وزارة التعليم العالي والبحث العلمي
الجامعة التقنية الجنوبية
المعهد التقني /العمارة
قسم :تقنيات المختبرات الطبية

الحقيبة التدريسية لمادة :

امراض دم1 / نظري

Hematology 1 /Theoretical

Second stage

تدريسي المادة
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الفصل الدراسي الاول

جدول مفردات مادة امراض دم1

الاسبوع	المفردات
1	Introduction importance of hematology .study the blood contains.
2	The haemotopoiesis in fetus ,children and adult
3	The normal red blood cells ,importance , structure ,erythropoiesis and function.
4	Polycythemia ,causes ,clinical signs and laboratory diagnosis.
5	Study red cell morphology in health and disease .abnormality of RBC in size
6	Abnormality of RBC in shape
7	Abnormality of RBC in colour
8	The normal Hb,of the blood contain and importance
9	Study the types of normal Hb .types
10	Common Hb. Variant
11	Anemia .definition ,classification ,and types
12	Anemia ,causes ,clinical signs and laboratory finding
13	Megaloblastic anemia and pernicious anemia
14	Aplastic anemia and hemolytic anemia
15	Sickle cell anemia ,acquired anemia , and autoimmune hemolytic anemia

Aim of Hematology study:

Studying of hematology for second stage aimed to :

Knowing medical system and tests that occur in laboratory and diagnosis the disease case .

Target group:

Pupils second stage /technical medical laboratory

Educational techniques used :

1-blackborad and pens

2-interactive whiteboard

3-Data show

4-laptop

5-showing scientific films

6-powerpoint

First week

Introduction importance of hematology .study the blood contains.

- **Educational objective:**

The student should be able to :

1- Know important of hematology .
2- Know components of blood

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly.

Activities Used:
1- Interactive classroom activities
2- Brainstorming questions
3- Group activities (if required)
4- Homework
5- Online homework (classroom)
6- Quick written exam .

Hematology: is the science which deals with blood contains in normal and abnormal (healthy and diseases).
Hematology study aid to:
1-the causes of bloody diseases.
2-Diagnosis of these diseases.
3-Treatment of these diseases.

Blood:
Blood is a connective tissue in fluid form composed from blood cells suspended in a liquid called blood plasma. It is considered as the 'fluid of life' because it carries oxygen from lungs to all parts of the body and carbon dioxide from all parts of the body to the lungs. It is known as 'fluid of growth' because it carries nutritive substances from the digestive system and hormones from endocrine gland to all the tissues. The blood is also called the 'fluid of health' because it protects the body against the diseases and gets rid of the waste products and unwanted substances by transporting them to the excretory organs like kidneys.

PROPERTIES OF BLOOD:

1–Color: Blood is red in color. Arterial blood is scarlet red because it contains more oxygen and venous blood is purple red because of more carbon dioxide

2-Volume: Average volume of blood in a normal adult is 5 L. In a newborn baby, the volume is 450 ml. It increases during growth and reaches 5 L at the time of puberty. In females, it is slightly less and is about 4.5 L. It is about 8% of the body weight in a normal young healthy adult, weighing about 70 kg.

3–Reaction and pH: Blood is slightly alkaline and its pH in normal conditions is 7.4.

4-Specific gravity: Specific gravity of total blood : 1.052 – 1.061 Specific gravity blood cells : 1.092 – 1.101 Specific gravity of plasma : 1.022 – 1.026.

5- **Viscosity:** Blood is five times more viscous than water. It is mainly due to red blood cells and plasma proteins.

COMPOSITION OF BLOOD :

Blood contains of the: 1-cellular portion called blood cells .

2-liquid portion: there are two types known: 1- Serum 2-Plasma

BLOOD CELLS :

Three types of cells are present in the blood contain 45% of blood volume and consist of :

1. Red blood cells or erythrocytes ,is most common cells .
2. White blood cells or leukocytes .
3. Platelets or thrombocytes .

Plasma:

Plasma is a straw-colored clear liquid part of blood. It contains 91% to 92% of water and 8% to 9% of solids. The solids are the organic(glucose, acid fatty , amino acid, urea ,lactic acid ..) and the inorganic substances (Na, Chloride,…etc) gives the normal values of some important substances in blood, contain coagulate factors added to blood protein(albumin, fibrinogen, immunoglublin) .

Serum:

Serum is the clear yellow-colored fluid that oozes from blood clot. When the blood is shed or collected in a container, it clots. In this process, the fibrinogen is converted into fibrin and the blood cells are trapped in this fibrin forming the blood clot. After about 45 minutes, serum oozes out of the blood clot. For clinical investigations, serum is separated from blood cells and clotting elements by centrifuging. Volume of the serum is almost the same as that of plasma (55%). It is different from plasma only by the absence of fibrinogen, i.e. serum contains all

the other constituents of plasma except fibrinogen. Fibrinogen is absent in serum because it is converted into fibrin during blood clotting.
Thus, Serum = Plasma – Fibrinogen

Functions of blood :

1-Nutritive function : Nutritive substances like glucose, amino acids, lipids and vitamins derived from digested food are absorbed from gastrointestinal tract and carried by blood to different parts of the body for growth and production of energy.

2-Respiratory function :Transport of respiratory gases is done by the blood. It carries oxygen from alveoli of lungs (statured with O2at 89-99% at rest) to different tissues and carbon dioxide from tissues to lung (alveoli).

3-Excretory function :Waste product formed in the tissues during various metabolic activities are removed by blood and carried to the excretory organs like kidney, skin, liver, etc. for excretion.

4-Transport of hormones and enzymes: Hormones which are secreted by ductless (endocrine) glands are released directly into the blood. The blood transports these hormones to their target organs/tissues. Blood also transports enzymes .

5-Regulation of water balance :Water content of the blood is freely interchangeable with interstitial fluid. This helps in the regulation of water content of the body.

6- Regulation of Acid-Base balance: Plasma proteins and hemoglobin act as buffers and help in the regulation of acid-base balance .

7- Regulation of body temperature : Because of the high specific heat of blood, it is responsible for maintaining the **thermoregulatory** mechanism in the body, i.e. the balance between heat loss and heat gain in the body.

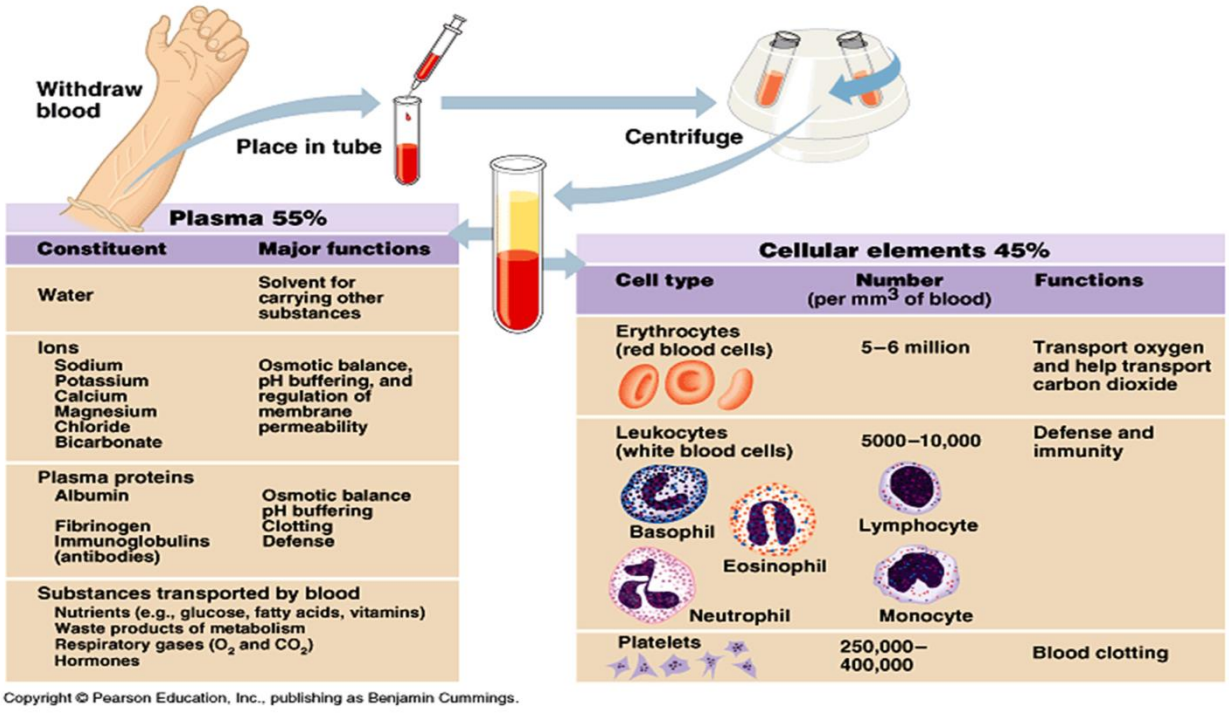
8-Storage function: Water and some important substances like proteins, glucose, sodium and potassium are constantly required by the tissues. Blood serves as a readymade source for these substances. And, these substances are taken from blood during the conditions like starvation, fluid loss, electrolyte loss, etc.

9-Defensive function: Blood plays an important role in the defense of the body. The white blood cells are responsible for this function. Neutrophils and monocytes engulf the bacteria by phagocytosis. Lymphocytes are involved in development of immunity. Eosinophils are responsible for detoxification, disintegration and removal of foreign proteins.

10- Transport of Hydrogen ion: some oxyhemoglobin loses O2 and become deoxyhemoglobin this compound binds to hydrogen ion in much greater

affinity than oxygenated blood.

11-Hadraulic function: The restriction of blood flow can be used in specialized tissue to engorge blood in it like in jumping in which blood forced flow and engorge into the leg under pressure resulting straighter them giving powerful for jumping without need to bulky muscular leg.



Evaluation methods :

1-Immediate feedback (formative assessment).
2-Involving students in self-assessment (correcting their own mistakes).
3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/What the causes of the following:

1-blood is called the fluid of health.
2-blood volume different between male and female.
3-blood more viscous than water.

Reference :

1- A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674
2- Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Second week

The hematopoiesis in fetus ,children and adult

-Educational objective:

The student should be able to :

1-Know the mechanism of hematopoiesis process in fetus ,children .

2-Know the mechanism of hematopoiesis process in adult .

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:

1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5- Online homework (classroom)
6-Quick written exam .

Erythropoiesis:

DEFINITION :

Erythropoiesis is the process of the origin, development and maturation of erythrocytes. Hemopoiesis or hematopoiesis is the process of origin, development and maturation of all the blood cells. This process start by stem cell which is non-recognizable morphologically. This is a well-defined and recognizable lineage of nucleated red cell in the marrow is called Erythroblast which produced from stem cell. Erythroblast give pronormoblast which suffer from many changes resulting erythrocyte ,these changes are :

1-Reduction in cell size .
2-reduction in nucleus size .
3-Ripening of cytoplasm .

Maturation time from pronoroblast until erythrocyte 7 days. There are stages present in erythropoiesis :

1-Multiplication maturation stage: it start from erythroblast until intermediate normoblast.

2- maturation stage: it include late normoblast and reticulocyte.

3-Rlease stage : it contain reticulocyte and erythrocyte.

Site of Hemopoiesis (Erythropoiesis):

-In Fetal Life :

In fetal life, the erythropoiesis occurs in three stages:

1-Mesoblastic Stage :I is start from few days after fertilization of ova until less than the first two months of embryonic life, the RBCs are produced from mesenchyme (mesoderm) of yolk sac.

2-Hepatic Stage :It begin 2-7 month of embryonic life, liver is the main organ that produces RBCs. Spleen and lymphoid organs are also with minimal role involved in erythropoiesis.

3-Myeloid Stage :After 3 months of embryonic life, the RBCs are produced from red bone marrow and liver.

Sites of haemopoiesis

0 – 2 months (yolk sac) 2 – 7 months (liver, spleen) 3 – 9 months (bone marrow)	**Fetus**
Infants	Bone marrow (practically all bones)
Adults	Vertebrae, ribs, sternum, skull, sacrum and pelvis, proximal ends of femur

IN NEWBORN BABIES, CHILDREN AND ADULTS :

In newborn babies, growing children and adults, RBCs are produced only from the red bone marrow.

