Hematology Introduction

APPROACH TO PATIENT WITH HEMATOLOGICAL DISORDER

BY:

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The study of blood is one of the most fascinating branches of clinical medicine. Almost all diseases produce changes in the blood at some time during the course of the illness

Primary disorders of the blood and blood-forming organs account for only a small percentage of a haematologist's practice.

Most patients who are referred with haematological abnormalities have diseases in other systems.

Most anaemias are due to blood loss, infection, renal failure, malignant disease, and malnutrition or parasitic infestation. Anaemia may be the first indication of a chronic urinary tract infection, hypothyroidism, pituitary failure, bacterial endocarditis, polymyalgia rheumatica.

An approach to patients with haematological disorders

History:

In taking a history from a patient who is suspected of having a haematological disorder, certain factors are of particular importance.

symptoms are of great importance, particularly

- ***WEIGHT LOSS,***
- ***NIGHT SWEATS,***
- ***BONE PAIN, AND***
- ***PRURITIS.***

gastrointestinal and haemostatic functions are particularly relevant to diseases of the blood. A detailed dietetic, sore tongue, bleeding gums, dysphagia, dyspepsia, disturbance of bowel habit suggestive of malabsorption, and rectal bleeding. Patients are often referred to haematological departments for investigation of easy bruising, is there is an inborn bleeding tendency. These include circumcision, dental), menstruation, surgical procedures

Family histories are particularly important for the diagnosis of blood diseases. It is essential to ask for a family history of ,
the red-cell enzyme (G6PD),
A detailed personal history is also essential.Cigarette- or cigar-smoking in polycythaemia.
Alcohol can produce remarkably diverse haematological changes. A detailed occupational history (lead exposure).

Physical examination:

The examination of a patient with a haematological disorder : On general inspection it is essential to examine the skin carefully for evidence of bruising, purpura, infiltration, or ulceration,
Jaundice is an important sign.

Pigmentation of the skin is common in patients with iron overload, both primary and secondary to repeated transfusion.

There is an association between vitiligo and pernicious anaemia.

The nails should be examined for unusual fragility; flattened, spoon-shaped nails, koilonychia, which are supposed to be diagnostic of chronic iron deficiency, are now rarely seen.

Systematic approach to lymph-node examination.

- A detailed examination of the mouth should include the state of the tongue, mucous membranes, gums, teeth, and. Glossitis, in iron-deficiency and megaloblastic anaemia. Gingival hypertrophy in patients with acute leukaemia, and in some individuals with megaloblastic anaemia due to phenytoin therapy.
- Oral infection, often associated with ulceration, is very common in neutropenic patients. The teeth may be badly formed and the bite may be abnormal in patients with severe forms of thalassaemia.
- Dental abscesses are common in patients with neutropenia. Telangiectases may be found on the lips and oral mucous membranes of patients with hereditary telangiectasia.

On abdominal examination the most important questions are the size of the liver, and whether there is splenomegaly Examination of the musculoskeletal system may be particularly important in patients with coagulation defects such as haemophilia or Christmas disease, hemarthrosis. Muscle haematomas are also common and are easily missed.The joints have other important associations with blood disorders.

A mild refractory anaemia is a very common accompaniment of rheumatoid arthritis. Painful arthritis of the large joints may be the presenting symptom of primary haemochromatosis, and Gout

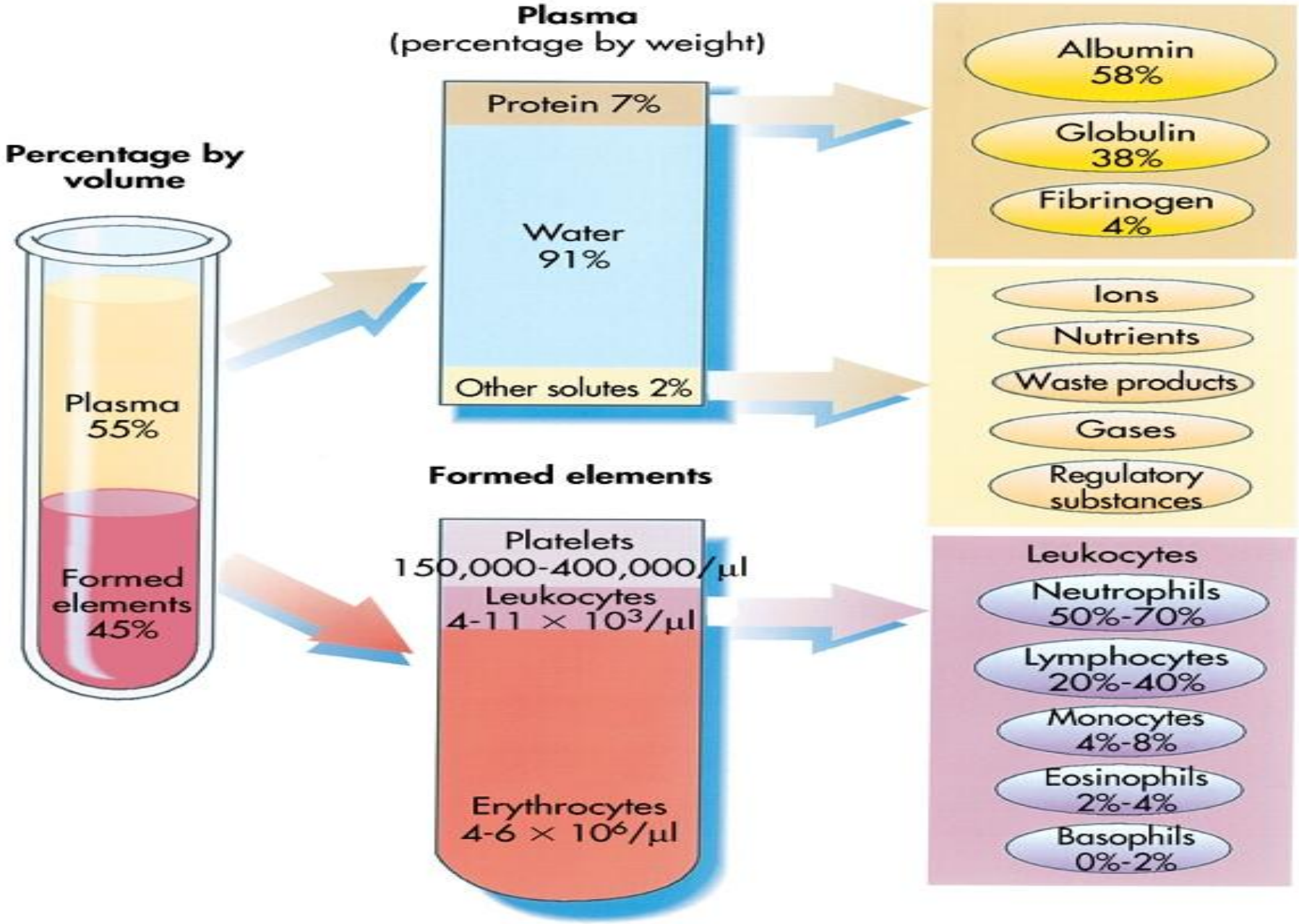
The use of the laboratory:

