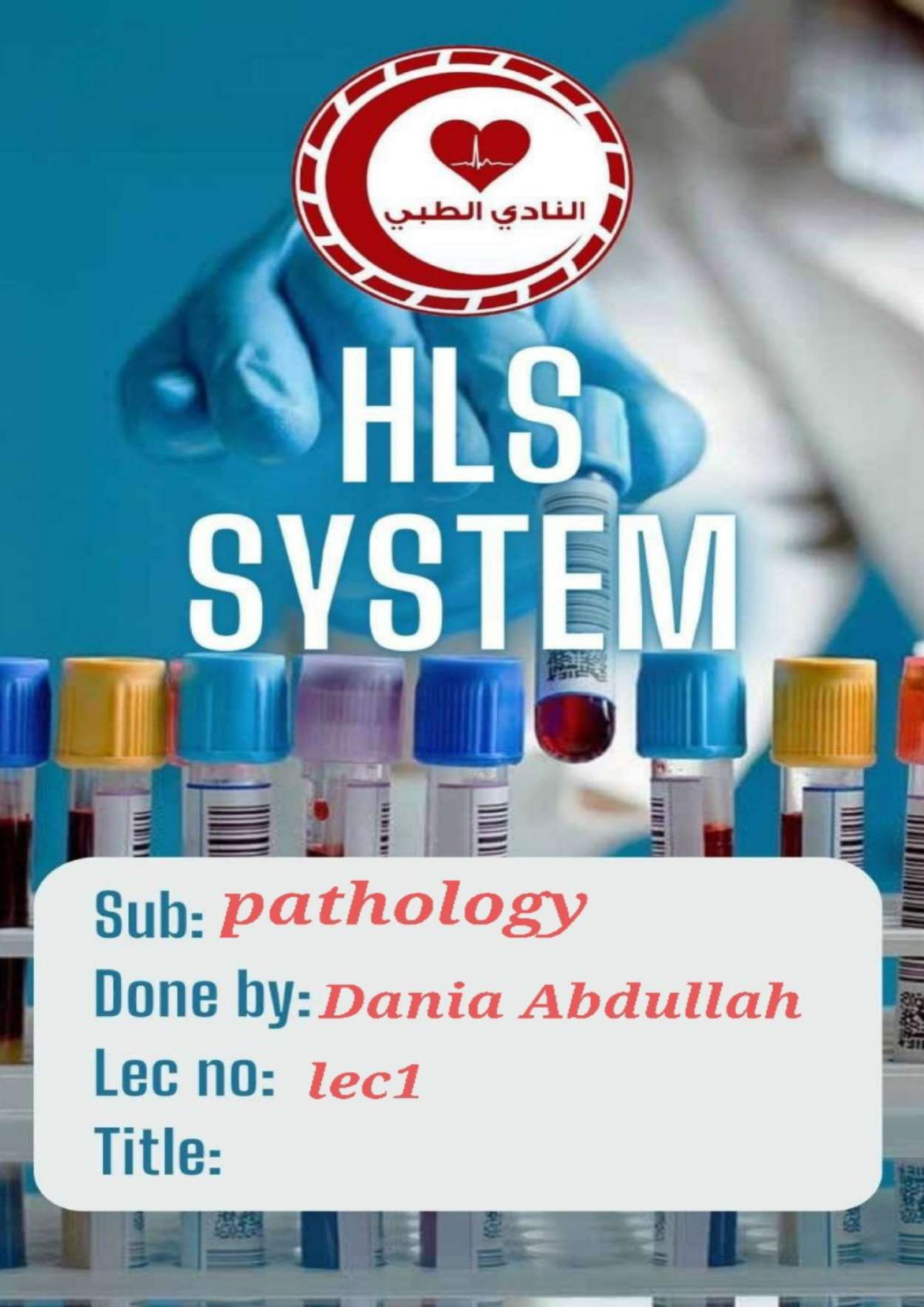


Sub: *pathology*

Done by: *Dania Abdullah*

Lec no: *lec1*

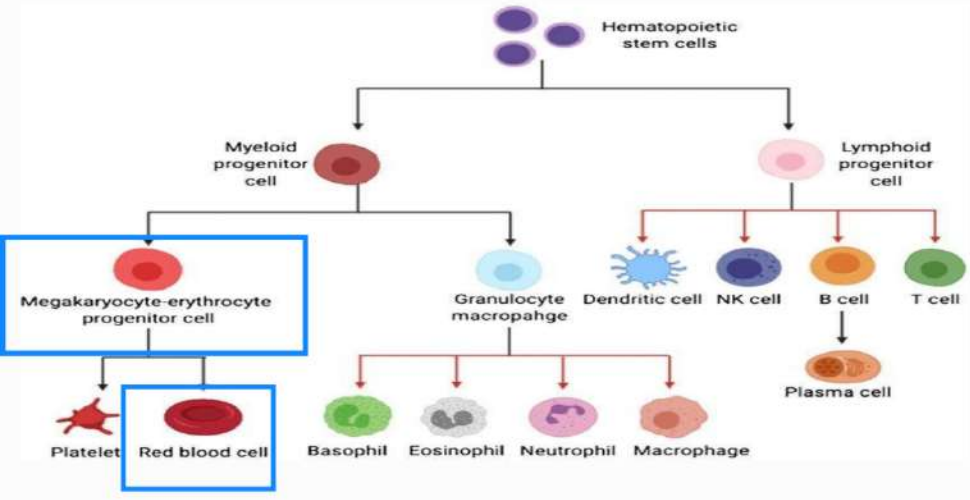
Title:

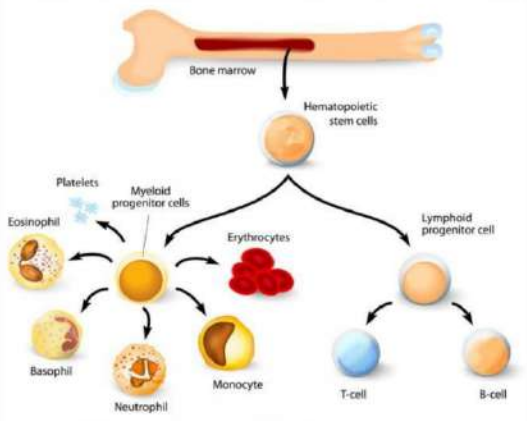
LECTURE(1) SUMMARY

Hematopoiesis: is the formation of blood cellular components.

