Foundation Block

Physiology team 441

8-
Blood physiology 2
(3-Anemia and polycythemia)

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physiology
441

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Editing File

Color index

- Main Text
- Important
- Dr's notes
- Female
- Male
- Extra

Objectives

At the end of this lecture student should be able to:

- Summarize the synthesis of Hemoglobin and Its structure, functions, types of HB.
- Describe essential elements needed for RBC formation (proteins,vitamins: B12, Folic acid, Vitamin C).
- Describe the process of Vit B12 - Folic Acid ,absorption and its malabsorption.
- Recognize hemoglobin structure and its functions.
- Discuss iron metabolism (absorption, storage, transport).
- Describe the fate of old RBC.
- Describe anemia and its causes ,physiological consequences and clinical picture.
- Know how to differentiate between the different types and causes of anemia.
- Recognize causes of polycythemia, Define, and physiological consequence.

★ Haemoglobin

- Globular protein
- Heme + Globin

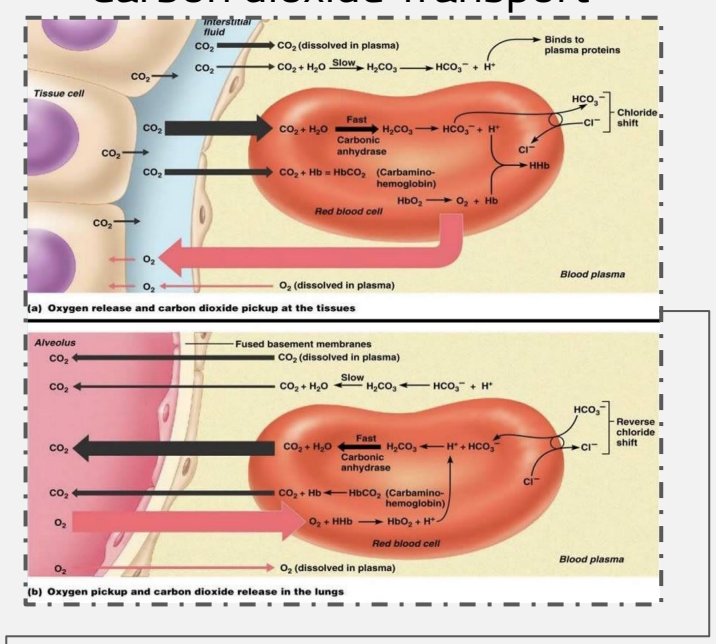
Synthesis:

1-

It occurs in the mitochondria of the developing RBC in bone marrow.

1- Transferrin: attaches to surface receptor.
2-Iron (F2+) is released and transported to mitochondria where it combines with protoporphyrin ring to form heme.
3- Heme combines with α and β protein chains formed on the ribosomes to make hemoglobin.

Carbon dioxide Transport



Average Value:

2-

Haemoglobin (Hb) = 14-16 gm/dl
-in male: 13.5-17.5 g/dl (16 g/dl).
-in female: 12-15.5 g/dl (14 g/dl).
Infant: 14-19 g/dl.
-N.B: concentration of plasma protein = 7 g/dl

This slide was found only in male slides

Chemical Reactions of HB:

3-

1- Oxygenation;
Oxyhemoglobin (Normal).

2-Oxidation;
Methemoglobin (Abnormal).

3- Co2;
Carbamino hemoglobin (Normal).

4- Co;
Carboxy hemoglobin (Abnormal).

Oxygenation and oxidation;

- When hemoglobin carries oxygen, the Hb is **oxygenated**. The iron atom in Hb is still in the ferrous state.
- **Oxidized** hemoglobin is called Met-Hb; then iron is in ferric state and the oxygen carrying capacity is lost.

Extra

★ Haemoglobin

Types of Hb;

4-

Types of Hb;

of normal Hb:

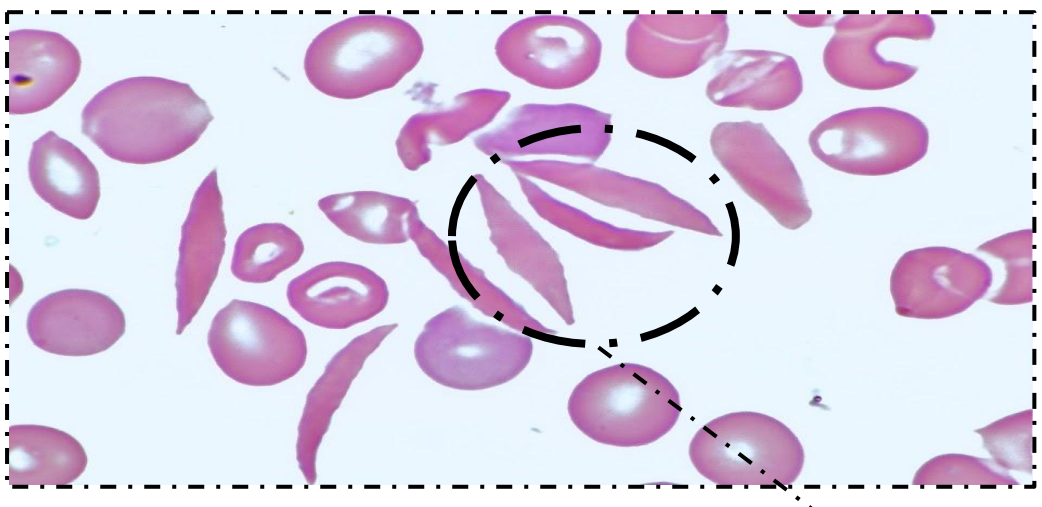
- -**Hb A** (2 alpha & 2 beta chains) (adult Hb) (98%).
- -**Hb A2** (2 alpha & 2 delta chains) (2%).
- -**Hb F** (2 alpha & 2 gamma chains) (Hb of intrauterine life)(fetal). (Higher affinity to oxygen , extract the oxygen of the mother's blood (Hb-A)).

of abnormal Hb:

1-Thalassemia:
Decreased synthesis of the globin polypeptide chains.(Hb-A).

