MAYO CLINIC | School of Continuous Professional Development

32ND ANNUAL

INTERNAL MEDICINE BOARD REVIEW 2023

June 5-9, 2023



©2023 Mayo Foundation for Medical Education and Research | WF2079364-1

MAYO CLINIC | School of Continuous Professional Development

THE ABNORMAL CBC

PRESENTATION SUBTITLE HERE

Carrie Thompson, MD
Division of Hematology
Mayo Clinic – Rochester





©2023 Mayo Foundation for Medical Education and Research | WF2079364-2

DISCLOSURE OF RELEVANT FINANCIAL RELATIONSHIP(S) WITH INELIGIBLE COMPANIES

- Nothing to disclose

REFERENCES TO OFF-LABEL USAGE(S) OF PHARMACEUTICALS OR INSTRUMENTS

- Nothing to disclose

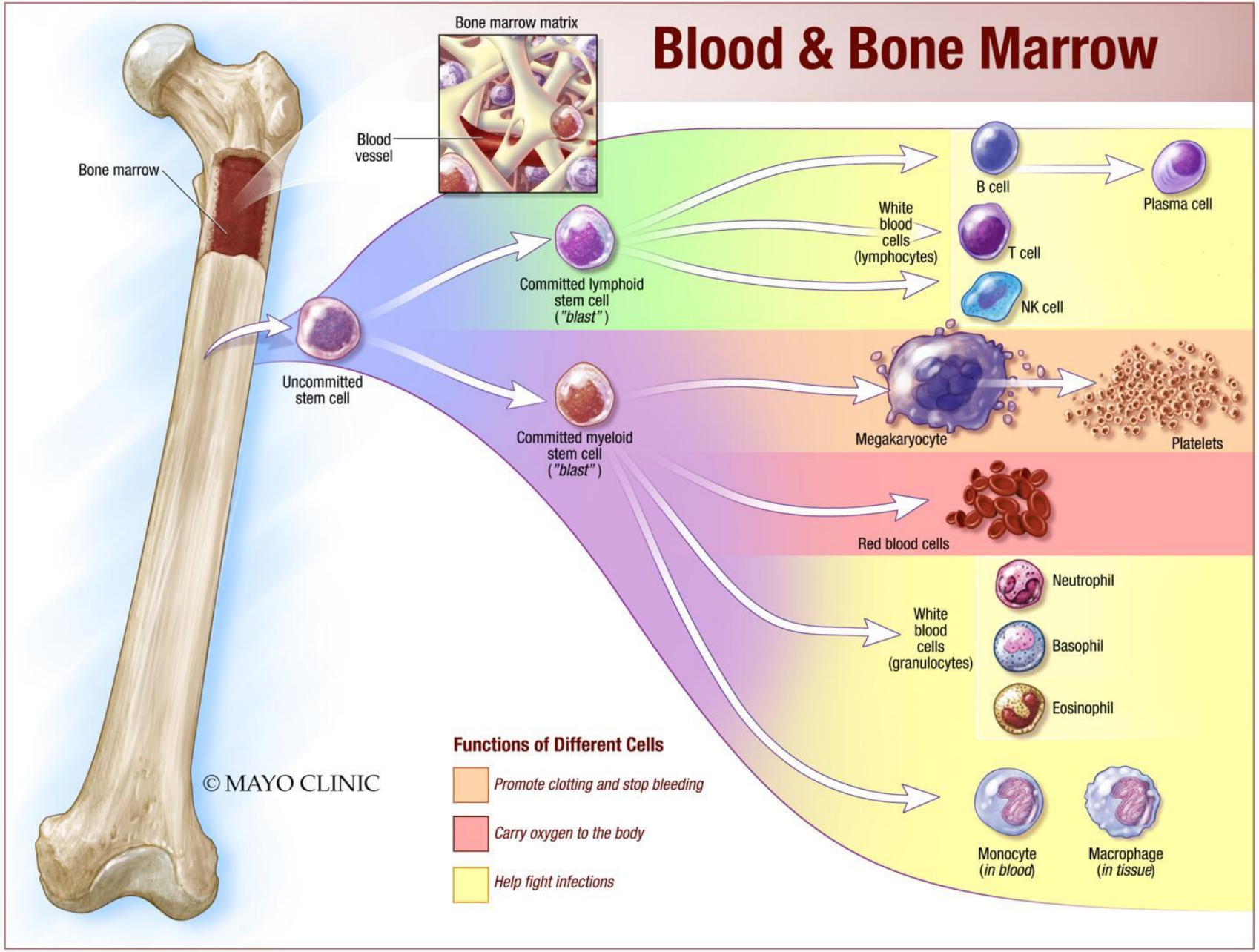
All relevant financial relationships have been mitigated.

©2023 Mayo Foundation for Medical Education and Research | WF942168-3

LEARNING OBJECTIVES

- Summarize the evaluation of abnormal red blood cell counts
- Describe evaluation of abnormal white blood cell count
- Recall the diagnosis and treatment of TTP
- Identify and evaluate pancytopenia
- Review the evaluation of elevated platelet counts

©2023 Mayo Foundation for Medical Education and Research | WF942168-4



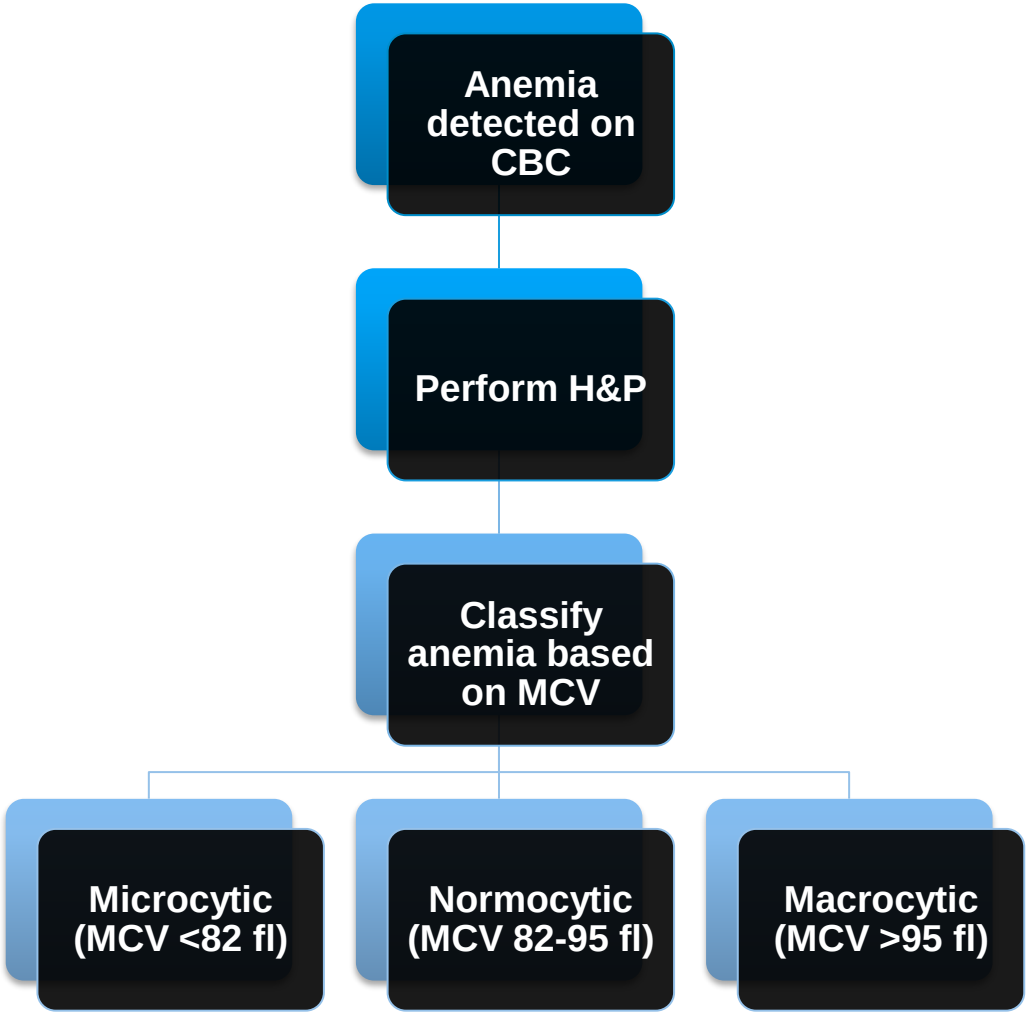
©2023 Mayo Foundation for Medical Education and Research | WF942168-5

