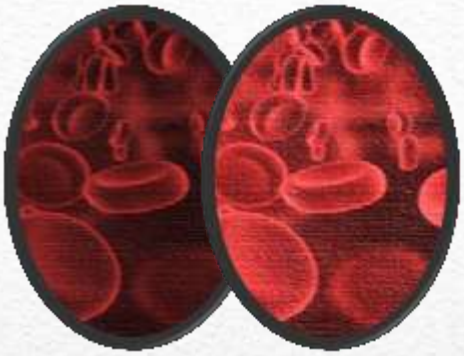
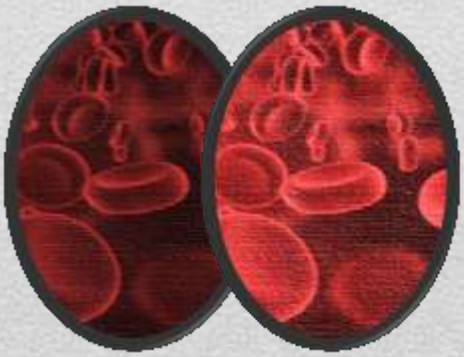


Haematology

Summary for the Important Points

Done By: Khulood Al-Raddadi



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You should only memorize these values.

Normal Values (NV)

- **RBCs:**
  - **Hemoglobin(g/dL):** **Male = 13.5-17.5** **Female = 11.5-15.5**
  - **Red Cell Count ($\times 10^{12}$):** **Male = 4.5-6.5** **Female = 3.9-5.6**
  - **Hematocrit (PCV) (%):** **Male = 40-52** **Female = 36-48**
  - **Mean Cell Volume (MCV) (fL): 80-95**
  - **Mean Cell Hemoglobin (MCH) (pg): 27-34**
  - **Mean Cell Hemoglobin Concentration (MCHC) (g/dL): 30-35**
  - **Life span 120 days.**

- **WBCs:**
  - **WBC count ($\times 10^9$/L): = 4-11.**
  - **Neutrophils = 1.5-6.5** **Lymphocyte = 1.2-3.4** **Monocytes = 0.1-0.6**
  - **Bands = 0-0.7** **Eosinophils = 0-0.5** **Basophils = 0-0.2**

- **Platelets:**
  - **Normal count ($\times 10^9$/L): 150-400.**
  - **Life span: 7-10 days.**
  - **Normal Platelet Size (MPV) (Fl) = 7.3-11.1**

- **Adult Hb: A ($\alpha 2$- $\beta 2$) = 95-97%**
  A2 ($\alpha 2$- $\delta 2$) = 2.5-3.5%
  F ($\alpha 2$- $\gamma 2$) = 0.5-1.5%

  } Percentages in Adults

1- Normal types of Haemoglobin and Thalassaemia

- **Hemoglobin formation**:

Stage	Site of formation	Globin chain
Embryonic Stage first 2 months	**Yolk sac**	**α ζ ε γ**
Fetal Stage 2nd to 7th month	**Liver, spleen**	**α γ** "β&δ in small amount"
Before Birth "7th month" until birth	**Bone marrow**	
After Birth + adulthood	**Bone marrow**	**α β** mainly **γ** & **δ** in small amount

- Chromosome **16** >> **(α + ζ).**
- Chromosome **11** >> **(ε γ β δ)**.
- Alpha (**α**) chains are made of **141** amino acids.
- Beta (**β**) chains are made of **146** amino acids.
- **Types of Hemoglobin:** (Refer to the (NV) – page 1).
    - Adult Hb: **A** (α2- β2), **A2** (α2- δ2) and **F** (α2- γ2).
    - Embryonic Hb: **Gower I - Gower II – Portland**.
    - Abnormal Hb: **H - Bart's** (<0.5% at birth) – **Lepore.**
- If Hb **A2 > 3.5 → β** thalassaemia (β is absent).
- If Hb **A2 < 1.5 → α** thalassaemia (α is absent).
- Hb **F** is a fetal and adult hemoglobin.
- Hb **Bart's** is normal to present at birth in minimal amount (less than 0.5%), but it has to disappear after that or it will be abnormal (α thalassaemia).