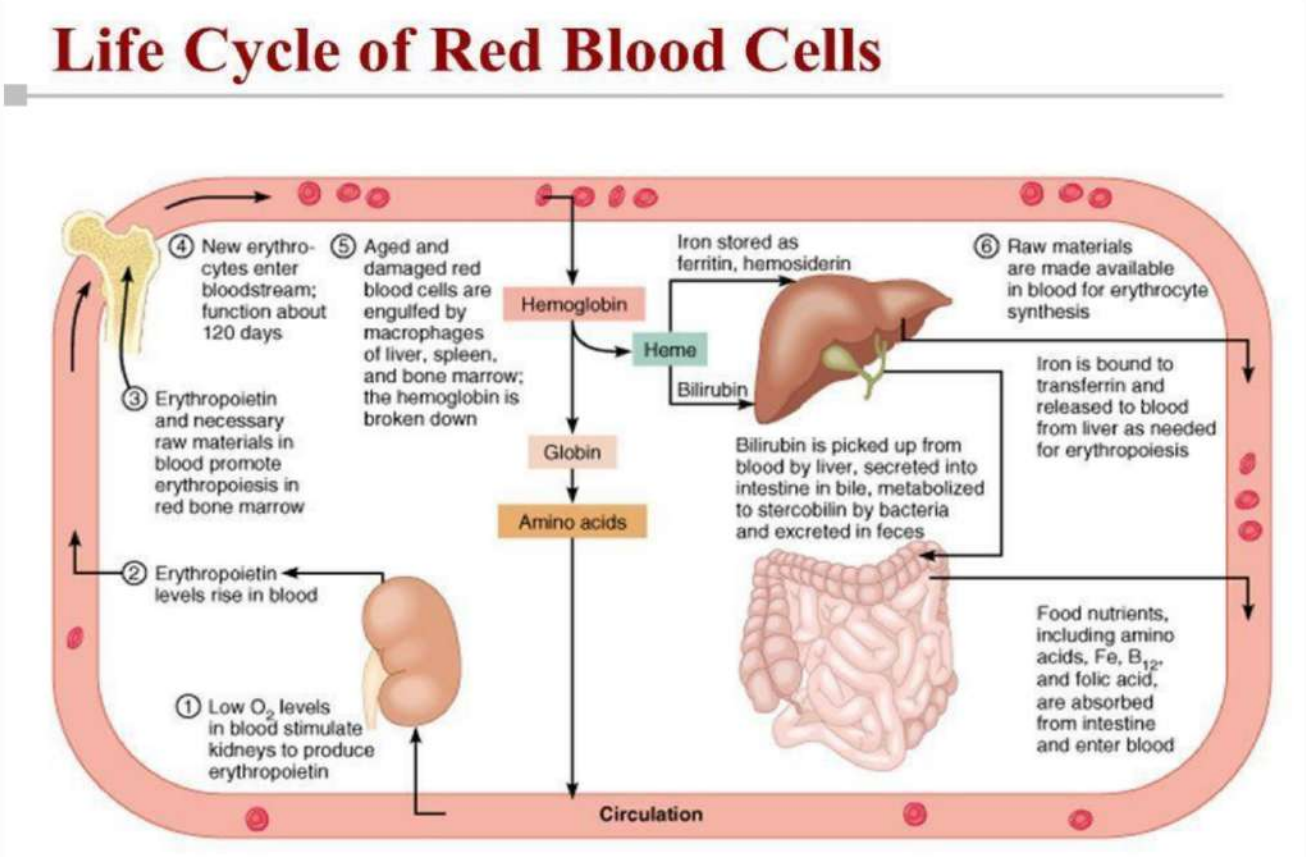
-prenatally, it occurs in the yolk sack, then in the liver and lastly in the bone marrow.
- In adults it occurs in the bone marrow and lymphatic tissues.

#NOTE: in crtain diseases erythropoiesis also occurs outside the bone marrow (spleen and liver), this is termed extramedullary hematopoiesis.





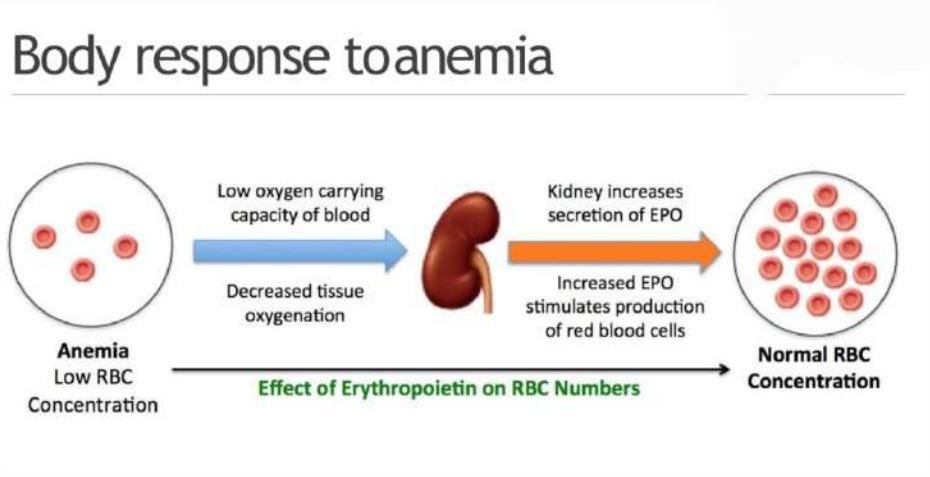
Erythropoiesis: is the process which produces red blood cells (erythrocytes).
= the development from erythropoietic stem cell to mature red blood cell.