APPROACH TO THE ABNORMAL CBC

- History and trend of blood counts
- Straight to bone marrow biopsy
  - Blasts in peripheral blood
  - Severe pancytopenia

©2023 Mayo Foundation for Medical Education and Research | WF942168-6

ANEMIA



©2023 Mayo Foundation for Medical Education and Research | WF942168-7

CASE #1

- 45 yo female presents for evaluation of fatigue and low back pain x last 3 months.
- PMHx: migraines, menorrhagia
- PE: pale, cracking at sides of lips (angular chelitis), otherwise normal
- Labs: WBC 5.2, Hgb 8.0 g/dL, platelets 290
- MCV 67 fL, RDW 16

©2023 Mayo Foundation for Medical Education and Research | WF942168-8

WHAT IS THE NEXT BEST STEP IN EVALUATION?

A. Reticulocyte count

B. Serum iron, TIBC, % saturation

C. ESR and CRP

D. Ferritin

E. All of the above

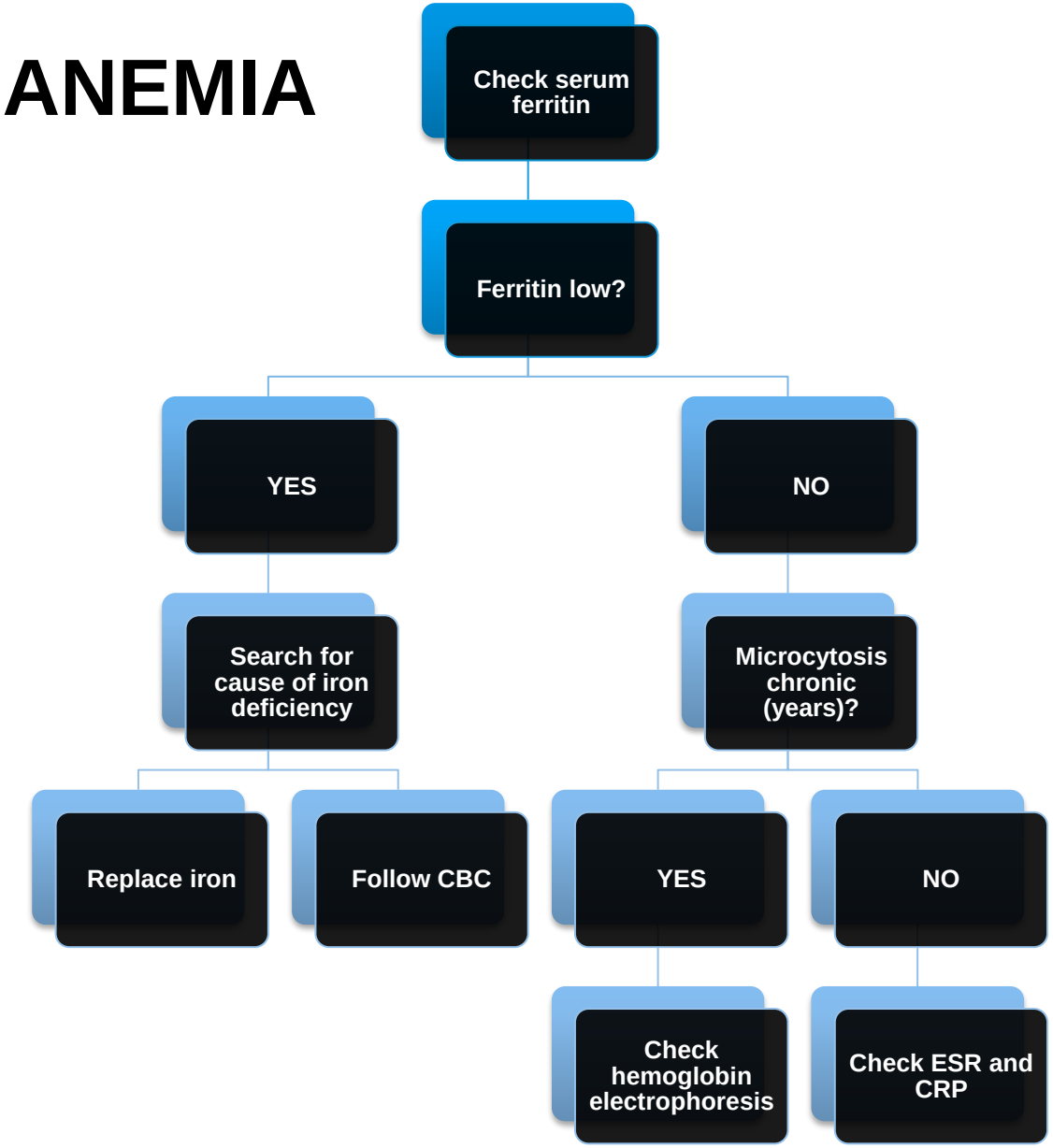
©2022 Mayo Foundation for Medical Education and Research | WF942168-9

