EVALUATION OF COMPLETE BLOOD COUNT (CBC)

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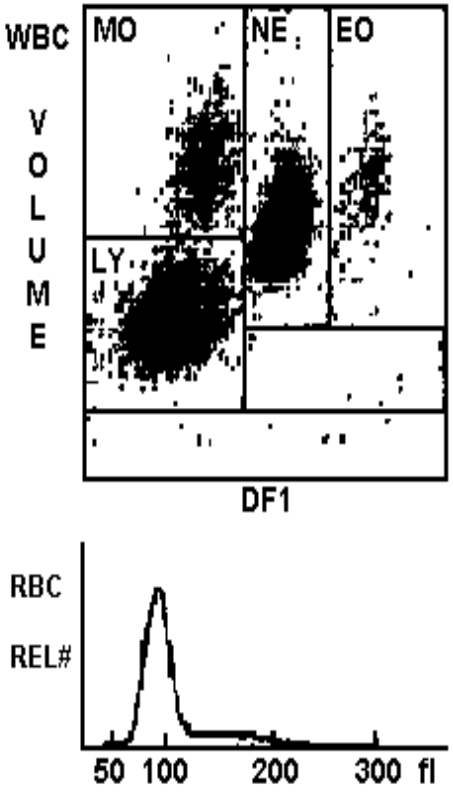
CBC Indications

- Detect hematologic disorder, i.e. leukaemia
- Evaluate known or suspected anaemia and related treatment
- Monitor blood loss and response to blood replacement
- Monitor hematologic status during pregnancy
- Monitor progression of non-hematologic disorders, such as chronic obstructive pulmonary disease, malabsorption syndromes, cancer, and renal disease
- Monitor response to chemotherapy
- Evaluate undesired reactions to drugs that may cause blood dyscrasias
- Provide screening as part of a general physical examination

CBC parameters

- **1) White blood cells (WBC) count**
  - Differential **(5 diff)**
    - **Neutrophils**
    - **Lymphocytes**
    - Monocytes
    - Eosinophils
    - Basophils
- **2) Red blood cells (RBC) count**
  - MCV, MCH, MCHC, RDW
  - **Hemoglobi**n (Hgb), Hct
- **3) Platelets (PLT) count**



WBC	6.8	
	%	#
NE	52.6	3.6
LY	36.7	2.5
MO	7.8	0.5
EO	2.5	0.2
BA	0.4	0.0
RBC	5.29	
HGB	16.2	
HCT	47.0	
MCV	88.8	
MCH	30.7	
MCHC	34.5	
RDW	12.5	
PLT	179	
MPV	8.4	

CBC Normal Ranges

Parameter	Male	Female
RBC count (10^6/µL)	4.7-6.1	4.2-5.4
Hb gr/dL	**13-16.5**	**12-16**
Hct %	38.3-48.9	35.5-47.9
WBC count (10^6/µL)	**4.0-10.0**	**4.0-10.0**
PLT count (10^6/µL)	**150-400**	**150-400**

White blood cell differential

- Leukocytes
  - Granulocytes
    - **Neutrophils** **40-75%**
    - Bands 0-8%
    - Eosinophils 0-4%
    - Basophils 0-2%
  - Lymphocytes 15-45%
  - Monocytes 0-12%