2-Sickle cell anaemia :
Abnormal sequence of the amino acids in the globin polypeptide chains.
(There is no decrease in synthesis of globin).

*Abnormality in the polypeptide chain leads to an abnormal Hb (hemoglobinopathies.) e.g. thalassemias, sickle cell (HbS).



Extra:
Why females have lower Hemoglobin levels than males?
The main reason is not menstrual cycle, but the Androgens (Especially Testosterone), They speed up the process of Erythropoiesis.

★ Haemoglobin

5-

Function of Hb:

1- Transportation of respiratory gases.

- Carriage of O2: Hb reversibly bind O2 to form oxyhemoglobin, affect by pH, temperature, H+.

- Carriage of CO2: Hb bind CO2 = carboxyhemaglobin.

2- Buffer: (any protein acts as a buffer).

Breakdown:

(Hb is broken into its component).

1- globin;
>> (amino acids) Protein pool.
2- Haem ;
>> Iron(reused).
>> Porphyrin is converted to **bilirubin.**

* **Jaundice** is caused by buildup of **bilirubin**, which is a waste material in the blood results from the breaking down of Hb.

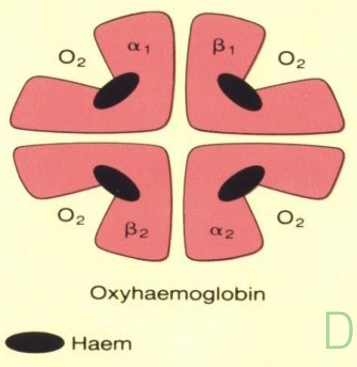
6-

Structure:

-Consist 4 chains each formed of heme & polypeptide chain (globin).
- Composed of **4 subunits** (2 alpha & 2 beta chains), each unit contains haem (iron-porphyrin).
-iron in the haem is ferrous (Fe++), **combines reversibly** with oxygen.
-Heme consist of protoporphyrin ring + iron (F2+).

-Each Hemoglobin molecule can have 4 Oxygen molecules(O2).
-Accounts for more than 95% of protein in RBC.
-Concentration of Hb in the Blood Measured as g/dl (grams per deciliter, or per 100 ml).
-It is a Globular protein.

Iron in the haem combines reversibly with oxygen and carbon dioxide reversibly .
But , irreversibly with carbon monoxide.
.Carbon Monooxide poisining .يصير فيه تسمم irreversible إذا مسك الهيموجلوبين في CO وماتركه يعني



Devoid of oxygen

★ Essential elements for RBCs formation and maturation:

Amino acids:

- formation of globin in haemoglobin.
- severe protein deficiency leads to anaemia.

Iron:

- formation of haemoglobin.
- Deficiency leads to anaemia.

★ Nutrients required for Erythropoietin:

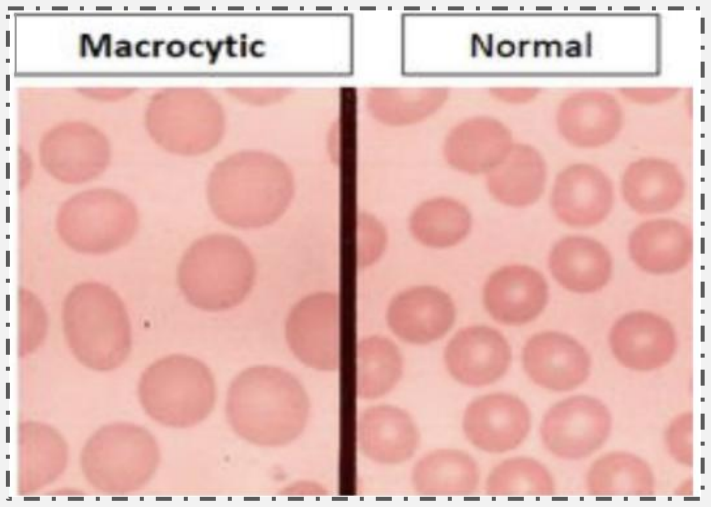
Vitamins:

Essential for DNA synthesis and maturation Rbcs في المراحل الأولى لتصنيع	(present in vegetables life & is heat liable إذا انطبخ يروح as folic acid): important for iron absorption.	important for haem production its deficiency leads to microcytic hypochromic anaemia.
B12 (cyanocobalamin) & folic acid.	Vitamin C (Ascorbic acid).	Pyridoxine (B6)

Other components:

- Iron.
- Amino acids.
- Trace elements (Cobalt, Copper, Zinc).

★ Vitamin B12 and Folic acid:



Importance:

- final Maturation factor for the RBCs .
- Essential for DNA synthesis.
  (early stages which have nucleus in uterus).