1. Up to the age of 20 years: RBCs are produced from red bone marrow of all bones (long bones and all the flat bones).

2. After the age of 20 years: RBCs are produced from membranous bones like vertebra, sternum, ribs, scapula, iliac bones and skull bones and from the ends of long bones. After 50 years of age, the proportion of active marrow decline as fat increase , the shaft of the long bones becomes yellow bone marrow because of fat deposition and looses the erythropoietic function. In adults, liver and spleen may produce the blood cells if the bone marrow is destroyed or fibrosed. Collectively bone marrow is almost equal to liver in size and weight.

It is also as active as liver. Though bone marrow is the site of production of all blood cells, comparatively 75% of the bone marrow is involved in the production of leukocytes and only 25% is involved in the production of erythrocytes.

But still, the leukocytes are less in number than the erythrocytes, the ratio being 1:500. This is mainly because of the lifespan of these cells. Lifespan of erythrocytes is 120 days whereas the lifespan of leukocytes is very short ranging from one to ten days. So the leukocytes need larger production than

erythrocytes to maintain the required number.

Stages of maturation :

Blood cell formations have 3 stages to recognize into erythrocytes, leucocytes, and platelets :

1-Multiplication maturation stage : it occur by division of the cells to increase its number.

2-Gradual maturation stage : include development and recognizable of the cells .

3-Relase stage :it occur after maturation stage when migrate all the mature cells to peripheral blood stream

PROCESS OF ERYTHROPOIESIS:

Stem cells :

Stem cells are the primary cells capable of self-renewal and differentiating into specialized cells . **Hemopoietic stem cells** are the primitive cells in the bone marrow, which give rise to the blood cells. Hemopoietic stem cells in the bone marrow are called **uncommitted pluripotent hemopoietic stem cells** (PHSC). PHSC is defined as a cell that can give rise to all types of blood cells. In early stages, the PHSC are not designed to form a particular type of blood cell. And it is also not possible to determine the blood cell to be developed from these cells: hence, the name uncommitted PHSC (Fig.). In adults, only a few number of these cells are present. But the best source of these cells is the umbilical cord blood. When the cells are designed to form a particular type of blood cell, the uncommitted PHSCs are called **committed PHSCs**. Committed PHSC is defined as a cell, which is restricted to give rise to one group of blood cells

Committed PHSCs are of two types:

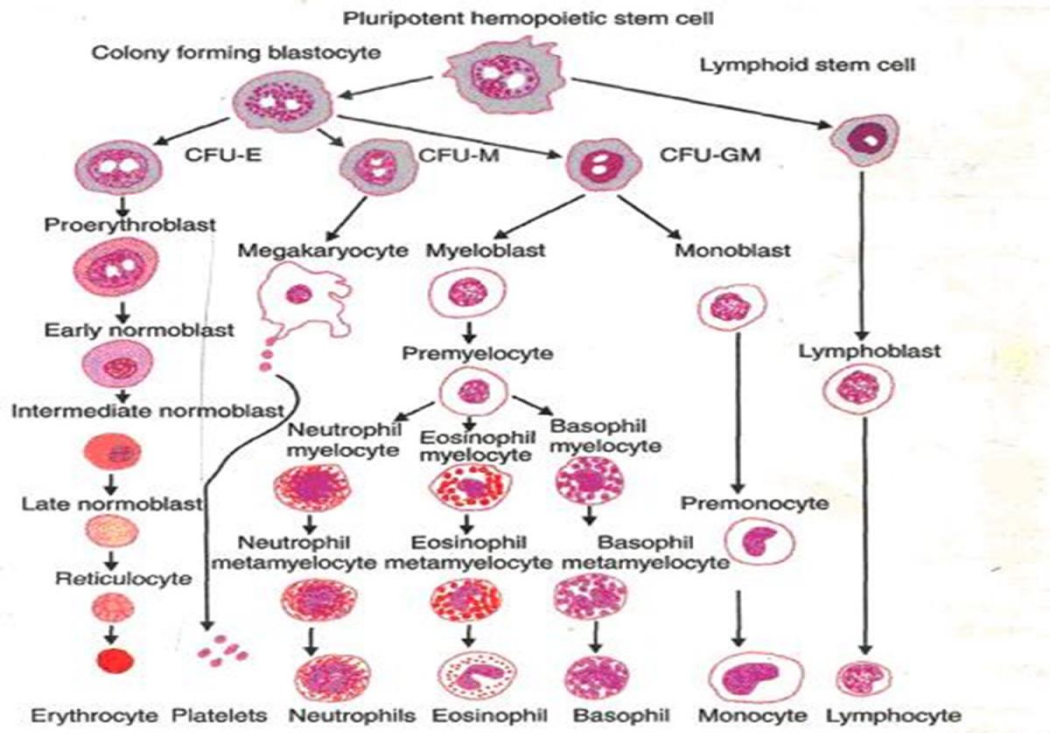
1. Lymphoid stem cells (LSC) which give rise to lymphocytes and natural killer (NK) cells.

2. Colony forming blastocytes, which give rise to myeloid cells. Myeloid cells are the blood cells other than lymphocytes. When grown in cultures, these cells form colonies hence the name colony forming blastocytes. Different units of colony forming cells are:

i. Colony forming unit-erythrocytes (CFU-E) – Cells of this unit develop into erythrocytes.

ii. Colony forming unit-granulocytes/monocytes (CFU-GM) – These cells give rise to granulocytes (neutrophils, basophils and eosinophils) and monocytes.

iii. Colony forming unit-megakaryocytes (CFU-M) – Platelets are developed from these cells



E 10-2: Stages of erythropoiesis. CFU-E = Colony forming unit—Erythrocyte, CFU-M = Colony forming unit—Megakaryocyte, CFU-GM = Colony forming unit—Granulocyte/Monocyte

STAGES OF ERYTHROPOIESIS:

Various stages between CFU-E cells and matured RBCs are (Fig. 10.2):

1. Proerythroblast
2. Early normoblast
3. Intermediate normoblast.
4. Late normoblast
5. Reticulocyte
6. Matured erythrocyte

1-Proerythroblast (Megaloblast)

Proerythroblast or megaloblast is the rounded or oval first cell derived from CFU-E. It is very large in size with a diameter of about 12-20 µ. Its nucleus is large and occupies the cell almost completely(80% of cytoplasmic space). The nucleus has two or more nucleoli and a reticular network. Proerythroblast does not contain hemoglobin. The cytoplasm is basophilic in nature have ferritin granules. Proerythroblast multiplies several times and finally forms the cell of next stage called early normoblast. Synthesis of hemoglobin starts in this stage. However, appearance of hemoglobin occurs only in intermediate normoblast.

2-Early Normoblast:

The early normoblast is little smaller than proerythroblast with a diameter of about

10-16 µ. In the nucleus still large have chromatin Condensation and deeply staining, the nucleoli disappear. The condensed network becomes dense. The cytoplasm is basophilic in nature. So, this cell is also called basophilic erythroblast. This cell develops into next stage called intermediate normoblast .

3-Intermediate Normoblast Cell:is smaller than the early normoblast with a diameter of 8-14 µ. The nucleus is still present (small). But, the chromatin network shows further condensation. The hemoglobin starts appearing. Cytoplasm is already basophilic. Now, because of the presence of hemoglobin, it stains with both acidic as well as basic stains. So this cell is called polychromophilic or polychromatic erythroblast. This cell develops into next stage called late normoblast

4-Late Normoblast :

Diameter of the cell decreases further to about 8 -10 µ. Nucleus becomes very small with very much condensed chromatin network and it is known as inkspot nucleus. Quantity of hemoglobin increases. And the cytoplasm becomes almost acidophilic. So, the cell is now called orthochromic erythroblast. In the final stage of late normoblast just before it passes to next stage, the nucleus disintegrates and disappears. The process by which nucleus disappears is called pyknosis. The final remnant is extruded from the cell. Late normoblast develops into the next stage called reticulocyte.

5-Reticulocyte:

Reticulocyte is flat non-nucleate, disc shaped ,otherwise known as immature RBC. It is slightly larger than matured RBC. The cytoplasm contains the reticular network or reticulum, which is formed by remnants of disintegrated organelles. Due to the reticular network, the cell is called reticulocyte. The reticulum of reticulocyte stains with supravital stain. In newborn babies, the reticulocyte count is 2% - 6% of RBCs, i.e. 2 – 6 reticulocytes are present for every 100 RBCs. The number of reticulocytes decreases during the first week after birth. Later, the reticulocyte count remains constant at or below 1% of RBCs. The number increases whenever production and release of RBCs increase. Reticulocyte is basophilic due to the presence of remnants of disintegrated Golgi apparatus, mitochondria and other organelles of cytoplasm. During this stage, the cells enter the blood capillaries through capillary membrane from site of production by diapedesis. Important events during erythropoiesis is given in Table (1)

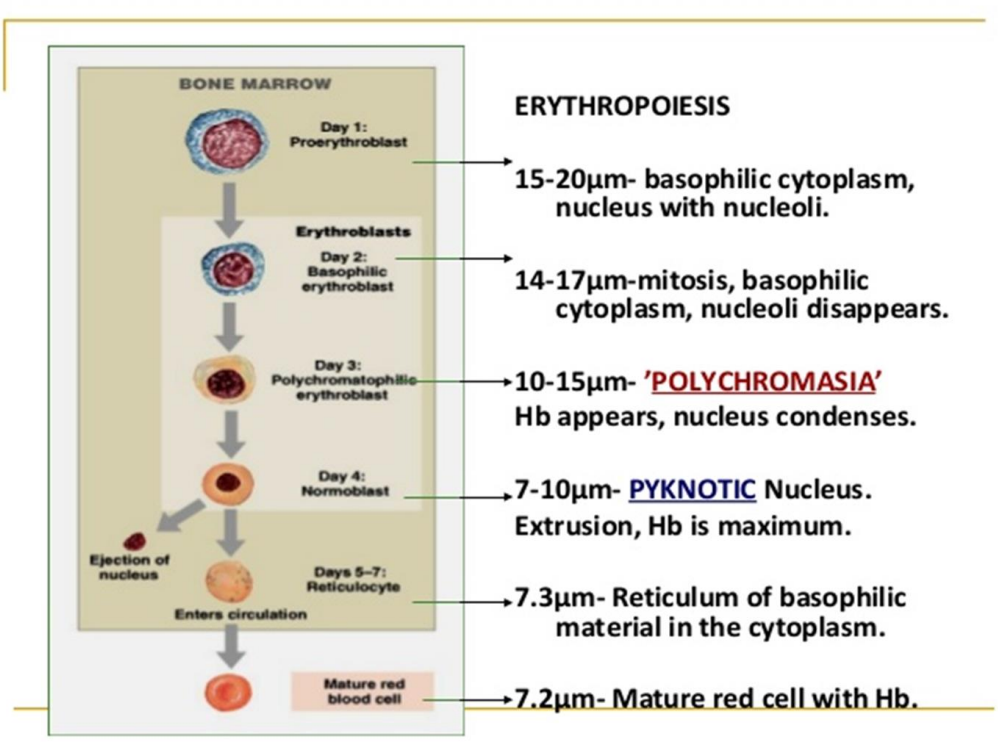
6-Matured Erythrocyte:

Reticular network disappears and the cell becomes the matured RBC and attains the biconcave shape. The cell decreases in size to 7.2 µ diameter. The matured RBC is with hemoglobin but without nucleus. It requires 7 days for the development and maturation of RBC from proerythroblast. It requires 5 days up to the stage of

reticulocyte. Reticulocyte takes 2 more days to become the matured RBC.

Table (1) : Important events during erythropoiesis

Stage of erythropoiesis	Important event
Proerythroblast	Synthesis of hemoglobin starts
Early normoblast	Nucleoli disappear
Intermediate normoblast	Hemoglobin starts appearing
Late normoblast	Nucleus disappears
Reticulocyte	Reticulum is formed. Cell enters capillary from site of production
Matured RBC	Reticulum disappears Cell attains biconcavity



Control of erythropoiesis :

This control system operates in the following manner :

1-Alteration in hemoglobin concentrations of the blood lead to changes in tissue oxygen tension within the kidney (hypoxia).

2-In response to hypoxia ,secreted hormones called erythropoietin which induce primitive marrow cells to differentiate into pronormoblast then resulting an increase in production of erythrocyte .

3-This in turn leads to an increase in size of the erthron and an increase in tissue oxygen levels .

Evaluation methods :

1-Immediate feedback (formative assessment).

2-Involving students in self-assessment (correcting their own mistakes).