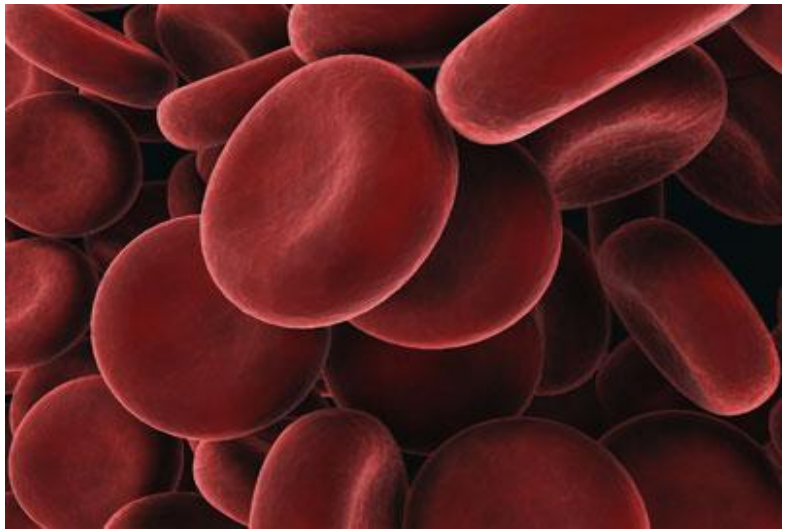
Symptoms/Findings

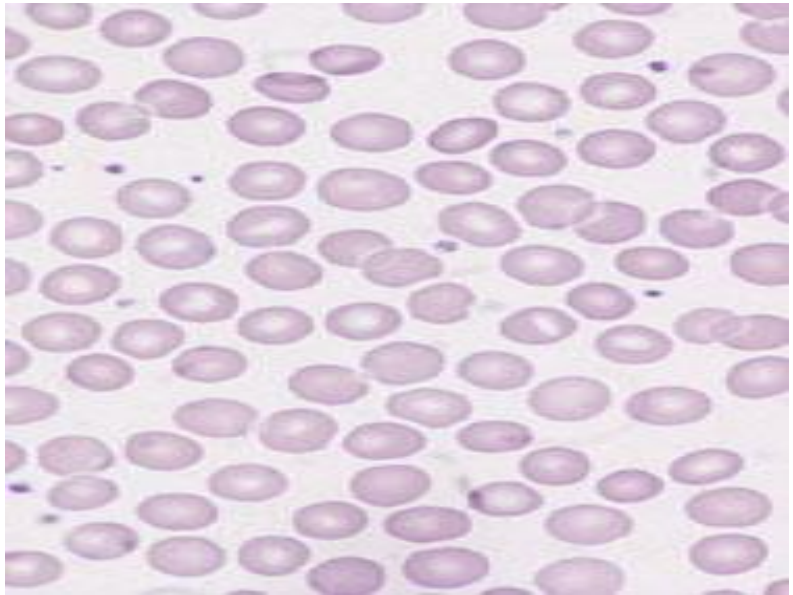
Type of Cell	High	Low
RBCs	Clots, strokes	Dyspnea, hypoxia, fatigue, pallor
WBCs	Clots, strokes	Infections
Platelets	Clots, strokes	Bleeding

RBC

Red Blood Cells (RBCs)

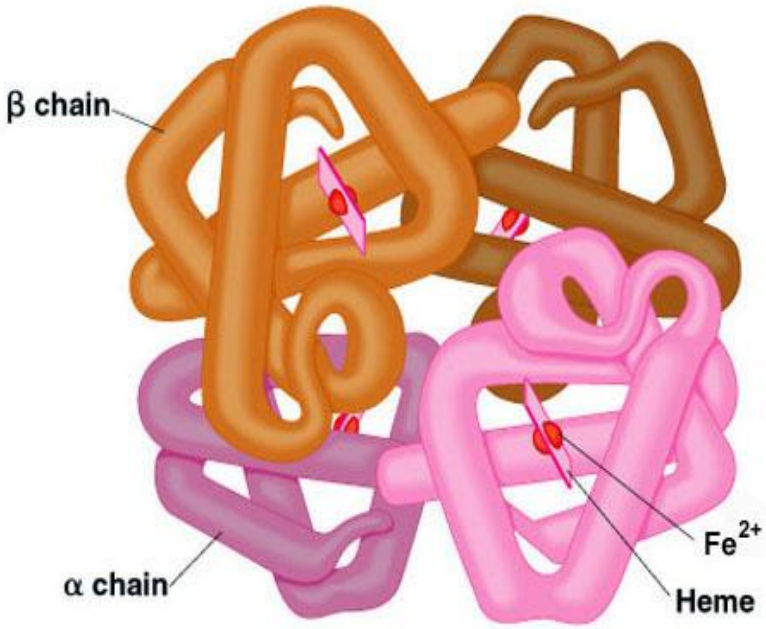
- **Largest cellular** component of blood
  - **about 40-45% of blood volume**
- Normal range for men: 4.5 - 5.9 $x10^6/mm^3$
- Normal range for women: 4.0 - 5.2 $x10^6/mm^3$
- Consist of mostly **hemoglobin**





Hemoglobin (Hb)

- **Red pigment molecule** which gives RBCs (and blood) its color
- Contains 4 molecules of heme and 4 of globin (2 alpha chains and 2 beta chains)
- **Each molecule of heme contains one iron ion**
- It is a parameter that is used to **measure anemia**
- Its expressed in g/dL
  - Normal range for women:
    - **12 - 16 g/dL**
  - Normal range for men:
    - **13 – 16.5 g/dL**



Molecular structure

Anemia

- Defined by **measurement of Hb concentration**
  - Patients are “anemic” when Hb is > 2 standard deviations below normal or
  - **WHO criteria define anemia as hemoglobin level lower than 12 g/dL in women and 13 g/dL in men**
- Almost 1/3 of the world population is anemic!
  - **Most common anemia is iron deficiency anemia in the world**