❖ **α - THALASSAEMIA:** **(Normal:** 4 copies of α-globin gene)

Silent carrier has 3 copies - **Trait** has 2 copies are **absent**.
Hb H: 3 copies are **absent** - **Hydrops fetalis:** absence of all 4.

- **Blood film:** fragile, small size RBCs, target cells and hypochromic microcytic anemia.
- **HbH α-thalassemia:** Golf Ball cell Appearance and target cells (in supravital stain).

❖ **β - THALASSAEMIA:** A2 > 3.5 %

β-thalassemia major : both alleles and HbA are absent, Hb <7 g/dl (very severe).
β-thalassemia intermediate: two abnormal β+ alleles, Hb >7 g/dl (moderate to severe).
β-thalassemia minor: one abnormal allele (trait, asymptomatic or mildly symptomatic).
β-thalassemia minima (Silent like α thalassemia trait).

- **Blood film:** Target cells, Nucleated RBCs and hypochromic microcytic anemia.
- **Clinical Manifestations:** "Severe types of Thalassaemias: Hb H and β – Thal. major "
    - Pallor and Jaundiced.
    - Hepato-splenomegaly and Skeletal Deformity.
    - Iron Overload manifestations.
    - Thalassemic face in β-thalassemia major.
    - Hair on ends appearance in x-ray.
- **Management:**
    - For further investigation (DNA analysis) and electrophoresis to confirm the diagnosis.
    - Iron chelation therapy (Deferiprone) to ↓ iron overload.

2- Anaemia

- (Refer to the (NV) – page 1).
- All stages of the RBC can synthesize Hb, except for the last stage (erythrocyte).
- Highest amount of Hb synthesis occurs in intermediate normoblast stage.
- Hb carries O2 from the lungs to the body's tissues, and maintains the shape of RBC.
- Hematopoietic stem cell: 1- Self renewal 2- Cell differentiation (T. Factor: EPO – GATA1).
- According to MCV: Microcytic - Normocytic - Macrocytic.
- According to MCH: Hypochromic – Normochromic.
- Anemia of chronic disease is normocytic normochromic anemia.
- Symptoms appear if Hb less than 9g/dL.
- **Clinical Features:**
  - Weakness - Headache - Pallor - Lethargy - Dizziness (Related to anemia)
  - Palpitation (tachycardia) - Angina - Cardiac failure (compensatory mechanism)
- **Classification of Anaemia:**

Defect in	Results in	Type of Anaemia
Prophyrin	Sidroblastic anemia	Hypochromic microcytic anemia
Iron	Iron def. anemia	
Globin chain	Thalassemia	
DNA synthesis	Megaloblastic anemia - MDS	Macrocytic anemia
RBC count	↓ RBC count (Hemolysis)	Normocytic normochromic anemia

- **Iron:**
  - Storage forms of iron in Liver and Macrophages: Ferritin – Haemosiderin.
  - Carried in the blood via transferrin in the ferric state.
  - Hepcidin is produced in the liver & it is the major hormonal regulator of iron.
  - Entering of Iron is controlled by DMT-1 while Haem is controlled by HCP-1.
  - Hepcidin has –ve effect on iron release and absorption.
  - High level of hepcidin decreases the release of iron from the macrophages, and decreases iron absorption in the intestine.
  - Factors favoring absorption: Acid (vitamin C) – Pregnancy and Iron deficiency.
  - Factor reducing absorption: Tea, alkalines and increased hepcidin level.
- **IDA (Iron deficiency Anemia):**
  - **Causes:** GIT Bleeding – Immaturity – Pregnancy.
  - In IDA: Stores, MCV/MCH and Hemoglobin are LOW.
  - In latent stage: Hb is normal while Stores and MCV/MCH are LOW.
  - **Signs and symptoms:** anaemia +/- bleeding with:
    - Koilonychia.
    - Angular stomatitis and/or glossitis.
    - Dysphagia (pharyngeal web "Plummer-Vinson syndrome")
  - **Blood film:** Microcytic hypochromic anemia with:
    - Anisocytosis (variation in size).
    - Pokiliocytosis (variation in shape).
  - **Studies:**
    - ↑ TIBC
    - ↓ Serum iron, serum ferritin and transferrin saturation.