ANSWER

D. Ferritin

©2023 Mayo Foundation for Medical Education and Research | WF942168-10

MICROCYTIC ANEMIA



©2023 Mayo Foundation for Medical Education and Research | WF942168-11

IRON DEFICIENCY ANEMIA: ETIOLOGY

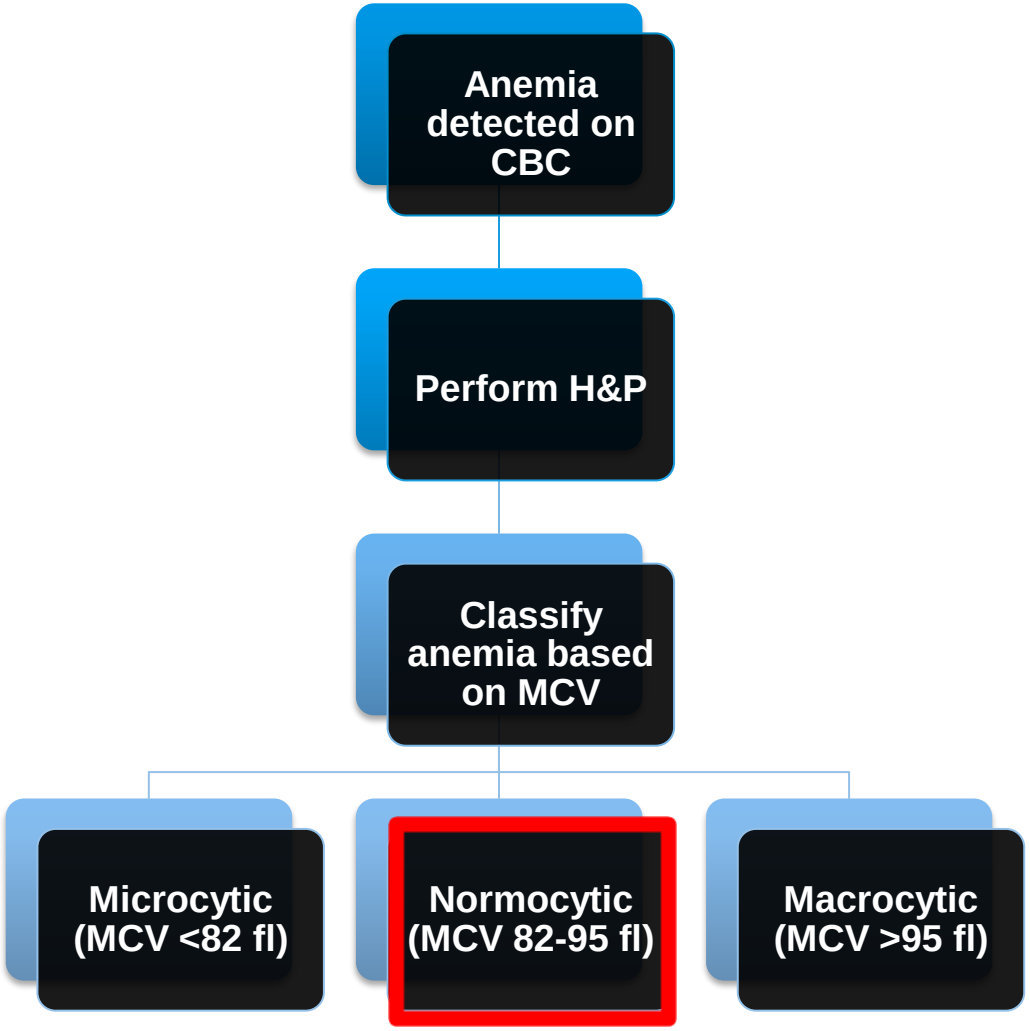
- Blood loss:
  - GI bleeding (upper or lower, often subclinical)
  - Menorrhagia
  - Multiple pregnancies
  - Blood donation
- Decreased iron absorption:
  - Vegan diet
  - Bariatric surgery
  - Celiac disease

©2023 Mayo Foundation for Medical Education and Research | WF942168-12

	Serum iron	Total Iron Binding Capacity (TIBC)	Transferrin Iron Percent Saturation (Serum Iron/TIBC)	Serum Ferritin
Normal range	40-180 µg/dL	250-450 µg/dL	25-35%	18-300 ng/mL
Iron deficiency	Low < 40 µg/dL	High > 350 µg/dL	< 15%	Low < 12 ng/mL (<41 ng/mL)
Anemia of chronic disease	Low < 40 µg/dL	Low < 300 µg/dL	> 15%	Normal to high

©2023 Mayo Foundation for Medical Education and Research | WF942168-13

ANEMIA



©2023 Mayo Foundation for Medical Education and Research | WF942168-14

NORMOCYTIC ANEMIA: ETIOLOGY

- Renal insufficiency/erythropoietin deficiency
- Anemia of chronic inflammation
- Hemolysis
  - Elevated LDH, direct bilirubin, reticulocyte count
  - Spherocytes → autoimmune
  - Schistocytes → MAHA – TTP, DIC, valve
  - Others: drugs (G6PD deficiency), PNH, congenital

©2023 Mayo Foundation for Medical Education and Research | WF942168-15

CASE #2

- A 51-year-old man presents for evaluation of fatigue. Follows with cardiologist but not seen by you in 3 years
- PMHx: morbid obesity s/p gastric bypass 2010, HTN, hyperlipidemia, DM type II, CAD, PVD, peripheral neuropathy
- Meds: Metformin, Metoprolol, Lisinopril, Simvastatin, ASA, Acetaminophen, MTV
- SH: Lives alone, 35 pack yr tob hx (quit 2010), occ beer, works in sales
- WBC 2.9, Hgb 8.3 g/dL, plts 145, MCV 104 fL
- Others: Calcium 8.2, albumin 4.0, creatinine 1.1, LDH 240, AST 23, ALT 31, tbili 1.2

©2023 Mayo Foundation for Medical Education and Research | WF942168-16

WHAT ARE THE MOST LIKELY FINDINGS ON PERIPHERAL BLOOD SMEAR?

