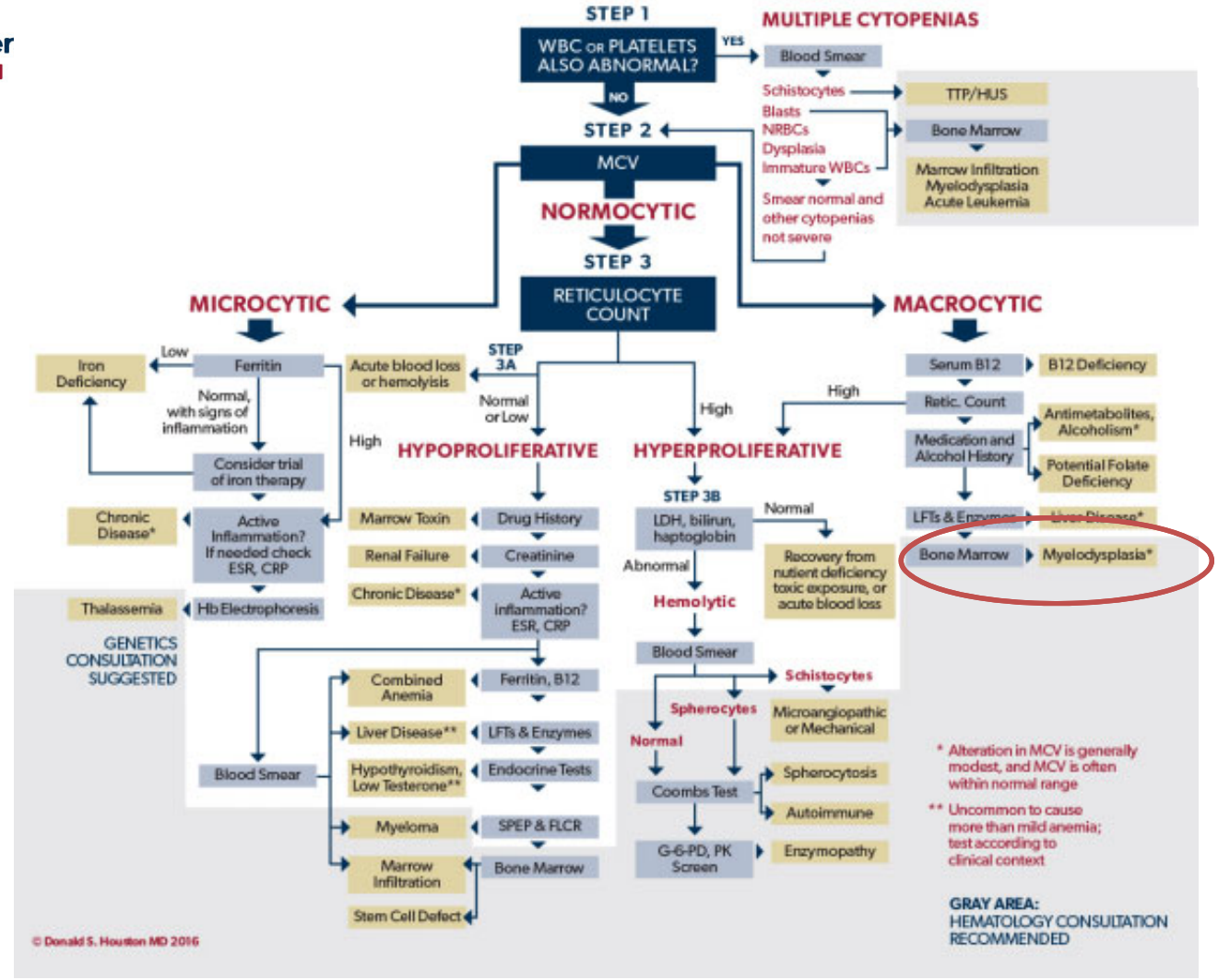
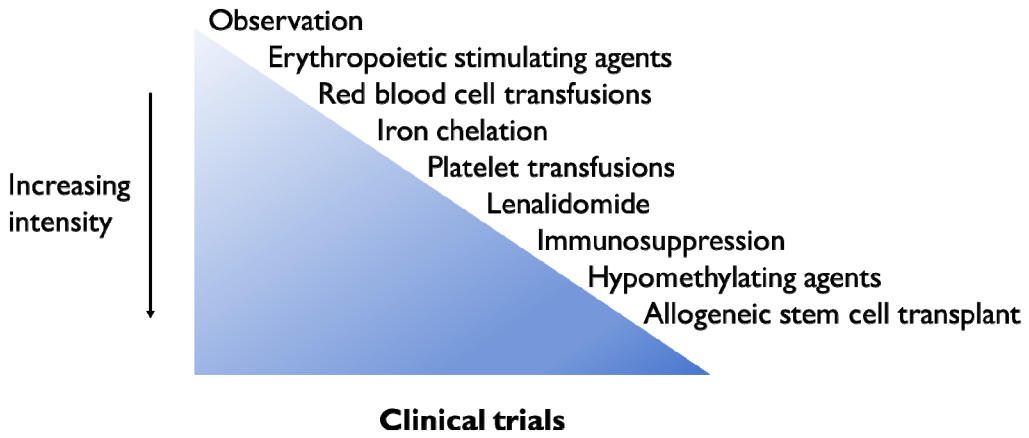


