Doctor.021

no. 1

# HLS
# PATHOLOGY


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# ANEMIA

## Definition

- Reduction of oxygen carrying capacity of blood secondary to decrease in red cell mass
- Leads to tissue hypoxia
- Practically, measure by Hemoglobin concentration, and Hematocrit

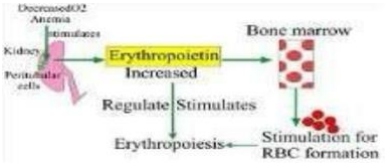
Missured either by (hematocrit g/dl) or hb consentration (%)

## Anemia and erythropoietin

- Anemia (hypoxia) triggers production of erythropoietin (Activates erythropiosis in bone marrow)
  Erythropoietin production can increase RBC production 5 folds in acute anemia, It's a potent hormone and in healthy patients the compensation is fast and complete
- Causes compensatory erythroid hyperplasia in bone marrow (BM)
- In acute anemia, production can increase by 5x or more in healthy people
- In severe cases, causes extramedullary hematopoiesis in secondary hematopoietic organs (spleen, liver and lymph nodes)
- Exceptions: anemia of renal failure (kidney is the organ responsible for erythropoietin production), anemia of chronic Inflammation (Explained in the recorded lecture : **https://elearning.ju.edu.jo/moodle10/mod/h5pactivity/view.php?id=370318)**

  Long duration high erythropoietin levels effects (in chronic forms of anemia ex thalassemia major) can not be corrected

  High erythropoietin levels on the long run causes a condition called extramedullary hematopiosis (production of RBCs out of bone marrow ( like spleen, liver, or even lymph nodes and causes hypertrophy in those organs)



## Classification according to cause

3 main categories

1- Blood loss

2- Diminished RBC production (Decreased bone marrow production)

- Iron deficiency anemia
- Anemia of chronic inflammation
- Megaloblastic anemia
- Aplastic anemia
- Pure red cell aplasia
- Myelophthisic anemia
- Myelodysplastic syndrome
- Anemia of renal failure
- Anemia of hypothyroidism

3- Increased destruction (hemolytic anemia)

Distruction either happens outside of the RBCs (induced by other factors eg malaria induced hemolysis or (mechanical damage), Or it happens inside the RBC due to a preexisting defect

- **Extrinsic factors** (infection, antibody, mechanical)
- **Intrinsic** RBC abnormalities:

1)Hereditary (membrane, enzyme, Hg abnormalities)

2)Acquired (Paroxysmal nocturnal hematuria)

## Classification according to morphology blood film

Blood smear (examination of blood samples via microscope).

We use this classification to reach to a diagnosis (How we decide what kind of anemia the patient has).
We preform a blood smear then use automated devices for testing.
This how we preform a CBC (complete blood count).
Normal values differ slightly between different testing devices.

### -**Size**: Normo, Micro, Macrocytic (MCV)

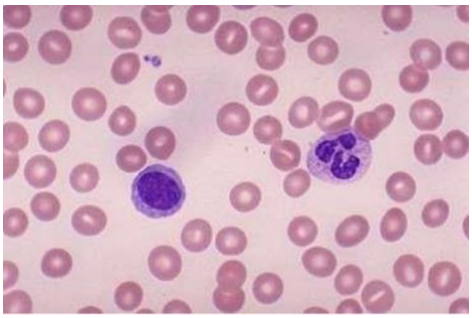
We usually compare the RBC to a lymphocyte to judge on its size (the size of one RBC is in similar diameter to a lymphocyte's nucleus.

### -**Color**: Normo, Hypochromic (MCH)

### -**Shape**: Anisopoikelocytosis (Or just Poikelocytosis): (spherocytes, sickle, schistiocytes), (RBC distribution width: Reflects Anisopoikelocytosis, High = abnormal shapes )

Hypochromic microcytic anemia usually reflects impaired Hg synthesis Heme (iron) or globulin deficiency

Macrocytic anemia reflects stem cell disease and defect in maturation



## RBC indices

In the good old days poor physicians had to do everything manually even counting RBCs and WBCs -thank god for technology- back then a physician could barely get the results for 10 patients in a day now we can get thousands in a way shorter time

- Can be directly measured, or automated
- Slight variation is present between labs, geographic areas (high altitude , higher Hb conc.)

- Sex (males typically have higher Hb concentrations due to androgens, while females may have lower levels during menstruation), age (neonates generally have higher Hb levels), race (African populations may have lower Hb levels compared to others), and mobility status (less physical activity can be associated with lower Hb concentrations)

- Reticulocyte count is used to distinguish between hemolytic anemia (where there is an increased destruction of red blood cells, prompting the bone marrow to produce more reticulocytes (immature red blood cells) meaning high reticulocyte count) and aregenerative anemia (occurs when the bone marrow fails to produce an adequate number of red blood cells, resulting in a low reticulocyte count.)