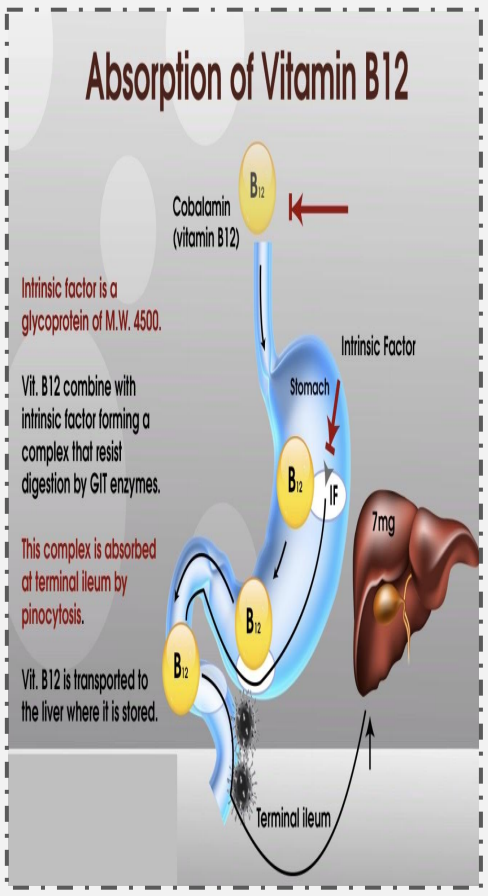
Dietary source:

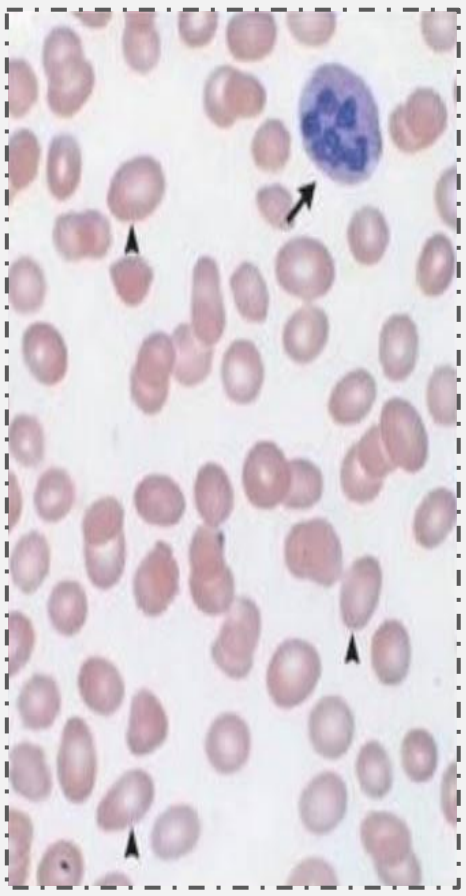
meat, milk, liver, fat, green vegetables.

Manifestation of deficiency:

- Macrocytic (megaloblastic) anaemia.
- Abnormal large.
- Fragile cells & oval shape.
- Failure of nuclear maturation & division.
- short life span.
- reduced RBC count & Hb.

*Macrocytic (megaloblastic anemia).





	Vitamin B12	Folic acid
Origin of source	Animal sources only (meat, liver, milk,...etc).	Animal and plant sources (meat, liver, fruits, vegetables). Easily destroyed by cooking.
Storage	In the liver in large amounts , enough for 3-4 years.	In the liver in very small amounts.
Causes of deficiencies	1- Defective absorption (pernicious anaemia). 2- Defective storage (liver diseases). 3- Dietary deficiency (very rare).	1- Dietary Deficiency (Important cause). 2- Defective absorption. 3- Defective storage (liver diseases).
Absorption	Intrinsic factor is secreted by parietal cells of the stomach to bind vitamin B12 and helps its absorption. Absorption occurs in terminal ileum, so macrocytic anaemia occurs in: 1- distal small intestine diseases. 2-deficiency of intrinsic factor lead to **malabsorption** of vit B12 (pernicious anaemia).	Mainly in the jejunum.

★ iron:

1-iron:

Total amount in the body = 3- 5 gm, distributed as follows:

1- Hb (65-75%).

2-storage iron (available) (20-30%) in the liver, spleen & bone marrow (ferritin).

3-intracellular oxidative enzymes(1%)(non-available).

4-transport or plasma iron. Myoglobin (4%).

2-Iron storage(1gm):

-site:
reticuloendothelial cells (liver, spleen, bone marrow).

-Iron is stored in two forms:

- Ferritin: (apoferritin + iron).
- Haemosiderin (one of the complications of excessive blood transfusion): insoluble complex molecule in the liver, spleen, bone marrow.

3-Iron Absorption:

-Absorption mainly in the duodenum.
-Iron must be absorbed in the Ferrous form (Fe 2+).

4-Iron transport:

Iron is transported in plasma (bloodstream) carried on the carrier protein:
in the form of (Transferrin).
Transferrin = "apotransferrin + iron".

5-Forms :

1- organic.
2- inorganic.

8-Iron deficiency:

Causes:
1 – Blood loss (the most important cause).
2 – Dietary deficiency.
3 – Defective absorption.
4 – Defective storage (liver diseases).

Results in blood film:
Microcytic anemia.

7-Factors decreasing iron absorption:

- Phosphates, phytates & oxalates in diet.
- Achlorhydria (decreased Hcl) , gastrectomy.
- Malabsorption syndromes or chronic diarrhea.

6-Daily intake:

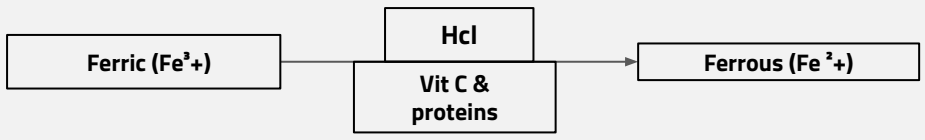
10 -20 mg/day.

★ iron:

9-Steps of iron absorption:

1-Iron in food: is in the oxidized form (ferric)(Fe^{3}+), to be absorbed it is reduced to the ferrous state (Fe^{2}+).
2-When Ferric reaches the stomach:

Reduction in the stomach



3-**Duodenum & upper part of small intestine:**
-Active transport of ferrous ions at the luminal border.
-once in the intestinal mucosal cell iron is attached to a non-ferritin protein carrier & either;
- transported across the serosal border to be picked up by transferrin.
(transport protein).
Or
- stored as ferritin by combining with apoferrtin.
(carrier protein).