Prognosis & treatment

- Lower risk: median OS 5-8 years
- Higher risk: median OS 1-2 years

- Treatment depends on risk & clinical circumstance



Greenberg, Blood, 2012
Della Porta, Leukemia, 2015

Case 1 revisited

- Mild cytopenias, observed for a number of years
- Treated with EPO with good response (x 18 months)
- Currently on RBC transfusion q2 weeks; iron chelation

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Take home messages

- Most commonly presents with macrocytic anemia +/- pancytopenia
- Bone marrow biopsy is required for diagnosis & risk stratification
- Treatment is highly dependent on risk status

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Case 2: Referral for leukocytosis

- 71-year-old woman
- Past history of hypertension, dyslipidemia
- Normal CBC February 2016
- WBC 22, ANC 1, Hb 78, MCV 102, Reticulocytes 27, Platelets 14
- Blood film: ~80% blasts; auer rods

IMPRESSION: leukocytosis, blasts, anemia / thrombocytopenia

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Leukocytosis

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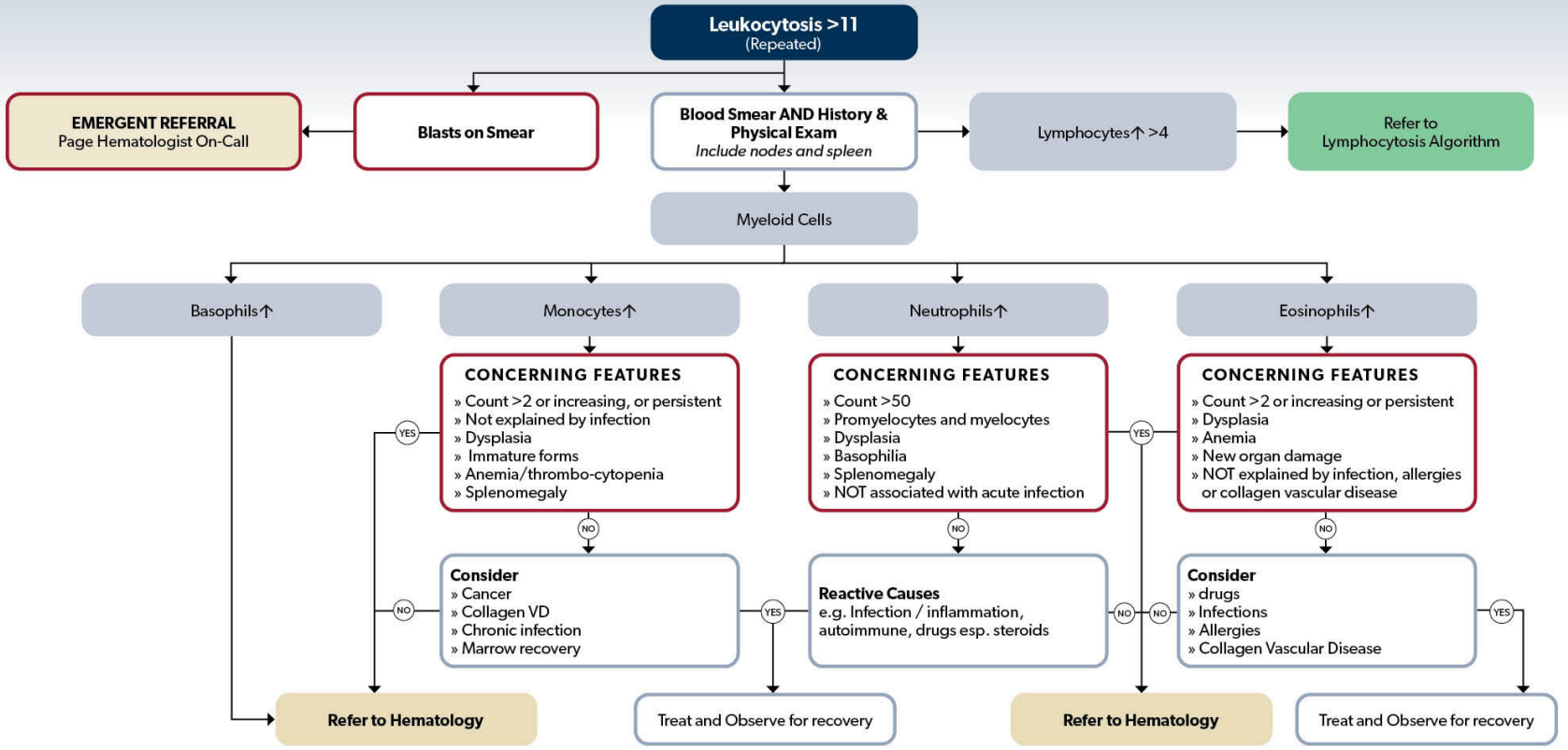

