Reviewed By Tarfa Alsharidi

MED439 KING SAUD UNIVERSITY

Approach to CBC Abnormalities

Objectives:

1. Practical approach to CBC
2. How to approach coagulation defect

439 Team Leader:
Nourah Alklaib

439 Team Member:
Muneerah Alsadhan

Editing File

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- Slides / Reference Book
- Doctor notes
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- Important
- Extra

Hematopoiesis - Cell development (Extra)

Hematopoiesis is blood cell production. Your body continually makes new blood cells to replace old blood cells so you have a steady blood supply. Hematopoiesis starts before birth and continues as a cycle throughout life.

Hematopoiesis includes the production of all blood cell types including:

Red blood cells (erythrocytes):

Red blood cells, or erythrocytes, carry oxygen from your lungs to organs throughout your body. They also carry carbon dioxide to your lungs so you can get rid of it by exhaling it. Your blood has more red blood cells than any other type of blood cell. The production of red blood cells is called erythropoiesis. Red blood cell production occurs in your bone marrow. An HSC matures into a precursor cell called an erythroblast. An erythroblast becomes an immature red blood cell called a reticulocyte. Finally, a reticulocyte develops into a mature red blood cell.

White blood cells (leukocytes):

White blood cells, or leukocytes, fight infection and protect your body from harmful invaders, or germs. They also destroy abnormal cells. The production of white blood cells is called leukopoiesis.
Broadly, the types of white blood cells are:

- Neutrophils
- Basophils
- Eosinophils
- Monocytes
- Lymphocytes (B-cells, T-cells and natural killer cells).

Neutrophils, basophils and eosinophils have similar functions and can be grouped together and called granulocytes. The other types of white blood cells are monocytes and lymphocytes.

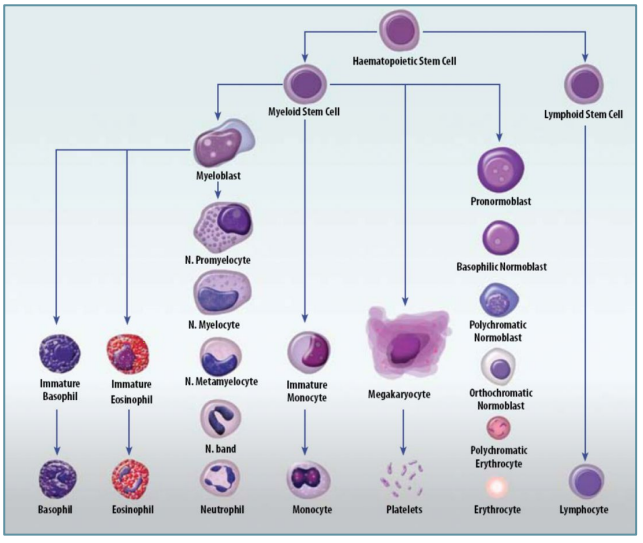
Platelets (thrombocytes)

Platelets, or thrombocytes, are sticky cell fragments that clump together to form a clot if you're injured. They create a seal in damaged tissue that prevents you from losing too much blood. The production of platelets is called thrombopoiesis.

Where does hematopoiesis occur?

The most common site of blood cell production is the spongy tissue inside of your bones called bone marrow. Hematopoiesis that occurs in your bone marrow is called medullary hematopoiesis. Blood cells get made in your bone marrow and released into your bloodstream.

Less often, hematopoiesis takes place in other parts of your body, like your liver and spleen. Hematopoiesis that occurs outside of your bone marrow is called extramedullary hematopoiesis.



Practical approach to CBC

Components of CBC	
Parameter	**Description**
RBC	• Absolute number of RBCs contained in a certain volume of blood
Hemoglobin (Hb)	• Oxygen-transporting protein found in RBCs
Hematocrit (Hct) (Packed Cell Volume)	• Ratio of RBC volume to total blood volume
Mean corpuscular volume (MCV)	• Measure the average size of red blood cells • You should always look to the MCV and specify if it's microcytic. normocytic or macrocytic anemia, you should never mention it's anemia only
Mean corpuscular hemoglobin (MCH)	• Average mass of hemoglobin in each RBC • MCH is always calculated for a single RBC and therefore decreases if the RBC size decreases.
Mean corpuscular hemoglobin concentration (MCHC)	• Measure the hemoglobin concentration of all RBCs. • In contrast to MCH, MCHC is independent of RBC size because it is calculated for the total mass of all RBCs.
Red blood cell distribution width (RDW)	• Measures the variation in RBC volumes
Reticulocyte count	• Percentage of all RBCs that are reticulocytes (immature red blood cells) • Represents erythropoietic activity
Total WBC count	• A measure of the number of WBCs in the unit volume of blood (Counts the total WBCs in a unit volume of blood)
Differential WBC count	• A measure of the proportions of each type of WBC in the blood (Counts each type of WBCs)
Platelets	• Measures the number of platelets present in a specific volume of blood.
Mean Platelet Volume (MPV)	• MPV is a measurement of the average size of platelets in a blood sample.