WHAT ARE HEMATOLOGICAL DISORDERS

- BENIGN
  - NAEMIAS
  - LEUKOPENIAS
  - PLATELETS DISORDERS
- MALIGNANT:
  - PLASMA CELLS DISORDERS
  - LYMPHOPROFLERATIVE DISEASES
  - LEUKEMIAS
- MYELOFIBROSIS

Components of Blood

- Plasma
  - 55%
- Blood Cells
  - 45%
  - Three types
    - Erythrocytes/RBCs
    - Leukocytes/WBCs
    - Thrombocytes/Platelets



From Thibodeau GA, Patton KT: *The human body in health and disease*, ed 3, St. Louis, 2002, Mosby.

Erythrocytes/Red Blood Cells

- Composed of hemoglobin
- Erythropoiesis
  - = RBC production
    - Stimulated by hypoxia
    - Controlled by erythropoietin
      - Hormone synthesized in kidney
- Hemolysis
  - = Destruction of RBCs
  - Releases bilirubin into blood stream
  - Normal lifespan of RBC = 120 days

RED BLOOD CELLS

- Transport oxygen via hemoglobin from lungs to peripheral tissues and organs
- RBC (Varies with altitude):
  - **M: 4.7 to 6.1 x10^12 /L**
  - **F: 4.2 to 5.4 x10^12 /L**
- Biconcave disc shape with diameter of about 8 μm
- **Function:**
  - Transport hemoglobin which carries oxygen from the lung to the tissues
  - Acid –base buffer.
- **Life span 100-120 days.**

Erythrocytosis due to Appropriate Increases in Erythropoietin

- Life at high altitude
- High affinity hemoglobins
- Cardiopulmonary disease
- Obesity-Hypoventilation syndrome
- Obstructive sleep apnea
- High carboxyhemoglobin levels

Hemoglobin & Hematocrit

- **Hemoglobin :**
  - M: 13.8 to 17.2 gm/dL
  - F: 12.1 to 15.1 gm/dL

- **Hematocrit : (Packed Cell Volume)**
- It is ratio of the volume of red cell to the volume of whole blood.
  - M: 40.7 to 50.3 %
  - F: 36.1 to 44.3 %

MCV & MCHC

- **MCV =** Mean Corpuscular Volume
  - MCV indicates the Red cell volume (Size) HCT/RBC = 80-100fL
  - **Small = Microcytic**
  - **Normal = Normocytic**
  - **Large = Macrocytic**
- **MCHC=** Mean Corpuscular Hemoglobin Concentration = 26-34%
  - Both the MCH & MCHC tell Hb content of RBC
  - Decreased = Hypochromic
  - Normal = Normochromic
  - **INCREASED = Hereditary Spherocytosis**

MCH & RDW

- **MCH (Mean Corpuscular Hemoglobin)**
  - = 27-32 pg
- **RDW (Red cell Distribution Width)**
  - It is correlates with the degree of Anisocytosis
  - Normal range from 10-15%

Reticulocyte Count

- Reticulocytes (Immature Red Blood Cells)
  - Calculating proportion within circulation assists in determining cause of anemia
    - Normal is 1-2%
    - **Low :** Suggests decreased production (i.e. nutritional or marrow problem)
    - **High :** Suggests bleeding or premature destruction of RBCs (i.e. Hemolysis)
- This important value is needed in the evaluation of any anemia.

The Three Basic Measures

	Measurement	Normal	Range
A.	RBC count	5 million	4 to 6
B.	Hemoglobin	15 g%	12 to 17
C.	Hematocrit	45	38 to 50

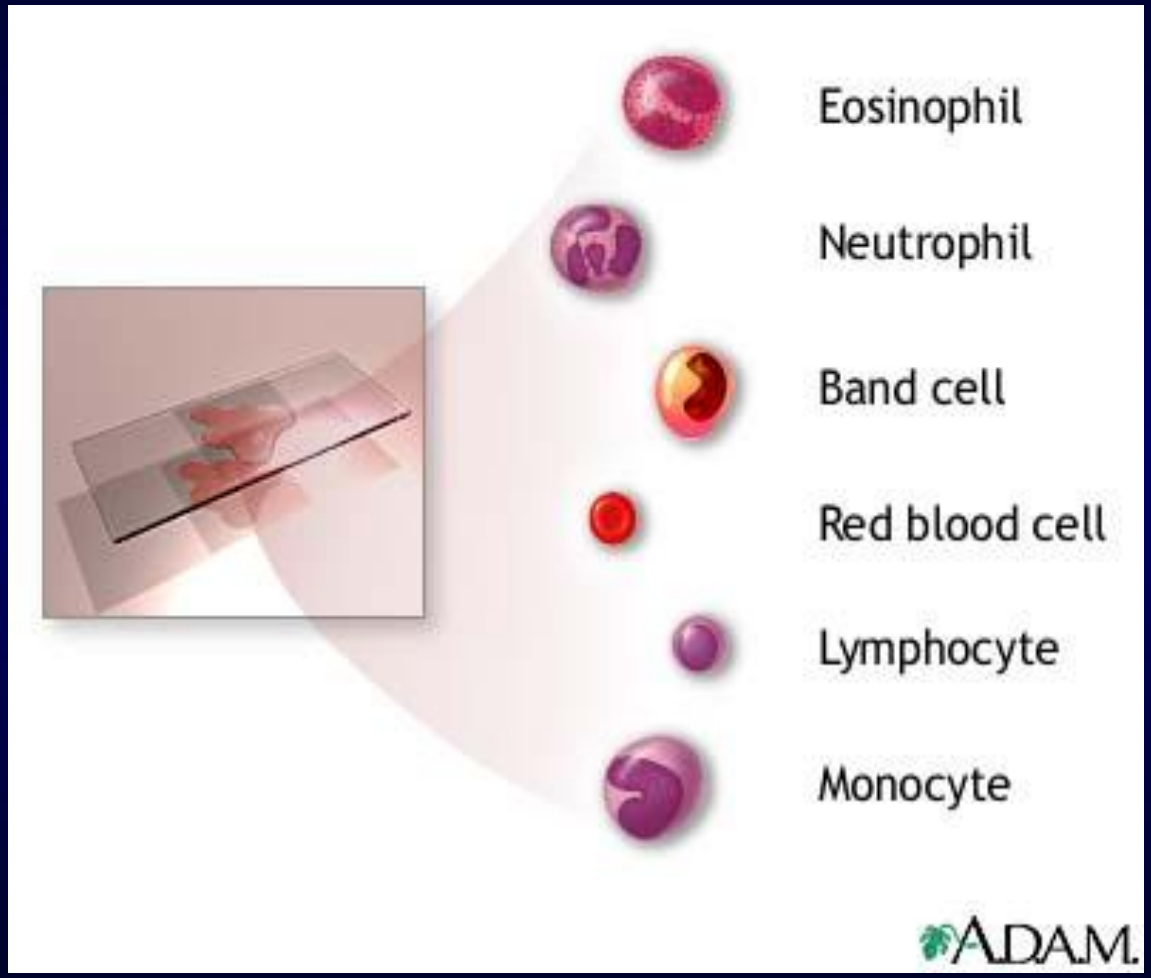
A x 3 = B x 3 = C - This is the rule of thumb