A. Hypersegmented neutrophils

B. Blasts

C. Rouleaux

D. Dysplastic changes

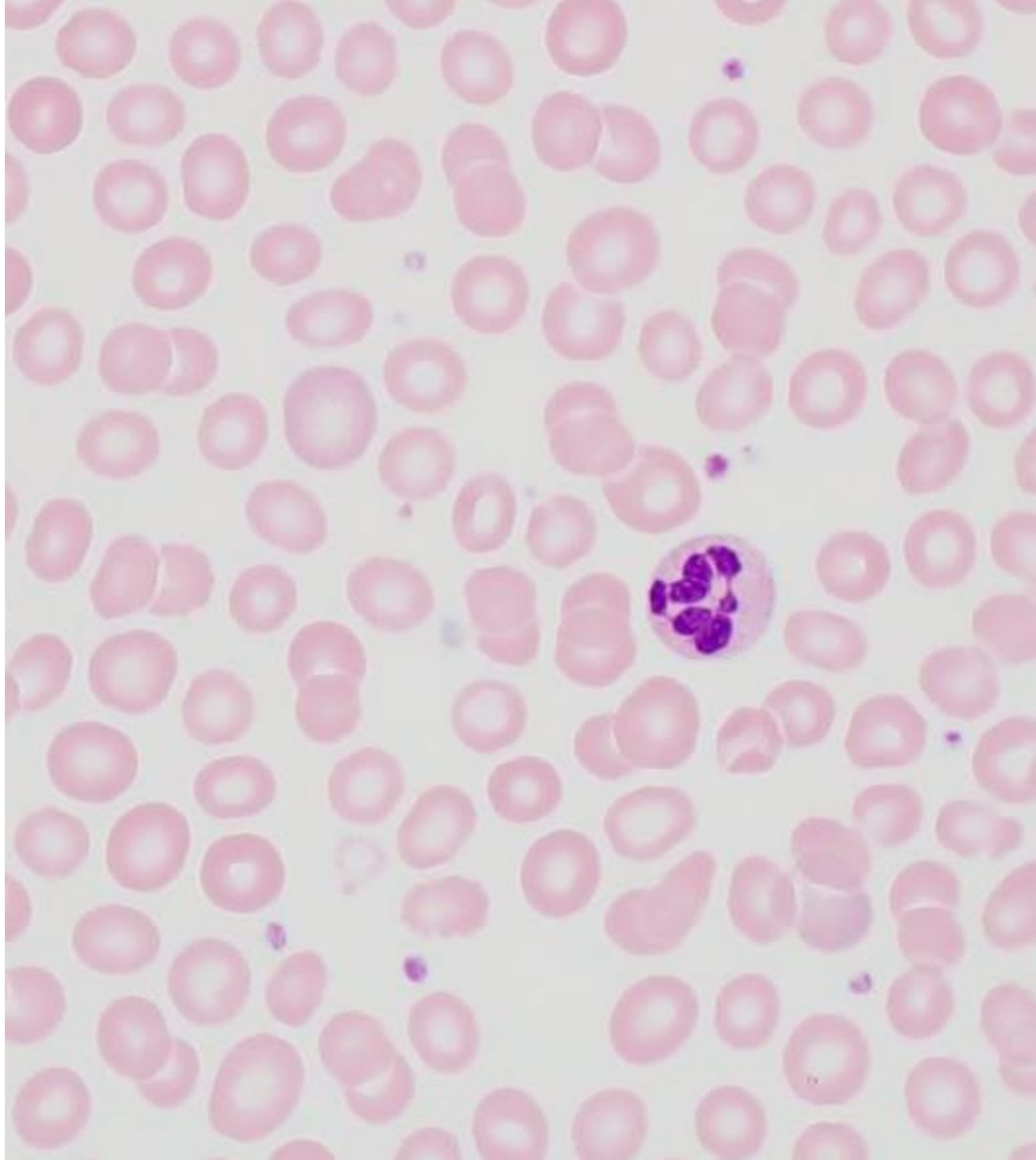
E. Burr cells (echinocytes)

©2022 Mayo Foundation for Medical Education and Research | WF942168-17

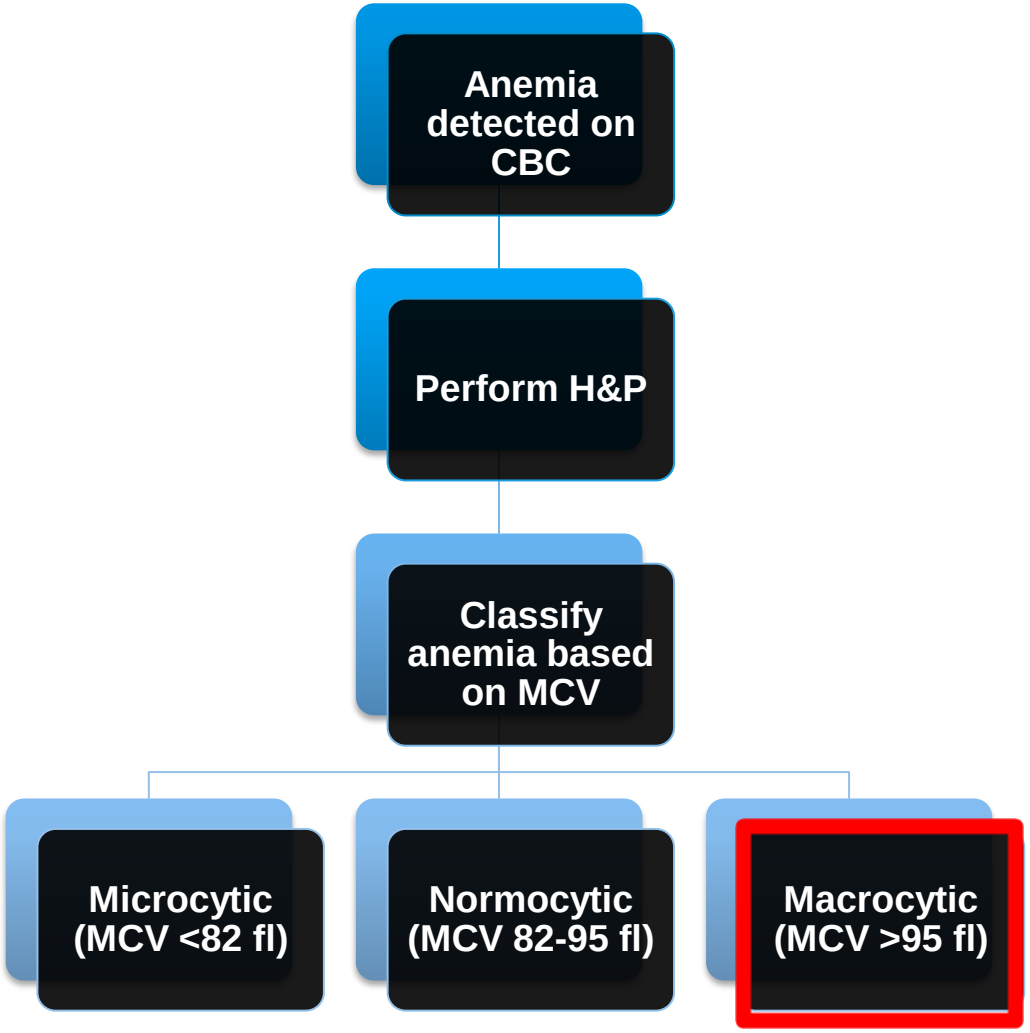
ANSWER

- A. Hypersegmented neutrophils

This patient has pancytopenia and macrocytosis. The most likely diagnosis is Vitamin B12 deficiency due to malabsorption (hx of gastric bypass surgery). Hypersegmented neutrophils are a classic finding in vitamin B12 deficiency.

