

Abnormal CBC: Diagnostic approach

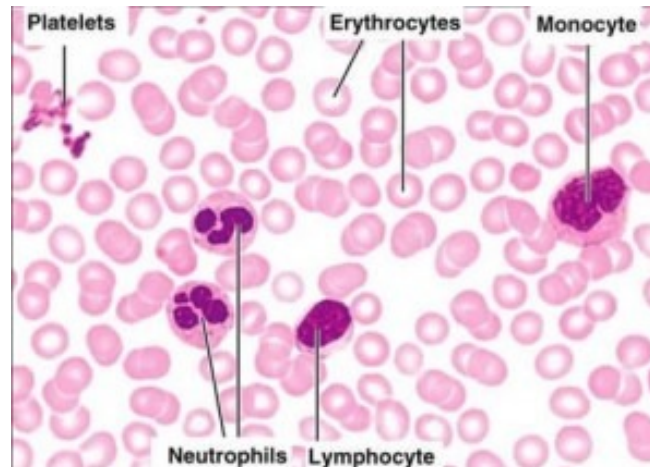
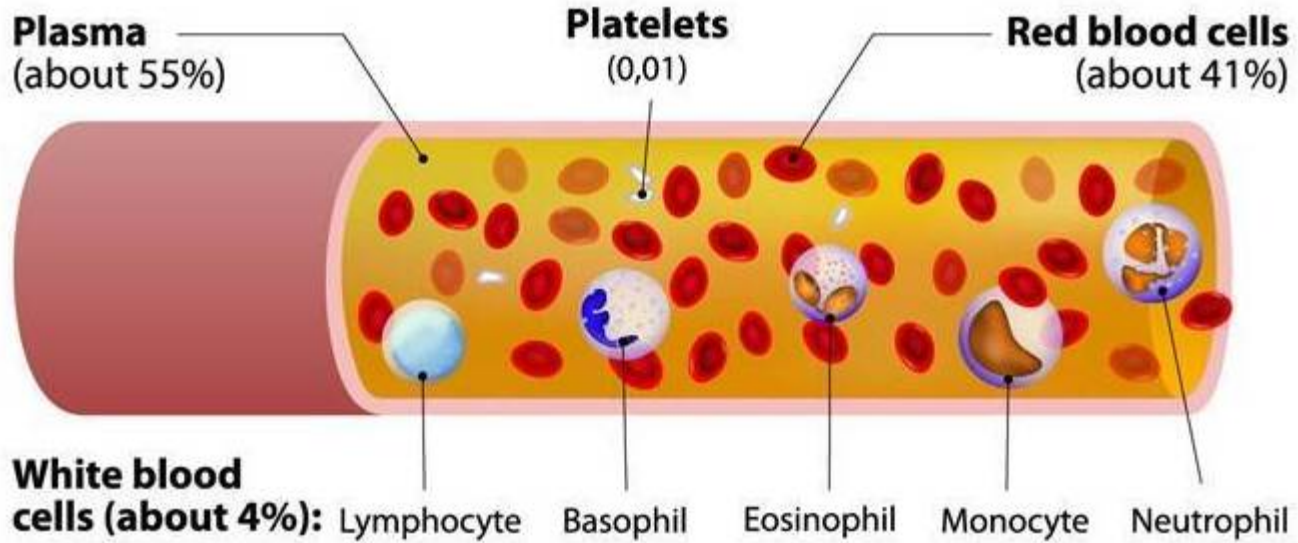
Ranju Kunwor, MD, MS, FACP

Assistant professor

SSM Health/SLU

- Nothing to disclose.