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Leukocytosis

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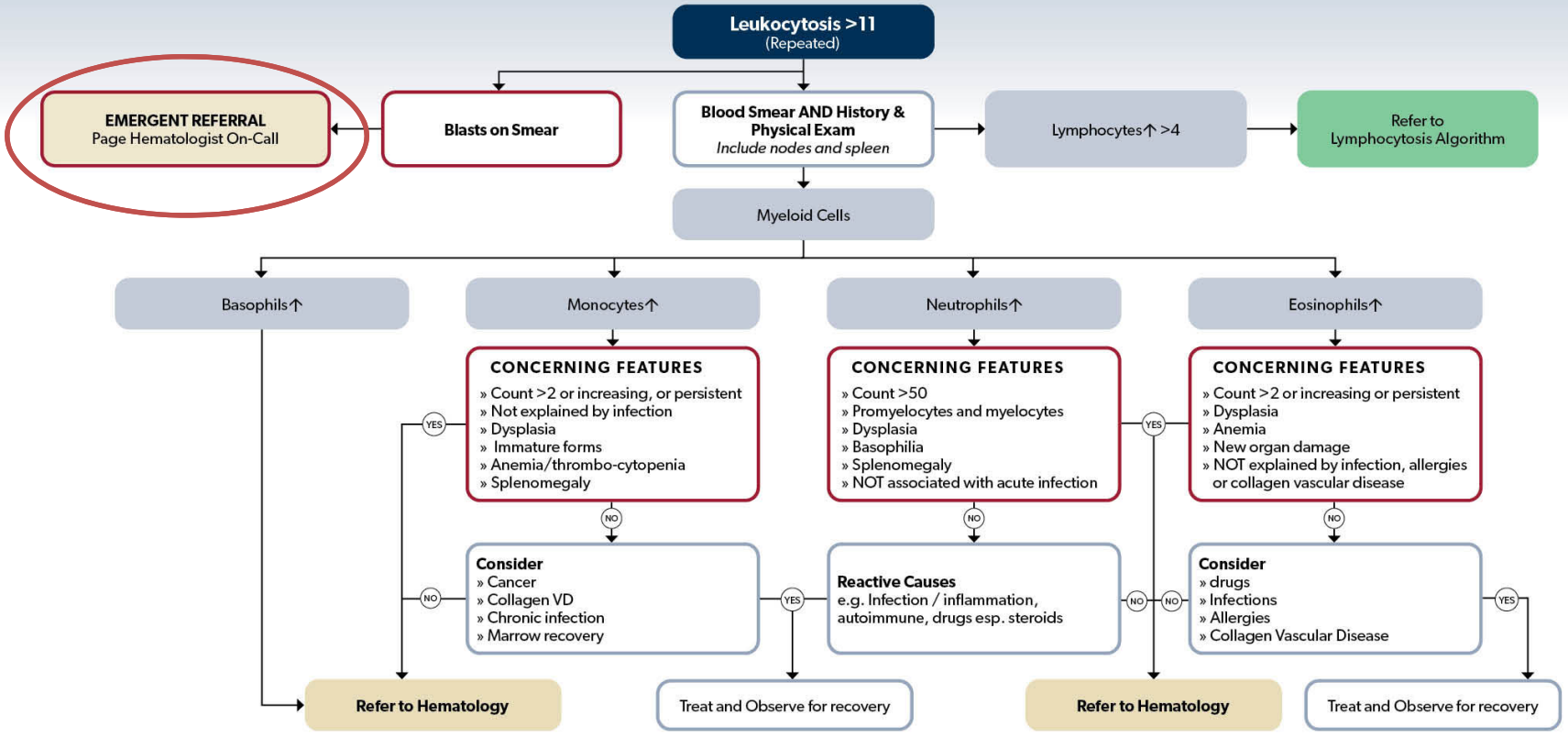