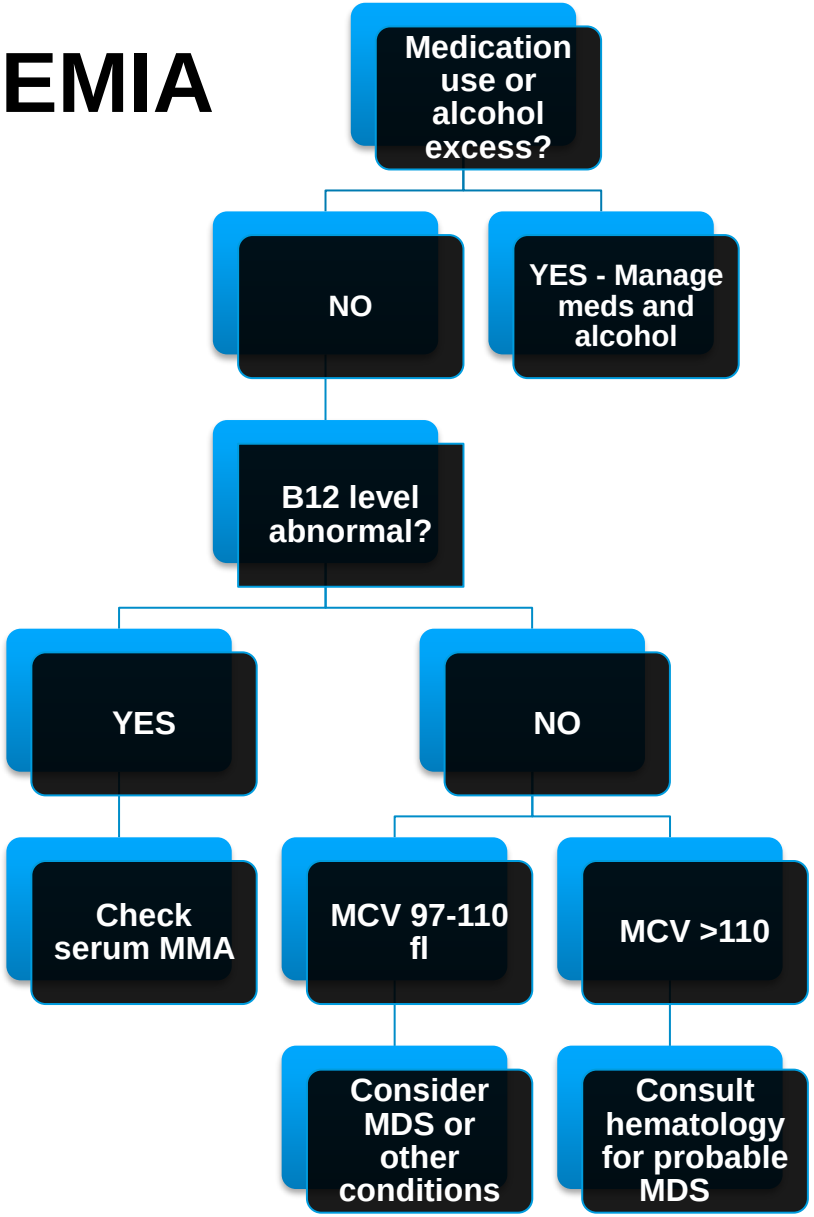


ANEMIA



©2023 Mayo Foundation for Medical Education and Research | WF942168-19

MACROCYTIC ANEMIA



©2023 Mayo Foundation for Medical Education and Research | WF942168-20

NUTRITIONAL DEFICIENCIES: LABORATORY STUDIES

- Measure vitamin B12 +/- folate
  - Low B12 = deficient
  - Borderline B12 = maybe deficient, further workup
    - Elevated homocysteine occurs with either B12 or folate deficiency
    - Elevated Methylmalonic acid occurs with B12 deficiency

©2023 Mayo Foundation for Medical Education and Research | WF942168-21

DIFFERENTIAL OF MACROCYTOSIS

- Medications
- Alcohol use
- Liver disease
- Reticulocytosis
- Hypothyroidism
- B12, folate, copper deficiency
- Nitrous oxide abuse
- Myelodysplastic syndrome

©2023 Mayo Foundation for Medical Education and Research | WF942168-22

ERYTHROCYTOSIS: TOO MANY RBC

- Polycythemia vera leads to increase in hemoglobin – and sometimes ↑WBC,↑platelets
  - Associated with thrombosis
    - Consider PV in patients with VTE in unusual places, such as portal bed
  - JAK2 mutation

©2023 Mayo Foundation for Medical Education and Research | WF942168-23

ERYTHROCYTOSIS WORKUP

- Step 1: repeat CBC in 1 month
- Step 2: determine if clonal vs. secondary
  - Check epo level
    - Clonal
      - Low epo level
      - Then check JAK2 V617F mutation (+ in 97% of PV)