Anemia Work-up

Initial tests

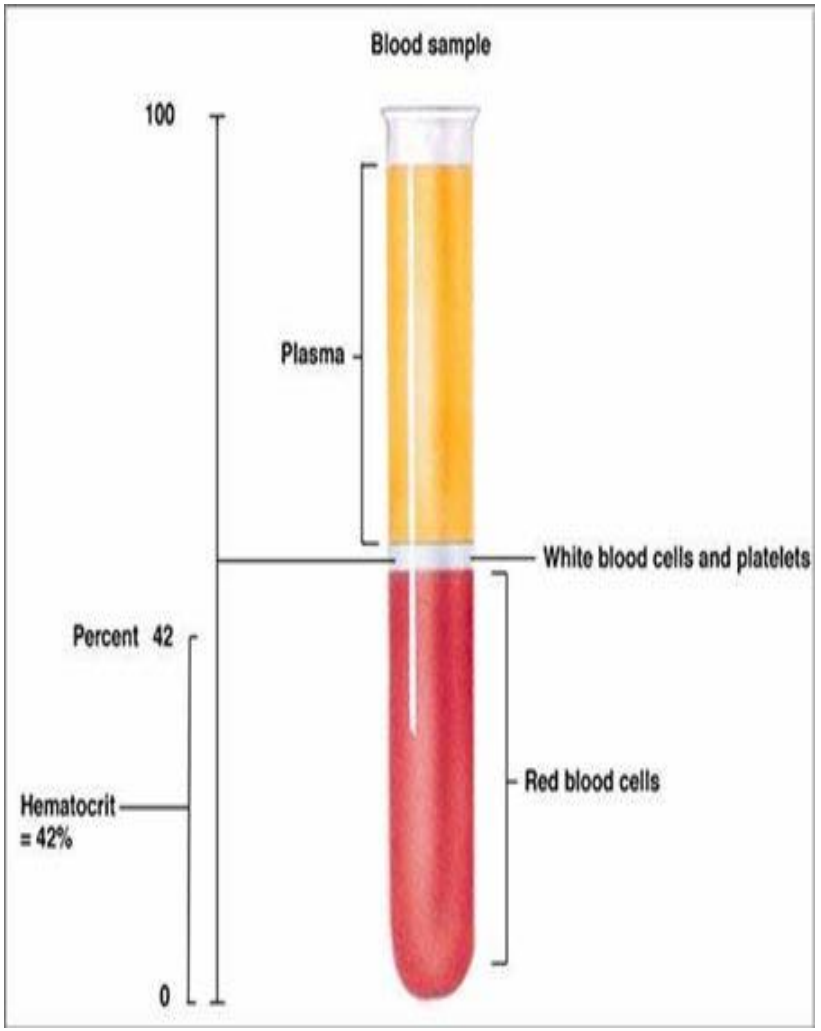
- **CBC:**
  - Hb (severity)
  - MCV (type)
  - WBC/platelets
    - Bone marrow disease
    - Megaloblastic anemia
- **Blood film exam**

Additional tests

- **Reticulocyte count**
  - Increased with **hemolysis**
  - Decreased with marrow disease or suppression
- **Hematinics**
  - **Ferritin, Vit-B12, Folate**
- Creatinine
- LFTs
- CRP
- Protein electrophoresis
- TSH

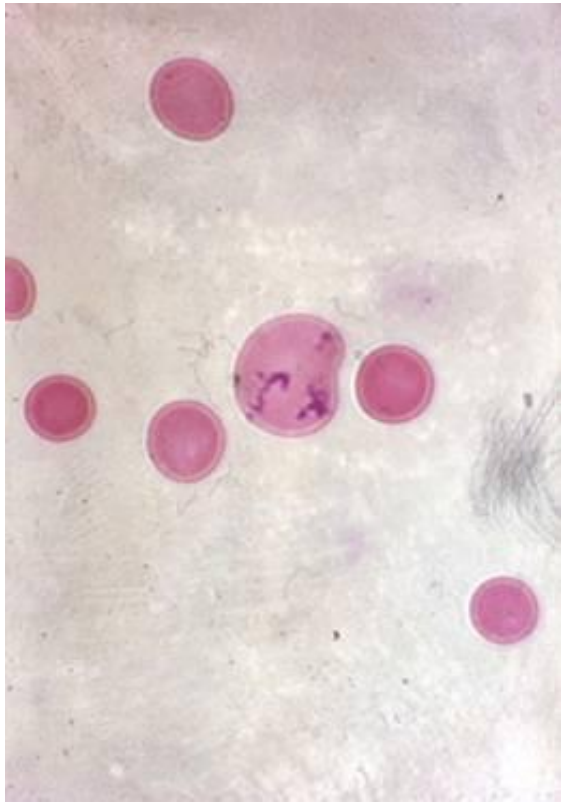
Hematocrit (Hct)