3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/Enumerate only: 1-organs of hemopoiesis for each age group
2-stages of erythropoiesis with important event for each stage.
3-Enumerate changes of intermediate stage of erythropoiesis

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674
2- Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Third week

The normal red blood cells ,importance , structure ,erythropoiesis and function.

Educational objective:

The student should be able to :
1-Know the normal red blood cells properties .
2-Know the importance , structure of RBC.
3-Know the erythropoiesis and function of RBC.

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:
1-Interactive classroom activities
2- Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

Erythrocyte ,Red blood cells (RBC) :

Mature Red blood cells (RBCs) also known as erythrocytes (erythros = red) are the non-nucleated. Red color of the red blood cell is due to the presence of the coloring pigment called hemoglobin. RBCs play a vital role in transport of respiratory gases. RBCs are larger in number compared to the other two blood cells, and marked by RBC count ranges between (4.7 – 6.1 million/cu mm) of blood in adult males, it is (4.2-5.4 million/cu mm) in adult females,

Normal shape :

Normally, the RBCs are disk shaped and biconcave (dumbbell shaped). In fixed blood smears appear circular , non-nucleus and lack organelles. Central portion is thinner and periphery is thicker. The biconcave contour of RBCs has

some mechanical and functional advantages.

Advantages of Biconcave Shape of RBCs :

1. Biconcave shape helps in equal and rapid diffusion of oxygen and other substances into the interior of the cell.
2. Large surface area is provided for absorption or removal of different substances.
3. Minimal tension is offered on the membrane when the volume of cell alters.
4. Because of biconcave shape, while passing through minute capillaries, RBCs squeeze through the capillaries very easily without getting damaged.

Normal size :

Diameter: 7.2 µ (6.9 to 7.4 µ).
Thickness : At the periphery it is thicker with 2.2 µ and at the center it is thinner with 1 µ. This difference in thickness is because of the biconcave shape.
Surface area : 120 sq µ. Volume : 85 to 90 cu µ.

Normal structure:

Red blood cells are non-nucleated. Only mammal, which has nucleated RBC is camel. Because of the absence of nucleus in human RBC, the DNA is also absent. Other organelles such as mitochondria and Golgi apparatus also are absent in RBC. Because of absence of mitochondria, the energy is produced from glycolytic process. Red cell does not have insulin receptor and so the glucose uptake by this cell is not controlled by insulin. It is cannot synthesis of protein or carry out oxidative reactions associated mitochondria or undergo mitosis. RBC has a special type of cytoskeleton, which is made up of actin and spectrin. Both the proteins are anchored to transmembrane proteins by means of another protein called ankyrin. Absence of spectrin results in hereditary spherocytosis. In this condition, the cell is deformed, losses its biconcave shape and becomes globular (spherocytic). The spherocyte is very fragile and easily ruptured (hemolyzed) in hypotonic solutions

properties of Red blood cells:

Rouleaux formation : When blood is taken out of the blood vessel, the RBCs pile up one above another like the pile of coins. This property of the RBCs is called rouleaux (pleural = rouleau) formation . It is accelerated by plasma proteins globulin and fibrinogen

Specific gravity : Specific gravity of RBC is 1.092 to 1.101

Packed cell volume :

Packed cell volume (PCV) is the proportion of blood occupied by RBCs expressed in percentage. It is also called hematocrit value. It is 45% of the blood and the plasma volume is 55%

Suspension stability :

During circulation, the RBCs remain suspended uniformly in the blood. This

property of the RBCs is called the suspension stability.

Physiology of mature Red blood cells :

1-A surface membrane **.**

2-Cytoplasm which is divided into : a-hemoglobin b- stroma

Erythrocyte membrane : is made from three layers **:**

1-Outer layer from glycoprotein molecules which carry the mucopolysaccharides ,blood group antigens and absorbed protein .

2-Middle layer is a phospholipid bilayer stabilized by cholesterol .

3- Inner layer has protein molecules extending toward the cell interior.

The erythrocyte surface bears a negative charge .

Hemoglobin content : It has 28% from the erythrocyte mass.

Metabolism : Erythrocyte has two metabolic pathways :

Glycolysis and glutathione metabolism . The energy derived from glycolysis is used to maintain selective exchanges of ions a cross unite membrane that result in potassium retention and sodium expulsion.

Life span of Red blood cells :

Average lifespan of RBC is about 120 days after the lifetime the senile (old) RBCs. About 1% of erythrocytes removed from circulation by phagocytes are destroyed in reticuloendothelial system particularly those of splenic pulp .

Determination of Lifespan of Red Blood Cells:

Lifespan of the RBC is determined by radioisotope method. RBCs are tagged with radioactive substances like radioactive iron or radioactive chromium. Life of RBC is determined by studying the rate of loss of radioactive cells from circulation.

Fate of Red blood cells:

When the cells become older (120 days), the cell membrane becomes more fragile. Diameter of the capillaries is less or equal to that of RBC. Younger RBCs can pass through the capillaries easily. However, because of the fragile nature, the older cells are destroyed while trying to squeeze through the capillaries. The destruction occurs mainly in the capillaries of red pulp of spleen because the diameter of splenic capillaries is very small. So, the spleen is called ‘graveyard of RBCs. Destroyed RBCs are fragmented and hemoglobin is released from the fragmented parts. Hemoglobin is immediately phagocytized by macrophages of the body, particularly the macrophages present in liver (Kupffer cells), spleen and bone marrow. Hemoglobin is degraded into iron , globin and porphyrin. Iron combines with the protein called apoferritin to form ferritin, which is stored in the body and reused later. Globin enters the protein depot for later use. Porphyrin is degraded into bilirubin, which is excreted by liver through bile. Daily 10% RBCs, which are senile, are destroyed in normal young healthy adults. It auses release of about 0.6 g/dL of hemoglobin into the plasma. From this 0.9 to 1.5 mg/dL bilirubin is formed.

FUNCTIONS OF RED BLOOD CELLS :

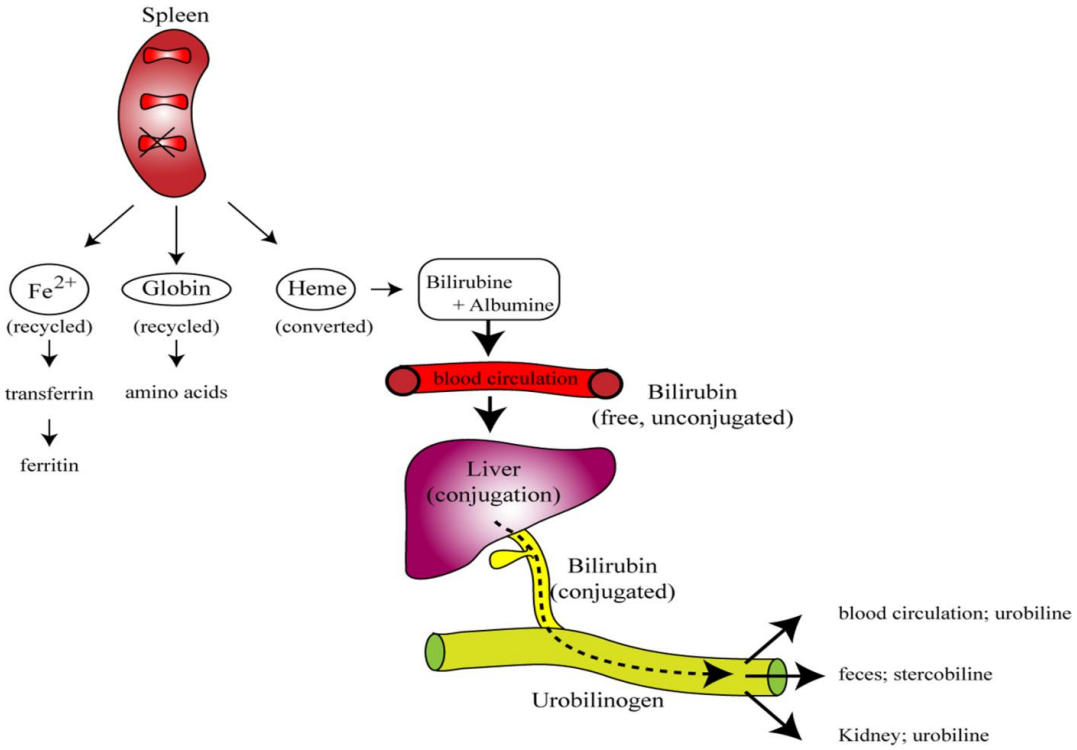
Major function of RBCs is the transport of respiratory gases. Following are the functions of RBCs:

1-Transport of Oxygen from the Lungs to the Tissues Hemoglobin in RBC combines with oxygen to form oxyhemoglobin. About 97% of oxygen is transported in blood in the form of oxyhemoglobin.

2-Transport of Carbon Dioxide from the tissues to the lungs Hemoglobin combines with carbon dioxide and form carbhemoglobin. About 30% of carbon dioxide is transport RBCs contain a large amount of the carbonic anhydrase. This enzyme is necessary for the formation of bicarbonate from water and carbon dioxide. Thus, it helps to transport carbon dioxide in the form of bicarbonate from tissues to lungs. About 63% of carbon dioxide is transported in this form.

3-Buffering Action in Blood Hemoglobin functions as a good buffer. By this action, it regulates the hydrogen ion concentration and thereby plays a role in the maintenance of acid- base balance.

4-In Blood Group :Determination RBCs carry the blood group antigens like A antigen, B antigen and Rh factor. This helps in determination of blood group and enables to prevent reactions due to incompatible blood transfusion



Evaluation methods :

1-Immediate feedback (formative assessment).

2-Involving students in self-assessment (correcting their own mistakes).

3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/Answer the following:

1- Enumerate only three advantages of RBC shape.
2- RBC's don't have a nucleus or endoplasmic reticulum, How can get the energy ?
3- cytoskeleton of RBC made of _____,____ .
4- Senile RBCs are destroyed in _____system.
5- The cell which can give rise all types of blood cells called _____.

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674
2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Fourth week

Polycythemia ,causes ,clinical signs and laboratory diagnosis

Educational objective:

The student should be able to :

1-Know the polycythemia disorder and types .
2-Know causes of polycythemia.
3-Know the signs and laboratory diagnosis of polycythemia

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:

1-Interactive classroom activities
2- Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

Polycythemia, causes, clinical signs and laboratory diagnosis

Variation in number of Red blood cells :

PHYSIOLOGICAL VARIATIONS :

A . Increase in RBC Count:

Increase in the RBC count and hemoglobin per liter (High PCV) is known as polycythemia leading to increase blood viscosity. It occurs in both physiological and pathological conditions. When it occurs in physiological conditions it is called physiological polycythemia. The increase in number during this condition is marginal and temporary. It occurs in the following conditions:

1. Age: At birth, the RBC count is 8 to 10 million/cu mm of blood. The count decreases within 10 days after birth due to destruction of RBCs causing physiological jaundice in some newborn babies. However, in infants and growing children, the cell count is more than the value in adults.

2. Sex :Before puberty and after menopause in females the RBC count is similar to that in males. During reproductive period of females, the count is less than that of males (4.5 million/cu mm).

3. High altitude Inhabitants of mountains (above 10,000 feet from mean sea level) have an increased RBC count of more than 7 million/cu mm. It is due to hypoxia (decreased oxygen supply to tissues) in high altitude. Hypoxia stimulates kidney to secrete a hormone called erythropoietin. The erythropoietin in turn stimulates the bone marrow to produce more RBCs

4. Muscular exercise :there is a temporary increase in RBC count after exercise. It is because of mild hypoxia and contraction of spleen. Spleen stores RBCs. Hypoxia increases the sympathetic activity resulting in secretion of adrenaline from adrenal medulla. Adrenaline contracts spleen and RBCs are released into blood .

5. Emotional conditions RBC count increases during the emotional conditions such as anxiety. It is because of increase in the sympathetic activity as in the case of muscular exercise.

6. Increased environmental temperature: increase in atmospheric temperature increases RBC count. Generally increased temperature increases all the activities in the body including production of RBCs.

7. **After meals** :there is a slight increase in the RBC count after taking meals. It is because of need for more oxygen for metabolic activities.

B. Decrease in RBC Count :

Decrease in RBC count occurs in the following physiological conditions:

1-High barometric pressures :At high barometric pressures as in deep sea, when the oxygen tension of blood is higher, the RBC count decreases.

2-During sleep : RBC count decreases slightly during sleep and immediately after getting up from sleep. Generally all the activities of the body are decreased during

sleep including production of RBCs.