The elements of blood



	Latest Ref Rng & Units
WBC	4.0 - 10.7 x10E9/L
RBC	4.30 - 5.80 x10E12/L
Hemoglobin	13.3 - 17.5 g/dL
Hematocrit	38.7 - 51.1 %
MCV	80.0 - 98.0 fL
MCH	26.7 - 33.6 pg
MCHC	31.7 - 36.3 g/dL
RDW-CV	11.3 - 14.8 %
Platelet Count	150 - 420 x10E9/L
MPV	7.8 - 11.4 fL
Neutrophils %	41.0 - 74.0 %
Lymphocytes %	17.0 - 47.0 %
Monocytes %	3.0 - 11.0 %
Eosinophils %	0.0 - 7.0 %
Basophils %	0.0 - 1.6 %
Immature Grans	0.0 - 1.0 %
Neutrophil Absolute	1.60 - 7.50 x10E9/L
Lymphocytes Absolute	1.00 - 4.40 x10E9/L
Absolute Monocytes	0.15 - 1.00 x10E9/L
Eosinophils Absolute	0.00 - 0.60 x10E9/L
Absolute Basophils	0.00 - 0.13 x10E9/L
RBC	4.30 - 5.80 x10E12/L
RDW	11.3 - 14.8 %
Granulocytes %	41.0 - 74.0 %
Granulocytes Absolute	1.60 - 7.50 x10E9/L
Monocytes Absolute	0.26 - 1.07 x10E9/L
Basophils Absolute	0 - 0.08 x10E9/L
Immature Granulocytes %	0.0 - 1.0 %
RDW-CV	12.1 - 14.9 %
nRBC Auto	<=0.0 /100 WBC

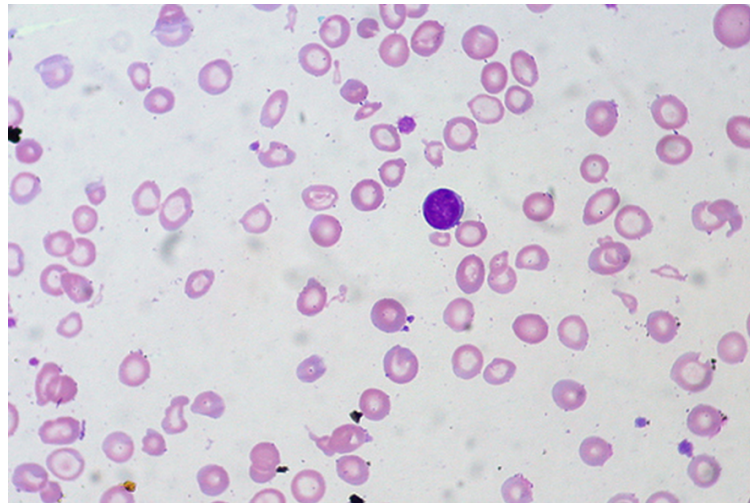
Red Cell Indices

- Mean Corpuscular Volume [Hctx10/RBC]
80-99 fL
How is the size?
- Red Cell Distribution Width
11-15.8%
Variation in size
- Mean Corpuscular Hemoglobin [Hbx10/RBC]
26-34 pg
Amount of Hb per RBC
- Mean Corpuscular Hemoglobin Concentration [Hbx100/Hct]
32-37.5 g/dL of erythrocytes

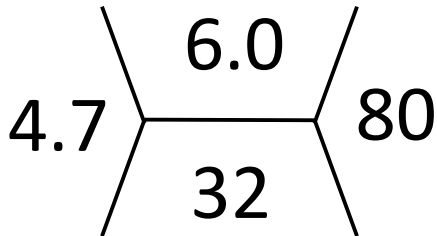
Case #1

52 y/o female with bipolar and migraines who presented with worsening fatigue x 2 months with approx 20 lbs unintentional weight loss over the past 2 years. Has had poor appetite but no specific food aversions / cravings.

PE: malnourished with some pallor; no hepato-splenomegaly. No masses, icterus



Case #1



MCV 72

RBC 5.0m/mm³

Retic: 1.3; Absolute count 25.9

RDW: 31.4

Iron: 64, TIBC 459, Sat 14%, Ferritin 10

B12 1002, Folate 5.9

Haptoglobin: 25, LDH 238

HBV, HVC and HIV are negative

Diagnosis ?