Check whether this holds good in given results

If not -indicates micro or Macrocytosis or Hypochromia.

Leukocytes/White Blood Cells

- 5 types
  - Basophils
  - Eosinophils
  - Neutrophils
  - Monocytes
  - Lymphocytes



Definitions : White Cell Numbers

- **Leukemoid Reaction**
  - Benign excessive leukocytosis
  - Accompanied by an exaggerated neutrophilia
  - And a left shift in response to an **infection**
  - The WBC > 50 x 10^9/L
- **Leukocyte Alkaline Phosphatase**
  - Stain used to differentiate a leukemoid from a leukoerythroblastic reaction

Leukocytes : WBC

- The normal range: 4 – 11x10^9 /L
- **Two types of WBC:**
  - 1) **Granulocytes consist of:**
    - Neutrophils: 50 - 70%
    - Eosinophils: 1 - 5%
    - Basophils: up to 1%
  - 2) **Agranulocytes consist of:**
    - Lymphocytes: 20 - 40%
      - B-cells
      - T-cells
    - **Monocytes**: 1 - 6%

WBC

- **The type of cell affected depends upon its primary function:**
- **<u>Production of WBC's increases in response to :</u>**
  - Infection
  - Presence of steroids
  - Decreased reserve of leukocyte pool in bone marrow
  - In bacterial infections, neutrophils are most commonly affected
  - In viral infections, lymphocytes are most commonly affected
  - In parasitic infections, eosinophils are most commonly affected.

Granulocytes

- Visible granules in the cytoplasm.
- Granules contain:
  - Enzymes
  - Other biochemicals that serve as signals and mediators of the inflammatory response
- **Neutrophils** – Phagocytes
- **Eosinophils** – Red granules, Associated with allergic response and Parasitic worms
- **Basophils** – Deep blue granules - Release heparin, histamine and serotonin

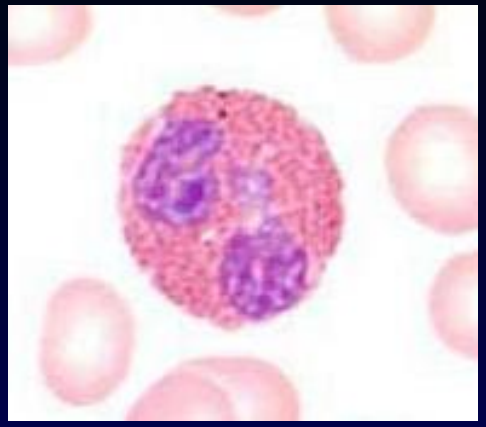
Quantitative Changes

- **Granulocytosis**
  - Increase in the count of all or one of the granulocytic component
    - Neutrophils
    - Basophils
    - Eosinophils
- **Agranulocytosis**
  - Decrease in the count of all or one granulocytic component

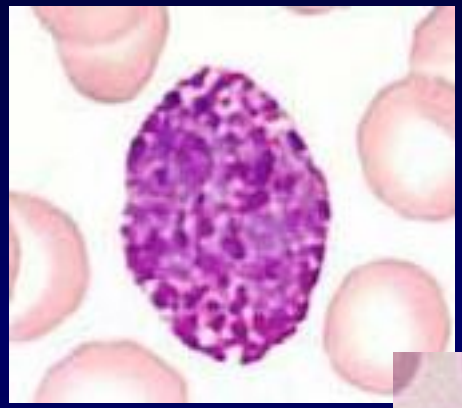
Peripheral Blood Morphology

- Erythrocytes
- Granulocytes
  - Neutrophils
  - Eosinophils
  - Basophils
- Platelets
- Monocytes
- Lymphocytes (B & T cells)