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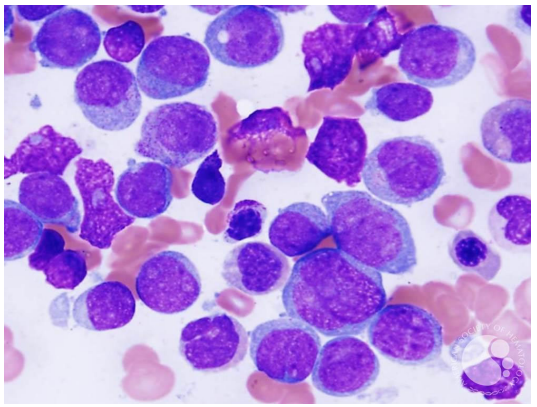
Additional information



- Feeling unwell x 3 weeks
- Intermittent fevers; COVID swab negative
- Easy bruising, minor epistaxis

- Bone marrow biopsy: 80% blasts (consistent with acute myeloid leukemia)

ASH Image Bank

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What is acute leukemia?

- Blood cancer
- Can progress quickly (days – weeks)
- Abnormal blasts (leukemia cells) often replace healthy bone marrow resulting in cytopenias

Epidemiology of acute leukemia

- Acute myeloid leukemia (AML) accounts for ~ 90% of acute leukemia in adults
- Median age 70 years
- In MB, ~ 50 – 75 new diagnoses / year

Clinical manifestations

- Constitutional symptoms
- Fatigue, weakness
- Anemia (pallor, heart failure)
- Thrombocytopenia (bleeding)
- Leukopenia / leukocytosis (infection)

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Diagnosis of acute leukemia

- Leukocytosis (blasts) OR pancytopenia
  - Peripheral blood or bone marrow blasts >20%

- Early mortality related to bleeding & infection
- Delayed treatment associated with reduced survival

Sekeres, Blood, 2009
Walter, JCO, 2011

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Pancytopenia

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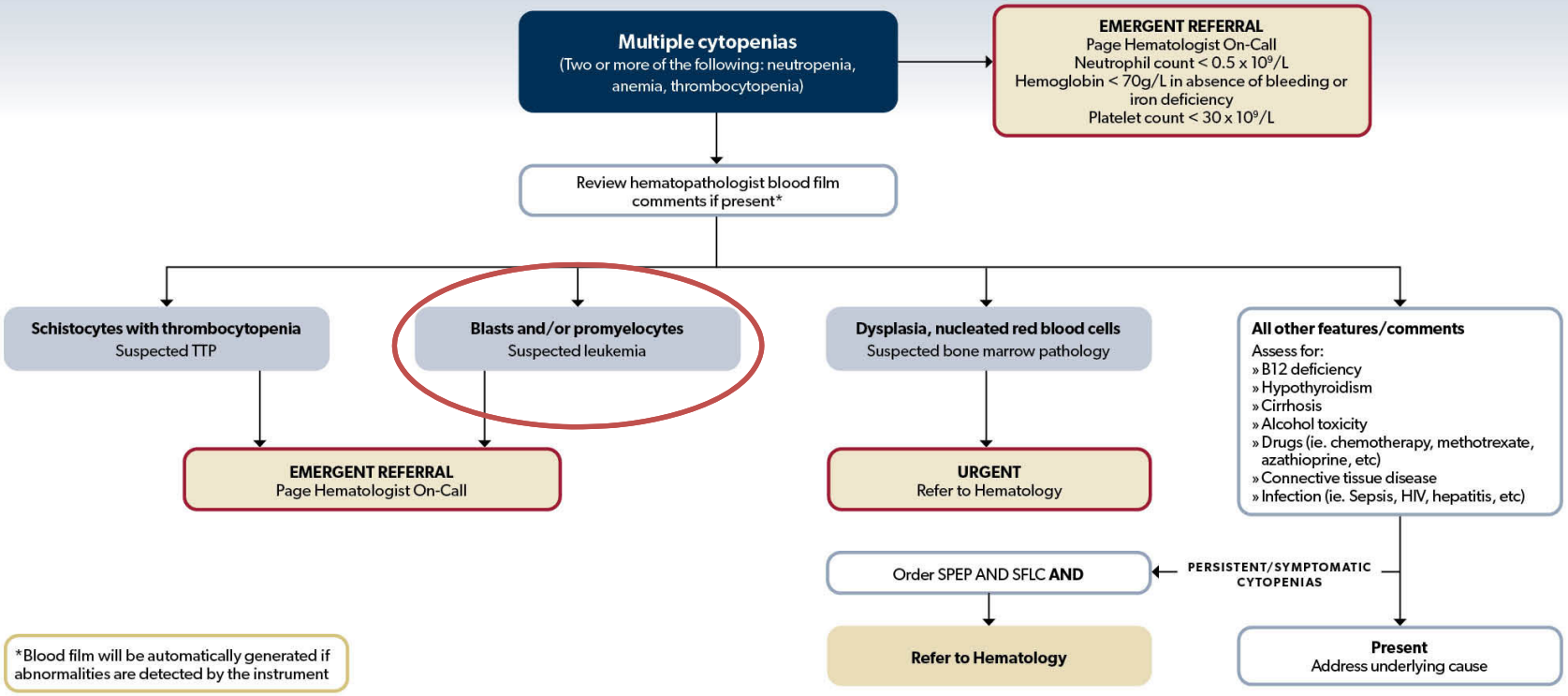