Reticulocytes are Larger , have DNA streaks makes it slightly basophilic, low percentage 0.5-1.5 % of RBCs

As we said before there's always a slight variation so always look at the normal range, There's also a slight differences due to different ages races and sex and there's always exceptions eg in pregnancy (lower hb), neonates (higher hb).

| | Units | Men | Women |
|---|---|---|---|
| Hemoglobin (Hb) | g/dL | 13.2–16.7 | 11.9–15.0 |
| Hematocrit (Hct) | % | 38–48 | 35–44 |
| Red cell count | $\times 10^6/\mu L$ | 4.2–5.6 | 3.8–5.0 |
| Reticulocyte count | % | 0.5–1.5 | 0.5–1.5 |
| Mean cell volume (MCV) | fL | 81–97 | 81–97 |
| Mean cell Hb (MCH) | pg | 28–34 | 28–34 |
| Mean cell Hb concentration (MCHC) | g/dL | 33–35 | 33–35 |
| Red cell distribution width (RDW) | | 11.5–14.8 | |

*Reference ranges vary among laboratories. The reference ranges for the laboratory providing the result should always be used in interpreting a laboratory test.

## Clinical features of anemia

- Dizziness due to hypotension
- Fatigue due to hypoxia
- Pallor obvious when examining the conjunctiva, nail-beds, sclera of the eye.
- Headache

**Adaptive changes:** (with prolonged hypoxia)

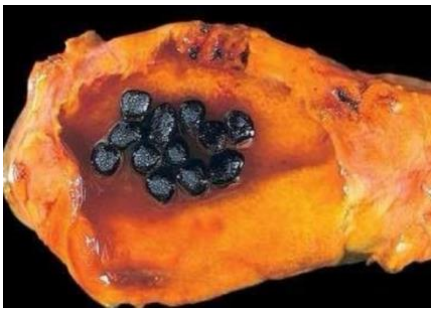
- Tachycardia
- Tachypnea
- Increased redcell 2,3-diphosphoglycerate. Facilitates the delivery of O2 (This molecule binds to hemoglobin and, in doing so, effectively displaces oxygen molecules, making it easier for hemoglobin to unload oxygen where it's needed most)

If the patient has heart or lung diseases, symptoms will be worse

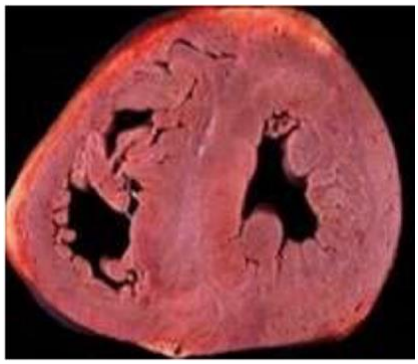
## Clinical symptoms in special types of anemia

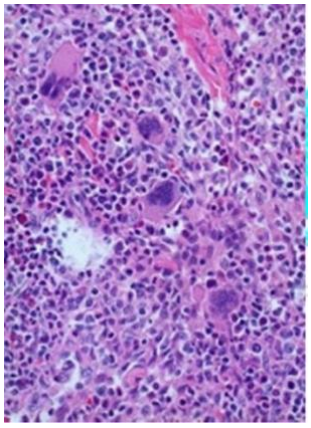
1- Chronic hemolytic anemia: jaundice ,pigmented gall bladder stones, red urine

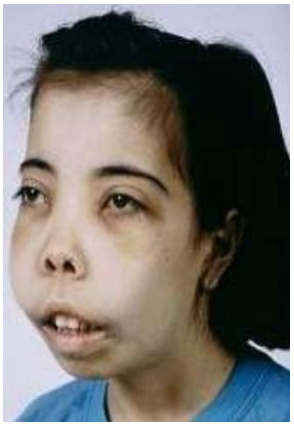
Hemolysis-> degradation of hemoglobin-> turns to bilirubin which is not soluble and gets deposited in tissue and causes the yellowish discoloration (jaundice)
It also forms pigmented (black) gallbladder stones different from the cholesterol white stones, Hemoglobin also after RBCs hemolysis could pass through the kidney and cause red coloration of the urine (not bleeding)

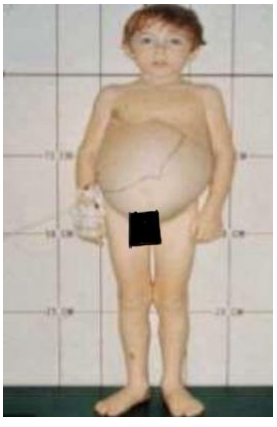


2- Extramedullary hematopoiesis: splenomegaly, hepatomegaly
3- Thalassemia major and sickle cell anemia: growth retardation, bone deformity (prominent cheeks and jaw), secondary hemochromatosis (damage to heart, endocrine glands) Due to prolonged exposure to high levels of erythropoietin









Prolonged exposure to erythropoietin can also suppress the hormone hepcidin, which plays a crucial role in blocking iron absorption. As a result, patients may absorb excessive amounts of iron from their diet, and since the body has limited mechanisms to excrete iron (primarily through the normal shedding of epithelial cells), it can accumulate in tissues, including the heart (leading to cardiomegaly and potentially heart failure) and endocrine glands, causing physical damage and in this phase it's usually fatal (secondary hemochromatosis).