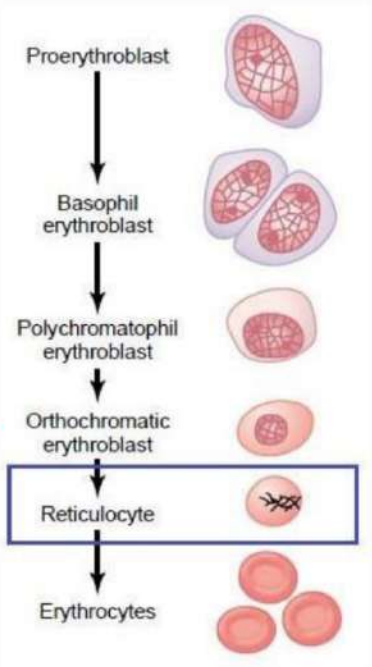
Complete blood count:

- RBC COUNT: the # of RBCs/unit of volume.
- Hemaocrit: a measure of the propotion of blood that is composed of RBCs.
- MCV: the average size of the RBCs.
- MCH: the average amount of Hemoglobin/RBC.
- MCHC: the average amount of hemoglobin in a given volume of RBCs
- RDW: the variation in size of RBCs in a sample.

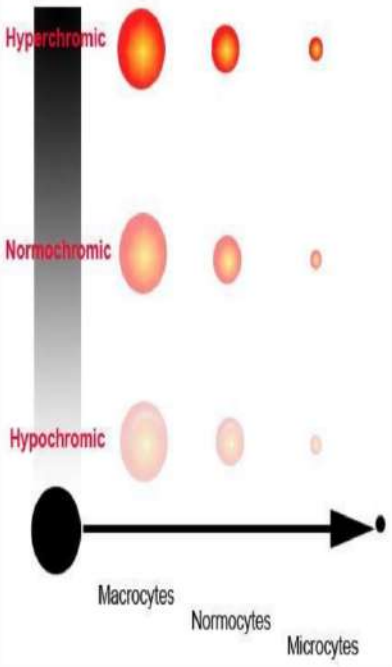
Reticulocyte count: percentage of the total number of RBCs.
#note: normally reticulocyte count is about 1-2%.



ANEMIA: is the reduction in the oxygen transporting capacity of blood, which results from a reduction of the total circulating red blood cell mass to below normal levels.



- MCV - Mean Corpuscular Volume, a measurement of the average size of RBCs (fl)
- MCH - Mean Corpuscular Hemoglobin - the mean cell hemoglobin (pg/cell) picogram per cell
- MCHC - Mean Corpuscular Hemoglobin Concentration - the mean concentration of hemoglobin per volume of red cells (gm/dl)
- RDW - Red Cell Distribution Width - a variation in the size of RBCs