3. Pregnancy : In pregnancy, the RBC count decreases. It is because of increases the plasma volume also resulting in hemodilution. So, there is a relative reduction in the RBC count

PATHOLOGICAL VARIATIONS :

Pathological polycythemia is the abnormal increase in the RBC count. Red cell count increases above 7 million/ cu mm of the blood. Polycythemia is of two types:

1-primary polycythemia
2-secondary polycythemia
Or other classification of polycythemia :
1-True (absolute) polycythemia :divided in to :
a. primary polycythemia (Idopathic poly. Or stear poly. ,Neoplastic poly.)
b. secondary polycythemia
2-Relative polycythemia

Primary Polycythemia – Polycythemia Vera:

Primary polycythemia is otherwise known as polycythemia vera. It is a disease characterized by persistent increase in RBC count above 14 million/cu mm of blood due to mutation HSCs or RBC progenitors in bone marrow, RBC production occurred out of erythropoietin control. This is always associated with increased white blood cell count above 24,000/cu mm of blood. Polycythemia vera occurs in myeloproliferative disorders like malignancy of red bone marrow.

Lab diagnosis: Increase in RBC, Hb. PCV, WBC, and Platelets count

Secondary Polycythemia:

This is secondary to some of the pathological conditions (diseases) such as:
1-Associated with hypoxia :
a. Respiratory disorders like chronic pulmonary disease (emphysema).
b. Congenital heart disease .
c. Ayerza's disease (condition associated with hypertrophy of right ventricle and obstruction of blood flow to lungs).
d. Chronic carbon monoxide poisoning.
e. Poisoning by chemicals like phosphorus and arsenic.
f. Repeated mild hemorrhages.
g-hypoventilation syndrome associated with obesity (pick wickian syndrome).
h- heavy smoking (carboxyhaemoglobin).
I- Metahaemoglobinemia (rarely).
2- Due to inappropriate erythropoietin increase in :
A-Benign and malignant tumors of kidney ,liver, C.N.S. Uterus, Ovary.
B-Renal diseases (hydronephrosis, vascular impairment ,cyst, renal artery stenosis

3-Associated with adrenocortical steroids or androgens :
a-adrenal hypercriticism .
b-Virilizing tumor.
c-Androgens used therapeutically and blood doping (as in athletes).
4- Associated with chronic chemical exposure :
a-nitrites, sulfonamide ,other substances producing methaemoglobin and sulphaemoglobin .
b-Cobalt ,shellac components ,various alcohols .

All these conditions lead to hypoxia which stimulates the release of erythropoietin. Erythropoietin stimulates the bone marrow resulting in increased RBC count

Lab diagnosis: increase in RBC ,PCV, Hb only but the WBC and Platelets at normal range .

Symptoms and signs of polycythemia:

Increase RBC count lead to increase in blood viscosity make shortage oxygen delivery to tissue causes very cyanosis degree and symptoms:

Symptoms:

-Headache ,pruritus, dyspnea,
-Weakness ,itching Pruritis (aquagenic) ,Dizziness
-Visual disturbance (blurred vision) ,Weight loss
-high blood pressure .
-fever and night sweats, Red skin (face, hands , and feet).
-Hemorrhage in gastrointestinal tract ,uterine, cerebral.
-Thrombosis in arterial ,cardiac ,cerebral ,peripheral venous ,deep or superficial leg venous .
-Gout (due to raise of uric acid production) and peptic ulceration rarely .

Signs

-Splenomegaly 66-70%
-Skin plethora 67%
-Hepatomegaly 40%
-Conjunctival plethora 59%
-Systolic Hypertension 72%

2) Relative polycythemia :

It which there is increased in total plasma in the body and the total number of RBC is normal, it is called " Pseudopolycythemia" which caused by concentration of plasma by :

a-stress
b-Dehydration :water deprivation, vomiting
c-Plasma lose :burns, enteropathy b. irregulation of fluid in the body

this condition is occur in the middle age .

Laboratory finding :

1-Raised erythrocytes count ,hematocrite, and hemoglobin.

2-Neutrophilic leukocytosis (50% cases) and in some cases basophilic .

3-Raise neutrophilic alkaline phosphatase score .

4-Raised platelets count (50% cases).

5-increase serum vitamin B 12 binding capacity.

6-bone marrow hyper cellular with prominent megakaryocytes

Diagnosis-Revised WHO Criteria:

- Major criteria

-Hemoglobin >18.5 g/dL in men, 16.5 g/dL in women

-Presence of JAK2 617V>F or other functionally similar mutation such as JAK2 exon 12 mutation

-Minor criteria

-Bone marrow biopsy showing hypercellularity for age with trilineage growth (panmyelosis) with prominent erythroid, granulocytic, and megakaryocytic proliferation

-Serum erythropoietin level below the reference range for normal

-Endogenous erythroid colony formation in vitro

Workup:

-H/H -EPO JAK2 mutation) -Bone marrow	-Sa O2	- JAK2 screen (95-100% pts with PV have

EEC: endogenous erythroid colony formation

Evaluation methods :

1-Immediate feedback (formative assessment).

2-Involving students in self-assessment (correcting their own mistakes).

3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/Comparative between polycythemia vera and secondary polycythemia.

Q2/ Enumerate the causes of polycythemia emotional conditions.

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674

2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Five week
Study red cell morphology in health and disease .abnormality of RBC in size

Educational objective:
The student should be able to:
1-Know red cell morphology in health and disease.
2-Know normal RBC size .

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:
1- Interactive classroom activities
2- Brainstorming questions
3- Group activities (if required)
4- Homework
5- Online homework (classroom)
6-Quick written exam .

Morphology of RCB in health and disease:

1-Discuss aspects of red cell morphology related to size
Normal RBC:
-Size: Normocyte ,measure 6.2-8.2µm (7.2µm)
-Colour: Normochromic
In disease abnormality in the RBC pictures due to four causes:
1-Abnormal erythropoiesis which may be effective or ineffective.
2 -Inadequate hemoglobin formation.
3 -Damages or changes effect erythrocytes after leaving bone marrow.
4-Attempts by bone marrow to compensate for anemia by increase erythropoiesis

Abnormal erythrocyte morphology is found in pathological states that may be :
- abnormalities in size (anisocytosis).
- In shape (poikilocytosis).
-In hemoglobin content or the presence of inclusion bodies in erythrocyte.

1-Variation in erythrocyte size (anisocytosis)
In healthy ,Red blood cells have a diameter within 6-8.5M (7.2M) can vary in size from smaller than normal, microcytes, to larger than normal, macrocytes.

When red cells of normal size, microcytes and macrocytes are present in the same field, the term anisocytosis.

1-Microcytosis:
Morphology:
- Decrease in the red cell size. Red cells are smaller than ± 7µm in diameter (>6µm) .The nucleus of a small lymphocyte (± 8,µm) ,is a useful guide to the size of a red blood cell. Smaller than a nucleus of the lymphocyte, MCV is decrease to less than 80fL,the area of central pallor is greater than 1/3 of the cell ,low hemoglobin content as a result from fragmentation of the number erythrocytes or macrocyte as occur with many types of abnormal erythropoiesis.

Found in:
- Iron deficiency anemia
- Thalassemia
- Sideroblastic anemia
- Lead poisoning
- Anemia of chronic disease
- liver disease
- alcoholism

2-Macrocytosis:
Morphology:
Increase in the size of a red cell. Red cells are larger than 9µm in diameter(diameter of 9-12 microns,1.5-2 times larger than normal red cells).They are uniform in size ,it occur when there is increased erythropoiesis. May be round or oval in shape, and MCV is also increase (above 80-100fL) and increase hemoglobin content, the diagnostic significance being different.

Found in :
- Folate and B12 deficiencies (oval)
- Ethanol (round)
- Liver disease (round)
- Reticulocytosis (round)
-Megaloblastic anemia
-Aplastic anemia
- Hemolytic anemia

3-Megalocytes
-Megalocytes are large (greater diameter may measure 12pm) often oval shaped cell with increased haemoglobin content with MCV exceed 120fL, they are result of decreased DNA synthesis, frequently due to vitamin B12 and/or folic acid deficiencies, and associated with some leukaemia chemotherapy .
-Decreased DNA synthesis causes the nucleus in the developing red cells to mature at a slower than normal rate.

2- **Pseudomacrocytes**
-appears larger than the lymphocyte but in contrast to megalocytes has an area

of central pallor.

-size is the result of exaggerated flattening and thus the presence of the central pallor.

-in patients with cirrhosis of the liver, obstructive jaundice, post splenectomy.

two types of macrocytes:-

1-True macrocytes (megalocytes). Increased MCV, MCH

2-Pseudomacrocytes. Normal MCV, MCH

Evaluation methods :

1-Immediate feedback (formative assessment).

2-Involving students in self-assessment (correcting their own mistakes).

3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/Fill in the blanks:

1-Red cells are smaller than a nucleus of the lymphocyte called. _____

2 -pathological conditions for Macrocytosis. _____, _____

3-Red cells have long axis is twice the short axis called. _____

4-The index value which used to adequate hemoglobin concentration.____

5-cause of rouleaux formation _____ ,_____.

Reference :

2- A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674

2- Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Six week

Abnormality of RBC in shape

Educational objective:
The student should be able to:
1-Know red cell morphology in health and disease.
2-Know normal RBC shape .

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:
1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

2-Discuss aspects of red cell morphology related to shape
II- Variation of red cells shape (Poikilocytosis) RBCs may have different shapes:
1- Spherocytosis /Microspherocytes:
Morphology:
Red cells are more spherical. Lack the central area of pallor on a stained blood film, cells which have a decreased surface-to-volume ratio.
-Their diameter is less and their membrane thickness greater than normal red cells
-they appear to be round, darkly-stained cells without central pallor.
-Associated with abnormalities in membrane protein, lipid loss and excessive flux Na+ across the membrane.
Found in :
- Hereditary spherocytosis (genetic defect of RBC cell membrane)
- Immune hemolytic anemia
- Zieve's syndrome
- Microangiopathic hemolytic anemia.
2-Target Cells: (Codocytes)
Morphology:
Red cells are thinner than normal ,they have an area of increased staining which appears in the area of central pallor then stained peripheral ring adhere to the cell membrane surrounded them .

-It appear less staining than normal one.
-Codocytes appear in conditions which cause the surface of the red cell to increase disproportionately to its volume.
-This may result from a decrease in haemoglobin, as in iron deficiency anemia, or an increase in cell membrane.

Found in

-Obstructive liver disease
- Severe iron deficiency
-Thalassemia
-Sickle cell anemia
-Haemoglobinopathies (S and C)
- Post splenectomy
-obstructive jaundice

This deformity happen due to loss of elasticity of red cell membrane because of changes in composition of membrane and its change in :
1- Fat composition.
2- Effect of bile salt regarded on blood in obstructive jaundice, these salts are fat emulsifier which cause the loss of elasticity of red cell membrane.

3- Ovalocytes:

Morphology:

oval shape red blood cell **Found in:**

- Thalassemia major.
- Hereditary ovalocytosis.
- Sickle cell anemia
-megaloblastic anemia

4- Elliptocytosis

Morphology:

The red cells are oval or elliptical in shape. Long axis is twice the short axis .Less than 1% of red cells in normal blood are oval.

Found in:

-Hereditary elliptocytosis .
- Megaloblastic anemia.
- Iron deficiency .
- Thalassemia .
- Myelofibrosis

5- Tear Drop Cells (Dacrocyte):

Morphology:

Red cells shaped like a tear drop or pear which could be considered to be discocytes with a single drawn out spicule .

Found in:

- Bone marrow fibrosis.
- Megaloblastic anemia .
- Iron deficiency .
- Thalassemia
- Tumor metastasis ,myeloid metaplasia (in bone marrow).
-Tuberculosis.