WBC

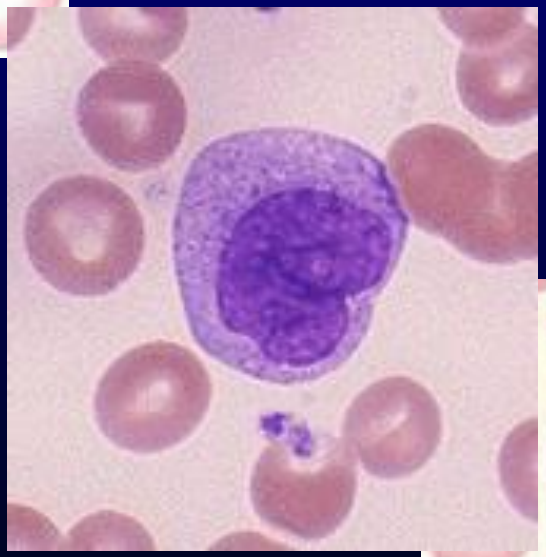


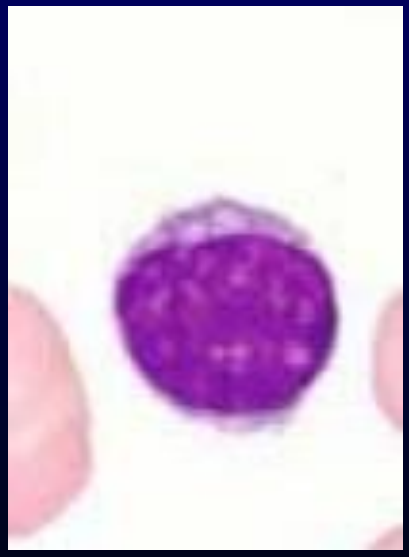
Eosinophil



Basophil

Band Cell

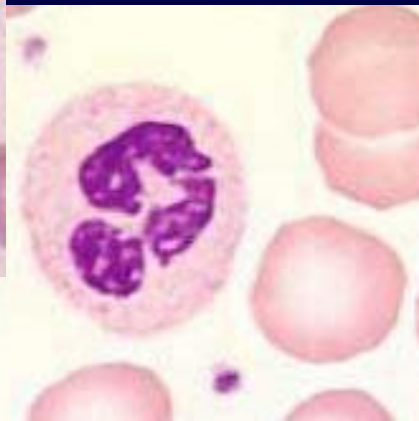




Monocyte

Lymphocyte

Neutrophil



Neutrophilia

- Conditions associated with **neutrophilia** are:
  - 1-Bacterial infections (most common cause)
  - 2-Tissue destruction
    - Tissue infarctions
    - Burns.
  - 3- Leukemoid reaction
  - 4-Leukemia

NEUTROPHILIA (>7.5 x 10^9/L)

- Increase in the Neutrophils and / or its precursors
  - In adults count >7.5 x 10^9/L but the counts are age dependent
- Increase may results from alteration in the normal steady state of
    - Production
      - Increased progenitor cell proliferation
      - Increased frequency of cell division of committed neutrophil precursors
    - Transit
      - Impaired transit to tissue
    - Migration
    - Destruction

NEUTROPHILIA

- **Causes of Neutrophilia**
  - Infection
    - Bacterial
  - Inflammatory conditions
    - Autoimmune disorders
    - Gout
  - Neoplasia
  - Metabolic conditions
    - Uraemia
    - Acidosis
    - Haemorhage
  - Corticosteroids
  - Marrow infiltration/fibrosis
  - Myeloproliferative disorders

NEUTROPHILIA

- **Acute Neutrophilia**
  - Mobilized rapidly by stress
  - Suggested by adrenaline stress test
  - Due to reduced neutrophil adhesion
    - Bacterial infection
    - Stress
    - Exercise
  - Slower rise when cells are released from the bone marrow storage pool
    - Steroid
    - Infections .
  - Steroids also reduces the passage to the tissues

NEUTROPHILIA

- **Chronic Neutrophilia**
  - Long term corticosteroid therapy
  - Chronic inflammatory reactions
  - Infections or chronic blood loss
  - Infections
    - Less common organisms e.g poliomyelitis
- **Leukemoid Reactions**
  - Applied to chronic neutrophilia with marked leucocytosis (>20 x 10^9/L)
  - The usual feature is the shift to the left of myeloid cells
  - Causes include
    - Infections
    - Marrow infiltration
    - Systemic disease (AGN & Acute liver failure)

Causes of Neutrophilia

- **Infections**
  - Primarily bacterial
- **Drugs/Hormones**
  - Epinephrine
  - Corticosteroids
  - Lithium
  - Venoms/Poisons/Toxins
- **Tissue necrosis**
  - Acute gout
  - Burns
  - Trauma
  - Infarcts
- **Other**
  - Autoimmune disorders
  - Stress
  - Severe physical activity
  - Pregnancy
  - Acute hemorrhage
  - Post-splenectomy
  - MPD
- **Metabolic**
  - Ketoacidosis
  - Uremia
  - Eclampsia
  - Thyrotoxicosis

NEUTROPENIA

- Absolute reduction in the number of circulating neutrophils
- **Definition:**
  - Less than the normal absolute count
  - Greatly influenced by patient age and race.
    - Middle Eastern populations
  - Subclasses include mild, moderate and severe
- Mild (1- 1.5 x 10^9/L)
- Moderate (0.5 – 1 x 10^9/L)
- Severe (<0.5 x 10^9/L)
  - Symptoms are rare with the neutrophil count above 1 x 10^9/L
  - Bacterial infections are the commonest
  - Fungal, viral and parasitic infection are relatively uncommon

Neutropenia

- This may result from
  - 1-Decreased bone marrow production
    - BM hypoplasia.
  - 2-Ineffective bone marrow production
    - Megaloblastic anemias and myelodysplastic syndromes.
  - 3- post acute infection
    - Typhoid fever, brucellosis.

Neutropenia Pathophysiology

- Defects inside or outside the Bone Marrow
  - Decreased proliferation [failure of cells - aplasia]
  - Decreased maturation [insufficient number of precursors undergoing abnormal maturation]
  - Decreased survival [increased destruction and/or rapid removal of cells]
  - Distribution [total body pools are normal, circulating numbers are reduced]

Neutropenia < 2.5 x 10^9/L

- **Causes**
  - Reactions to Drugs
    - BM ablative therapy
  - Infections
    - HIV/Hepatitis
    - Typhoid/ miliary TB
    - Malaria
  - Immune Disorders
    - SLE
  - Neoplasm
  - BM Failure
    - Megaloblastic Anemia
    - Aplastic Anemia
  - Hypersplenism
  - Idiopathic

Causes of Neutropenia

- Physiologic
  - In African-Americans
- Drugs –
  - Anti-psychotics,
  - Anti-epileptics,
  - Anti-thyroid, and
  - Some antibiotics (Gold, Sulfa)
- Chemotherapy
- Infections: Viral, Overwhelming bacterial sepsis, TB, Fungal
- Immune - SLE, RA (Felty syndrome)
- Familial
- Hypothyroidism, Hypopituitarism

(NEUTROPENIA) contd.

- **Causes of Neutropenia**
  - Racial
  - Congenital
  - Cyclical neutropenia
  - Marrow aplasia
  - Marrow infiltration
  - Megaloblastic anemia
  - Acute infections
  - Typhoid, Miliary TB, viral hepatitis
  - Drugs
  - Irradiation exposure
  - Immune disorders
    - HIV
    - SLE
    - Felty's syndrome
    - Neonatal isoimmune and autoimmune neutropenia
  - Hyperslplenism

(NEUTROPENIA) contd.