©2023 Mayo Foundation for Medical Education and Research | WF942168-24

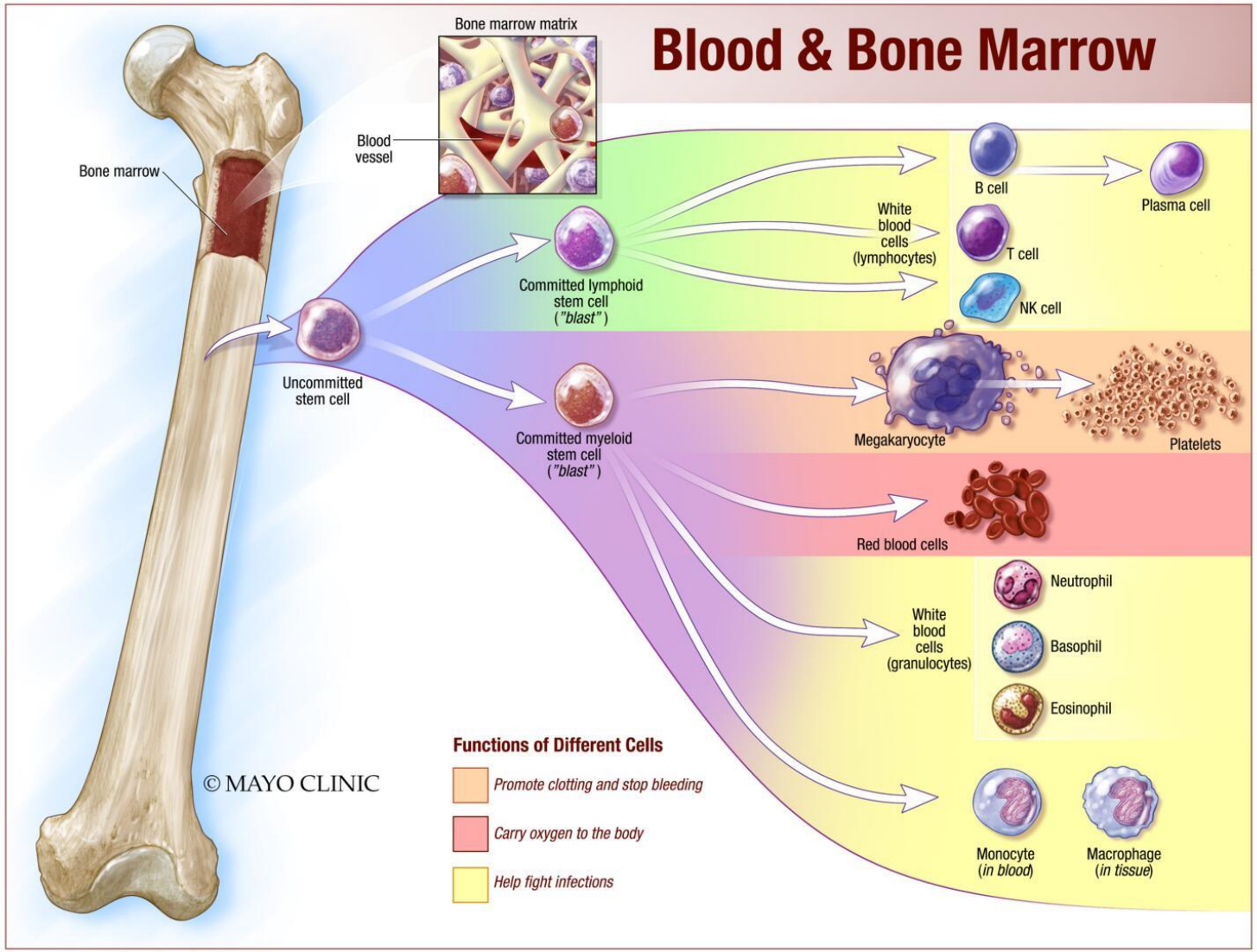
SECONDARY ERYTHROCYTOSIS

- 1- Due to epo-response to hypoxia
  - High altitude, smoking, sleep apnea, congenital heart disease,
- 2- Due to epo-producing tumors
- 3- Due to drugs
  - Androgens and erythropoietin

©2023 Mayo Foundation for Medical Education and Research | WF942168-25

LEUKOCYTOSIS: TOO MANY WBC

- Check WBC differential
- Check peripheral blood smear
  - Immature cells?
    - Blasts = acute leukemia
  - Mature leukocyte types?
    - Neutrophils
    - Lymphocytes



©2023 Mayo Foundation for Medical Education and Research | WF942168-26

NEUTROPHILIA

- Reactive (leukemoid reaction)
  - Infection, inflammation, malignancy, drugs
- Myeloid malignancy
  - Acute leukemia, myelofibrosis, CML, other MPD

©2023 Mayo Foundation for Medical Education and Research | WF942168-27

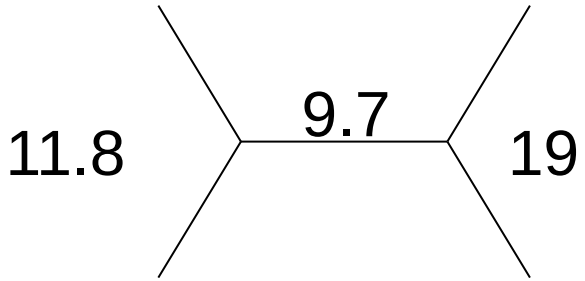
LYMPHOCYTOSIS

- Reactive
  - Viral infection
- Malignancy
  - Chronic lymphocytic leukemia (CLL)
  - LGL leukemia
  - Others
    - Hairy cell leukemia, mantle cell lymphoma, splenic marginal zone lymphoma, etc.
- Workup = Flow cytometry study

©2023 Mayo Foundation for Medical Education and Research | WF942168-28

CASE #3

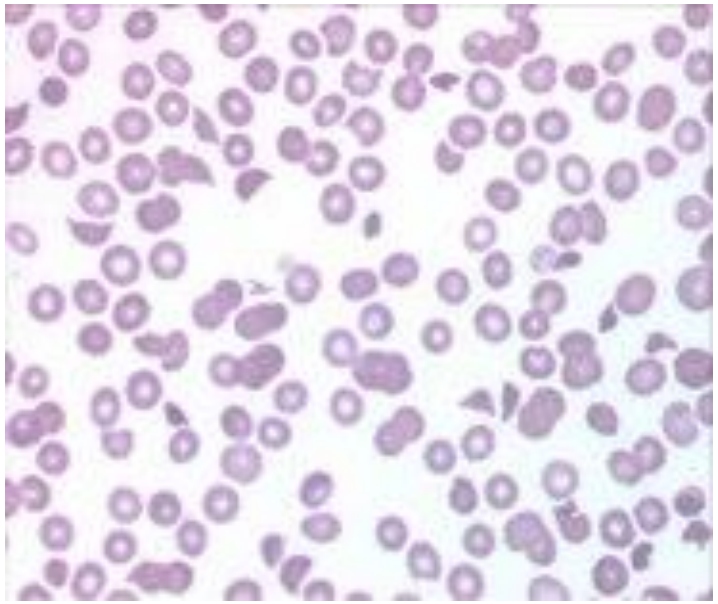
- 28 yo F presented to ER with fever, fatigue, N/V
- PMHx: S/P tonsillectomy
- Meds: Yasmin oral contraceptive
- SH: smoker, 1 ppd for 10 years
- Exam: T 38.2, no distress, slightly confused, otherwise normal



©2023 Mayo Foundation for Medical Education and Research | WF942168-29

CASE #3, CONTINUED

- Peripheral smear



- INR 0.9, APTT 27
- Haptoglobin < 14, LDH 612, total bilirubin 4.7

©2023 Mayo Foundation for Medical Education and Research | WF942168-30

WHAT SHOULD BE THE NEXT STEP IN PATIENT MANAGEMENT?

A. IVIG 1 mg/kg and Prednisone 1 mg/kg
B. Urgent plasmapheresis
C. Platelet transfusion
D. Check heparin-PF4 antibodies

©2022 Mayo Foundation for Medical Education and Research | WF942168-31

ANSWER

B. Urgent plasmapheresis

- This patient has TTP. Plasmapheresis is life-saving treatment.