- Hematocrit (Hct) is the percent of a volume of whole blood occupied by intact red blood cells.
- proportion of blood occupied by erythrocytes.
- Measured in percent.
  - Normal range for women:
    - 35.5-47.9%
  - Normal range for men:
    - 38.3– 48.9%



Reticulocyte

- **Immature red blood cells without a nucleus**
- Calculating proportion within circulation assists in determining cause of anemia
- **Normal is 0.5-2.5%** (40-100x10^9/L)
- ***Low*** suggests **decreased production** (i.e. nutritional or marrow problem)
- ***High*** **suggests <u>bleeding</u> or premature destruction of red blood cells (i.e. <u>hemolysis</u>).**



Mean Corpuscular Volume (MCV)

- MCV is **the average size** of red blood cells.
- Measured in fentolitres (fL)
- Normal range: 80-100 fL
  - **Low = "microcytic"** ("too small") = **<80 fL**
  - **High = "macrocytic"** ("too big") = **>100 fL**
  - **Normal = "normocytic"** ("just right") = **80-100 fL**

Mean Corpuscular Hemoglobin (MCH)

- MCH is **the amount of hemoglobin** in an average red blood cell.
- MCH = Hb / red cell count x10 (pg/cell)
- Normal range: 26-34 pg/cell
- Low MCH (hypochromic):
  - Iron deficiency

Mean Corpuscular Hemoglobin Concentration (MCHC)

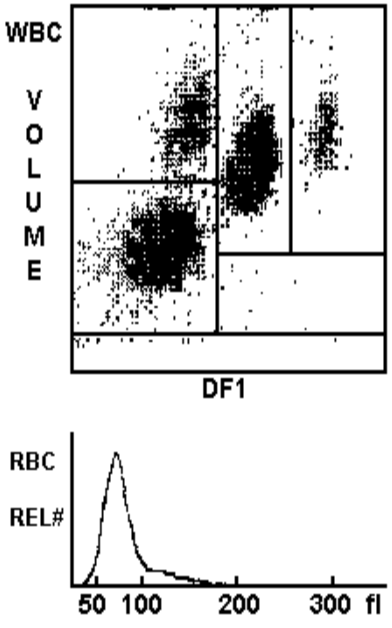
- MCHC is **concentration of Hb** per unit red cell volume.
- MCHC = Hb / Hct x 100 (g/dL).
- Normal range: 31-37 g/dL
  - "Hypochromic" = "too pale" (MCHC < 31 g/dL)
  - "Normochromic" = "just right" (MCHC: 31-37 g/dL)
  - **MCHC > 37 g/dL is associated with hereditary spherocytosis.**
  - **Low MCHC is typical of iron deficiency anemia.**

RDW (Red cell distribution width)

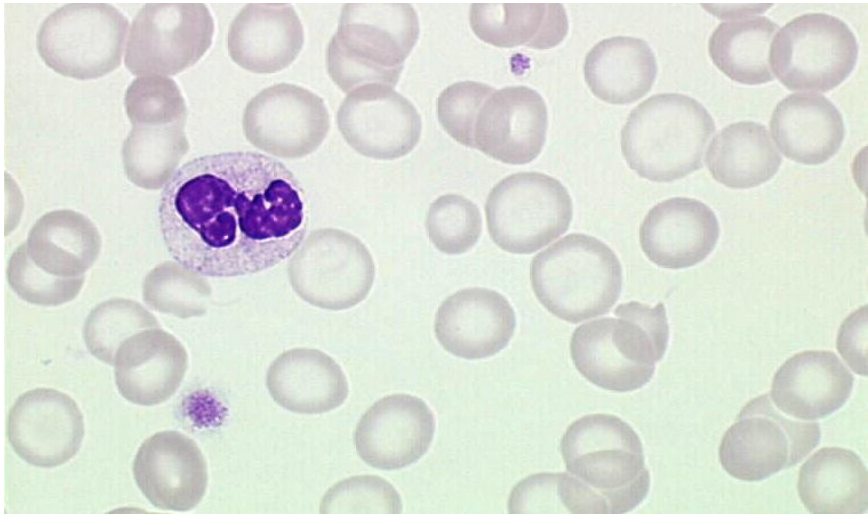
- Measured the **variability of red cell sizes**
- Large values indicate great variations
- Normal range: 11.5-14.5%
- On a peripheral blood smear, high RDW is described as **"anisocytosis"**
- Help to distinguish IDA from thalassemias (microcytic anemias)
  - < 12% → Thalassemia
  - > 14% → Iron deficiency anemia

Microcytic Anemia

- Microcytosis – small cells (**MCV<80 fL**)
- **Most common type** of anemia encountered in primary care
- Differential diagnosis
  1. **Iron deficiency (most common)**
  2. **Thalassemia**
  3. **Chronic disease**
  4. Sideroblastic anemia
  5. Lead poisoning
- Check iron studies and Hb electrophoresis