- Cyclical neutropenia
  - Regular recurring episodes of severe neutropenia ($<0.2 \times 10^9/L$) usually lasting for 3-6 days
  - Can be familial & inherited with maturation arrest
  - Three suggested mechanisms for cyclical neutropenia
    - Stem cell defect & altered response to growth factors
    - Defect in humoral or cellular stem cell control
    - Periodic accumulation of an inhibitor

Management of Neutropenia

- Remove the cause if possible
- Treat any infection aggressively
- Role of
  - Growth factors
  - Splenectomy

(EOSINOPHILIA)

- Increase in the eosinophil count must prompt for further investigation (>0.6 x 10^9/L)
- The causes of eosinophilia can be considered under following headings
  - Allergy
    - Atopic, Drug sensitivity and Pulmonary eosinophilia
  - Infection
    - Parasites (Helminths , recovery from infections
  - Malignancy
    - Hodgkin's disease, NHL and MPD
  - Drugs
  - Skin disorders , Autoimmune disorders
  - Gastrointestinal disorders
  - Hypereosinophilic syndrome

Eosinophils Function

- Granulocytes with large, refractile, orange-pink granules.
- Nucleus is typically bilobed.
  - 1-5% of WBC =0.04-0.4x10^9/L
- **Functions include all PMN functions,**
  - Chemotaxis
  - Phagocytosis
  - Killing of phagocytosed bacteria
  - Serving as effector cells for antibody-dependent damage to parasites,
  - Regulation of immediate-type hypersensitivity reactions
    - Inactivation of histamine and leukotrienes released by basophils and mast cells

Causes of Eosinophilia

- Neoplasm
- Allergy/asthma
- Addison's disease
- Collagen vascular disease
- Parasites

(EOSINOPHILIA) Contd.

- **Hypereosinophilic syndrome**
  - Criteria of diagnosis
    - Peripheral blood eosinophil >1.5 x 10^9/L
    - Persistence of counts more than 6 months
    - End organ damage
    - Absence of any obvious cause for eosinophilia
  - Organ most commonly involved
    - Heart
    - Lung
    - Skin
    - Neurological

(MONOCYTOSIS)

- Absolute monocyte count is age dependent
- Absolute count $>0.8 \times 10^9/L$
- Have no marrow reserves
- Useful harbinger of engraftment
- Most commonly seen in conditions with increased cell damage -
- Causes of monocytosis can be grouped as
  - Infections
    - Chronic infection (TB, Infective endocarditis)
    - Recovery from Acute infection
  - Malignant disease
    - MDS, AML, HD, NHL
  - Connective tissue disorders
    - Ulcerative colitis, Sarcoidosis, Crohn's disease
  - Post splenectomy
- Strenuous exercise

(BASOPHILIA)

- Basophils are least common of the granulocytes
- Reference range for adult is $0 – 0.2 \times 10^9/L$
- Most commonly associated with hypersensitivity reactions to drugs or food
  - Allergies
  - Irradiation
  - Viral infections
  - Inflammatory conditions e.g RA, Ulcerative Colitis are also sometime associated with basophilia
  - Myeloproliferative disorders

Agranulocytes

- Granules too small to be visible
- **Monocytes** – Become macrophages
- **Lymphocytes** – B cells and T cells = Immune functions

Lymphocyte Function

- Lymphocytes have an oval nucleus, with a thin rim of blue cytoplasm.
  - 20-40% of WBC =1.55-3.5x10^9/ L
- There may be a few very fine purplish-red granules.
- The nuclear border is smooth.
- Lymphocytes live for years.
- Functions in immune regulation and production of hematopoietic growth factors.
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  - immune regulation and
  - production of hematopoietic growth factors.

Causes of Lymphocytosis

- T cells: cellular
  - For viral infections
- B cells: humoral (AAntibody)
- Natural Killer Cells
- Lymphocytosis – may indicate
  - Viral infection
    - Infectious mononucleosis, CMV .
  - Bacterial infection : whooping cough (pertussis), syphilis, brucellosis
- TB
  - Stress.
  - Steroid therapy
- Chronic Lymphocytic Leukemia (CLL)
- Lymphomas and Waldenstrom's macroglobulinemia

Lymphocytosis
Absolute count >5.5 x 10^9/L

- The blood contain only few percent of total body lymphocytes
- The most consistent variation is seen with age
- **Normally:**
  - 60-80% circulating lymphs are T-cells
    - [2:1 CD4/CD8]
  - 10-20% are B-lymphs
  - 5-10% are natural killer or NK cells

(LYMPHOCYTOSIS)

- Non-malignant causes of lymphocytosis
  - Infections
    - Viral infections
      - Infectious mononucleosis
      - CMV
      - Rubella, hepatitis, adenoviruses, chicken pox,dengue
    - Bacterial infections
      - Pertussis
      - Healing TB, typhoid fever
    - Protozoal infections
      - Toxoplasmosis
  - Allergic drug reactions
  - Hyperthyroidism
  - Splenectomy
  - Serum sickness
  - Recovery from acute infections

Causes of Lymphocytopenia

- Immunodeficiencies, including HIV/AIDS
- Immunosuppresive drugs, including corticosteroids
- Lymphomas
- Granulomatous diseases, including sarcoid, TB
- Alcoholism, malnutrition, zinc deficiency

Lymphopenia
Absolute lymphocyte count <0.6 x 10^9/L

- There are three types of abnormalities:
  - Decreased production
  - Increased destruction
  - Changes in distribution

Lymphopenia

- **Decreased production**
  - SCID = severe combined immunodeficiency
  - Protein-calorie malnutrition
  - Zinc deficiency
- **Increased destruction**
  - HIV infection
  - Radiation therapy
  - Neoplastic chemotherapy
  - SLE
- **Redistribution**
  - Glucocorticoid therapy
  - Anesthesia
  - TB
  - Influenza
  - Burns
- **Other**
  - Hodgkin's
  - Myasthenia gravis

Monocyte Function

- Largest white cell normally found in the periphery
- Has a folded nucleus with uneven countour
- Slate grey cytoplasm--there may be vacuoles
- Monocytes live about 2 - 3 months,
- Functions Include:
  - Chemotaxis,
  - Phagocytosis,
  - Killing of some microbes,
  - Antigen presentation,
  - Release of IL-1 and TNF, which stimulates bone marrow stromal cells to produce growth factors, including: GM-CSF, G-CSF, M-CSF, and IL-6.
  - Precursors of tissue macrophages

Causes of Monocytosis

- Bacterial infection: TB, Syphilis, SBE, Typhoid, Brucellosis
- Protozoal infex: Malaria
- Rickettsial infex: RMSF, Typhus
- Myelodysplastic Syndromes
- Leukemias
- IBD

Abnormal Results of WBC

- **(Leukocytosis) may indicate:**
  - Infectious diseases
  - Inflammatory disease (such as rheumatoid arthritis or allergy)
  - Leukemia
  - Severe emotional or physical stress
  - Tissue damage (e.g. necrosis, or burns)
- **(Leukopenia) may result from:**
  - Decreased WBC production from BM.
  - Irradiation.
  - Exposure to chemical or drugs.