Absorption in the duodenum & upper part of small intestine.

transferrin : glycoprotein + iron
Apotransferrin: glycoprotein without iron.

Rate of absorption is determined by the rate of iron loss from the body.
And is regulated by the hepatic protein (Hepcidin).

10-Iron absorption is dependent by:

- Size of iron stores.
(لو مليان المخزن يقل الامتصاص).
- Rate of erythropoiesis.
(لو زاد يزيد الامتصاص).
- The rate of iron loss from the body.

Normally, 10- 15% of ingested iron will be absorbed.
It's regulated by the protein (hepcidin).

11-Iron excretion:

- 0.5 -1.0 mg [(mainly feces, skin) ,urin, cutting hair and nails].

- Daily loss of iron is 0.6 mg/day in males & 1.3 mg/day in females.

12-sources :

Animal and plant
(Liver, beef, meat,fruits,mutton, fish, egg yolk,beans,lentils & green vegetables).

★ Anemia:

This slide was found only in female slides

(عرَض وليست مرض)

Definition:

Decreased Hb concentration, the number of RBC, and Oxygen supply to tissues below the normal level of the same age and gender.

Due to:

- Decreased RBCs count below normal level for same age and gender.

- Hb load in each RBC (MCH) below normal level.

Signs and symptoms:

are due to ↓ oxygen supply to tissues.

❑ **depending on the severity:**

Dr.Nervana Mostafa notes these tables isn't Important;

1-symptoms:

1-Pale skin. (pallor)

2-Fatigue, Weakness, Tiring easily.

3-Breathlessness (tachypnea), Racing heart or palpitations (tachycardia).

4-Cold intolerance.

5-Reduce in oxygen carrying capacity lack of O2 for ATP and heat production

6-Postural (orthostatic) hypotension: Drop in blood pressure when standing from a sitting or lying position, this may happen after acute blood loss, like a heavy period.

2-Signs:

01 Pallor: an abnormal loss of skin or mucous membrane color.

02 Concentration difficulties, Racing heart or palpitations.

03 Koilonychia: is when the nail curves upwards (becomes spoon-shaped).

04 Loss of appetite, Frequent, and Becoming irritated easily.

05 Angular stomatitis: deep cracks and splits form at the corners of the mouth.

06 Strange food cravings, and headaches.

07 Tachycardia and tachypnea: due to compensatory sympathetic stimulation.

This slide was found only in female slides

★ Full (Complete) Blood Count (FBC, CBC):

1

- MCV (mean corpuscular volume):

- The MCV shows the size of the red blood cells.

$$MCV = \frac{Hct}{RBC}$$

Dr.Nervana Mostafa notes these tables is Very very Important; فقط القيم الي عليها مربع عاده بتطبقونها بالعملي اكثر.

Complete blood count	Result	Reference values
WBC	7.36 × 10.e9/L	(4-11)
RBC	5.12 ×10.e12	(4.2-5.5)
HGB	15.4 g/dl	(12-16)
HCT	45%	(37-47)
MCV	87.9 fl	(80-94)
MCH	30 pg	(27-32)
MCHC	34 g/dl	(32-36)
RDW	11.4 %	(11.5-14.5)
Platelet count	183 × 10.e9/L	(140-450)
MPV	9.43 fl	(7.2-11.1)

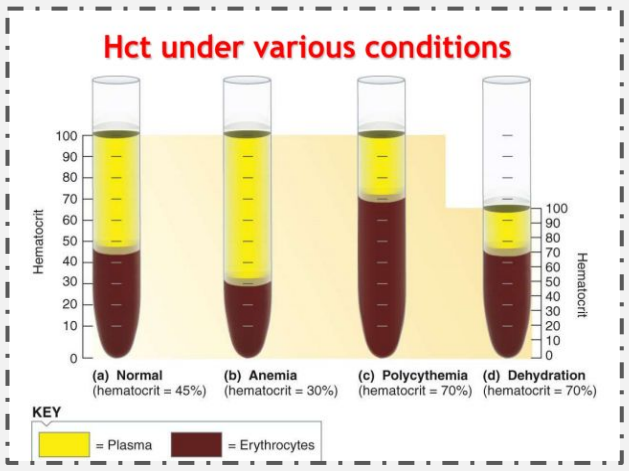
WBC: White blood cells, RBC: Red blood cells, HGB: Hemoglobin, HCT: Hematocrit, MCV: Mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: Mean corpuscular hemoglobin concentration, RDW: Red cell distribution width, MPV: Mean plasma volume.