WBC	5.5		
	%		#
NE	54.7		3.0
LY	34.1		1.9
MO	7.5		0.4
EO	3.0		0.2
BA	0.7		0.0
RBC	4.28	L	
HGB	9.7	L	
HCT	29.9	L	
MCV	69.7	L	
MCH	22.6	L	
MCHC	32.4	L	
RDW	18.4	H	
PLT	331		
MPV	8.8		

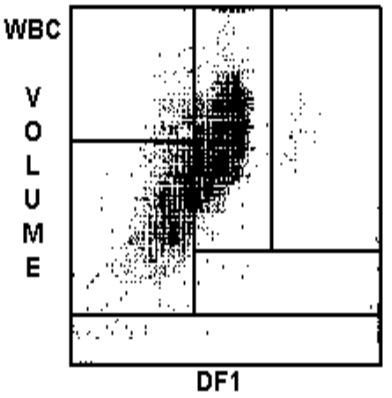


Microcytic Anemia

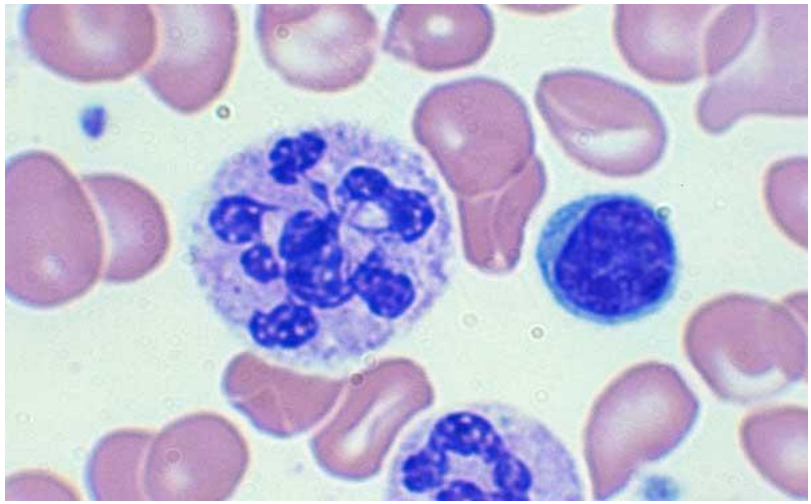
Diagnosis	Ferritin	Serum Iron (Fe)	TIBC	Transferrin Saturation (TS)	Hb electrophoresis
Iron deficiency	↓	↓	↑	↓	N
Chronic disease	N or ↑	↓	↓	N or ↑	N
Thalassemia	N or ↑	N	N	N or ↑	HbA2 ↑

Macrocytic Anemia

- Macrocytosis – large cells (**MCV >100 fL**)
- Differential diagnosis
  - **B12 vit deficiency**
    - **Pernicious anemia (most common)**
  - **Folate deficiency**
  - **Alcohol**
  - **Medication**
- Check vitamin B12, RBC folate, fasting homocysteine (HC), and methylmalonic acid (MMA)
  - HC and MMA are *elevated* in subclinical B12 and folate deficiency



WBC	12.1	H		
	%		#	
NE	71.1		H 8.5	H
LY	15.9		L 1.9	
MO	3.3		0.5	
EO	0.5		L 0.1	
BA	8.7		H 1.1	H
RBC	2.69	L		
HGB	10.6	L		
HCT	31.6	L		
MCV	117.6	H		
MCH	39.6	H		
MCHC	33.7			
RDW	14.1			
PLT	578	H		
MPV	7.2	L		



Hemolytic Anemia

- History and physical findings
  - **Jaundice** is common (due to increased ind bil)
  - **Splenomegaly**
- Laboratory findings
  - **Elevated reticulocyte count**
    - Reflects bone marrow compensating for peripheral RBC destruction
  - **Elevated LDH**
  - **Elevated ind. bilirubin**
  - **Decreased haptoglobin**
  - Abnormal cells on peripheral blood smear examination
    - For example: sickle cell, schistocytes

Hemolytic Anemia

- Congenital
  - **Membrane defects**
    - Hereditary spherocytosis
    - Hereditary elliptocytosis
  - **Enzyme defects**
    - G6PD (glucose 6 phosphate dehydrogenase) deficiency (most common)
  - **Hemoglobin defects** – diagnosed by hemoglobin electrophoresis
    - Thalassemias
      - Group of diseases characterized by globin chain (alpha and beta) imbalance
    - Sickle cell disease
      - Hb S gene carried by 8% of African Americans
      - RBCs are sickle-shaped
      - characterized by hemolysis, vascular occlusion