Evaluation of Anemia Based on MCV

Microcytic Anemia (MCV < 80 fL)

- Iron deficiency anemia
- Anemia of chronic disease
- Thalassemia
- Sideroblastic anemia
- Lead poisoning

Normocytic Anemia (MCV 80–100 fL)

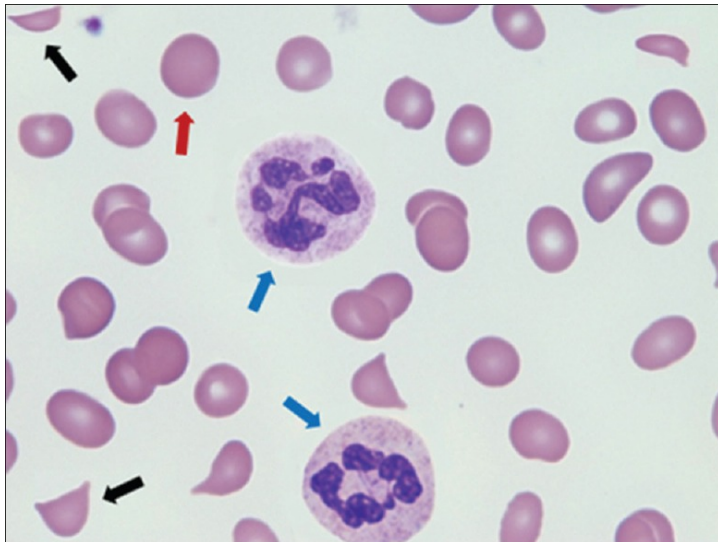
- Acute blood loss
- Hemolysis (AIHA, G6PD, sickle cell, etc.)
- Anemia of chronic disease
- Aplastic anemia
- Bone marrow infiltration
- Chronic kidney disease
- Endocrine disorders

Macrocytic Anemia (MCV > 100 fL)

- Vitamin B12 deficiency
- Folate deficiency
- Alcohol use disorder
- Liver disease
- Hypothyroidism
- Medications (hydroxyurea, methotrexate, etc.)
- Myelodysplastic syndrome
- Reticulocytosis

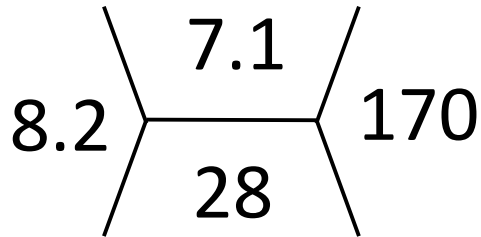
Case #2

57 yo female with Asthma, IgG2 Deficiency who presented with worsening SOB and fatigue x 2 weeks. On Augmentin for presumed sinus infection. Normal diet but minimal red meat. No EtOH use.



Smear: Blood smear reveals normochromic with significant anisocytosis (microcytic and macrocytic) and polikocytosis including schistocytes, red cell fragmentation with slightly higher degree of polychromasia. Normal platelet number and morphology without clumping. WBC's show normal differential with occasional hypersegmented neutrophils.

Case #2



MCV 104

Retic: 2.3%; Absolute count 52

RDW: 25.6

Iron Studies: normal

Hapto < 10

LDH 5980

Tbili 2.5 (Direct 0.4)

B12 150

Homocysteine, MMA Pending

Intrinsic Factor

DAT (-)

Diagnosis ?

Evaluation of Anemia Based on MCV

Microcytic Anemia (MCV < 80 fL)

- Iron deficiency anemia
- Anemia of chronic disease
- Thalassemia
- Sideroblastic anemia
- Lead poisoning

Normocytic Anemia (MCV 80–100 fL)