Parameter	Description
Erythrocyte Sedimentation Rate (ESR)	• Is a blood test that can show if you have inflammation in your body. Inflammation is your immune system's response to injury, infection, and many types of conditions, including immune system disorders, certain cancers, and blood disorders.
Blood film	• A blood film, also known as a blood smear or peripheral blood smear, is a laboratory test that involves examining a thin, spread-out layer of blood cells on a glass slide under a microscope. It allows for the evaluation of the size, shape, and arrangement of different types of blood cells, including red blood cells (erythrocytes), white blood cells (leukocytes), and platelets.

Practical approach to CBC

Parameter	Formula
MCV	$\frac{\text{Hematocrit x 10}}{\text{RBCs count x } 10^{12}/\text{L}}$
MCH	$\frac{\text{Hemoglobin (Hb)}}{\text{RBCs count x } 10^{12}/\text{L}}$
MCHC	$\frac{\text{Hemoglobin}}{\text{Hematocrit}}$

All haematology results need to be interpreted in the context of a thorough history and physical examination, as well as previous results.

History and clinical examination

Important features of history and clinical examination

	Pallor	Jaundice[1]	
	Fever[2]	Lymphadenopathy[2]	
	Bleeding[3]	Bruising[3]	
	Hepatomegaly	Splenomegaly	
	Exposure to drugs[4]	Exposure to toxins	
	Fatigue	Weight loss	

Frequency and severity of infections, mouth ulcers & recent viral illness

1. Due to hemolysis
2. Increased due to leukemia or infection
3. Due to coagulation cascade defects or platelets deficiency (coagulation defects cause hemarthrosis "joint bleeding" due to hemophilia and platelets deficiency cause mucocutaneous bleedi "petechiae"
4. Especially chemotherapy

Pancytopenia can be caused by anything that causes the bone marrow to produce a few blood cells, such as bone marrow toxicity due to chemotherapy or aplastic anemia.

RBCs

Useful to use MCV to classify the anemia

Microcytic	Normocytic	Macrocytic
MCV < 80 fl	MCV 80 – 100 fl	MCV > 100 fl

Causes of each type of anemia

Microcytic

- Iron deficiency (IDA): Due to sleeve gastrectomy, menorrhagia and pregnancy
- Thalassaemia
- Anemia of Chronic disease (usually normocytic and can be microcytic)

A 20 y/o male complaining of iron deficiency anemia and he doesn't do bariatric surgery what is the differential diagnosis? IBD or celiac disease and we should do celiac and IBD serology.
A 75 y/o female complaining of iron deficiency anemia what is the differential diagnosis? Malignancy and we should refer the patient immediately to GI for EGD, colonoscopy and fecal occult blood .

Normocytic

- Bleeding
- Early nutritional anemia (iron, B12, folate deficiencies)
- Anemia of renal insufficiency (CKD is the most common cause)
- Anemia of chronic disease/chronic inflammation
- Hemolysis
- Primary bone marrow disorder

Bleeding and hemolysis cause rapid drop in hemoglobin (more than 1g/dl within a week)

Macrocytic

- Alcohol
- Liver disease
- B12 or folate deficiency (Megaloblastic) (If the MCV is more than 120 it indicates vitamin B12 deficiency)
- Thyroid disease
- Some drugs (especially hydroxyurea)

Features might help in distinguishing between IDA and Thalassemia (Extra)

Feature	IDA	Thalassemia
RBC	Low, Low normal	High, High normal
MCV	Mild to moderate low (most likely above 70) ~80	Very low (< 70) ~60
RDW	Mostly High	Mostly Normal
Mentzer index: MCV/RBC	> 13	< 13

RBCs

Types of polycythemia (Extra)

Relative

Decreased plasma volume

Is a condition characterized by an apparent increase in red blood cells count without an actual increase in the total number of RBCs.