2

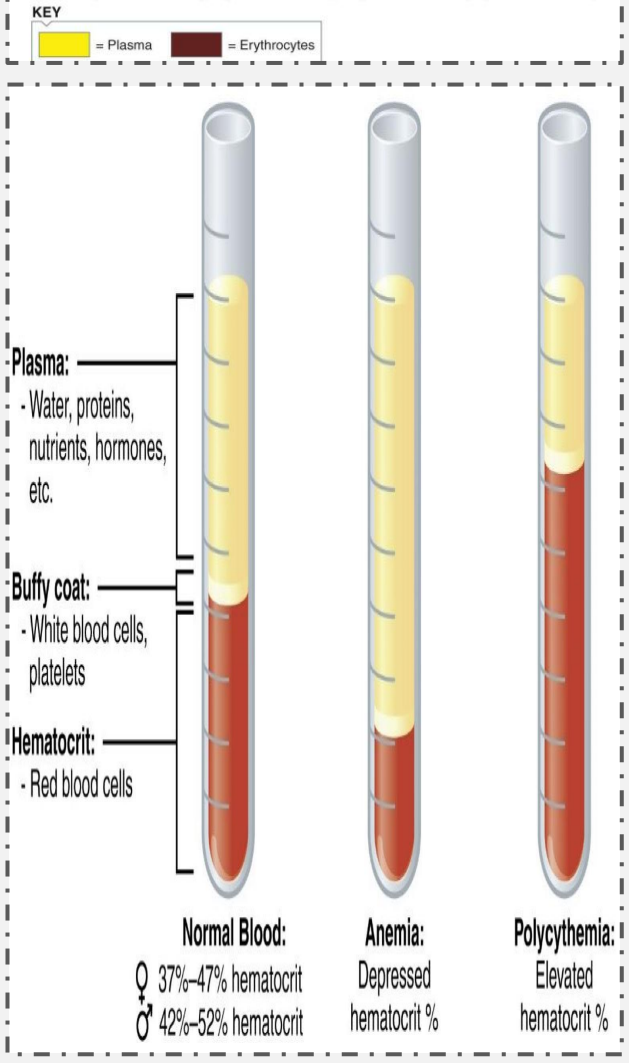
- MCH (mean corpuscular hemoglobin):

- The MCH value is the amount of hemoglobin in an average red blood cell.

$$MCH = \frac{Hgb}{RBC}$$



★ HCT Under various conditions:



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★ Types Of Anemia (Hemoglobin is low) :

01 Microcytic hypochromic:

Causes:
Iron deficiency.

- microcytic = smaller size.
- hypochromic = less hemoglobin.
- increased zone of central pallor.
-decrease in MCV and MCH.

- anisocytosis = variation in size.
-poikilocytosis= variation in shape.

1-The RBC's = smaller than normal.

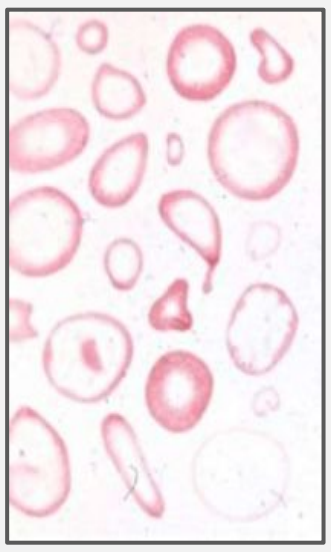
2- Increased zone of central pallor.

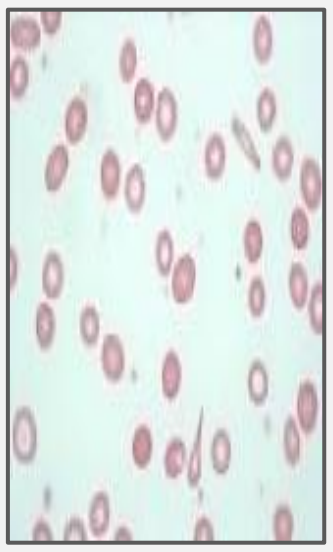
3-this is indicative of a microcytic (smaller size of each RBC) and Hypochromic (less hemoglobin in each RBC) anemia.

4-Increased anisocytosis (variation in size)

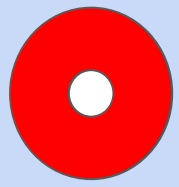
5-Increased poikilocytosis (variation in shape).

Decrease in Hb content, RBCs count, PCV(HCT value)
MCV= 70 μ^3
MCH=22 pg





02 Normocytic normochromic:



Causes:
Acute blood loss.

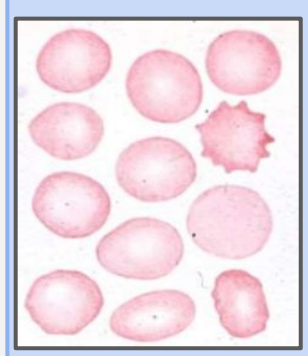
- Normal HB (in each RBC).
- normal RBCs' size.
- normal MCV and MCH.

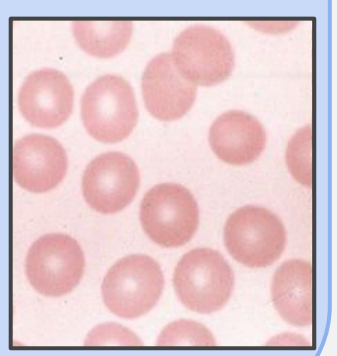
The decrease in the RBCs count will lead to decrease the total number of Hb in the blood.

1- Hb level is low.

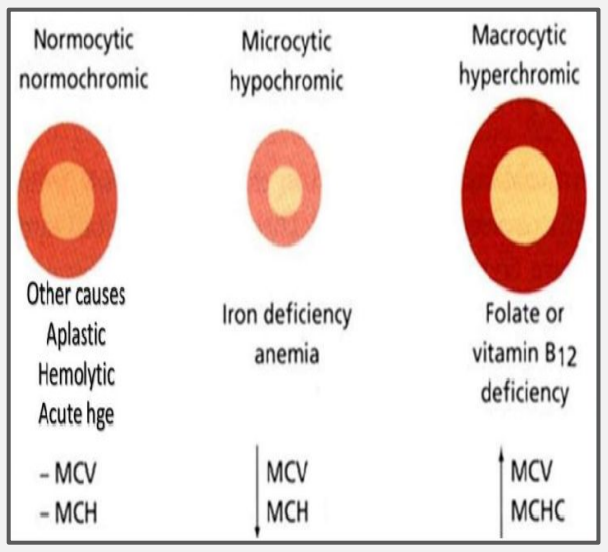
2-Normal RBCs' size.