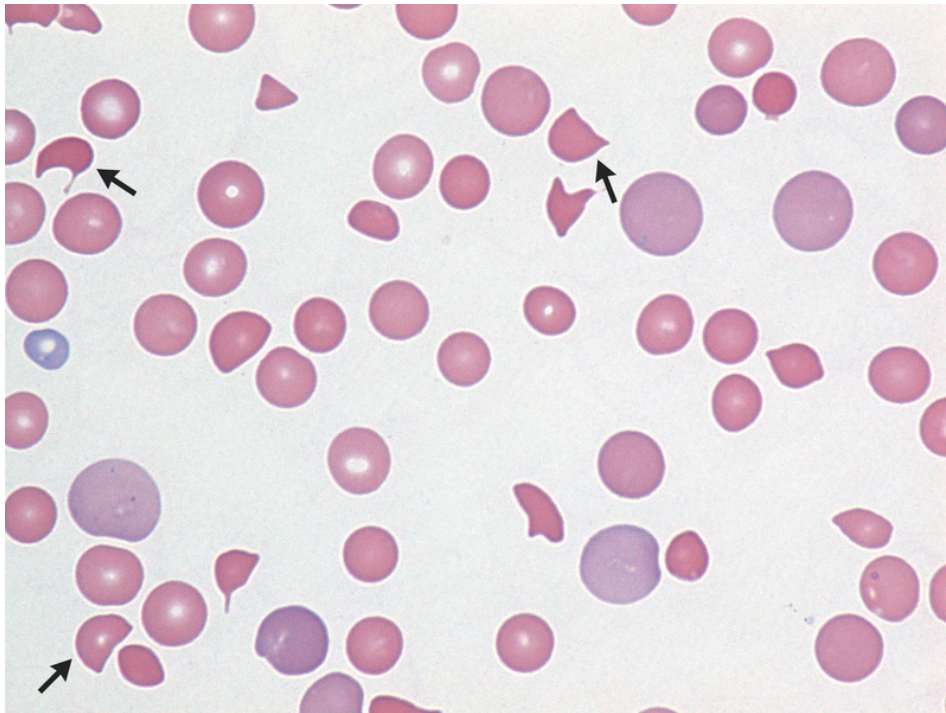
- Acute blood loss
- Hemolysis (AIHA, G6PD, sickle cell, etc.)
- Anemia of chronic disease
- Aplastic anemia
- Bone marrow infiltration
- Chronic kidney disease
- Endocrine disorders

Macrocytic Anemia (MCV > 100 fL)

- Vitamin B12 deficiency
- Folate deficiency
- Alcohol use disorder
- Liver disease
- Hypothyroidism
- Medications (hydroxyurea, methotrexate, etc.)
- Myelodysplastic syndrome
- Reticulocytosis

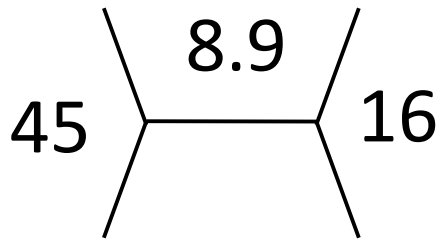
Case #3

56 yo female with recently diagnosed DVT and obstructive jaundice leading to ERCP with pancreatic head mass, returning with AMS and abdominal pain. Path showed biliary adenocarcinoma. Consult for Thrombocytopenia?



Smear: Blood smear reveals with significant anisopolikocytosis with variability of chromasia (some normal, hypo). Target cells, schistocytes, spherocytes all identified. Very low platelet number and morphology normal, no clumping. WBC's with significant neutrophilia and myeloid lineage with left shift .with mature monocytes, neutrophils, lymphocytes present.

Case #3



MCV 85

Retic: 12%; Absolute count 370

RDW: 25.6

LDH 1200

Haptoglobin – undetectable

PT 20, PTT 30, INR 1.8

D-Dimer: 8000

Fibrinogen – 86

AST/ALT – elevated

T Bili 4.8

Cr: 0.6

Diagnosis ?

Case # 4

A 56-year-old man is hospitalized for evaluation of fever and cough for the past 5 days. His past medical history includes type 2 diabetes mellitus and hypertension. He is not on corticosteroids or other immunosuppressive therapy.

On examination, temperature is 38.8 °C (101.8 °F), pulse 110/min, blood pressure 112/64 mm Hg, respiratory rate 22/min, and oxygen saturation 93% on room air. Lung auscultation reveals crackles over the right lower lung field.

Laboratory studies:

WBC count: 38,000/ μ L (reference 4,000–10,000/ μ L)

Differential: 87% neutrophils, 8% bands, 2% lymphocytes, 2% monocytes, 1% eosinophils

Hemoglobin: 13.5 g/dL

Platelets: 290,000/ μ L

Peripheral smear: mature neutrophils with toxic granulations and Döhle bodies

Serum leukocyte alkaline phosphatase (LAP) score: elevated

Chest x-ray: right lower lobe consolidation

Which of the following is the most likely diagnosis?

- A. Acute myeloid leukemia (AML)
- B. Chronic myeloid leukemia (CML)
- C. Leukemoid reaction (reactive leukocytosis)
- D. Acute lymphoblastic leukemia (ALL)
- E. Polycythemia vera

Answer: Leukemoid reaction

Leukemoid reaction is a marked elevation in WBC count (often $>30,000$ – $50,000/\mu\text{L}$) due to a severe infection, stress, inflammation, or other reactive process.