    } Thalassemia is the opposite
  - **Diagnosis:** Perl's stain (normally, iron appears blue).

3- Hemolysis and Haemoglobinopathies

- **Types of Hemolysis:**
  - (Intra-corpuscular - Congenital – Intravascular - in the circulation) "like HbS".
  - (Extra-corpuscular - Acquired – Extravascular – in the RES).

	Extravascular Hemolysis	Intravascular Hemolysis
Laboratory Features	↑ Serum unconjugated bilirubin ↑ Urine urobilinogen ↑ Faecal stercobilinogen ↑ LDH	Haemoglobinaemia Haemoglobinuria Haemosiderinuria
It is important to understand the picture in slide 7 and make sure you go through all the labels in it.		

- **Haemolytic Anaemia:**
  - Congenital:
    - Sickle cell disease
    - Enzymopathies.
  - Acquired: Red cell fragmentation syndrome, cardiac valves and a lot of diseases.
- **Hb C:** α2 β2 6 GLU → LYS.
- **Sickle Cell Anaemia "HbS":** α2 β2 6-GLU → VAL
  - **Clinical Manifestations:**
    - Foot and hand syndrome.
    - Leg ulcer.
    - Short middle finger.
    - Hair on end (X-Ray).
  - **Laboratory Diagnosis:**
    - CBC: Low Hb.
    - **Blood Film:** irreversible sickle cells, target cells and normocytic normochromic anemia.
    - Sickle Solubility Test: +ve.
    - Hb Electrophoresis.
    - Genetic Study.
  - **Indications for:**
    - Blood Transfusion:
      - Severe painful crisis associated with severe haemolysis.
      - Pregnancy.
  - Patient with Sickle cell anemia have high risk of Salmonella "infections in general".

4- White blood cells

- Most important regulating factors are for hematopoiesis: SCF (Stem cell factor) & FLT3-L.
- G-CSF can be given clinically to stimulate the hematopoiesis in severe neutropenia.
- EPO is given in severe anemia to stimulate RBCs production.
- (Refer to the (NV) – page 1).
- **Neutrophils:**
  - (2–5 lobes) - Short lived (≈6 days) and highly motile.
  - Chemotaxis: IL-8, TNF γ & C5a.
  - Killing Mechanisms:
    - Intracellular: Phagocytosis (Superoxide Hydrogen peroxide).
    - Extracellular: Degranulation (Lysozyme, NADPH oxidase and MPO) and NETs.
  - Leukemoid reaction: (neutrophilia with left shift) → sign of infection.
    - Associated with: Toxic granulation - Vaculation - Döhle bodies.
- **Lymphocytes:**
  - Important in the immune system
  - Composed of: T-cells – B-cells – NK cells.
- **Monocytes:**
  - Single well-defined nucleus and very fine granulation.
  - Matures into different types of macrophages
- **Eosinophils:**
  - Nucleus with two lobes and bright red coarse cytoplasm
  - Functions: Anti-Parasitic - allergic reactions
- **Basophils:**
  - Bluish-black granules and mature to tissue mast cells
  - Functions: release Heparin and Histamine - allergic reactions
- **Causes of abnormalities:**

Situation	Important Causes
Neutrophilia (>6.5)	Benin: Bacterial infection. Malignant: Chronic Myeloid leukemia (CML).
Neutropenia (≤ 0.5)	Congenital: Kostmann syndrome - Benign neutropenia - Cyclical neutropenia. Aplastic anemia, SLE and some bacterial infections (Typhoid).
Lymphocytosis	Viral infection: infectious mononucleosis (IMN). Bacterial infection: Pertussis, tuberculosis and brucellosis. Chronic lymphocytic leukemia (CLL).
Monocytosis	Chronic infection: (TB, Brucellosis). Acute leukemia (AML M5). Chronic Myelomonocytic leukemia (CMML).
Monocytopenia	Hairy cell leukemia (HCL).
Eosinophilia	C H I N A = all the causes. Important ones: Idiopathic "Hypereosinophilic syndrome", eosinophilic leukaemia and MPN " Myeloproliferative neoplasm".
Basophilia	Neoplasia (CML).
Leukoerythroblastic	Primary Myelofibrosis.