3-Decreased number Of RBCs.





Decrease in Hb content, RBCs count, PCV(HCT value)
MCV= 90 μ^3
MCH=30 pg



02 Macrocytic (megaloblastic):

Causes:
Folic acid (folate) or vit B12 deficiency.

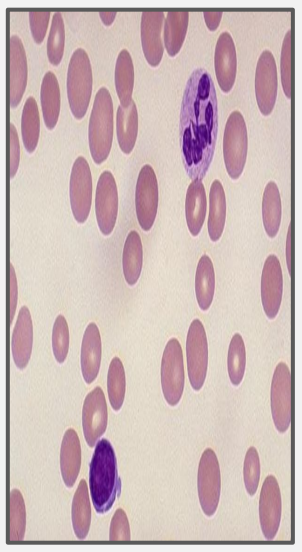
- The hypersegmented neutrophil and also that the RBC are almost as large as the lymphocyte.
- There are fewer RBCs.
- increase in MCV and MCH.

1-Hypersegmented neutrophil and also the RBCs are almost as large as the lymphocyte.

2- There are fewer RBCs.

Note:
the hypersegmented neutrophils and also that the RBC are almost as large as the lymphocyte.
Note:
that there are fewer RBCs.

Decrease in Hb content, RBCs count, PCV(HCT value)
MCV= 110 μ^3
MCH=38 pg



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Causes Of Anemia:

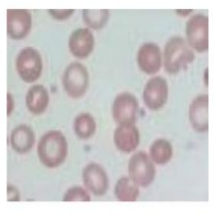
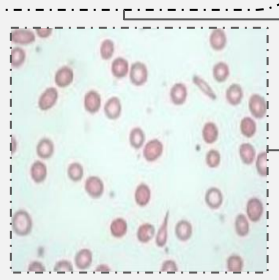
– Extrinsic Abnormalities:

1- Infections
2- Malaria
3- Mycoplasma

-Intrinsic Abnormalities:

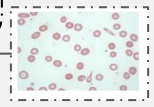
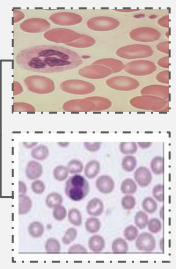
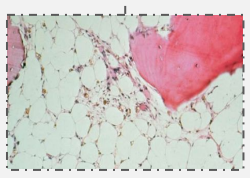
Hereditary Spherocytosis- Thalassemia- Sickle Cell Anemia- G6PD deficiency.

1-Bleeding
(RBC loss without RBC Destruction).

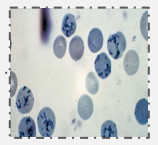
- Acute
  - **Accident: cause:** Hemorrhage. (RBC return to normal 3-6w).
  - **- normocytic. -normochromic.**
  - 
- Chronic
  - **Iron deficiency anaemia:**
    - Menstruation.
    - Gynecological disorders.
    - -cancer.
    - GIT bleeding (peptic ulcer- Bilharziasis- piles- Parasitism Hookworms).
    - **microcytic hypochromic anaemia** (ulcer, worms).
  - 

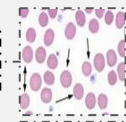
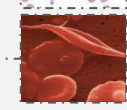
Causes:
- Trauma
- Disorders: e.g. Cancer, ulcer.

2-Decreased RBCs production

- *Nutritional deficiency :*
  - 1- Iron deficiency leads to: **(microcytic hypochromic anaemia).**
  - 
  - 2-Vit. B12 & folic acid leads to: **megaloblastic anaemia**. ***Pernicious anaemia***: is a special type of megaloblastic anaemia due to *intrinsic factor deficiency* causing vit B12 deficiency.
  - 
- Increased demands :
  - (childhood & pregnancy)
  - –Renal disease (lack of erythropoietin production).
- *Bone marrow failure* (aplastic anemia) :
  - **Due to:**
    - a- irradiation or excessive X-ray usage.
    - b- drugs e.g. chloramphenicol.
    - c- invasion of bone marrow by (secondary cancer cells or fibrosis).
  - 

3-destruction of RBCs :
Haemolytic anaemia=Reticulocytosis



- Intrinsic Abnormalitie:
  - Incompatible blood transfusion.
  - Malaria.
  - Mycoplasma.
  - Infections.
- Intrinsic Abnormalitie:
  - Abnormal Cell Membrane Defect → (spherocytosis) rigid.
  - 
  - Abnormal Hb → (Hb S) = Sickle cell anaemia.
  - 
  - Erythroblastosis fetalis.
  - Enzymatic defect:
    - glucose 6 phosphate dehydrogenase deficiency (G6PD).
    - - is an *inherited* condition.
    - -The body doesn't have enough of the enzyme G6PD, which helps (RBCs) function normally.
    - This deficiency can cause **hemolytic anemia**, usually after exposure to certain medications, foods, or even infections.
  - Hereditary.
  - Thalassemia.

– Intrinsic Abnormalities:

- Hereditary.
- Spherocytosis .
- Thalassemia.
- Sickle Cell Anemia.
- G6PD deficiency.
- Erythroblastosis fetalis.

– Extrinsic Abnormalities:

- Infections.
- Malaria.
- Mycoplasma.
- Incompatible blood transfusion.