©2023 Mayo Foundation for Medical Education and Research | WF942168-32

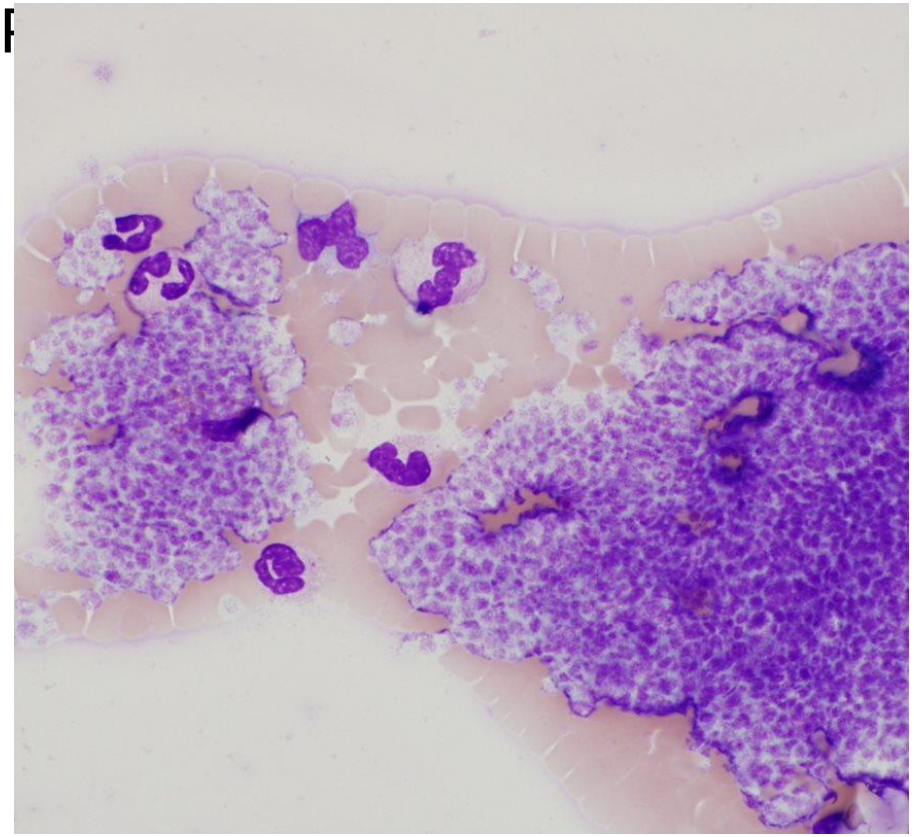
APPROACH TO THE ABNORMAL PLATELET COUNT

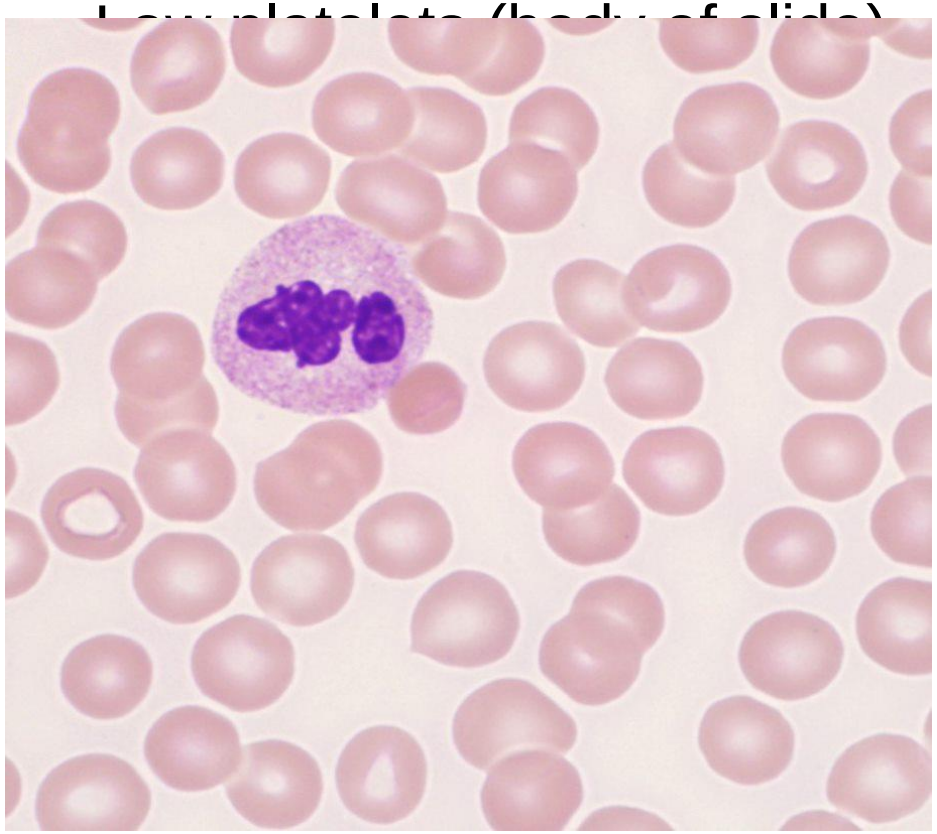
- History and trend of blood counts
- Determine if this is true thrombocytopenia
- Is this a thrombocytopenic emergency?

©2023 Mayo Foundation for Medical Education and Research | WF942168-33

APPROACH TO THROMBOCYTOPENIA: 1ST STEP PERIPHERAL SMEAR

- P

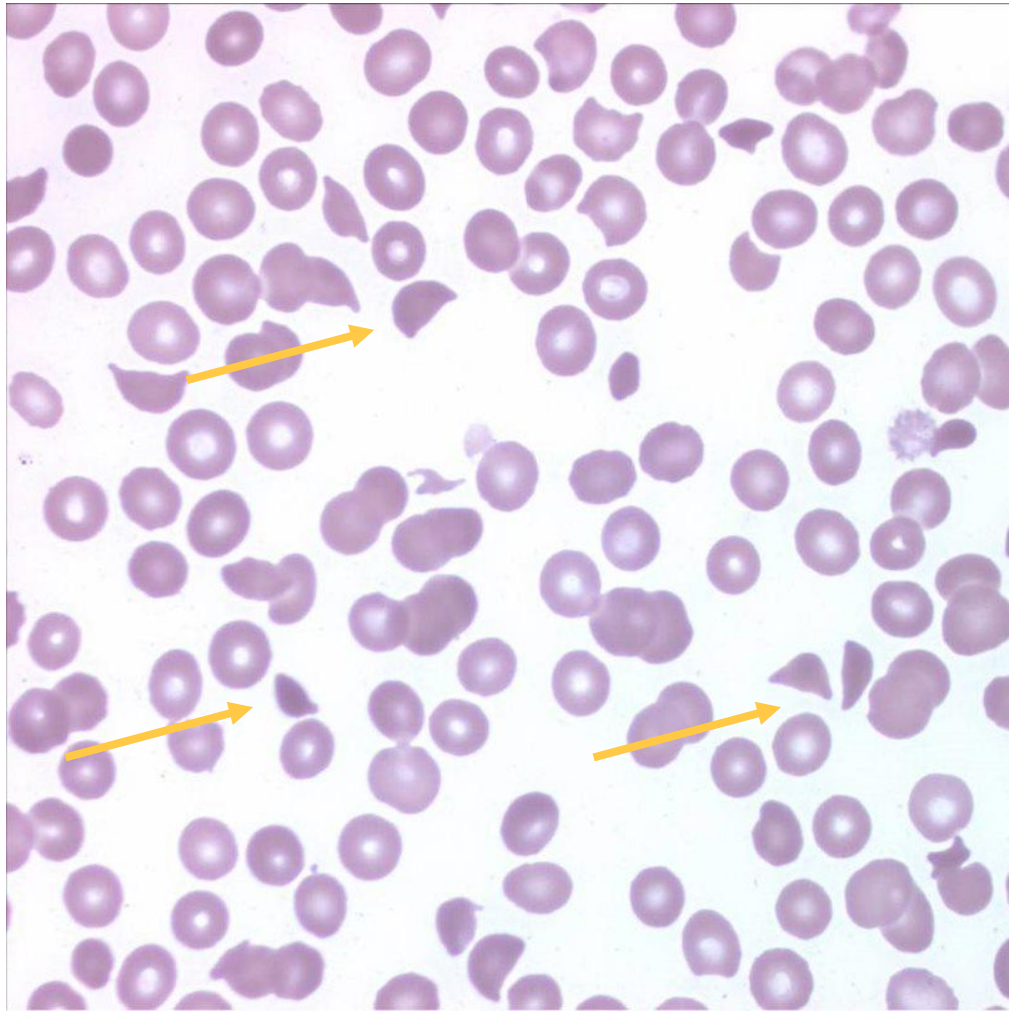




©2023 Mayo Foundation for Medical Education and Research | WF942168-34

APPROACH TO THROMBOCYTOPENIA: 1ST STEP PERIPHERAL SMEAR

- Schistocytes = RBC fragments
- Produced by mechanical damage in circulation
  - May be caused by thrombotic microangiopathy (TMA) = hematological emergency