6- Blister cell:
Morphology:
Have acentric hallow area.
Found in: Microangiopathic hemolytic anemia.
7- Schistocytosis:
Morphology:
Fragmentation of the red cells. red cell fragments which are formed when fibrin strands come in contact with circulating red cells. The strands cut a small piece from the original cell.
Found in:
1- certain genetically disorders as thalassemia and hereditary elliptocytosis
2-Aqcuired disorders of red cell formation (megaloblastic anemia, Iron deficiency anemia).
3-As the sequences of mechanical stress in Microangiopathic hemolytic anemia, Mechanical hemolytic anemia.
4-As a result of direct thermal injures as in severe burns.
8- Stomatocytosis:
Morphology:
Red cells with a central linear slit or stoma. Seen as mouth-shaped form in peripheral smear.
- The cause for this deformity is decrease pH.
Found in :
- Alcohol excess (alcoholism) .
- Alcoholic liver disease .
- Hereditary stomatocytosis .
- Hereditary spherocytosis
9- Echinocyte ,Burr (crenation) cell:
Morphology:
Red cell with uniformly spaced, short pointed projections(spicules). Red cell with 30 or more, short blunt projections which are regularly distributed on their surface on their surface. They are small cells or fragment cells, they are: a-small fragments of cells of varying shape, sometimes round in shape with sharp angles or spines .
b-large cells or irregular or round contour from which fragments have been split off.
c- normal un fragmented adult red cells and reticulocyte.
Found in :
- hemolytic anemia
- Uremia.
- Megaloblastic anemia.
-pyruvate kinase deficiency
-neonatal liver disease
10- Keratocytes (horn cell):
Morphology:
Part of the cell fuses back leaving two or three horn-like projections. The keratocyte is a fragile cell and remains in circulation for only a few hours.

Found in:
- Uraemia .
- Severe burns .
- EDTA artifact .
- Liver disease

11- Acanthocytosis (spiny cells):

Morphology:

are red blood cells with irregularly spaced projections (3-12 spicules), these projections very in width but usually contain a rounded end.

-Smaller than normal and have little or no central pallor.

-Acanthocytes refer to abnormal phospholipid metabolism (have an excess of cholesterol)

-Large numbers of these cells on a smear can be of diagnostic significance. **Found in:**

- Hereditary acanthocytosis,50-100% of blood cells.

-Liver disease (cirrhosis),rarely in hepatitis.

- Post splenectomy
- Anorexia nervosa and starvation

-lipid disorders

12- Rouleaux Formation:

Morphology:

Stacks of RBC's resembling a stack of coins. Stacking of RBCs due to increased plasma proteins coating RBCs (in patient with high ESR) .

Found in:
- Hyperfibrinogenaemia
- Hyperglobulinaemia
- Chronic inflammatory disorders.
- Multiple myloma

13- Red cell-agglutination:

Morphology:

Irregular clumps of red cells. Antibody-mediated Irregular clumping , temperature dependent. Several types of irregular contracted cells can be distinguished in toxin or drug or chemical induced hemolytic anemia.

Found in:
- Cold agglutinins
- Warm autoimmune hemolysis

14- Sickle Cells (Drepanocytes):

Morphology:

Sickle shaped red, are formed as a result of the presence of hemoglobin S in the red cell. As the red cell ages, it becomes less flexible or deformable and becomes rigid as it passes through the low oxygen tension atmosphere of the small capillaries in the body.

-In the absence of oxygen, hemoglobin S polymerizes into rods, causing the sickle cell shape. Sickle cells can be somewhat pointed at the ends,

Found in: Hb-S disease

-Most sickled cells can revert back to the discoid shape when oxygenated.
-About 10% of sickled cells are unable to revert back to their original shape after repeated sickling episodes.

15- Nucleated red blood cells.
These red blood cells are released from the bone marrow early into the blood stream, due to the need for oxygen. Normal red blood cells do not contain a nucleus on a peripheral smear.

16-Envelope Form Cell:
Found in
Thalassaemia -
-Sickle cell anemia

17-Knizocyte:
-A streak of hemoglobin through the centre of the cell.
-In some hemolytic anemia cases.

Target Cells	Central Hemoglobin; target shaped	Liver Disease; Thalassaemia, Abnormal Hb; Iron Deficiency
Echinocyte	Short specula's, equally-spaced	Uremia, Hypokalemia, Artifact
Acanthocyte	Speculated, Irregular	Liver disease (Alcohol), Post-spleenoctomy.
Spherocyte	Spherical, no central pallor	HS, immune Hemolytic anemia
Shistocyte	Fragmented RBC, Helmet cells	MAHA, burns
Ovalocyte	Oval / Elliptical shaped	Hereditary elliptocytosis, Megaloblastic anemia.
Sickle Cell	Bipolar speculated shape " banana" shaped	Hb S-containing hemoglobinopathy
Teardrop cell	Single elongated extremity	Myelophthistic changes
Bite cells	Irregular gap in membrane	G6PD deficiency

Abnormality with inclusion bodies :is the presence foreign bodies in inside erythrocyte, includes :

1-Howell-Jolly Bodies:

There are nuclear remnant ,they appear as small round cytoplasmic red cell inclusion with same staining characteristics as nuclei, may be seen in sickle cell anemia. These bodies are DNA that densely staining dark purple (violet) particles within the red blood cell.

Found in

1-Post splenectomy
2-Megaloblastic anemia
3-Leukemia

2-Siderotic Granules (Pappenheimer Bodies):

These are iron containing granules in red blood cells that are seen because the iron is aggregated with mitochondria and ribosomes. They appear as faint violet or magenta specks, often in small clusters, due to staining of the associated protein.
They are associated with:
-severe anemia and thalassemia.
- hemolytic anemia,
-infections
-post-splenectomy.

3-Basophilic stippling:

Considerable numbers of small basophilic inclusions in red cells is granules of RNA seen within the red blood cell. The granules stain blue to purple distributed throughout the cell surface.

Found in

-Thalassemia
-Megaloblastic anemia
-Hemolytic anemia
- Liver disease
-Toxicities such as Heavy metal poisoning

4-Heinz Bodies:

Represent denatured hemoglobin deep purple bodies (methemoglobin - Fe+++) within a cell, some laying close to periphery of the red cells and other attach to outer surface .With a supravital stain like crystal violet, Heinz bodies appear as round blue precipitates. Presence of Heinz bodies indicates red cell injury and is usually associated with G6PD-deficiency.They are found in some forms of hemolytic anemia.

5-**Cabot Rings:**

Reddish-blue threadlike rings or figure 8 pattern in RBCs of severe anemia's.
These are remnants of the nuclear membrane or remnants of microtubules and.
Very rare finding in patients with
-Megaloblastic anemia -severe anemia.
-lead poisoning.
-Dyserythropoiesis

6-Parasites of Red Cell:

Two organisms are have a tendency to invade the RBCs

1-All 4 species of the malaria parasite will invade RBCs. We will see the Plasmodium of different species in RBCs..

2-Theileria microti (Bebesia microti).

7-Erythroblast:is used as genetic term to describe all nucleated erythrocyte .In normal marrow the pronormoblast is the first cell, recognizable as definitely belonging to erythroid series .From it the erythrocyte develops through a succession of maturing erythroblast, early normoblast ,intermediate normoblast, late normoblast developing erythrocyte. The process of normoblastic maturation is characterized by the following progressive changes :

a- **Diminution in cell size**.

b- **Ripening of cytoplasm** in stain proportion ,this is accompanied by change in color from deep blue to pink due to progressive formation of acidophil staining haemoglobin and simultaneous loosening of the ribose nucleic acid which responsible for basophilic of the cytoplasm .

c- Diminution of the nucleus :this is manifest by loss nucleoli, decrease in total size and size relative to cytoplasm progressive clumping and condensation of the chromatins and Deeping in color ,the time for maturation from pronormoblast to mature red blood cell about 7 days.

8- pronormoblast. **9- early normoblast**

10- intermediate normoblast. **11- late normoblast.**

12-Reticulocyte

Inclusion	Composition	Appearance	Condition
Basophilic stippling	Precipitated ribosomes	Evenly dispersed fine or coarse granules	- Lead poisoning - Thalassaemia , other anemia.
Howell-Jolly bodies	DNA in origin Nuclear Fragment	Dense, round blue granule	Post – Splenectomy
Pappenheimer bodies	Iron-containing granules	Small blue granules in clusters	Anemia's
Heinz bodies	Denatured Hemoglobin	Round blue precipitates	G6PD
Cabot Rings	Remnants of Nuclear membrane	Reddish-blue thread like rings	Severe anemia, Lead poisoning.
Organism		Small blue inclusion	Malaria Babesiosis

Evaluation methods :

1-Immediate feedback (formative assessment).
2-Involving students in self-assessment (correcting their own mistakes).
3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/Give one feature of morphology for the cells:

1-Keratocytes
2- Blister cell
3-spherocyte
1- knizocyte

Q2/Write the causes of the following:

1- pappenheimer bodies 2- Basophilic stippling

Reference :

1- A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674
2- Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Seven week

Abnormality of RBC in colour

Educational objective:
The student should be able to:
1-Know red cell morphology in health and disease.
2-Know normal RBC colour .

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:
1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

Red Cell Morphology

Discuss aspects of red cell morphology related to color

III -Variation In Erythrocyte Color

-A normal erythrocyte has a pinkish-red color with a slightly lighter-colored center (central pallor) when stained with a blood stain, such as Wright stain.
-The color of the erythrocyte is representative of hemoglobin concentration in the cell.
-Under normal conditions, when the color, central pallor, and hemoglobin are proportional, the erythrocyte is referred to as Normochromic.

RBC Color

-the central area (1/3 of the cell) is white, while buff-colored haemoglobin is visible in the outer 2/3 of the cell.

- The unit to measure the amount of hemoglobin per cell is mean corpuscular hemoglobin, or MCH .
- The MCH is simply the average amount of hemoglobin in one red blood cell, from a particular sample .
- Its reference range is 27pg – 31pg , meaning that there is typically between 27pg and 31pg of hemoglobin in a single red blood cell
  - The other unit for haemoglobin content of a red blood cell is mean corpuscular haemoglobin concentration (MCHC).
  - The MCHC is reflective of the concentration of packed red blood cells (so blood

excluding plasma) that is haemoglobin.

- It basically translates to the amount of haemoglobin present in the cellular component of blood, and thus excluding plasma. Its reference range is 32g/dL – 36g/dL

-A decreased amount of haemoglobin is referred to as hypochromasia or hypochromic.

-MCHC values of 30% or less reflect this condition. -Hyperchromasia and hyperchromia, refer to a hypothetical situation rather than an actual occurrence.

1-Hypochromia

Is used to describe a decrease in intensity of hemoglobin color at varying degree . Increased central pallor and decreased hemoglobin concentration, the central pallor occupies more than the normal third of the red cell diameter. Hypochromia is associated with decrease in MCHC. However cell which are thinner than normal may appear slightly hypochromic but MCHC is still normal .

There are two conditions that a RBC must satisfy in order to be classified as a hypochromic cell. These are:

1- The central zone of pallor of the RBC must be greater than 1/3 of the diameter of the cell.

2-The MCH must be below 27pg/cell and/or the MCHC must be below 32g/dL.

Found in

-Iron deficiency anemia

-Thalassemia

-Sideroblastic anemia .

-any of the conditions leading to Microcytosis.

❖ They are two possible causes :-

1-Abnormal thinness of erythrocyte.

2-A lowered hemoglobin concentration result from impaired hemoglobin synthesis as in sideroblastic anemia .Rarely, the failure of globin synthesis cause lower hemoglobin as in thalassemia

2- Hyperchromia\Polychromasia

Mean increase the intensity of stain of erythrocyte in which central area of pallow is lost so the cell appear more deep staining, this appearance due to increase in thickness of cell not in to increase concentration of hemoglobin so MCHC normal. Red cells stain shades of blue-gray as a consequence of uptake
of both eosin (by hemoglobin) and basic dyes (by residual ribosomal RNA). Often slightly larger than normal red cells and round in shape – round macrocytosis (high MCV).

Found in

- Any situation with reticulocytosis –for example bleeding, hemolysis or response to heamatinic factor replacement.

-Megaloblastic anemia or spherocyte in spherocytosis occur due to increase cell thickness.

3-Polychromasia (reticulocyte) /polychromatophilia :

Young erythrocyte which have not yet completely with lost their nucleic acid (residual RNA) affinity for basic component of the Romanowsky stains and assumes a degree of blue staining proportional to the amount of RNA ,it is normally present only in small number in peripheral blood film, they stain as reticulocyte .It general marked polychromasia indicated active blood regeneration ,they are slightly larger than normal mature erythrocyte (macrocyte). Polychromasia term used to indicate the increased presence of non-nucleated immature erythrocyte (polychromatophilic erythrocyte) Appears as bluish gray color of RBC on Wrights stain smear due to prescience RNA . Residual RNA indicates immaturity of cell.

Found in :

-Reticulocyte

-Target cell – also called leptocyte ,the Maxican hat cell or codocyte.