Hemolytic Anemia

- **Acquired**
  - Classified according to site of RBC destruction and whether mediated by immune system
    - Intravascular / Extravascular
    - Autoimmune / Non-immune
  - Causes
    - Autoimmune
      - Warm (IgG-mediated) ; most common
      - Cold (IgM-mediated)
    - Transfusion of incompatible blood
    - Prosthetic valves
    - TTP/HUS
    - DIC
    - Cancer
    - Drugs

Hemolysis Work-up

Initial evaluation

1. Ind. bilirubin- increased
2. Reticulocyte - increased
3. LDH - increased
4. Haptoglobin - decreased

Additional tests

- Blood film
  - **Polychromasia**
  - Spherocytes
  - Sickle cells
- Hb electrophoresis
- Direct Antiglobulin (Coombs) test

Polycythemia / Erythrocytosis

- **Abnormal *elevation* of hemoglobin**
  - **Men – Hb >16.5 g/dL** (Hct ≥49%), **Women – Hb >16 g/dL** (Hct ≥48%)
  - **Secondary**
    - **More common**
    - RBC production in response to increased EPO production
      - **EPO level is usually high**
    - Usual etiology is **chronic hypoxia** (COPD, sleep apnea)
  - Primary (**Polycythemia Vera)**
    - Uncommon
    - **RBC production independent of EPO**
    - **EPO level is low**
    - **Positive JAK-2 is diagnostic**
    - May be associated with leukocytosis, thrombocytosis, & splenomegaly

WBC

Leukocytosis

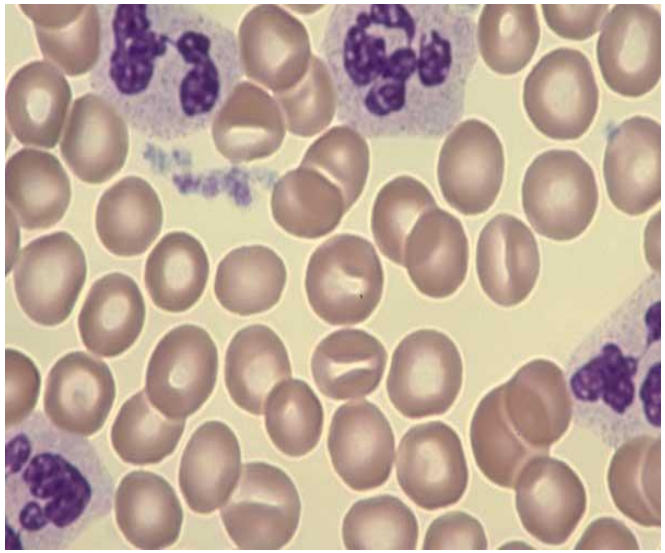
- **Leukocytosis= > 10-12,000/µL**

  - **Acute infections**
  - Leukemia, Polycythemia Vera, other malignancies
  - Toxins & Drugs
  - Trauma or tissue injury (e.g., surgery)
  - Uremia
  - Coma
  - Eclampsia
  - Thyroid storm
  - Acute hemolysis
  - Acute hemorrhage
  - Splenectomy
  - Tissue necrosis

Neutrophilia

Neutrophilia = greater than 7500/µL

- **Infections (acute bacterial infections)**
- Connective tissue disorders
- Medications (especially steroids, growth factors)
- Cancer (solid tumors & Myeloproliferative disorders)
- Cigarette smoking
- Stress (physiologic, seizure, trauma)
- Acute haemorrhage
- Tissue necrosis
- Acute haemolysis
- Idiopathic



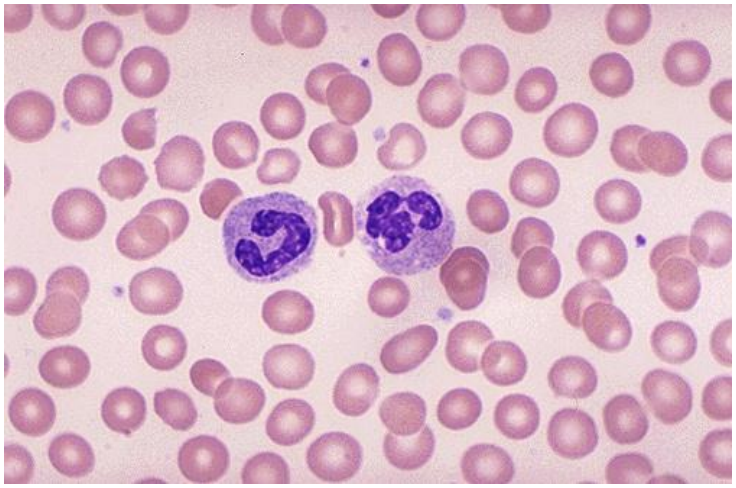
Lymphocytosis

- **Lymphocyte count >4000/µL**
- First consideration is a viral infection or any chronic infections
  - **Viral infections**
    - HBV, HCV, Infectious mononucleosis (EBV), CMV, Rubella, hepatitis, adenoviruses, chicken pox, dengue
  - Bacterial infections
    - Pertussis, Tuberculosis, Typhoid fever
  - Protozoal infections
    - Toxoplasmosis
  - Drug Reaction
  - Hyperthyroidism
  - Stress
    - Trauma, MI, cardiac arrest, sickle crisis
  - Malignancy
    - ALL, CLL, lymphoma