5- Megaloblastic Anemia

- (Refer to the (NV) – page 1).
- **Microcytic, Hypochromic Anemia:** Iron deficiency, sideroblastic anemia and thalassemia.
  - If MCV < 80 fL (Low) and MCH <27pg (Low).
- **Normocytic, Normochromic Anemia:** renal disease.
- **Macrocytosis with Normoblasts:** Chronic alcoholism – MDS - Chronic liver disease.
- **Macrocytosis:** Alcohol, Liver disease, Reticulocytosis, Hypothyroidism, Myelodysplasia, Pregnancy and Newborn.

❖ **Megaloblastic Anemia:** (Abnormal synthesis of DNA).

- **Causes:**
  - Cobalamin (vitamin B12) deficiency.
  - Folate deficiency.
  - Drugs: hydroxyurea and anitfolate drugs (e.g. methotrexate).
- Vitamin B12 and Folate are stored in the liver.

	Vitamin B12	Folate
Time to develop deficiency	2-10 years	5 months
for absorption	IF and TC2	Intestinal folate conjugase
Site of absorption	Terminal ileum	Duodenum and jejunum

- Causes of deficiencies are due to defect in the factors, receptors or sites of absorption, e,g: Inadequate intake, Veganism, inadequate secretion of intrinsic factor, total or partial gastrectomy, malabsorption and congenital intrinsic factor deficiency.
- Vitamin B12 deficiency: ↑ Homocysteine level, ↓Methionine → abnormalities in CNS.
- **Clinical Features:**
  - Neuropathy due to vit. B12 "mainly" and folate deficiency:
    - Subacute combined degeneration of the cord and psychiatric symptoms.
  - Neural tube defect (NTD): due to deficiencies of both in the mother.
    - Spina bifida.
    - Genetic mutation in 5, 10 methylene tetrahydrofolate reductase → NTD.
- Neuropathy and hypersegmented neutrophils are classical to Vitamin B12 deficiency.
- **Hematological findings:**
  - **Blood film:** "Peripheral Blood":
    - Oval macrocytes. "large cells"
    - High MCV.
    - Hypersegmented neutrophils. "B12 def."
  - **Bone Marrow:**
    - Giant and abnormally shaped megakaryocytes.
    - Hypercellular marrow.
    - Megaloblast (large erythroblast).
- **Treatment:**

	Vitamin B12	Folate
Compound	Hydroxocobalamin	Folic acid
Route	Intramuscular	Oral
Prophylactic	Total gastrectomy Ileal resection	Daily in Pregnancy – Hemolysis Dialysis - Prematurity

6- Acute Leukemia

- It differs from Chronic in the presence of blasts in the peripheral blood "Acute Leukemia".
- AL is in blasts (precursors) while CL is mainly in mature cells.
- Mutations Block differentiation + Enhance proliferation + Decrease apoptosis.
- Defect in Myeloid stem cell → AML while Lymphoid stem cell → ALL.
- AML mainly in Adults "worse" While ALL mainly in children.

❖ **AML: (usually in Adult)**

- Blasts should count 20% or more of total cells.
- Myeloblasts (AML) have granular cytoplasm and Auer rods , while Lymphoblasts (ALL) have a granular cytoplasm and May be vacuolated (like in L3).
- **Stem Cell Markers:** (CD34 & TDT).
- **Main lineage markers are:**
  - Myeloid: MPO - CD13 - CD33 - CD14 - CD41 - CD64 - CD235a
  - B-Lymphoid: CD10 - CD19 - CD22 - CD79a
  - T-Lymphoid: CD3 - CD4 -CD5 - CD7 - CD8
- Subtypes of AML (M0-M8) + cytogenetic abnormalities.
- **FAB Classification:** (Based on Morphology and Flow Cytometry)

FAB	Features	GENETICS	Molecular
M2	Maturation	t(8,21)	AML1-ETO
M3	Promyelocytic	t(15,17)	PML-RARA
M4	Granulocytic & monocytic	t(16,16) or Inv(16,16)	CBFB-MYH11
M5	Monoblastic - Monocytic	t(9,11)	MLLT1-MLL
FAB	**Features**	**MARKERS**	
M6	Erythroid	CD235a	
M7	Megakaryocytic	CD41	