-An RBC with a peripheral ring of Hb plus a central condensation of Hb in the area of pallor or "bull's eye appearance"

- Found in patients with hemoglobinpathay and thalassemia Reticulocyte

4-Anisochromasia (Dimorphism)

Refer to different abnormality of color in same field , indicates the presence of both normochromic and hypochromic

Found in :

-Iron deficiency anemia .

-Responding to iron therapy or after blood transfusion of normal blood to patient with hypochromic .

-sideroblastic anemia.

What Abnormal Results Mean

This test is used to diagnose the cause of anemia. The following are the types of anemia and their causes:

-Normocytic/ normochromic (NC/NC) anemia is caused by sudden blood loss, prosthetic heart valves, sepsis, tumor, long-term disease or aplastic anemia.

-Microcytic/ hypochromic anemia is caused by iron deficiency, lead poisoning, or thalassemia.

-Microcytic/ normochromic anemia results from a deficiency of the hormone erythropoietin from kidney failure.

-Macrocytic /normochromic anemia results from chemotherapy, folate deficiency, or vitamin B-12 deficiency.

Evaluation methods :
1-Immediate feedback (formative assessment).
2-Involving students in self-assessment (correcting their own mistakes).
3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/compare between hypochromic and hyperchromic
Q2/Enumerate pathological conditions for Polychromasia (reticulocyte) /polychromatophilia

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674
2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Eight week

The normal Hb of the blood contain and importance

Educational objective:
The student should be able to:
1-Know normal Hb structure .
2-Know normal Hb contain , important .

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:
1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

The normal Hb of the blood ,contain and importance

Hemoglobin (Hb) : The red respiratory protein of erythrocytes ,Iron- bearing protein, red globular proteins which have a molecular weight of about 68000-64,500 deltons which is the main component of the RBC ,gives the red cell its color. In adult has about 630gm of hemoglobin containing about 2.2gm of Iron

.64,500 consisting of approximately 3.8% heme and 96.2% globin which is the main component of the RBC ,gives the red cell its color

Hb function:-

Hb is found in RBCs each100ml of arterial oxygenated blood carriers 19ml oxygen in combination with Hb and about 0.3ml of O2 in plasma.

its main function :

-Transport of O2 from lung to tissues.

-Transfer of CO2 from tissue to lungs.

-Buffering action, maintains blood pH as it changes from oxyhemoglobin (carrying O_2) to deoxyhemoglobin (without o_2) In the lungs, 1 g of hemoglobin combines readily with 1.36cc of oxygen by oxygenation to form oxyhemoglobin.

-Each red cell has 640 million molecules of Hb.

-Haemoglobin (Hb), protein constituting 1/3 of the red blood cells weight

Synthesis : Majority synthesized at the polychromatophilic normoblast, stage begins in proerythroblast

65% at erythroblast stage

35% at reticulocyte stage

Structure: Is a tetramers, 2 pairs un like polypeptide chains (consist of 4 polypeptide subunits)

-**Heme group**: protoporphyrin is linked at a specific site to each globin polypeptide chain ,made up of ringed structure called pyrrol rings, the building materials used to synthesis hem within the developing erythrocyte are amino acid glycine and succinic acid ,one molecule of glycine acid and one of succinic acid condense to give delta aminolaevulinic acid (A.L.A) .Two molecules of A.L.A are called aminolaevulinic acid anhydrase . Four of pyrrol rings react to form a tetra pyrrol rings ,additional structures of pyrrol rings form the protoporphyrin at the last stage link to Iron

Structures of Heme : a)Porphyrin ring

b)Ferrous iron

-Globin chain: major component of hemoglobin, some globin are made daily,

four chains: a)2 (α) Alpha chains (141)amino acid

b)2 Beta chains (146) amino acid

Heme: porphyrin ring with central iron. Iron is the site of attachment with O2.

Synthesis of : Haem & globin produced at two different sites in the cells :

Haem in mitochondria

Globin in polyribosomes

Processes necessary for normal synthesis of Hb :-

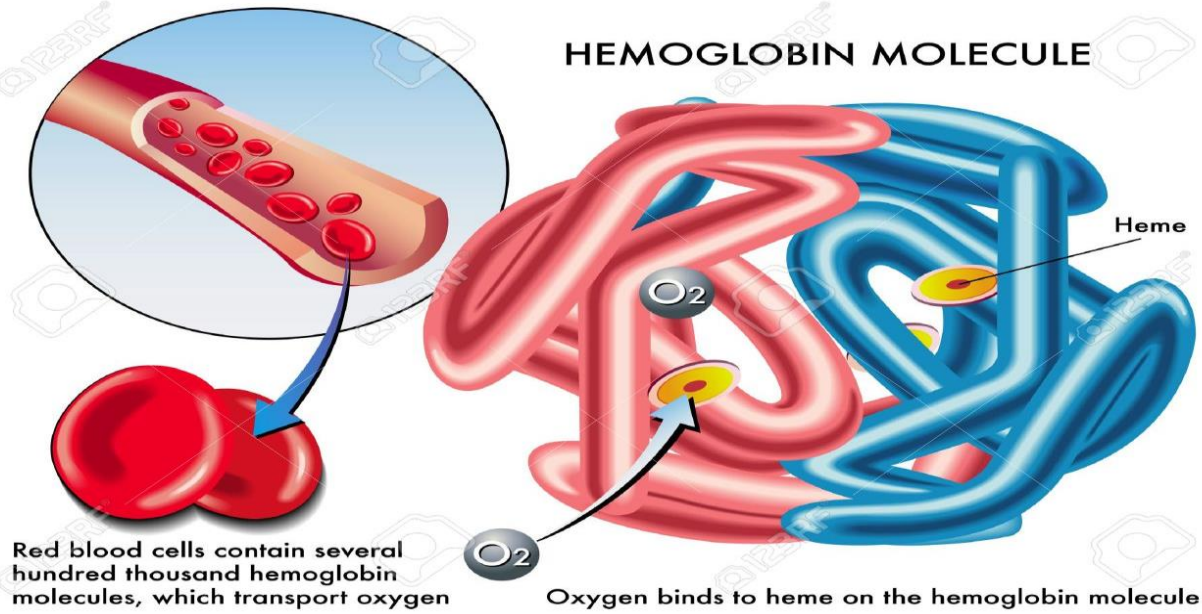
-Adequate iron supply & delivery

-Adequate synthesis of protoporphyrins

-Adequate globin synthesis

Chain of Events:

-Iron delivery & supply: Iron is delivered to the reticulocyte by transferrin
-Synthesis of protoporphyrins: Occurs in the mitochondria of RBC precursors mediated by EPO and vitamin B_6
Protoporphyrin + iron = heme
Regulation : Stimulated by tissue hypoxia
Hypoxia causes the kidneys to increase production of EPO, which increases RBC and hemoglobin production
There are 4 heme groups each attached to on globin chain. So one Hb molecule can carry up to 4 O2 molecules. According to sequence of amino acids in the primary structure of each chain, there are four types of chains: α, β, γ and δ.
Hemoglobin Reference Ranges
-Adults
Male 14-17.5 g/dL
Female12-15 g/dL
-Children
Birth 13.5-20.0 g/mL 6-12 years 11.5-15.5 g/mL
Iron in Hemoglobin is ferrous or ferric ? Why ?
• Iron in ferrous form (6 coordination)
4 bind with protoporphyrin
1 bind to histidine (globin)
1 free bind to O2 or CO2 respectively
• Where in ferric form we well have one bond missing (malfunctional hemoglobin)
• Heme and globulin are not isolated, the bind together by Iron.
Gas Transportation
• **Why we use hemoglobin as a transporter for oxygen ?**
1. Because of low solubility of oxygen in water.
2. Hemoglobin have a regulatory effect on oxygen concentration in lungs and tissues.
Note : all tissue required of oxygen and 20% of CO2 from metabolic wastes transport via Hb



Evaluation methods :

1-Immediate feedback (formative assessment).

2-Involving students in self-assessment (correcting their own mistakes).

3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/ 1-Structures of Heme consist of. _____,_____

2-Haemoglobin (Hb) constituting _____ of the red blood cells weight.

Q2/ -Why use hemoglobin as a transporter for oxygen ?

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674

2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Nine week

Study the types of normal Hb

Educational objective:
The student should be able to:
1-Know normal Hb types .
2-Know abnormal Hb types
3- know causes of abnormal Hb Types .

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:
1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

Types of Hb:

Hb A or HbA1: is the normal Hb in adults represents about 97% of total Hb, it is composed of 2 α and 2 β chains.

HbA2: minor adult Hb, comprised 3% of normal adult Hb. Composed of 2 α and 2 δ chains consider as diagnostic aid in beta-thalassemia and megalobastic anemia and decrease in Iron deficiency anemia and sideroblastic anemia

Hb Gower (Gower-1 (ζ2ε2), Hb Gower-2 (α2Aε2) or Hb Portland (ζ2γ) : embryonic hemoglobin's produced in the first three months of embryonic development, when blood cells are produced in the yolk sac.

HbF(fetal Hb): is the main Hb during fetal life and about 60% of normal Hb at birth then disappear gradually. It is composed of 2α and 2 γ chains.It have many character like :
1-Hb F has greater affinity for O2 than HbA so ensure O2 transfer from maternal circulation to fetus RBCs through placenta.
2-Hb F has special property of remarkable resistance to denaturation of extremes pH.

The erythrocyte of newborn contain about 80% Hb F,20% Hb A and less than 0.5% Hb A2.Hb F falls steadily following birth at about six months of age, it is increase in Varity of acquired hematological disorders include megaloblastic anemia ,sickle cell anemia ,and leukemia .

HBA1C : has glucose residues attached to β-globin chains – increased

amounts in DM . ***HbA1c could be used as a monitor for the control of the blood glucose level during the last 2 months for diabetic patients***

Hb A	Hb A_2	Hb F	
structure	$\alpha_2\beta_2$	$\alpha_2\delta_2$	$\alpha_2\gamma_2$
Normal %	96-98 %	1.5-3.2 %	0.5-0.8 %

Nonfunctional hemoglobin:

1-Carboxyhemoglobin

-Oxygen molecules bound to heme are replaced by carbon monoxide.

-Slightly increased levels of carboxyhemoglobin are present in heavy smokers and as a result of environmental pollution. Can revert to oxyhemoglobin.

2-Methemoglobin

Iron in the hemoglobin molecule is in the ferric (Fe_3) state instead of the ferrous (Fe_2) state. Incapable of combining with oxygen. The NADH-dependent enzyme methemoglobin reductase is responsible for converting methemoglobin back to hemoglobin .Can occur as a result of strong oxidative drugs or to an enzyme deficiency. Can revert to oxyhemoglobin

3-Sulfhemoglobin

Hemoglobin molecule contains sulfur. Caused by certain sulfur-containing drugs or chronic constipation. .Cannot revert to oxyhemoglobin and may cause death.

Evaluation methods :

1-Immediate feedback (formative assessment).

2-Involving students in self-assessment (correcting their own mistakes).

3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/ Mention Structure of "

a-Hb portland

b-HbF

C-Heme group

D- Hb A2

E-Cooley anemia

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674

2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Ten week

Common Hb. Variant:

Educational objective:
The student should be able to:
1- Know abnormal Hb types
2- know causes of abnormal Hb Types .