Neutropenia

- **Absolute neutrophil count (ANC) < 1500/µL**

- Many causes
  - **Bacterial infections**
  - **Viral infections**
    - Epstein-Barr, Hepatitis B, HIV
  - **Drugs, chemicals, toxic agents**
  - Radiation
  - Splenomegaly
  - Autoimmune disorders
    - SLE, Rheumatoid Arthritis, etc.
  - Bone marrow disorders

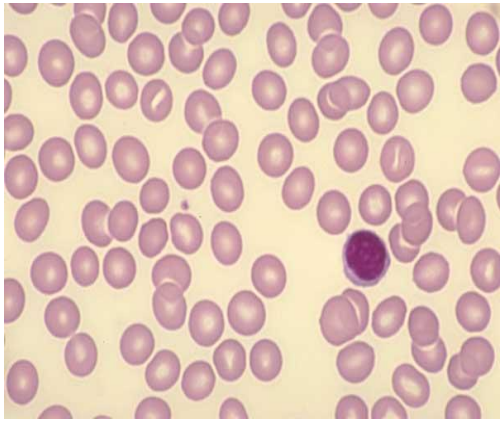


Neutropenia

Common Causes of Neutropenia
Cytotoxic agents
Antibiotics (Penicillins, Cephalosporins, Sulfonamides)
Anticonvulsants
NSAIDs
Antithyroid agents (Methimazole, PTU)
Phenothiazines
Allopurinol
Cimetidine
Diuretics (HCTZ, Spironolactone)

Lymphopenia

- **Lymphopenia = less than 1500/µL**

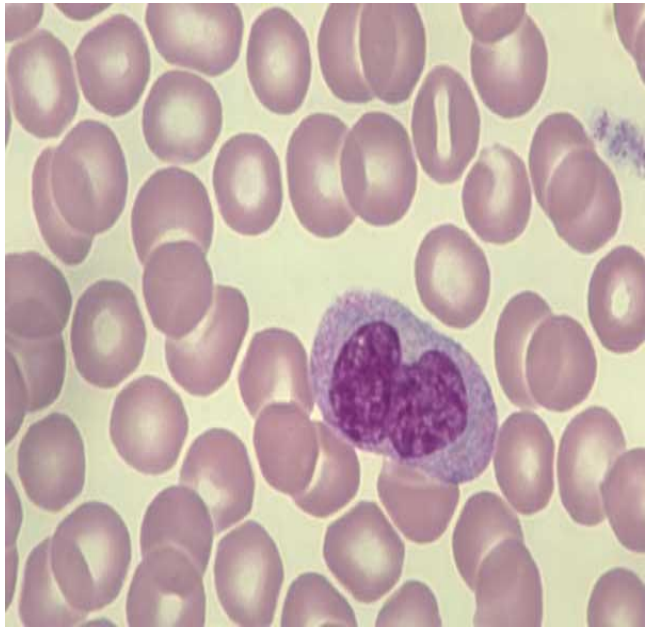


- Chemotherapy
- Radiation
- Steroids
- Aplastic anemia
- Hodgkin's disease and other malignancies
- Inherited immune disorders
- Acquired immunodeficiency syndrome (AIDS)
- ACTH-producing pituitary tumors (Cushing syndrome)