- **WHO Classification:** (Based on Genetics "Immunophenotype")
  - AML with recurrent genetic abnormalities has a good prognosis.
- **Clinical Features:**
  - Myeloid sarcoma - Gum hypertrophy - CNS disease (M4-M5)
  - DIC: Widespread activation of coagulation system (M3)
- **Prognosis:** is good with:
  - t(8;21), inv(16;16) or t(15;17)
  - Less than 60 yrs.
- **Chemotherapy Treatment**: all have the same protocol except M3: target "ATRA"

❖ **ALL: (usually in Adult):**

- Malignant lymphoid blasts.
- Subtypes of ALL (T or B cell).
- B-ALL has a better prognosis, especially: CD10 and t(12:21) "ETV6-RUNX1".
- L3 "Burkitt's" shows Vacculated cytoplasm and t(8,14) mutation.
- CNS relapse + Mediastinal mass (T-ALL).

7- Lymphoproliferative Disorders

- **Causes:**
  - **Benign:**
    - Acute: viral e.g. infectious mononucleosis (IMN).
    - Protozoal infections: toxoplasmosis and malaria.
    - Chronic infections: e.g. tuberculosis, syphilis.
  - **Malignant:** Chronic Lymphocytic Leukaemia (CLL).

- **Infectious Mononucleosis (IM):**
  - Epstein-Barr virus (EBV) → B-cell proliferation → T-cell proliferation → Viremia.
  - **Laboratory Findings:**
    - Atypical lymphocytes (due to proliferation of T cells not B cells).
    - EB virus specific (IgG).
- Pro-lymphocyte leukemia (PLL) → not a blast, it is a stage before maturation.

- **Chronic Lymphocytic Leukaemia (CLL):**
  - Proliferation of mature lymphocytes usually B lymphocytes.
  - Usually in elderly >60 and common in males.
  - Herpes Zoster infection mainly is seen with CLL.
  - **Laboratory Features:**
    - **Blood film**: Mature lymphocytes and smudge (smear) cells.
    - ↓ Immunoglobulin levels.
    - ↑ Uric Acid.
  - Presence of anemia or thrombocytopenia with Lymphocytosis indicates advanced stage) → Rechter's syndrome.
  - Diffuse involvement of bone marrow has a poor prognosis (local is good).

- **Hairy Cell Leukaemia (HCL):** Massive splenomegaly and monocytopenia.

- CD19 and SIg are +ve in CLL, PLL, HCL, FL and MCL (all cases of lymphoma).
- CD103 is +ve in HCL.
- In CLL: SIg and CD5 are +ve but CD22/FMC7 and CD79b are –ve.
- In MCL: all are +ve.

- **Hodgkin's Lymphoma:**
  - Multinucleated cell which is Reed – Sternberg.
  - Positive for CD 15 and CD 30.

- **Sezary syndrome** (cleft nuclei) and **T-cell cutaneous lymphoma** are malignancies of T-Cell, characterized by red man syndrome.

8- Chronic Leukemia

- CL occurs mainly in adults.
- Myeloproliferative Neoplasms (MPN) (Cytosis): CML – PV – ET – PMF.
  - Malignancy of myeloid cells (maturing cells) which are mainly granulocytes.
  - BCR-ABL1 is positive only in CML. Others are negative.
  - **Clinical Features:**
    - Organomegaly.
    - Progression to AML.

- **Chronic Myeloid Leukemia (CML):**
  - Predominant proliferation of granulocytic cells (Cytosis).
  - Between the ages of 40 and 60.
  - BCR-ABL1 gene fusion in the (Ph) chromosome which results from t(9,22).
  - The gene has a tyrosine kinase activity → uncontrolled proliferation.
  - **Clinical presentation:**
    - Marked leukocytosis, usually Neutrophilia.
    - Splenomegaly (Massive)
  - NAP score is low in CML and high in the leukemoid reaction.
  - **Phases:**
    - Chronic: Blasts ≤10% ,Basophils≤ 20% - stable.
    - Accelerated: 10-19% blasts (basophils ≥20%) – unstable.
    - Blastic: ≥20% blasts → AML.
  - **Treatment:** TKIs: Imatinib (Trade name: Gleevec).