Groups At High Risk of anaemia:

01 Menstruating women

02 Pregnant and breastfeeding women

03 Babies, especially if premature

04 People on weight reduction diets

05 Children going through puberty

06 Vegetarians

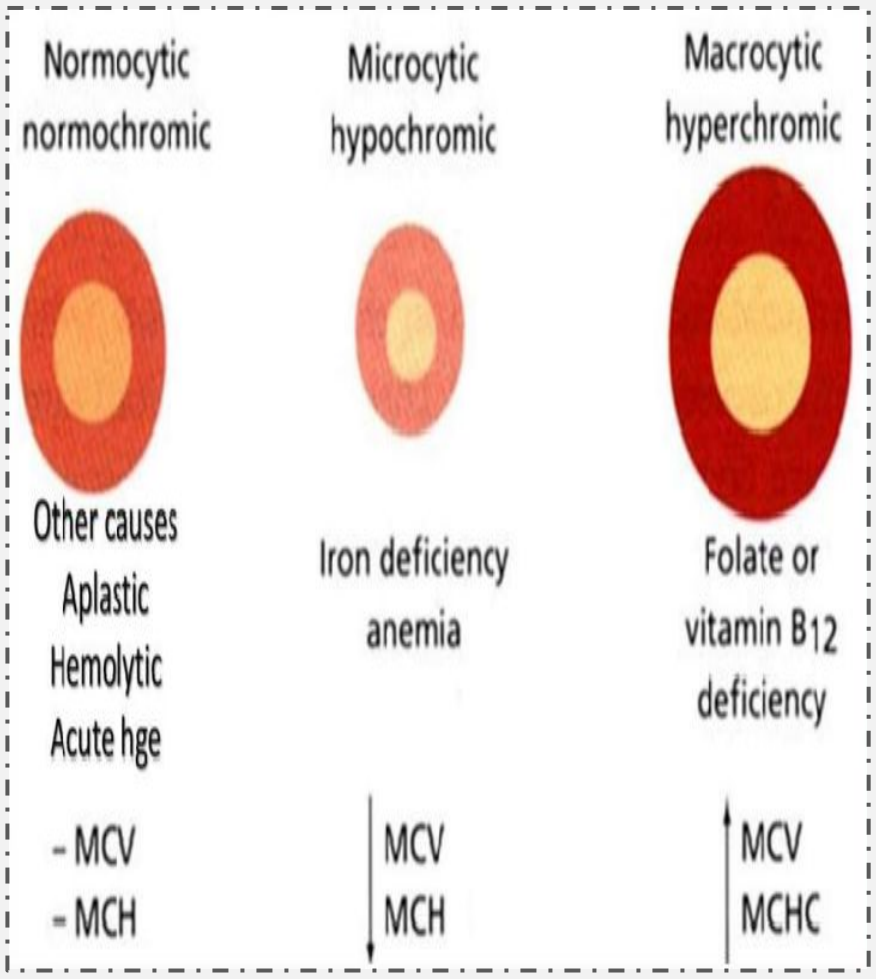
07 People with cancer, stomach ulcers and some chronic diseases

08 Athletes

★ Treatment of Anemia:

Treatment depends on the ***cause*** and ***severity***, but may include:

- Vitamin and mineral supplements. (in the case of deficiency).
- Iron injections . (if the person is very low on iron).
- Vitamin B12 oral or by injection . (required for pernicious anaemia).
- Folic acid supplement.
- Blood transfusions . [if required (Usually in severe cases)].



This slide was found only in male slides

Anemia and polycythemia:

Anemia is decrease in RBC mass as determined by Hct or Hb values below reference level.

The major causes of anemia are:

↓ Production or ↑ Loss

1- Decreased RBC production.
2-Increased RBC destruction.
3-RBC Loss without destruction.

Polycythemia is increase in RBC mass as determined by Hct or Hb values above reference level for age and gender.

This slide was found only in male slides

★ Haematological indices:

Indices	Male	Females
Hematocrit (Hct) (%)	47	42
Red blood cells (RBC) (10^6/L)	5.6	4.8
Hemoglobin (Hb) (g/dL)	16	14
Mean corpuscular volume (MCV) (fL)	90-95	
Mean corpuscular hemoglobin (MCH) (pg)	29	
Mean corpuscular hemoglobin concentration (MCHC) (g/dL of cells)	34	

MCV is the most accurate method of measuring red blood cells and most useful in classification of anemia.

(MCV) Mean corpuscular volume	The average volume of the RBCs.	Expressed in femtoliters (fL) or cubic micrometers.	$= \frac{Hct * 10}{RBC\ (—)\ 10^6\ \mu L}$	↑ 95 fl : Macrocytic anemia. Normal value (90-95 fl): normocytic anemia. ↓ 90 fl : Microcytic anemia.
(MCH) Mean corpuscular Hb	The average amount of hemoglobin inside a RBC.	Expressed in picograms (pg).	$= \frac{Hb * 10}{RBC\ (—)\ 10^6\ \mu L}$	↑ 33 pg: Hyperchromic. Normal value. (27-33 pg): normochromic ↓ 27 pg: Hypochromic.
(MCHC) Mean corpuscular concentration	The average concentration of hemoglobin in the RBCs.	Expressed as (gm/dl).	$= \frac{Hb * 10}{Hct}$	Normal value (32-36 g/dl) of RBCs.
Reticulocyte index	Reticulocytes are immature red blood cells (RBCs).		$= \frac{Hematocrit}{Normal\ Hematocrit}$	↑ 2% excessive RBC destruction or loss (Hemolytic anemia) ↓ 2% decreased production (Aplastic anemia)

Indices	Hematocrit (Hct)	RBC	Hb	MCV	MCH	MCHC
Male	47%	5.6x10^6/L	16 g/dL	90-95 fl	29 pg	34 g/dL of cells
Females	42%	4.8x10^6/L	14 g/dL			

★ Clinical correlation:

This slide was found only in male slides

Hereditary Spherocytosis:

Cause:

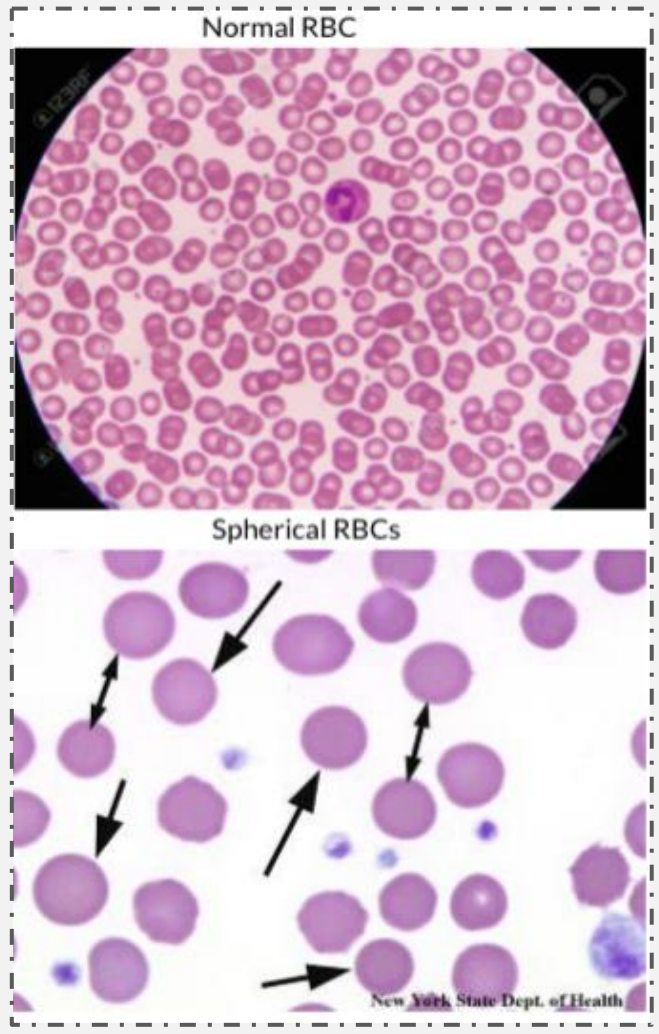
Congenital deficiency of the protein spectrin.

Manifestatio:

Anemia + spherical RBCs instead of the normal biconcave shape.

On blood film:

Loss of central pallor. Maybe polychromasi.



★ Polycythemia:

This slide was found only in female slides

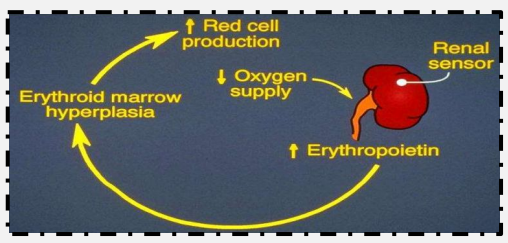
Definition:

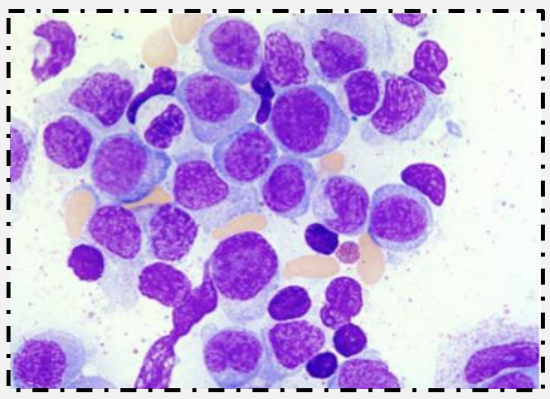
- increase in the number of RBCs per unit volume of blood.

Classification & Causes:

True or absolute

Complications of polycythemia: hyperviscosity of the blood





A-primary (unknown cause) **(Polycythaemia Rubra Vera- PRV)** (autoimmune disease).

uncontrolled RBC production (cancer of the bone marrow).

سمى برايمري لأن ما فيه سبب أدى للزيادة
More in female.

B-secondary due to hypoxia , Hypoxia occurs due to the increased release of Erythropoietin : high altitude, chronic respiratory or cardiac disease , smokers .

يسمى سكندري لأن بالبداية تحدث الهايبوكسيا وبعدها يحدث زيادة في إنتاج RBCs.

Hypoxia: deficiency in the amount of oxygen reaching the tissues.

Relative; (haemoconcentration)

in cases of dehydration loss of body fluid in vomiting, diarrhea, sweating.(البلازما قلت فبيان إن RBC زادت)
decrease in the volume of plasma.

Test yourself

MCQs

Q1: ..... is a special type of megaloblastic anaemia			
A- sickle cell anemia	B- pernicious anemia	C- Haemolytic anemia	D- None
Q2 : Which blood count shows the size of RBCs ?			
A- MCH	B- HCT	C- MCHC	D- MCV
Q3: Which type of Hb has highest affinity to oxygen ?			
A- Hb A	B- HB A2	C-Hb F	D- None
Q4 : B12 which combine with intrinsic factor , absorbed in ..... and stored in			
A- terminal ileum - liver	B- liver - terminal ileum	C- stomach -Terminal ileum	D- stomach -Liver

1-B 2-D 3-C 4-A

SAQs

Q1 : the treatment of anemia depends on ?

Q2: which type of anemia is erythroblastosis fetalis ?

Q3: what are iron storage forms ?

1- cause and severity

2-Haemolytic anemia

3-Ferritin and hemosiderin

MED441
KING SAUD UNIVERSITY

physiology 441

Foundation Block

Physiology team 441

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Bader Rajeh

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Arwa Alenzi
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Lama Aleyadhy
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Layan Almasri
Deema Almuhaimel
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