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

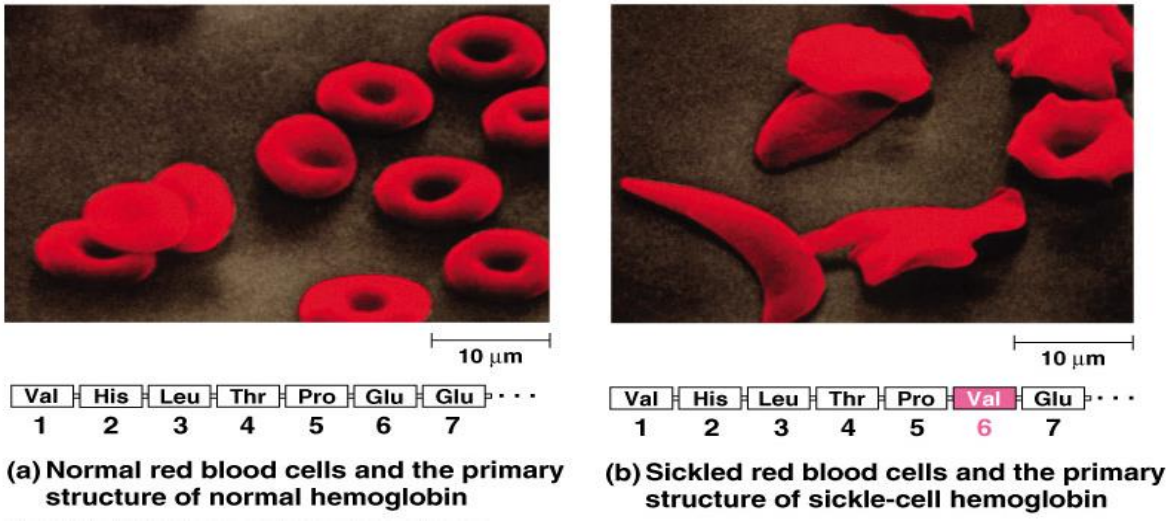
Activities Used:
1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

Mutations in hemoglobin (hemoglobinopathies):

Hemoglobinopathies are members of a family of genetic disorders caused by:
1- Production of a *structurally abnormal* hemoglobin molecule
(Qualitative hemoglobinopathies)
Or: 2- Synthesis of *insufficient quantities* of normal hemoglobin
(Quantitative hemoglobinopathies)
Or: 3- both (rare).

1- Sickle cell anemia (Hb S disease):

It is a genetic disorder of blood caused by mutation in β-globin chain resulting in the formation of Hb S. The mutation occurs in 6th position of β-chain where glutamic acid is replaced by valine (non polar). Valine residues aggregate together by hydrophobic interactions leading to precipitation of Hb within RBCs. RBCs assume sickle-shaped leading to fragility of their walls and high rate of hemolysis.



(a) Normal red blood cells and the primary structure of normal hemoglobin

(b) Sickled red blood cells and the primary structure of sickle-cell hemoglobin

Such sickled cells frequently block flow of blood in narrow capillaries and block blood supply to tissue (tissue anoxia) causing pain and cell death.

Note: The lifetime of erythrocyte in sickle cell is less than 20 days, compared to 120 days for normal RBCs.

Patients may be :

- Heterozygotes (Hb AS): mutation occurs only in one β-globin chain. These patients have sickle cell trait with no clinical symptoms and can have normal life span. HbS 35% while HbA 65% .

Or: Homozygotes (Hb SS): mutation occurs in both β-globin chain with apparent anemia and its symptoms. 90% HbSS and 10% HbA .

Symptoms: a-pain in stomach, legs ,arm**.** b- patients is tired and nervous.
c-ulceration in lower part of legs. d-prolong arm and legs .

2- Hb C disease: Like HbS, Hb C is a mutant Hb in which glutamic acid in 6th position of β-chain is replaced by lysine. RBCs will be large oblong and hexagonal. Found primarily in blacks, in area of west Africa , the gene may be as high as 28%. About 2% of blacks Americans are AC heterozygote while 1out of 10,000 are CC homozygote .it is the second most commonly variant worldwide . The heterozygous form (HbAC) is lack any clinical manifestation (asymptomatic),erythrocyte life is normal contain about 30% Hb C and 50-60% Hb A and slightly increase amount of HbA2.Stained blood film of AC show increase numbers of target cell. The homozygous form (Hb CC) causes anemia, tissue anoxia and severe pain.

3- Thalassemia: A group of genetic diseases in which a defect occur in the rate of synthesis of one or more of Hb chains(imbalance occurs in the synthesis of globin chains),but the chains are structurally normal. This due to defect or absence of one or more of genes responsible for synthesis of α or β chains leading to premature death of RBCs.

Types:

β -thalassemia: When synthesis of β chains is decreased or absent. There are two copies of the gene responsible for synthesis of β chains. Individuals with β globin gene defects have either :

-β -thalassemia minor (β –thalassemia trait) : when the synthesis of only one β –globin gene is defective or absent. Those individuals make some β chains and usually not need specific treatment.

β -thalassemia major (Cooley anemia): if both genes are defective.
Babies will be severely anemic during the first or second year of life and so require regular blood transfusion. Bone marrow replacement is more safe treatment (why?).

α-thalassemia: in which synthesis of α globin chain is defective or absent. There are four copies of gene responsible for synthesis of α globin chains so patients may have:

i - Silent carrier of α-thalassemia with no symptoms: if one gene is defective

ii- α-thalassemia trait: if two genes are defective.

iii- Hb H disease: if 3 α globin genes are defective, with mild to moderate anemia. The produced Hb will be β4 which is called HB H. Oxygen delivery to tissues will be blocked because Hb H (β4) has high affinity to O2 and not deliver it to tissues.

iv- Hydrops fetalis: when all 4 α globin genes are defective. It causes fetal death because α globin chains are required for synthesis of Hb F.

4 -Hb D

Hb D Punjab present in punjab region of India and Pakistan. Studies indicate that Hemoglobin D-Punjab accounts for over 55% of the total hemoglobin variants there. it is also sometimes called “D Los Angeles”. Hemoglobin D is the 4th most common hemoglobin variant. It developed as a response to the selective pressures of malaria in these regions of Asia.

1 -these individuals have normal Hb values with no evidence of hemolysis.

2-erythrocyte indices within normal limit.

3-some individuals have decreased osmotic fragility 4 -individuals doubly heterozygous for Hb D and B thalassemia.

5-usually individuals have mild anemia and minimal hemolysis.

6-People with hemoglobin D trait have slightly more hemoglobin A than hemoglobin D.

7 -Hemoglobin D Disease can cause mild hemolytic anemia and mild to moderate splenomegaly. The anemia usually occurs in the first few months of life, as fetal hemoglobin decreases and hemoglobin D increases

5 -Hb E

is an abnormal hemoglobin with a single point mutation in the β chain. At position 26 there is a change in the amino acid, from glutamic acid to lysine. Hemoglobin E is very common among people of Southeast Asian, Northeast Indian, Sri Lankan and Bangladeshi descent. The βE mutation affects β-gene expression creating an alternate splicing site in the mRNA at codons 25-27 of the β-globin gene. Through this mechanism, there is a mild deficiency in normal β mRNA and production of small amounts of anomalous β mRNA. The reduced synthesis of β chain may cause β-thalassemia

AE heterozygotes are commonly encountered ,they have no hematological abnormalities .As in Ac and As heterozygotes, the proportion of Hb E decease in individuals who have α-thalassemia.

6-Hb G Accra(korle-B4)

It is encountered quite frequently in central Africa. Hemoglobin G-Philadelphia can arise from one of two different mutations in the α-globin gene. Although both produce the same protein, the mutations occur in different ethnic groups and produce different patterns of abnormal hemoglobins. 1-there is no clinical or hematological manifestation associate with either the heterozygote or the homozygote state .

2-the erythrocyte from an individual homozygote for Hb krole B4 have normal appearance on blood smear.

3-No target cell

7 -Hb H

It is a tetramer composed of four normal ß chains .this abnormal hemoglobin is seen in some individuals with α-thalassemia.

8 -Hb I

it is most commonly encountered Alpha chain variant. They have no apparent clinical or hematological abnormalities. Heterozygous have about 25% Hb I and 75% Hb A ,this proportion is similar to other alpha chain variant and indirect evidence that each parent contributes two alpha chain gene .

Myoglobin (Mb) :

- It is formed of one heme molecule attached to one globin chain.
- It is found only in red skeletal muscles and cardiac muscle. It gives their tissues their characteristic red color.

-Myoglobin has much higher affinity for oxygen than hemoglobin. So it is unable to release it to tissues. In contrast, Hb reacts with oxygen reversibly to give it to tissues. Myoglobin concentration is increased in blood in a disease called myocardial infarction and in case of muscle trauma and myopathies.

Evaluation methods :
1-Immediate feedback (formative assessment).
2-Involving students in self-assessment (correcting their own mistakes).
3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/ Mention causes of the following:
1- Hb AS
2-Hb CC
3-Sulfahemoglobin
4-Hb H
5-Qualitiative hemoglobinopathies

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674
2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Eleven and twelve week

Anemia .definition ,classification ,and types
Anemia ,causes ,clinical signs and laboratory finding

Educational objective:
The student should be able to:

1- Know anemia meaning /definition
2- know anemia classification
3- know anemia types .
4- Know anemia causes
5- Know anemia clinical signs and laboratory finding

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:

1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

Anemia: definition, classification and types

Anemia is the blood disorder, deficiency in the oxygen-carrying capacity of the blood due to a diminished erythrocyte mass.
characterized by the reduction in:
1. Red blood cell (RBC) count
2. Hemoglobin content
3. Packed cell volume (PVC).

Generally, reduction in RBC count, hemoglobin content and PCV occurs because of:
1. Decreased production of RBC: **a)**low erythropoietin
b) Decreased marrow response to erythropoietin
2. Increased destruction of RBC (hemolysis)
3. Excess loss of blood from the body (bleeding).

All these incidents are caused either by inherited disorders or environmental influences such as nutritional problem, infection and exposure to drugs or toxins.

Anemia is a laboratory diagnosis:

Less than normal range of hematological parameters (CBC):

-RBC,WBC, ,platelets count ,hemoglobin concentration and PCV.
-Mean cell volume (MCV): is below 80 fL in microcytic anemia ,higher than 100fL in macrocytic anemia

Reticulocyte count important to determine is a hypo-proliferative or hyperproliferative anemia or observed the treatment progress in hypo-proliferative anemia.
-Blood bilirubin: High bilirubin (unconjugated bilirubin) indicate the jaundice which due to haemolysis (hemolytic anemia)or megaloblastic anemia.
-Iron blood : Iron level be low in Iron deficiency anemia which due to shortage in Iron storage in human body led to defect in haemoglobin synthesis .Microcytic ,hypochromic anemia observed in Iron deficiency anemia.

Laboratory Definition of Anemia:

Hgb: Women: <12.0 g/dL

Men: < 13 g/dL

Hct: Women: < 36

Men: < 39

Clinical symptoms and Signs of anemia:

The severity of symptoms may vary widely depending on :

1-The degree(severity) of anemia.

2-Time period over which anemia developed.

3-Age of patient.

4-The Hb oxygen dissociation curve.

5-Other medical conditions that are present.

-Decreased oxygenation

Exertion dyspnea (shortness of breath)

Dyspnea at rest

Weakness ,Headache, Fatigue

Tachycardia ,Bounding pulses and Roaring in the Ears

Widened pulse pressure (increase systolic blood pressure with a decreased diastolic blood pressure)

Lethargy, confusion **Decreased volume**

Signs :physical examination:

Fatigue - pale apparent in conjunctive ,palms, and face, nail beds (all mucous membrane in all side of the body) .

Muscle cramps

Postural dizziness

syncope

CLASSIFICATION OF ANEMIA:

Anemia is classified by two methods:

1. Morphological classification
2. Etiological classification.

MORPHOLOGICAL CLASSIFICATION:

Morphological classification depends upon the size and color of RBC.

a-Size of RBC is determined by mean corpuscular volume (MCV).

b-Color is determined by mean corpuscular hemoglobin concentration (MCHC).

By this method, the anemia is classified into four types.

1-Normocytic Normochromic Anemia:

Size (MCV) and color (MCHC) of RBCs are normal. But the number of RBC is less (as in hematological malignancies(chronic lymphocytic and large granular lymphocytic leukemia),rheumatic diseases, and infections).

2. Macrocytic Normochromic Anemia

RBCs are larger in size with normal color. RBC count is less. (causes is impaired DNA synthesis in the bone marrow leading to megaloblastic changes in the red cell precursors ,and from other mechanism as alcoholism, liver diseases, hypothyroidism ,and hemolysis or hemorrhage)

3-Macrocytic Hypochromic Anemia

RBCs are larger in size. MCHC is less, so the cells are pale (less colored).

4-Microcytic Hypochromic Anemia

RBCs are smaller in size with less color(Iron deficiency, anemia of chronic disease, thalassemia).

Normal ranges:

-Normocytic (MCV 90-100)

-Macrocytic (MCV >100)

-Microcytic(MCV<80)

Table: Morphological classification of anemia

Type of anemia	Size of RBC (MCV)	Color of RBC(MCHC)
Normocytic normochromic	normal	normal
Normocytic hypochromic	normal	less
Macrocytic hypochromic	large	less
Microcytic hypochromic	small	less

ETIOLOGICAL CLASSIFICATION:

On the basis of etiology (study of cause or origin), anemia is divided into five types:

1. Hemorrhagic anemia
2. Nutrition deficiency anemia
3. Hemolytic anemia
4. Aplastic anemia
5. Anemia of chronic diseases.