Key distinguishing features:

Predominance of mature neutrophils with a left shift (bands).

Toxic granulations and Döhle bodies on smear (morphologic evidence of reactive process).

Elevated leukocyte alkaline phosphatase (LAP) score (whereas LAP is low in CML).

In contrast:

CML may also present with marked leukocytosis, but peripheral smear shows more immature forms (myelocytes, promyelocytes, basophilia), and LAP is low.

Splenomegaly is common.

AML presents with blasts and anemia/thrombocytopenia.

ALL shows lymphoblasts, usually in younger patients.

Polycythemia vera presents with erythrocytosis, not isolated leukocytosis.

Thus, this patient with pneumonia, high WBC count, toxic changes on smear, and elevated LAP score has a leukemoid reaction.

Evaluation of Leukocytosis

Neutrophilia

Infection (bacterial)
Inflammation (tissue necrosis, vasculitis)
Medications (steroids, lithium, G-CSF)
Stress (surgery, trauma, exercise)
Myeloproliferative neoplasms (CML, PV, ET, PMF)
Smoking

Lymphocytosis

Viral infections (EBV, CMV, hepatitis, HIV)
Pertussis
Chronic lymphocytic leukemia (CLL)
Acute lymphoblastic leukemia (ALL)
Post-splenectomy

Monocytosis

Chronic infections (TB, syphilis, brucellosis, malaria)
Inflammatory/autoimmune (IBD, SLE, RA, sarcoidosis)
Recovery phase of neutropenia
Myelodysplastic syndromes
Chronic myelomonocytic leukemia (CMML)

Eosinophilia

Allergic disorders (asthma, eczema, drug reactions)
Parasitic infections (helminths)
Autoimmune (EGPA/Churg-Strauss, vasculitis)
Malignancy (Hodgkin lymphoma, T-cell lymphoma)
Hypereosinophilic syndrome

Basophilia

Myeloproliferative neoplasms (CML, PV, ET, PMF)
Allergic or hypersensitivity reactions
Chronic inflammation
Hypothyroidism
Infections (rare, TB, influenza)