©2023 Mayo Foundation for Medical Education and Research | WF942168-35

APPROACH TO THOMBOCYTOPENIA: 2ND STEP DETERMINE IF THIS IS AN EMERGENCY

- TTP/HUS
- Drug-induced, including HIT
- ITP with bleeding
- Catastrophic antiphospholipid Ab syndrome
- Post-transfusion purpura

©2023 Mayo Foundation for Medical Education and Research | WF942168-36

APPROACH TO THOMBOCYTOPENIA: 3RD STEP CONSIDER THE CLINICAL CONTEXT

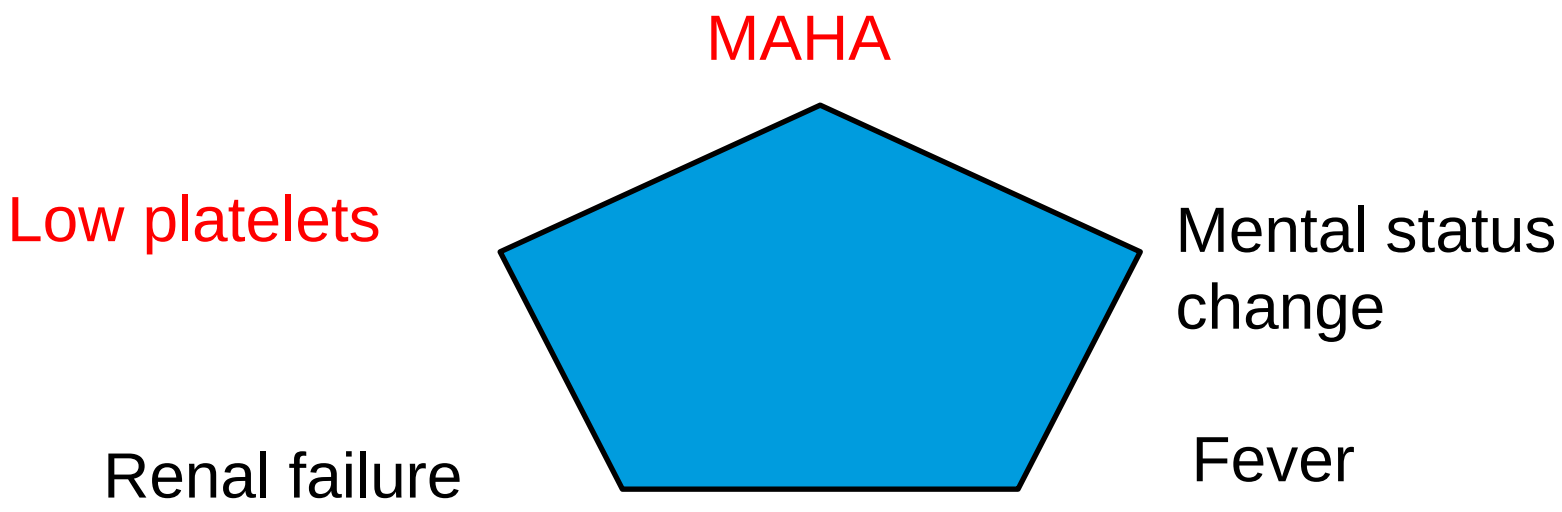
Clinical Context:	Consider this:
Postoperative setting	Dilutional, HIT
Medical patient	HIV, hepatitis C
Isolated low platelets	ITP
ICU	Sepsis, drugs, DIC, multifactorial
Cancer patients	DIC, TTP
Pregnancy	Gestational thrombocytopenia, ITP, preeclampsia, HELLP syndrome, TTP/HUS, acute fatty liver of pregnancy

©2023 Mayo Foundation for Medical Education and Research | MF942168-37

TTP

- Often strikes young adults, mainly females
- Due to autoantibodies vs. ADAMTS-13

Classic pentad:



©2023 Mayo Foundation for Medical Education and Research | WF942168-38

CASE #4

- A 34-year-old man is hospitalized after a motorcycle accident. He suffered multiple traumatic injuries, including splenic laceration requiring splenectomy and pneumothorax requiring chest tube placement.
- Today is postop day 7, he is clinically improving, and hopes to be discharged.
- CBC shows the following: WBC 10.5, hemoglobin 12.5 g/dL, and platelets 832.
- Platelet count was normal on the day of admission.

©2023 Mayo Foundation for Medical Education and Research | WF942168-41

WHAT IS THE NEXT BEST STEP?

A. BCR-ABL level

B. Peripheral blood smear

C. Dismiss home

D. Plateletpheresis

E. Start heparin therapy

©2022 Mayo Foundation for Medical Education and Research | WF942168-42

ANSWER

- C. Dismiss home

©2023 Mayo Foundation for Medical Education and Research | WF942168-43

REACTIVE THROMBOCYTOSIS

- Expected post-splenectomy
  - Peaks 1-3 weeks postop, normalizes within weeks
  - Generally not associated with thrombosis
    - Consider ASA 81 mg
  - If extreme (>1500K), risk of hemorrhage (acquired vWD)
- Other causes
  - Inflammatory conditions, infection, trauma, hemolysis, iron deficiency

©2023 Mayo Foundation for Medical Education and Research | WF942168-44

CLONAL THROMBOCYTOSIS

- Essential thrombocythemia (ET)
  - Increased risk of thrombosis if age >60 years and/or previous thrombosis
    - Platelet lowering agents + ASA
  - Increased risk of thrombosis if platelets >1 million

©2023 Mayo Foundation for Medical Education and Research | WF942168-45

SUMMARY: 4 TAKE-HOME POINTS

- Low ferritin is diagnostic of iron deficiency anemia
- Most common causes of macrocytosis are alcohol use, reticulocytosis, and vitamin B12 deficiency
- Workup lymphocytosis with peripheral blood flow cytometry to determine reactive vs. clonal
- Thrombocytopenia + schistocytes = TMA, DIC, or valvular hemolysis →call a hematologist

©2023 Mayo Foundation for Medical Education and Research | WF942168-46

THANK YOU

Thompson.Carrie@mayo.edu

@CaThompsonMD

©2023 Mayo Foundation for Medical Education and Research | WF942168-47

MAYO CLINIC | School of Continuous Professional Development

THANK YOU FOR JOINING US IN THIS COURSE



Rochester, Minnesota



Phoenix, Arizona



Jacksonville, Florida

©2023 Mayo Foundation for Medical Education and Research | WF942168-48