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Complications

- White blood cells (infection, leukostasis)
- Hemoglobin (symptomatic anemia, CHF)
- Platelets (bleeding)

- DIC (bleeding, thrombosis)
- Tumor lysis syndrome

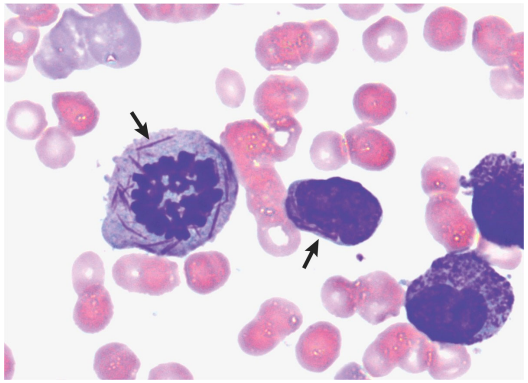
Assessment

- History & Physical
  - Infection
  - Bleeding (mucocutaneous, intracranial, GI)
  - Thrombosis (DVT, PE)
  - Organ dysfunction (head to toe)
    - Leukostasis

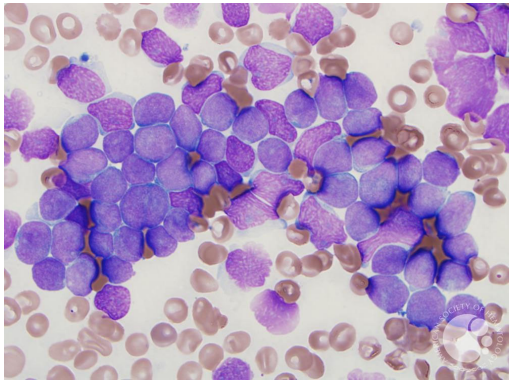
- Investigations
  - CBC, differential, blood film
  - Electrolytes, Ca, Mg, PO4, albumin
  - Creatinine
  - Liver enzymes
  - LDH, uric acid
  - DIC screen (INR, aPTT, fibrinogen, d-dimer)

Assessment

- Bone marrow biopsy
  - Determine type of leukemia (myeloid, lymphoid)
  - Cytogenetics / molecular testing



Acute myeloid leukemia



Acute lymphoblastic leukemia

Gordon, NEJM, 2017
ASH Image Bank

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Prognosis & treatment

Younger / fit	Older / unfit	Median OS
	Supportive care	3 months
Intensive chemotherapy (7+3)	Azacitidine	10 months
Stem cell transplant (SCT)	Azacitidine + venetoclax	15 months
(Targeted therapies)	Reduced intensity SCT	
	(Targeted therapies)	

Case 2 revisited

- Patient declined intensive chemotherapy & started azacitidine + venetoclax
  - Admitted to monitor for tumor lysis syndrome x 4 days, close follow-up at CCMB
  - Alive and well 5 months into treatment; counts normalized

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Take home messages

- Acute leukemia is a medical emergency with life-threatening complications
- Maintain high index of suspicion (leukocytosis, pancytopenia)
  - Blasts are always bad
- If any suspicion, phone hematologist on-call ASAP

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Thank you

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