Evaluation of Leukopenia

Neutropenia

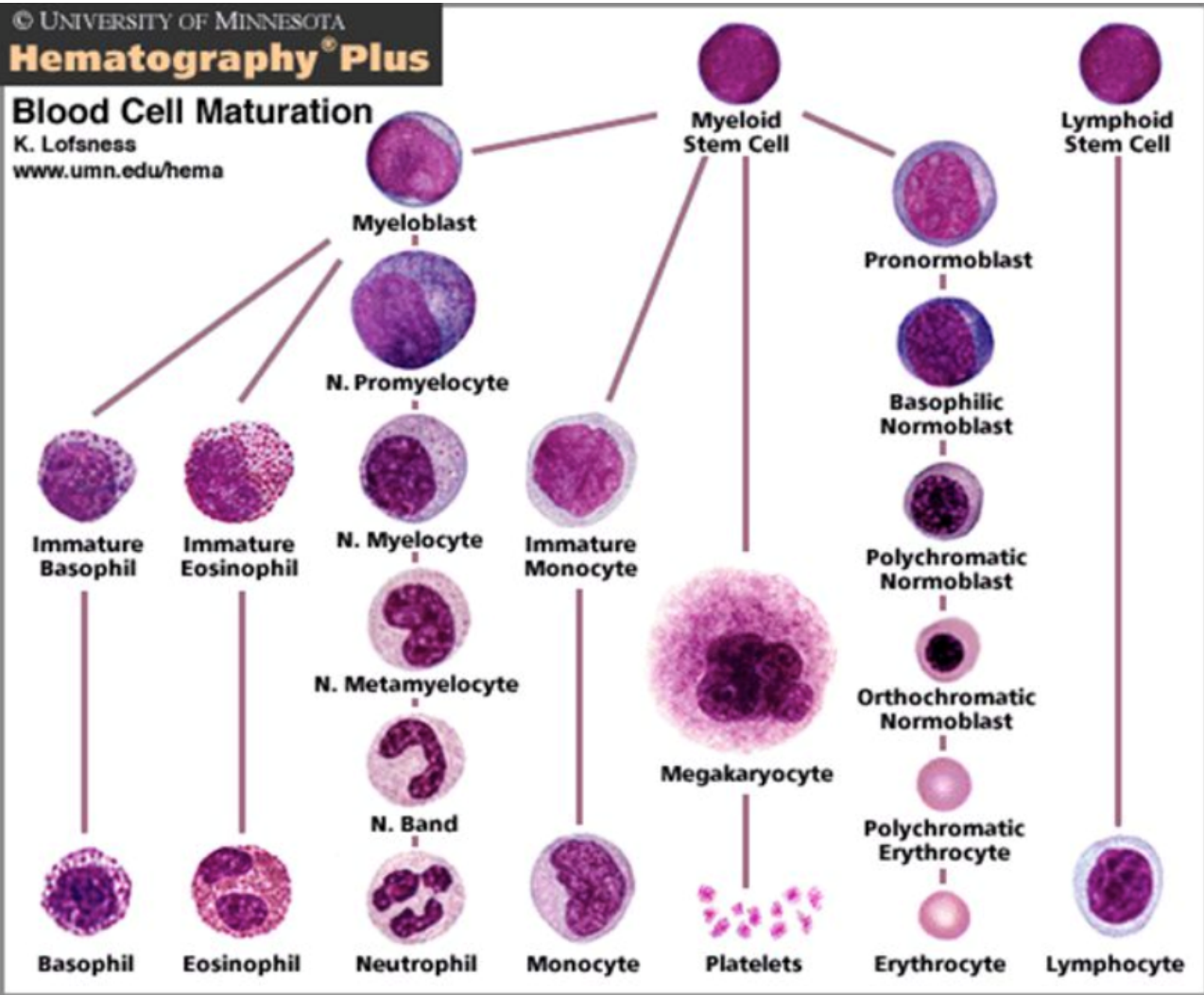
Infections (viral: HIV, hepatitis, influenza, parvovirus)
Drug-induced (chemotherapy, antibiotics, antithyroid drugs, clozapine)
Bone marrow failure (aplastic anemia, myelodysplastic syndromes, leukemia)
Autoimmune (SLE, rheumatoid arthritis, Felty's syndrome)
Nutritional deficiencies (vitamin B12, folate, copper)
Hypersplenism

Lymphopenia

Infections (HIV, COVID-19, viral hepatitis, sepsis)
Iatrogenic (glucocorticoids, chemotherapy, radiation)
Immunodeficiency syndromes (SCID, Wiskott-Aldrich)
Autoimmune diseases (SLE, rheumatoid arthritis)
Protein-energy malnutrition
Post-transplant or post-splenectomy

Blood Cell Maturation

K. Lofsness
www.umn.edu/hema



Evaluation of Thrombocytopenia

Decreased Production

Bone marrow failure
(aplastic anemia,
leukemia, MDS)
Infections (HIV, hepatitis,
parvovirus)
Nutritional deficiencies
(B12, folate)
Alcohol, liver disease
Congenital
thrombocytopenia
syndromes

Increased Destruction / Consumption

Immune
thrombocytopenia (ITP)
Drug-induced (heparin,
antibiotics)
Thrombotic
microangiopathies (TTP,
HUS, DIC)
Autoimmune diseases
(SLE, RA)
Infections / Sepsis
Hypersplenism

Sequestration / Pseudothrombocytopenia

Splenomegaly (cirrhosis,
portal hypertension)
Laboratory artifact
(platelet clumping, EDTA)

Case #5

- *A 58-year-old woman presents for evaluation of fatigue and easy bruising for the past month. She has no significant past medical history. Physical examination reveals pallor and scattered petechiae on her lower extremities.*
- *Laboratory studies show:*
 - Hemoglobin: 8.2 g/dL (normal: 12-16 g/dL)
 - Mean corpuscular volume (MCV): 104 fL
 - White blood cell count: $2.1 \times 10^9/L$ (normal: $4.0-11.0 \times 10^9/L$)
 - Absolute neutrophil count: $0.9 \times 10^9/L$
 - Platelet count: $48 \times 10^9/L$ (normal: $150-400 \times 10^9/L$)
 - Reticulocyte count: low
 - Peripheral smear: pancytopenia with occasional macrocytes; no blasts seen
 - Lactate dehydrogenase (LDH): elevated
 - Vitamin B12: normal
 - Folate: normal