These patients do not grow normally due to hypoxia, have enlarged abdomen (enlarged spleen and liver : if you take a tissue biopsy they'll look like bone marrow and you'll see Megakaryocytes, myeloid, erythroyed cells, They also have a distinctive bone shape : short structure, special skull shape called sickle face (larger bones because of the increase of hematopoietic cells)

## Anemia of acute blood loss

Sudden and fast, Could cause brain and major organ tissue necrosis leading to death

-Symptoms are related to decreased intravascular volume (hypovolemia and hypotension)

-If loss is >20% of blood volume, patient might have hypovolemic shock and die

We worry the most of shock so we could give fluids and depend on bone marrow to compensate the RBCs loss

- If a patient survived blood loss , the body responds by shifting fluid from interstitial to intravascular space, causing dilutional anemia and worse hypoxia (stays 2-3days)

Dilutional anemia occurs when a patient experiences bleeding that is subsequently stopped. For example, if a patient initially had a hemoglobin (Hb) concentration of 14 g/dL before bleeding, and it decreased to 10 g/dL due to the bleeding, it's not uncommon to find that the Hb concentration may decrease further to 8 g/dL after a few days. This decline does not necessarily indicate ongoing bleeding but is a result of a normal physiological response – the body shifts fluids from surrounding tissues into the bloodstream to restore blood volume, leading to a dilution effect on Hb concentration.

-Erythropoietin secretion is stimulated, activating BM erythropoiesis (needs 5-7days)

-In internal hemorrhage, iron is reclaimed from extravasated RBCs and used again in erythropoiesis

-In external and GIT hemorrhage, iron is lost, which complicates anemia

-The anemia is normochromic, normocytic, with reticulocytosis (bone marrow is active)

## Anemia of chronic blood loss

Arises from the gradual loss of blood in small amounts over an extended period

- Occurs when the rate of RBC loss exceeds regeneration
- Mostly occurs in gastrointestinal diseases (Peptic ulcers, hemorrhoids, colon cancer, small bowel inflammation), also in excessive menstruation
- Results in iron deficiency, anemia appears hypochromic and microcytic, low reticulocytes (decreased production).
  In this case there's always iron deficiency unlike acute blood loss anemia (deficiency only happens with external bleeding).

## TEST YOURSELF

**1. In anemia, what stimulates the production of erythropoietin in response to decreased oxygen-carrying capacity?**

**A) High iron levels**
**B) Low reticulocyte count**
**C) Tissue hypoxia**
**D) Elevated bilirubin levels**

**2. Reticulocyte count is used to distinguish between:**

**A) Hypothyroidism and hyperthyroidism**
**B) Hemolytic anemia and aregenerative anemia**
**C) Iron-deficiency anemia and megaloblastic anemia**
**D) Sickle cell anemia and thalassemia major**

**3.Which clinical symptom is commonly associated with anemia with prolonged hypoxia?**

**A) High blood pressure**

**B) Tachycardia**

**C) Increased oxygen saturation**

**D) Improved exercise tolerance**

**4.In patients with extramedullary hematopoiesis, which organs are most likely to become enlarged?**

**A) Lungs and kidneys**

**B) Spleen and liver**

**C) Heart and brain**

**D) Stomach and pancreas**

**5.What is a typical clinical feature of chronic hemolytic anemia?**

**A) Cyanosis**

**B) Jaundice**

**C) Hypertension**

**D) Increased platelet count**

**6.What is the term for the physiological response that leads to a decrease in hemoglobin concentration after bleeding has stopped?**

**A) Hypoxia**

**B) Dilutional anemia**

**C) Reticulocytosis**

**D) Hemolysis**

**Answers: 1)C / 2)B / 3)B / 4)B / 5)B / 6)B**

فاحشدوا ما شئتم من قوات وأجلبوا بخيلكم ورجلكم، براً وبحراً وجواً، فقد أعددنا لكم أصنافاً من الموت

ستجعلكم تلعنون أنفسكم، ولن تجدوا منّا ضعفاً أو جزعاً أو تراجعاً، وليس لكم منّا إلا السيف والنار.

- الناطق العسكري باسم كتائب القسام، أبو عبيدة.

**اللهمّ عليكَ باليهودِ الغاصبين، ربّنا اشدُد على قلوبهم فلا يؤمنوا حتّى يرَوا العذابَ الأليم،**

**اللهمّ أزِل مُلكهم، واقتُل جُندهم، ولا تجعل لهُم سبيلًا على عبادكَ المؤمنين.**

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