Manifestations of Leukocytosis

- Fever
- Malaise
- Weakness
- Others depend on each system which is involved
- » Chest: cough, SOB and chest pain
- » Abdomen: diarrhea, vomiting, dehydration.
- »CNS: headache, visual disturbance, Neck stiffness

Manifestations of Leukopenia

- Infection of the mouth and throat.
- Painful skin ulceration.
- Recurrent infection.
- Septicemia.

Platelets

- Small granular non-nucleated discs.
- Diameter about 2-4 μm
- Normal range; 150-300x10^9 /L
- Destroyed by macrophage cells in the spleen.
- Function; involved in coagulation and blood haemostasis.
- Life span 7-10 days

Numbers of Platelets

- **Increased (Thrombocythemia)**
  - Pregnancy.
  - Exercise.
  - Bleeding.
  - Splenectomy
- **Decreased (Thrombocytopenia)**
  - Viral infections.
  - Drugs.
  - Bone marrow destruction or suppression e.g. leukemia

Normal Clotting Mechanisms

- **Hemostasis**
  - Goal: Minimizing blood loss when injured
    1. Vascular Response
       - Vasoconstriction
    2. Platelet response
       - Activated during injury
       - Form clumps (Agglutination)
    3. Plasma Clotting Factors
       - Factors I – XIII
       - Intrinsic pathway
       - Extrinsic pathway

Manifestations of Throbocytopenia

- Petechial hemorhage.
- Easy bruising.
- Mucosal bleeding
  - Epistaxes.
  - Gum bleeding

Sign or symptom	Pathological basis
Tiredness, dyspnoea	Reduced oxygen-carrying capacity of blood due to anaemia
Mucosal pallor	Anaemia
Glossitis (Sore mouth, smooth tongue)	Mucosal effects of haematinic deficiency
Spoon-shaped nails	Due to iron deficiency
Jaundice	Bilirubin accumulation from haemolysis
Abnormal tendency to infections	Neutropenia, e.g. in leukaemia or hypoplastic anaemia Immune deficiency, e.g. in myeloma, and due to chemotherapy in leukaemia and lymphoma
Splenomegaly	Myeloid metaplasia in myeloproliferative disorders, red cell pooling and destruction in haemolytic anaemias, infiltration in leukaemias and lymphomas. Also non-haematological causes, e.g. portal hypertension
Lymphadenopathy	Infiltration with leukaemia or lymphoma. Non-neoplastic causes, e.g. infectious mononucleosis
Bone pain and fractures	Osteoclast activation in myeloma
Purpura, bruising, mucosal or traumatic bleeding	Thrombocytopenia or severe platelet dysfunction
Bruising, muscle and joint bleeding and traumatic bleeding	Severe coagulation factor deficiency

Enlarged lymph nodes	Neoplastic infiltration • primary (lymphoma) • secondary (metastases) Specific infections (e.g. tuberculosis, toxoplasmosis, infectious mononucleosis) Reactive hyperplasia
Enlarged spleen	Congestion (heart failure, portal hypertension) Storage disorder Neoplastic infiltration (leukaemia, lymphoma)
Susceptibility to infection	Immune deficiency • congenital • acquired (lymphoma, leukaemia, AIDS, iatrogenic)
Weight loss/ pyrexia	Interleukins produced by inflammatory or lymphomatous (i.e. type B symptoms) tissue acting on thermoregulatory centre in hypothalamus
Muscle weakness (myasthenia gravis)	Thymic hyperplasia or neoplasia
Howell–Jolly inclusions in red cells	Persistence of DNA fragments in red cells due to splenic atrophy

RED BLOOD CELLS

- **Erythropoietin (EPO)**
  - Growth factor produced by kidneys that is essential for RBC production and release
  - Sense tissue oxygen content
    - EPO increases when oxygen delivery to kidneys falls in setting of anemia and hypoxemia
      - Response is blunted or absent in patients with kidney disease

Assessment of the Hematologic System

- **History**
  - Past health history
  - Medications
  - Surgery or other treatments
- **Physical Examination**
  - Skin
  - Eyes
  - Mouth
  - Lymph Nodes
  - Heart and Chest
  - Abdomen
  - Nervous System
  - Musculoskeletal System

Diagnostic Studies of the Hematologic System

- Radiologic Studies
  - CT/MRI of lymph tissues
- Biopsies
  - Bone Marrow examination
  - Lymph node biopsies

TABLE 19-1 Common Laboratory Tests for Hematologic and Lymphatic Disorders

TEST	NORMAL ADULT VALUES	EXPLANATION	NURSING IMPLICATIONS
Complete Blood Count (CBC)			
Red Blood Cell (RBC) count ■ Men ■ Women	 4.6–6.0 million/μL (mm^3) 4.0–5.0 million/μL(mm^3)	Number of circulating RBCs in one microliter (cubic millimeter, or mm^3) of blood Reduced in hemorrhage, anemia, and chronic kidney disease Increased (polycythemia) in high altitude, cardiopulmonary disease	No fasting or special client preparation is necessary. Explain the test and the reason it is being done. Results may be affected by deficient or excess fluid volume.
Reticulocyte count	0.5%–1.5% of total RBC	Percentage of immature RBCs Used to help diagnose anemias and their underlying cause	No fasting or special client preparation is necessary. Explain the test and the reason it is being done.
Hemoglobin (Hgb) ■ Men ■ Women	 13.5–18 g/dL 12–15 g/dL	Amount of hemoglobin in 100 mL (1 dL) of blood Used to help diagnose anemias	No fasting or special client preparation is necessary. Do not draw a sample from an arm in which an IV is infusing. Explain why the test is being done. Results may be affected by deficient or excess fluid volume. No special preparation is required. Explain that these tests are used to help identify the underlying cause or type of anemias.
Hematocrit (Hct) ■ Men ■ Women	 40%–54% 36%–46%	Packed volume of RBCs in 100 mL of blood; reported as a percentage Used to help diagnose acute blood loss, anemias, and to monitor chronic diseases	
Mean corpuscular volume (MCV)	80–98 cuμ (fL)	Average volume of individual RBCs	
Mean corpuscular hemoglobin (MCH)	27–31 pg	Weight of the hemoglobin in an average RBC	
Mean corpuscular hemoglobin concentration (MCHC)	32%–36%	Average concentration (percent) of hemoglobin within RBC	