It is called "relative" because the increase in RBC count is relative to a decrease in plasma volume, rather than an absolute increase in RBC production.

Causes:

- Dehydration
- Alcohol
- Cigarette smoking
- Diuretics

Absolute

Increased RBCs mass

Primary

Erythropoietin independent

Causes:

Congenital:

- EPO receptor mutations

Acquired:

- Polycythemia Vera

Secondary

Erythropoietin dependent

Causes:

Central hypoxia:

- Cyanotic heart disease
- COPD
- Smoking
- Sleep apnea
- High altitudes

Local hypoxia:

- Renal artery stenosis
- Renal cysts
- ESRD
- Hydronephrosis

Pathological EPO production:

- Renal cell cancer
- Hepatocellular carcinoma

Medications:

- EPO analogues
- Androgens

Polycythemia Vera (Extra)

Polycythemia vera is a chronic myeloproliferative neoplasm most commonly caused by a gain of function mutation in the JAK2 gene, leading to erythrocytosis with or without increases in granulocytes and platelets.

Risk factors: Older age, Male sex, White race, Hypertension, DM, Obesity, Hyperlipidemia & Smoking.

Pathophysiology: The JAK2 (Janus kinase 2) oncogene codes for a non-receptor tyrosine kinase in hematopoietic progenitor cells. JAK2 is essential for the regulation of erythropoiesis, thrombopoiesis (megakaryopoiesis), and granulopoiesis. 98% of patients with polycythemia vera have a mutation in the JAK2 gene (gain of function) → ↑ tyrosine kinase activity →erythropoietin-independent proliferation of the myeloid cell lines → ↑ blood cell mass (erythrocytosis, thrombocytosis, and granulocytosis) → hyperviscosity and slow blood flow → ↑ risk of thrombosis and poor oxygenation.

Clinical features:

1- Increased blood viscosity:

- Hypertension: due to the increase need to pump thicker blood through the circulatory system.
- Headache, dizziness, visual disturbances & paresthesia.

2- Thrombosis: (Deep vein thrombosis, Myocardial infarction, Mesenteric, portal or splenic vein thrombosis).
3- Splenomegaly: in 70%. (polycythemia vera makes your spleen work harder than normal, which causes it to enlarge)
4- Hepatomegaly: in 40%.

Investigations:

1- CBC: RBC (increased), Hb (increased) | WBC & PLT (Mildly increased)
2- Blood smear: Excess of normocytic normochromic RBC. | ±Leukocytosis & thrombocytosis.(if it's associated with any MPN other than polycythemia, in polycythemia it's normal

Treatment: The Diagnosis of PV will initiate a treatment consisted of Venesection + Aspirin and may they use of Myelosuppressive drugs (Chemotherapy) such as hydroxyurea.

From doctor's slides

✩ Hb often accompanied by ✩PCV

- Can reflect decreased plasma volume (eg: dehydration, alcohol, cigarette smoking, diuretics) (Psudopolycythemia)
- Increased red cell mass (eg polycythaemia) This can be primary or secondary (True polycythemia)

WBCs

Neutrophils		
	High	**Low**
Details	—-	Significant levels < 0.5 x 10^9/L (high risk for bacterial infection) Neutropenia is a high risk of infection and it is a medical emergency so you need to give the patient antibiotic because the patient can end up with septic shock in less than 24h
Most common causes	• Infection (bacterial)/inflammation • Necrosis/malignancy • Any stressor/heavy exercise • Drugs (steroids + G-CSF) • CML	• Viral (overt or occult) • Autoimmune/idiopathic • Drugs (chemotherapy)
Red flags	• Person particularly unwell • Severity • Presence of left shift or blast	• Person particularly unwell • severity • Lymphadenopathy • Hepatosplenomegaly

Lymphocytes		
	High	**Low**
Details	Isolated elevated count not usually significant	Not usually clinically significant (HIV is the most common cause)
Most common causes	• Acute infection (viral) • Smoking • Hyposplenism • Acute stress response • Autoimmune thyroiditis • CLL (most common type of leukemia)	—-