- *Which of the following is the most appropriate next diagnostic test?*
 - A. Iron studies*
 - B. Bone marrow biopsy*
 - C. Erythropoietin level*
 - D. Antinuclear antibody (ANA) testing*
 - E. Parvovirus B19 serology*

Correct Answer: B. Bone marrow biopsy

Explanation:

The patient presents with pancytopenia, macrocytosis, and elevated LDH—all concerning for a bone marrow process such as myelodysplastic syndrome (MDS) or aplastic anemia. The absence of vitamin deficiencies and presence of cytopenias in multiple lineages make iron studies or erythropoietin level unhelpful at this stage. ANA testing may be warranted if there were clinical suspicion for autoimmune disease, but this would not be the initial test.

Bone marrow biopsy is essential to evaluate marrow cellularity, dysplasia, and to rule out hematologic malignancies.

Case #6

A 72-year-old man is seen for routine follow-up. He feels well and has no symptoms. Past medical history includes hypertension and type 2 diabetes mellitus. CBC shows:

- Hemoglobin: 13.6 g/dL
- MCV: 88 fL
- WBC: $6.0 \times 10^9/L$
- Platelets: $670 \times 10^9/L$

Repeat CBC 4 weeks later shows persistent thrombocytosis. Physical examination is unremarkable.

Which of the following is the most appropriate next step in evaluation?

- A. Bone marrow biopsy
- B. JAK2 V617F mutation testing
- C. Peripheral blood smear review
- D. C-reactive protein (CRP)
- E. Iron studies

Correct Answer: E. Iron studies

Explanation:

In an asymptomatic patient with isolated thrombocytosis, it is important to first evaluate for reactive causes, including iron deficiency, infection, or inflammation. Iron deficiency is a common cause of secondary thrombocytosis. JAK2 mutation testing is useful for evaluating clonal thrombocytosis (e.g., essential thrombocythemia), but not before ruling out reactive causes. Peripheral smear may help, but iron studies are more directly informative here.

Evaluation of Thrombocytosis

Primary (Clonal) Thrombocytosis

Essential thrombocythemia (ET)
Polycythemia vera (PV)
Primary myelofibrosis (PMF)
Chronic myeloid leukemia (CML)
Other myeloproliferative neoplasms

Secondary (Reactive) Thrombocytosis

Infections
Inflammation (RA, IBD, vasculitis)
Malignancy (solid tumors, lymphomas)
Iron deficiency anemia
Hemolysis
Splenectomy or hyposplenism
Post-surgery, trauma

Spurious/ Pseudothrombocytosis

Microspherocytes, fragments, or bacteria miscounted as platelets
Cryoglobulinemia
Laboratory artifact

Case #7

A 35-year-old woman presents with shortness of breath and dark urine in the mornings.

Labs

- Hemoglobin: 9.4 g/dL
- MCV: 100 fL
- WBC: $5.4 \times 10^9/L$
- Platelets: $220 \times 10^9/L$
- Reticulocyte count: elevated
- LDH: elevated
- Haptoglobin: undetectable
- Direct antiglobulin (Coombs) test: negative
- Peripheral smear: normocytic anemia with occasional schistocytes

Which of the following is the most appropriate next diagnostic test?

- A. Serum vitamin B12 level
- B. Hemoglobin electrophoresis
- C. Paroxysmal nocturnal hemoglobinuria (PNH) flow cytometry
- D. G6PD level
- E. ANA testing

Correct Answer: C. Paroxysmal nocturnal hemoglobinuria (PNH) flow cytometry

Explanation:

This patient has evidence of intravascular hemolysis (elevated LDH, undetectable haptoglobin, dark urine) with a negative Coombs test, suggesting non-immune hemolysis. The combination of hemolysis, fatigue, and hemoglobinuria, particularly in the morning, is classic for PNH. Flow cytometry for CD55/CD59 on blood cells is the diagnostic test of choice.

CBC summary

- Be inquisitive about any value outside of the normal range in CBC.
- Question is-
 - Is it clinically relevant?
 - What is the etiology?
 - How can we fix/treat?



THANK
YOU