TABLE 19-1 Common Laboratory Tests for Hematologic and Lymphatic Disorders (continued)

TEST	NORMAL ADULT VALUES	EXPLANATION	NURSING IMPLICATIONS
WBC count	4,500–10,000/μL (mm^3)	Measures the number of WBCs in circulating blood	No food or fluid restriction is required. Inquire about manifestations of acute infection or known chronic conditions that may affect WBC count. Decreased WBCs are seen in disorders affecting blood cell production and some infections. Increased WBCs are present in acute infection, leukemias, stress responses, and some acute and chronic diseases.
Differential WBC count		Provides more specific information about infections and disease processes	
Neutrophils	50%–70% (2,500–7,000/μL)	Rapid responders to infection and tissue damage Increase in acute infection and inflammation	
Eosinophils	1%–3% (100-300/μL)	Increase during allergic and parasitic conditions	
Basophils	0.4%–1.0% (40–100/μL)	Increase during healing; decrease in stress and allergic reactions	
Lymphocytes	25%–35% (1,700–3,500/μL)	Play a major role in immune response with B lymphocytes and T lymphocytes	
Monocytes	4%–6% (200–600/μL)	Second line of defense against bacterial infection and foreign substances	
Platelets	150,000–400,000/μL (mm^3)	The number of circulating platelets in the blood Low platelet count associated with bleeding; increased count may increase risk for abnormal clotting	No client preparation is required. Observe for manifestations of bleeding. Monitor count in clients undergoing chemotherapy.
Bleeding time	3–7 minutes	Used to screen for disorders caused by platelet dysfunction	Bleeding time is prolonged by ingestion of aspirin and anti-inflammatory drugs.

Coagulation Studies			
Prothrombin time (PT or protime)	10–13 seconds (varies by laboratory)	Evaluates the extrinsic clotting pathway; prolonged in warfarin (Coumadin) therapy	No food or fluid restrictions are necessary. The INR provides a more standardized measure of Coumadin therapy.
INR (International Normalized Ratio)	2–3.0	Used to evaluate Coumadin therapy (see Chapter 18 for therapeutic values)	
Partial thromboplastin time (PTT)	60–70	Used to evaluate clotting pathways and monitor heparin therapy	No food or fluid restriction is required. Values are increased in clotting factor deficiencies, heparin therapy, and aspirin ingestion.
Activated partial thromboplastin time (APTT, PTT)	20–35 seconds	More sensitive than PTT; evaluates the intrinsic clotting pathway; prolonged in heparin therapy	
Coombs' test	Negative	Performed to diagnose hemolytic anemias and evaluate transfusion reactions. The expected results are no detected antibodies to RBCs (indirect Coombs') or no detected RBC antigen–antibody complexes (direct Coombs').	No food or fluid restriction is required. Ask about previous transfusions or transfusion reactions. Report manifestations of transfusion reactions.
Hemoglobin electrophoresis	■ Hb A_1 95%–98% ■ Hb A_2 1.5%–4% ■ Hb F less than 2% ■ Hb C 0% ■ Hb D 0% ■ Hb S 0%	Performed to detect abnormal forms of hemoglobin associated with genetic hemolytic anemias (e.g., sickle cell anemia, thalassemia)	No food or fluid restrictions are required. Assess for and report manifestations of hemolytic anemias. Encourage the client to obtain genetic counseling.

TABLE 19-1 Common Laboratory Tests for Hematologic and Lymphatic Disorders (continued)

TEST	NORMAL ADULT VALUES	EXPLANATION	NURSING IMPLICATIONS
		Serum Iron Studies	
Iron	50–150 mcg/dL (10–27 mol/L)	Serum iron and body iron stores are measured to evaluate iron deficiency anemia.	Antibiotics, estrogen and testosterone, oral contraceptives, aspirin, and ethanol affect results.
Total iron-binding capacity	250–450 µg/dL	Measures the maximum amount of iron that can bind to transferrin, the protein that transports it	
Ferritin	Men: 15–445 ng/mL (15–445 µg/L) Women: 10–310 ng/mL (10–310 µg/L)	A measure of the amount of iron stored in body tissues	No food or fluid restrictions are required. Results in women are affected by age and use of oral contraceptives.
Transferrin	200–430 mg/dL (2.0–4.3 g/L)	Measures the protein that transports iron to the bone marrow for use in synthesizing hemoglobin	Avoid iron supplements for 12 hours before testing. Results are affected by pregnancy and use of oral contraceptives.
D-dimer	Negative	D-dimer is a fragment produced when fibrinolysis occurs. It is used primarily to diagnose disseminated intravascular coagulation.	No food or fluid restriction is required. Report manifestations such as unexplained bleeding. Monitor vital signs.

Common Laboratory Tests for Hematologic and Lymphatic Disorders

Schilling test	10%–40% of vitamin B_{12} excretion in 24 hr	Primarily used to diagnose pernicious anemia. This timed test evaluates the body's ability to absorb vitamin B_{12} from the GI tract. An oral dose of radioactively tagged vitamin B_{12} and an intramuscular vitamin B_{12} injection are administered, followed by collection of a 24-hour urine specimen.	Verify that client has given informed consent. Instruct the client to: ■ Withhold food and fluids for 8–12 hours before the test. ■ Avoid taking vitamin B supplements for 3 days before the test. May eat and drink after vitamin B_{12} injection is given. Observe for manifestations of anaphylaxis for at least 1 hour after administration of radioactive vitamin B_{12}. Collect a 24-hour urine sample (see Box 28-3 ), using rubber gloves to handle urine.

COMPLETE BLOOD COUNT

- White Blood Cells (WBC)
  - Differential
    - Neutrophils, Lymphocytes, Monocytes, Eosinophils, Basophils, Bands
- Red Blood Cells (RBC, Hgb, Hct)
- Platelets (PLT)
- Macrophages of the Reticuloendothelial (RE) system removes RBC's (spleen is major site of RBC clearance)
- RE system is Extravascular
  - 90% of normal RBC destruction occurs without release of hemoglobin into circulation.