Monocytosis

- **Monocytes count >1000/µL**

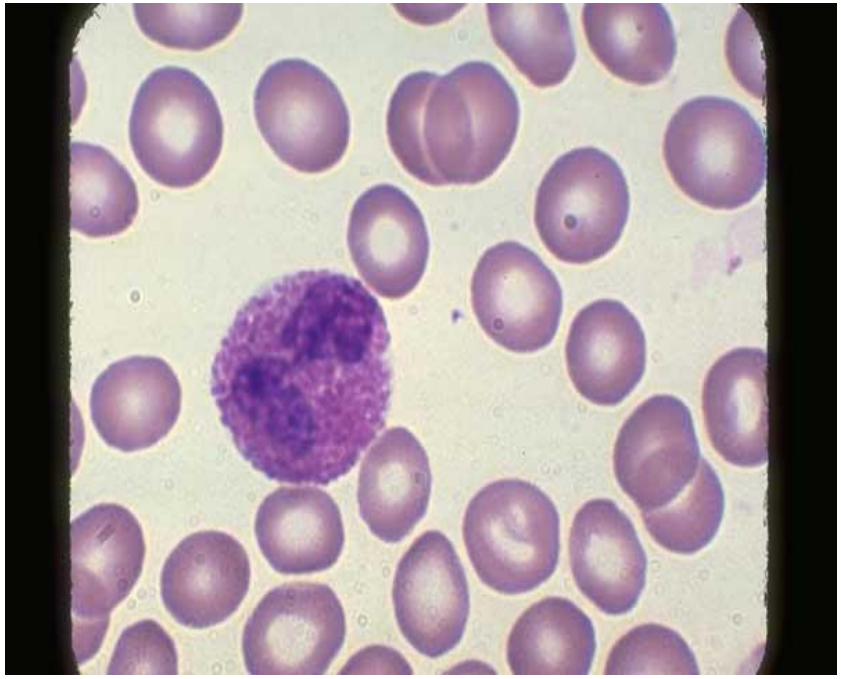
- Common:
  - **Acute infections** (recovery phase)
- Uncommon:
  - Infections (Tbc, malaria, typhoid fever)
  - Inflammatory bowel disease
    - Ulcerative colitis, Crohn's disease
  - Myeloproliferative disorders
    - Myeloid metaplasia, Polycythemia Vera, etc.
  - Leukemia (AML-M4/M5)
  - Lymphoma (HD/NHL)
  - MDS (CMML)



Eosinophilia

- **Eosinophil count >700/µL**

- Common:
  - **Allergic disorders** (including drug reactions)
- Uncommon:
  - **Parasite infection**
  - SLE, rheumatoid arthritis
  - Hypereosinophilic syndrome
  - Diffuse skin diseases
  - Leukemia and Lymphoma
  - Löffler's endocarditis



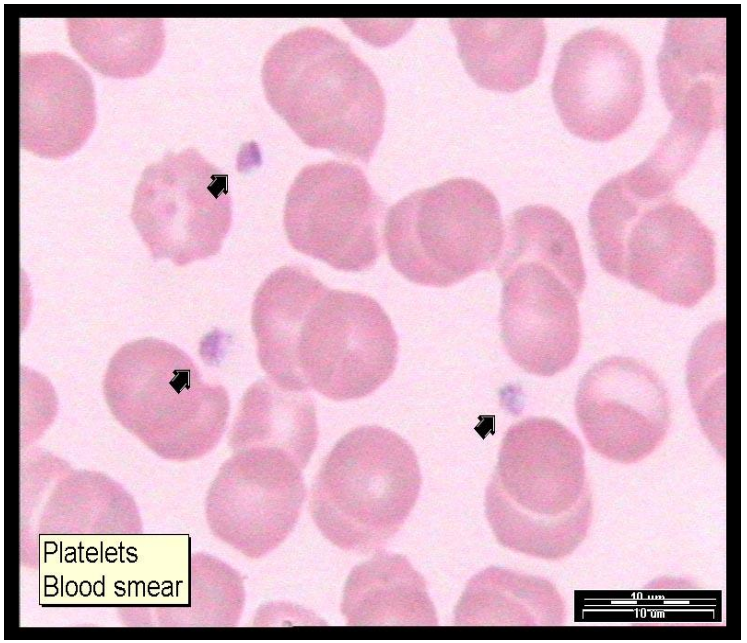
Basophilia

- Reference range for adult is 0-0.2 x 10^9/L
  - Rare:
    - Hypersensitivity reactions to **drugs** or food
    - Inflammatory conditions
      - RA, ulcerative colitis
    - Chronic myeloid leukemia (**CML**)
    - Hodgkin's disease

PLT

Thrombocytopenia

- **PLT count < 150,000/µL**
  - **Immune thrombocytopenia (ITP)**
  - **Drugs**
  - **Viral infection** (CMV, HBV, HIV)
  - Aplastic anemia
  - Hemolytic-uremic syndrome (HUS)
  - Thrombotic Thrombocytopenic Purpura
  - Leukemia
  - Malignancies
  - Sepsis
  - DIC
  - Hypersplenism
  - Pregnancy
  - Bone marrow infiltration



Thrombocytosis

- **PLT count > 400,000/µL**

- Common:
  - "Reactive" thrombocytosis related to
    - Acute trauma
    - Surgery
    - **Blood loss**
    - **Iron deficiency**
    - Chronic infections (i.e. osteomyelitis)
    - Inflammatory diseases (i.e. RA and ulcerative colitis)
    - **Splenectomy**
- Uncommon:
  - Essential thrombocytosis,
  - Polycythemia Vera, Some cancers

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