- **Myelodysplastic syndrome (MDS):**
  - Hypercellular bone marrow but pancytopenia in blood → No splenomegaly.
  - Variable genetic abnormalities mainly -5 and -7.

- **Chronic myelomonocytic leukemia (CMML):** (↑ monocytes and neutrophils).
  - MDS/MPN disease (Combination of both).
    - Features of MDS (dysplasia & enhanced apoptosis).
    - Features of MPN (marked proliferation).
  - Philadelphia chromosome must be negative.
  - CMML is –ve for BCR-ABL.
  - Blast must be less than 20%, if 20% and above → acute leukemia.

- **MPN (CML)** → Cytosis **MDS** → Cytopenia **MPN/MDS (CMML)** → Cytosis + Cytopenia.

9- MPN (PV – ET – PMF)

- BCR-ABL1 is positive only in CML. Others are negative.

- **Polycythemia Vera (PV): "Primary Polycythemia"**
  - Increase in total body red cell volume due to malignant proliferation.
  - (Refer to the (NV) – page 1).
  - ↑ Hb (>16.5 in women or >18.5 in men) or ↑ packed cell volume (PCV).
  - Primary Polycythemia: ↓ EPO but Normal plasma.
    - In 2nd Polycythemia: normal plasma but High EPO due to smoking or COPD.
    - In relative Polycythemia: plasma is low and RBCs is normal (dehydration).
  - **Clinical and Laboratory Features:**
    - JAK2 mutation in >95% - ↑ Hb - ↓ EPO
    - Splenomegaly in 70% - Thrombosis - ↑ viscosity
  - **Investigations:**
    - **CBC:** ↑ Hb and ↑ RBCs.
    - **Blood smear:** Excess of normocytic normochromic RBCs.
    - **Bone marrow:** Hypercellular bone marrow "high filtration".
  - ↑ Blasts → AML transformation.
  - **Treatment:** Venesection + Aspirin ± Myelosuppressive drugs (hydroxyuria).

- **Essential Thrombocythemia (ET):**
  - Neoplasm that involves primarily the megakaryocytic lineage & characterized by sustained thrombocytosis ≥ 450×10^9.
  - Exclusion of: CML, MDS, PV, PMF and reactive thrombocytosis.
  - JAK2 mutation (60%).
  - Very indolent (5% risk of AML transformation).
  - **Clinical presentation:** Asymptomatic (50%) - Thrombosis – Bleeding - Mild splenomegaly (50%).
  - **Treatment:** Aspirin with or without Hydroxyuria.

- **Primary Myelofibrosis (PMF):**
  - Proliferation of megakaryocytes & granulocytes.
  - **Blood picture:**
    - Leukoerythroblastic (Nucleated red blood cells and immature leukocytes).
    - Tear-drop cells.
  - **Bone marrow:** Deposition of fibrous connective tissue "Fibrotic bone marrow".
  - Massive splenomegaly.
  - JAK2 mutation (50%).
  - Risk of AML transformation (20%).

- **JAK2 mutation:**
  - Specific to 3 diseases: PV (95%) – ET (60%) – PMF (50%).
  - Point mutation leads to loss of auto inhibitory control over JAK2.
  - The mutated JAK2 is in a constitutively active state →Increased proliferation and Decreased apoptosis.

10- Blood Groups

- **Before donation:**
  - Hb (males>13, females>12).
  - Weight > 50k and age (17-70) yrs.
- ABO,H is the most important Blood Group, Rh is the 2nd one.

	Gr A	Gr B	Gr AB	Gr O
Cell type	A	B	AB	O
Ab	Anti- B	Anti- A	None	Both
Ag	A	B	Both	None

Gene	Allele	Transferase
A	A	---galactosaminyl---
B	B	---galactosyl---
O	O	None

- Commonest blood group is O then group A.
- O receives transfusion from O only, and donates to all the other types.
- AB receives transfusion from all types, but only donates to AB.
- Rh+ groups can receives from Rh+ and Rh-, but Rh- receives Rh- only.
- **Genotype:** A (AA or AO), B (BB or BO), AB (AB), O (OO).