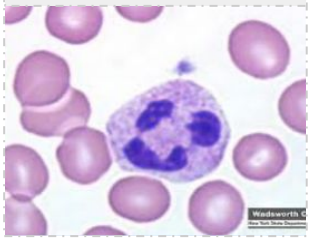
Monocytes		
	High	**Low**
Details	• Usually not significant • Watch levels > 1.5 x10^9/L more closely	• Not clinically significant

WBCs

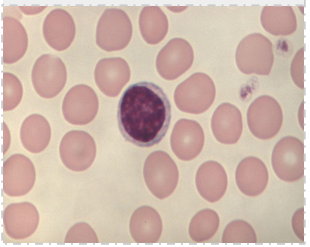
Eosinophils		
	High	**Low**
Details	—-	• No real cause for concern
Most common causes	• Allergy/atopy: asthma/hay fever • Parasites (less common in developed countries)	—-
Rare causes	• Hodgkins • Myeloproliferative disorders • Churg-Strauss syndrome (autoimmune disorder)	—-

Basophils		
	High	**Low**
Details	—-	• Difficult to demonstrate/no clinical significance.
Most common cause	• myeloproliferative disorders (CML)	—-

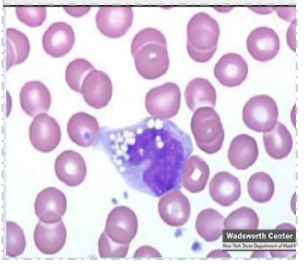
Neutrophils



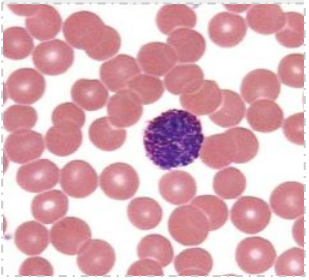
Lymphocytes



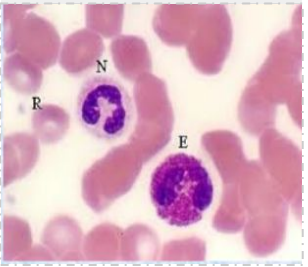
Monocytes



Basophils



Eosinophils



Platelets & Coagulation Cascade

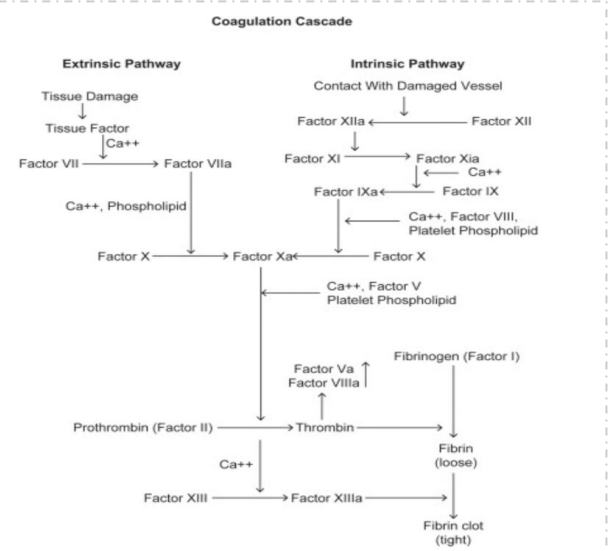
Platelets		
	High	**Low**
Details	• Significant levels > 500 x109/L	• Significant levels < 100 x109/L
Most common causes	• Reactive conditions: infection, inflammation • Pregnancy • Iron deficiency • Post splenectomy • Essential thrombocythemia	• Viral infection (Typically in pediatrics) • Idiopathic thrombocytopenic purpura • Liver disease • Drugs • Hypersplenism • Autoimmune disease • Pregnancy (Gestational thrombocytopenia is a benign condition and doesn't cause bleeding) • Artificial → confirm on blood film
Red flags	—-	• Bruising • Petechiae • Signs of bleeding

Prolonged PT is seen in:

- Vitamin K deficiency
- Warfarin therapy
- Liver disease

Prolonged PTT is seen in:

- Von Willebrand
- Hemophilia
- Heparin therapy
- Antiphospholipid syndrome



Coagulation cascade explanation

Prolonged PT and PTT is seen in:

- Deficiencies of the final common pathway factors such as factor V, prothrombin, fibrinogen, or factor X.
- Liver disease
- DIC

No all bleeding problems can be explained by this but most of it.

Warfarin acts on the **extrinsic** pathway whilst heparin acts on the **intrinsic** pathway.