Evaluation methods :

1-Immediate feedback (formative assessment).
2-Involving students in self-assessment (correcting their own mistakes).
3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/ Mention types of anemia according to morphology .
Q2/Enumerate cause of anemia

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674
2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Thirteen week

Hemorrhagic Anemia ,Megaloblastic anemia and pernicious anemia

Educational objective:
The student should be able to:

1- Hemorrhagic Anemia
2- Know megaloblastic anemia cause
3- know pernicious anemia causes
4- know clinical signs and laboratory finding

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:

1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

1-Hemorrhagic Anemia

Hemorrhage refers to excessive loss of blood. Anemia due to hemorrhage is known as hemorrhagic anemia. It occurs both in acute and chronic hemorrhagic conditions .

Acute hemorrhage:

Acute hemorrhage refers to sudden loss of a large quantity of blood as in the case of accident. Within about 24 hours after the hemorrhage, the plasma portion of blood is replaced. However, the replacement of RBCs does not occur quickly and it takes at least 4 to 6 weeks. So with less number of RBCs, hemodilution occurs. However, morphologically the RBCs are normocytic and normochromic. Decreased RBC count causes hypoxia, which stimulates the bone marrow to produce more number of RBCs. So, the condition is corrected within 4 to 6 weeks.

Chronic hemorrhage :

It refers to loss of blood by internal or external bleeding, over a long period of time. It occurs in conditions like peptic ulcer, purpura, hemophilia and menorrhagia due to continuous loss of blood, lot of iron is lost from the body causing iron deficiency. This affects the synthesis of hemoglobin resulting in less hemoglobin content in the

cells. The cells also become small. Hence, the RBCs are microcytic and hypochromic .

2-Nutrition Anemia

Deficiency anemia that occurs due to deficiency of a nutritive substance necessary for erythropoiesis is called nutrition deficiency anemia. The substances which are necessary for erythropoiesis are iron, proteins and vitamins like C, B12 and folic acid. The types of nutrition deficiency anemia are:

A-Iron deficiency anemia (I.D.A) :

Iron deficiency anemia is the most common type of anemia. It develops due to inadequate availability of iron for hemoglobin synthesis. RBCs are microcytic and hypochromic. **Causes of iron deficiency anemia:**

i. Loss of blood (chronic blood loss) as in uterine bleeding, gastrointestinal tract bleeding) .

ii. Decreased dietary intake of iron

iii. Poor absorption of iron from intestine (malabsorption)

v. Increased demand for iron in conditions like growth and pregnancy.

Symptoms of iron deficiency anemia are headache ,weakness, difficult in breath brittle nails, spoon shaped nails (koilonychias), brittle hair, glossitis (atrophy of papilla in tongue) and dysphagia (difficulty in swallowing) ,Ulcerations or fissures at the corners of the mouth, Pica is the habitual consumption of unusual substances like clay, ice, and starch.

Iron Deficiency Anemia – Lab Findings:

- CBC : RBC indices (MCV,MCH,MCHC) decreased .
- The blood film shows hypochromic, microcytic cells with occasional target cells and pencil-shaped poikilocytes. The reticulocyte count is low in relation to the degree of anemia.

-Serum Iron LOW (< 60 micrograms/dL)

-Total Iron Binding Capacity (TIBC) HIGH (> 360 micrograms/dL)

-Serum Ferritin LOW (< 20 nanograms/mL)

-Can be “falsely” normal in inflammatory states

B-Protein deficiency anemia:

Due to deficiency of proteins, the synthesis of hemoglobin is reduced. The RBCs are macrocytic and hypochromic .

C-Pernicious anemia or Addison’s anemia :

Pernicious anemia is the anemia due to deficiency of vitamin B12. It is also called Addison’s anemia. It is due to atrophy of the gastric mucosa because of autoimmune destruction of parietal cells. The gastric atrophy results in decreased production of intrinsic factor and poor absorption of vitamin B12, which is the maturation factor for RBC. RBCs are larger and immature with almost normal or

slightly low hemoglobin level. Synthesis of hemoglobin is almost normal in this type of anemia. So, cells are macrocytic and normochromic/hypochromic.

Causes B12 deficiency :

1-disorder of the ileum(intrinsic factor receptors are present on the ileal mucose) as in lymphoma.

2-pancreatic insufficiency(R protein).

3-consumption by fish tapeworm(*Diphyllobotherium latum*) .

D-Megaloblastic anemia .

Megaloblastic anemia is due to the deficiency of another maturation factor called folic acid. Here, the RBCs are not matured. The DNA synthesis is also defective, so the nucleus remains immature. The RBCs are megaloblastic and hypochromic. Features of pernicious anemia appear in megaloblastic anemia also. However, neurological disorders may not develop.

Causes:

1-inadequte diet

2-alcoholism (causes urinary folate excretion).

3-impeding liver storage.

4-decrease absorption(sprue, lymphoma).

5-increases demand as in pregnancy.

6-some medications causes folate deficiency

Evaluation methods :

1-Immediate feedback (formative assessment).

2-Involving students in self-assessment (correcting their own mistakes).

3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/ Mention causes of Megaloblastic anemia .

Q2/mention cause of Addison's anemia

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674

2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Fourteen week

Aplastic anemia and hemolytic anemia

Educational objective:

The student should be able to:

1-Know Aplastic Anemia causes
2-Know hemolytic anemia cause
3-know Hemolytic anemia causes and types
4- know clinical signs and laboratory finding

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:

1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

Hemolytic Anemia:

Hemolysis means destruction of RBCs. Anemia due to excessive hemolysis which is not compensated by increased RBC production is called hemolytic anemia. It is classified into two types:

A. Extrinsic hemolytic anemia(extravascular).
B. Intrinsic hemolytic anemia(intravascular) .

A. Extrinsic hemolytic anemia:

It is the type of anemia caused by destruction of RBCs within macrophages present in organs such as liver ,spleen ,or bone marrow by external factors. Healthy RBCs are hemolized by factors outside the blood cells such as antibodies, chemicals and drugs. Extrinsic hemolytic anemia is also called autoimmune hemolytic anemia.

Common causes of external hemolytic anemia:

i. Liver failure
ii. Renal disorder
iii. Hypersplenism
iv. Burns
v. Infections like hepatitis, malaria and septicemia
vi. Drugs such as penicillin, antimalarial drugs and sulfa drugs
vii. Poisoning by chemical substances like lead, coal and tar

viii. Presence of isoagglutinins like anti-Rh.
ix. Autoimmune diseases such as rheumatoid arthritis and ulcerative colitis .

B. Intrinsic hemolytic anemia(intravascular) :

It is the type of anemia caused by destruction of RBCs within the blood stream because of the defective RBCs. There is production of unhealthy RBCs, which are short lived and are destroyed soon. Intrinsic hemolytic anemia is often inherited and it includes sickle cell anemia and thalassemia. Because of the abnormal shape in sickle cell anemia and thalassemia, the RBCs become more fragile and susceptible for hemolysis .The intrinsic disorders include:

1-abnormal hemoglobins.
2-enzyme defects
3-membrane abnormalities.

Symptoms:

-increase in bilirubin.
-turbid plasma
-blood film show decrease in RBC, Hb, PCV, ESR, and increase WBC
The specific clinical sign :is hemoglobin urine

Aplastic Anemia:

Aplastic anemia is due to the disorder of red bone marrow. Red bone marrow is reduced and replaced by fatty tissues. Bone marrow disorder occurs in the following conditions:

i. Repeated exposure to X-ray or gamma ray radiation.
ii. Presence of bacterial toxins, quinine, gold salts, benzene, radium, etc.
iii. Tuberculosis.
iv. Viral infections like hepatitis and HIV infections.

In aplastic anemia, the RBCs are normocytic and normochromic.

- **Anemia of chronic diseases:**

or anemia of chronic inflammation, is a form of anemia seen in chronic infection, chronic immune activation, and malignancy. These conditions all produce massive elevation of Interleukin-6, which stimulates hepcidin production and release from the liver, which in turn reduces the iron carrier protein ferroportin so that access of iron to the circulation is reduced. Other mechanisms may also play a role, such as reduced erythropoiesis.

Anemia of chronic inflammation is the preferred term since not all chronic diseases are associated with this form of anemia.

Evaluation methods :
1-Immediate feedback (formative assessment).
2-Involving students in self-assessment (correcting their own mistakes).
3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/ Mention causes of Aplastic anemia .
Q2/mention types of Hemolytic anemia **with causes**

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674
2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical

Fifteen week

Sickle cell anemia ,acquired anemia , and autoimmune hemolytic anemia

Educational objective:
The student should be able to:
1-Know Aplastic Anemia causes
2-Know hemolytic anemia cause
3-know Hemolytic anemia causes and types
4- know clinical signs and laboratory finding

Lecture duration:
Theory (2) hour+ practical (4) hour /weekly .

Activities Used:
1-Interactive classroom activities
2-Brainstorming questions
3-Group activities (if required)
4-Homework
5-Online homework (classroom)
6-Quick written exam .

Intrinsic hemolytic anemia(intravascular) :

It is the type of anemia caused by destruction of RBCs within the blood stream because of the defective RBCs. There is production of unhealthy RBCs, which are short lived and are destroyed soon. Intrinsic hemolytic anemia is often inherited and it includes sickle cell anemia and thalassemia. Because of the abnormal shape in sickle cell anemia and thalassemia, the RBCs become more fragile and susceptible for hemolysis .The intrinsic disorders include:
1-abnormal hemoglobins.
2-enzyme defects
3-membrane abnormalities.

Symptoms:
-increase in bilirubin.
-turbid plasma
-blood film show decrease in RBC, Hb, PCV, ESR, and increase WBC
The specific clinical sign :is hemoglobin urine

Sickle cell anemia:
Sickle cell anemia is an inherited blood disorder, characterized by sickle-shaped red blood cells. It is also called hemoglobin SS disease or sickle cell disease. It is common in people of African origin. Sickle cell anemia is due to the abnormal hemoglobin called hemoglobin S (sickle cell hemoglobin). In this, αchains are normal and βchains are abnormal. The molecules of hemoglobin S polymerize into long chains and precipitate inside the cells. Because of this, the RBCs attain sickle (crescent) shape and become more fragile leading to hemolysis . Sickle cell anemia occurs when a person inherits two abnormal genes (one from each parent). In children, hemolyzed sickle cells aggregate and block the blood vessels, leading to infarction (stoppage of blood supply). The infarction is common in small bones. The infarcted small bones in hand and foot results in varying length in the digits. This condition is known as hand and foot syndrome. Jaundice also occurs in these children.

Thalassemia:
Thalassemia is an inherited disorder, characterized by abnormal hemoglobin. It is also known as Cooley's anemia or Mediterranean anemia. It is more common in Thailand and to some extent in Mediterranean countries. Thalassemia is of two types:
i-αthalassemia
ii. βthalassemia
The βthalassemia is very common among these two.
In normal hemoglobin, number of α and β polypeptide chains is equal. In thalassemia, the production of these chains become imbalanced because of defective synthesis of globin genes. This causes the precipitation of the polypeptide chains in the immature RBCs, leading to disturbance in erythropoiesis. The precipitation also occurs in mature red cells, resulting in hemolysis.

α-Thalassemia
αthalassemia occurs in fetal life or infancy. In this αchains are less, absent or abnormal. In adults, βchains are in excess and in children, γchains are in excess. This leads to defective erythropoiesis and hemolysis. The infants may be stillborn or may die immediately after birth .

β-Thalassemia
In βthalassemia, βchains are less in number, absent or abnormal with an excess of αchains. The αchains precipi tate causing defective erythropoiesis and hemolysis.

Evaluation methods :
1-Immediate feedback (formative assessment).
2-Involving students in self-assessment (correcting their own mistakes).

3. Final feedback (summative assessment), which refers to answering questions given as a class activity at the end of the lecture.

Q1/ compare Intrinsic hemolytic anemia(intravascular),extrinsic hemolytic anemia .
Q2/mention types of sickle cell anemia .

Reference :

1-A. Victor Hoffbrand; Paul A. H. Moss .(2011).Hoffbrand's Essential Haematology. Seventh Edition http://www.wiley.com/buy/9781118408674
2-Marshall Lichtman, Josef Prchal, et al.(2001) Williams Manual of Hematology Ninth Edition. McGraw Hill / Medical