- **Blood Transfusion:**
  - **Blood Compatibility Testing (Crossmatch):**
    - Front Type: determines antigens "this method is preferable".
    - Back Type: identifies Antibody.
  - **Rh phenotypes:** (Rh +ve or Rh –ve).
    - 2 genes control it: D and Ce (D is dominant).
    - 32.68 % of population has DCe/dce/R^1r.
  - **Mandatory Tests** on All Units of Blood:
    - ABO group, Rh type and blood-group antibodies.
    - Serologic test for syphilis, retroviruses and hepatitis
  - **After donation:**
    - RBCs are stored in fridge in 2 to 6 degrees for 35 days.
    - Platelets are stored in room temperature 20-25 degrees for 5 days with agitation.
    - Plasma is stored in the freezer -30 degree for 1 year (Clotting factors).

- **Complications** of Blood Transfusion: infections and hemolytic reaction.
- **Investigation** of a Hemolytic Transfusion Reaction: Clerical checks.

11- Haemostasis

- **Malignancy of platelets:** ET and M7.
- (Refer to the (NV) – page 1).
- **Formation:** Segmentation of the cytoplasm of the megakaryocyte in the BM.
- **Controllers:** Lysosomes, Dense body and **α**-granules.
- GPIa attached directly to the collagen but GPIb, GPIIb and GPIIIa attached through VWF.
- If VWF get diseased → GPIb, GPIIb and GPIIIa will be affected.
- **Bleeding time:** 3-8 minutes. It is associated with platelets functions and VWF not with the clotting factors.
- Clotting Factors activities are measured by PT and APTT.
- Extrinsic pathway is measured by PT (10-14 sec), intrinsic by APTT (30-40 sec).
- Extrinsic pathway covers factor 3 and 7, intrinsic covers 12, 11, 9 and 8.
- Common pathway covers factor 2, 5 and 10.
- We do **Coagulation Profile**, if:
    - PT is prolonged → problem with the Extrinsic pathway.
    - APTT is prolonged → problem with the Intrinsic pathway.
    - Both are prolonged → problem with the common pathway.
- **Hereditary vascular disorder:** Hereditary Haemorrhagic Telangiectasia.
- **Acquired vascular Disorder:** Allergic purpura - Paraproteinemia and amyloidosis - Vitamin C Deficiency (Scurvy).
- **Inherited disorders of platelet function:**
    - **Membrane abnormalities:**
        - Bernard – Soluier syndrome "Gp1b-IX-V deficiency" (-ve for Ristocetin).
        - Glanzmann Thrombasthenia "Gp llb/llla deficiency" (+ve for Ristocetin).
    - **α- granule deficiency:**
        - Gray platelet syndrome.
- **Acquired disorders of platelet function:** a lot of diseases.

- **Causes of Thrombocytopenia:** Autoimmune (ITP) - DIC.

1- Immune Thrombocytopenia (ITP):

- **Laboratory features:**
    - Increased numbers and size of megakaryocytes.
    - Reduced platelet life span.
    - Elevated levels of IgG.

2- Disseminated Intravascular Coagulation (DIC): (↑FDPS)

- **Causes:**
    - Infections.
    - Malignancies: (AML-M3)

- **Haemophilia A and B:**
    - If the coagulation factor activity <1 → Severe disease, joint deformity and crippling and spontaneous bleeding episodes.
    - Haemophilia A is due to defect in factor 8 while Haemophilia B in factor 9.

Haemophilia A	VW Disease
Normal bleeding time	Abnormal bleeding time
Normal platelets aggregation	Abnormal platelets aggregation

- **Von-Willebrand disease:**
  - **Classification:**
    - Type1: Quantitative partial deficiency.
    - Type2: Functional abnormality.
    - Type3: complete deficiency.

- **Screening Tests of Hemostasis:** الزبدة هنا

ST	Result	Defects
APTT	Prolonged	Factor 12-11-8-9
PT	Prolonged	Factor 7
TT	Prolonged	Factor 1 (Fibrinogen)
FDPS	High	DIC
Platelets count	Normal	Platelets dysfunction

"If your ship doesn't come in, swim out to meet it!" J.W.

❤ GOOD LUCK ❤