Complete Blood Count (CBC)

- Red Blood Cells (RBCs)
- Hematocrit (Hct)
- Hemoglobin (Hgb)
- Mean Corpuscular Volume (MCV)
- Mean Corpuscular Hemoglobin Concentration (MCHC)
- Red Cell Distribution Width (RDW)
- White Blood Cells (WBCs)
- Platelet

Diagnostic Studies of the Hematologic System: Complete Blood Count (CBC)

- WBCs
  - Normal 4,000 -11,000 μ/ℓ
  - Associated with infection, inflammation, tissue injury or death
  - Leukopenia-- ↓ WBC
  - Neutropenia -- ↓ Neutrophil count
- RBC
  - ♂ 4.5 – 5.5 x 10^6/ℓ
  - ♀ 4.0 – 5.0 x 10^6/ℓ
- Hematocrit (Hct)
  - The hematocrit is the percent of whole blood that is composed of red blood cells. The hematocrit is a measure of both the number of Red Blood Cells and the size of red blood cells.

Complete Blood Count (CBC)

- Platelet Count
  - Normal 150,000- 400,000
  - Thrombocytopenia-↓ platelet count
  - Spontaneous hemorrhage likely when count is below 20,000
- Pancytopenia
  - Decrease in number of RBCs, WBCs, and platelets

RBC : Peripheral Smear

- **Anisocytosis**
  - Refers to red cells which vary widely in size.
  - Different sizes of RBC
- **Poikilocytosis**
  - Refers to red cells that vary widely in shape.
  - Different Shapes of RBC
    - Thalassemia
    - Myelofibrosis
- **The RDW**
  - Mathematically measures the range of red cell sizes.

RBC : Peripheral Smear

- **Microcytosis**
  - Refers to red cells that are small.
  - **Associated with**
  - Iron deficiency
  - Thalassemias
  - Sideroblastic anemia
- **Hypochromasia**
  - Refers to red cells that have too little hemoglobin.
  - The area of central pallor is more than 1/3 the total red cell diameter.
  - This is measured by the MCH
  - Iron deficiency

RBC : Peripheral Smear

- **Macrocytosis**
  - Refers to large red cells.
  - **Associated with**
  - Elevated reticulocyte count
  - B12/folate deficiency
  - Liver disease
  - Hypothyroid
  - Chemotherapy
  - Anti-retroviral drug.
- **Basophilic Stippling**
  - Occurs in Lead poisoning
  - Occurs in Megaloblastic Anaemia
  - Dyshaemopoiesis

RBC : Peripheral Smear

- **Polychromasia young red cells (stain unevenly) – reticulocytes**
  - Haemolysis
  - Increased red cell turnover
- **Nucleated RBC Normoblasts**
  - Marrow infiltration
  - Myelofibrosis Leukoerytheroid anaemia
  - Severe haemolysis
- **Target cells :** Look like bulls-eyes.
  - Liver disease
  - Thalassemias
  - Hemoglobin C
  - Post splenomegaly

RBC : Peripheral Smear

- **Spherocytes**
  - Have a loss of central pallor.
  - **Can be seen in**
  - Hereditary spherocytosis
  - Autoimmune hemolysis (Microspherocytes)
  - Disseminated intravascular coagulation
  - Post-splenomegaly
- **Schistocytes** **(**Red cell fragments Intravascular haemolysis
  - They are a hallmark of Microangiopathic Hemolytic Anemia (MAHA)
  - Disseminated intravascular coagulation
  - Heamolytic uraemic syndrome
  - Thrombotic thrombocytopaenic purpura

RBC : Peripheral Smear

- **Sickle Cells**
  - Seen in sickle cell anemia.
- **Echinocytes, or Burr cells**
  - Have small, regular projections. Seen in renal disease
- **Acanthocytes, or Spur cells**
  - Have larger, irregular projections, and are seen in liver disease.

RBC : Peripheral Smear

- **Teardrop cells**
  - Seen in myelophthisic processes
  - Or diseases of marrow infiltration.
  - Deformed as it tries to squeeze out of the bone marrow
- **Howell-Jolly bodies**
  - Peripheral, small, round, purple inclusions within red cells that represent nuclear remnants.
  - They are seen after splenectomy
  - Or in cases of splenic hypofunction.
  - Dyshaemopoiesis

RBC : Peripheral Smear

- **Rouleaux are linear arrangements of red cells**
  - Typically described as "piles of coins on a plate"
  - They are typically seen in disorders with increased levels of immunoglobulin, such as
    - Multiple Myeloma
    - Waldenstrom's macroglobulinemia.
    - Non-specific inflammation raised ESR
    - Severe hypo-albuminemia can also lead to reouleux formation

RBC : Peripheral Smear

- **Red cell Agglutination**
  - Occurs when the red cells are coated with IgM.
  - IgM is large enough to bridge two red cells and cause agglutination.
  - Unlike rouleaux, the red cell clumps are not orderly and linear.

Infectious Mononucleosis

- Epstein-Barr virus
- Acute, self-limiting, febrile infection of B-cells
- Circulating reactive lymphocytes are primary CD8 T-cells
- Saliva from infected person is the main contagion
- Autocrine growth stimulation
- Infection in children under the age of 10 does not cause illness and result in life long immunity
- Clinical features
  - Fever, malaise, fatigue, sore throat, diagnostic red spots at the junction of soft and hard palate, splenomegaly
  - Blood picture shows leucocytosis (10 – 20 x 10^9/L) due to absolute increase in the number of lymphocytes
  - Diagnosis is by serological tests
  - There is no specific treatment

Mononucleosis

- Self-limiting lymphoproliferative disorder caused by the Epstein-Barr Virus
- Infects 90% of people
- Incorporates into DNA of B cells causing production of heterophil antibodies
- T Cells are produced to limit numbers of infected B cells
  - Accounts for increased numbers of lymphocytes.

Hyperviscosity Syndrome

- **Symptoms include:**
  - Headaches
  - Visual changes
  - Tinnitus
  - Dizziness
  - Paresthesias
  - Decreased mental acuity

Pancytopenia -- Differential Diagnosis

Leukemia / Lymphoma

Myelodysplasia

Myelofibrosis

HIV

Folate Deficiency

Aplastic Anemia

Paroxysmal Nocturnal Hemoglobinuria

Drugs

B12 Deficiency

Acute Alcohol Toxicity

If you see pancytopenia: Get a Bone Marrow Examination!!!


Thanks for attention
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