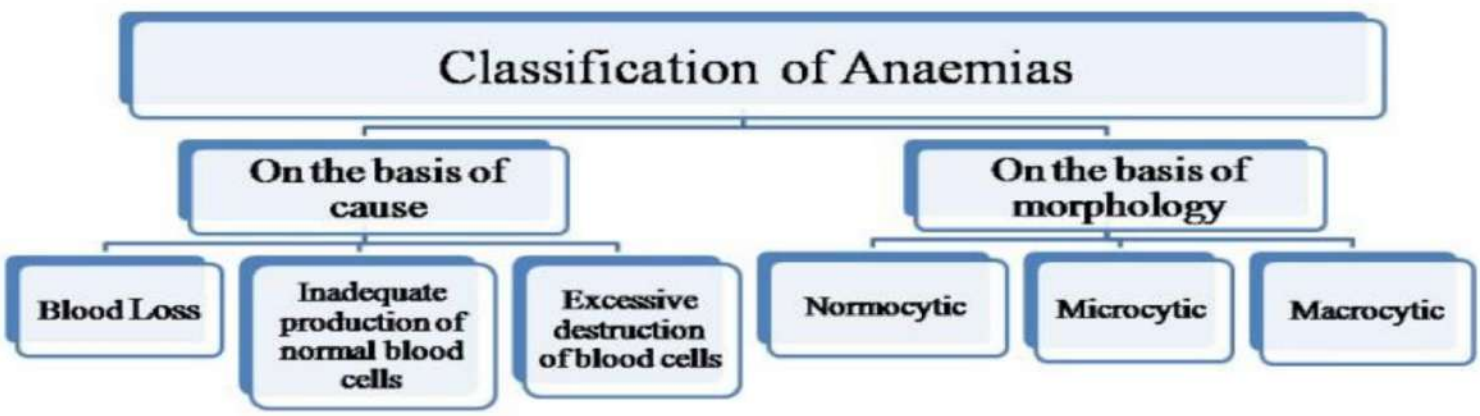


It can result from:

1) Excessive bleeding.
2) Increased red cell destruction.
3) Decreased red cell production.

in males: Hb < 13g/dl
in females: Hb < 12 g/dl

#note: Anemia is not a diagnosis, but a sign of disease.



Clinical cues:

Anemia in general: fainting, pallor, tachycardia
Hemolysis: jaundice, gallbladder sotones, red urine.

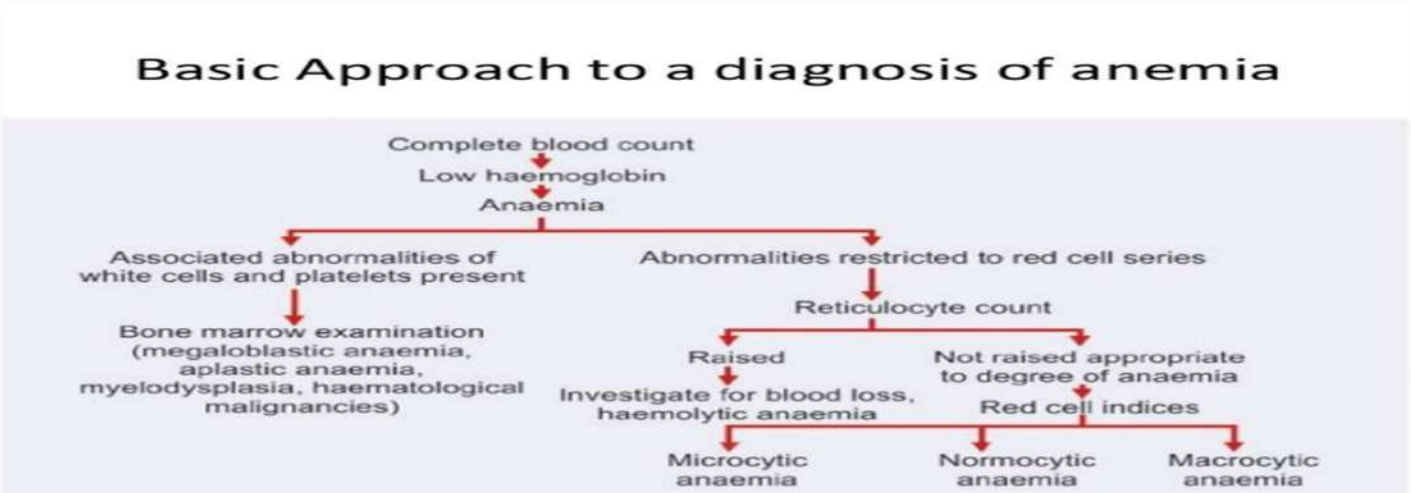
Approach:

1) do CBC/peripheral blood smear.
2)reticulocyte count
3) MCV, MCH, RDW
4) Bone marrow biobsy(not usually done)

Reticulocye count:

* anemias are categorized on the basis of the reticulocyte response.

* an elevated reticulocyte count implies a bone marrow response to either incresesed RBC destruction(hemolysis) or acute/chronic blood loss.
** reticulocyte count>2% then the BM is producing RBCs at accelerated pace



Microcytic anemia:

- The main problem in microcytic anemia is decreased production of Hb

-RBC is produced from subsequent division of erythroblasts, and during Hb deficiency, erythroblasts divides too much. As a result, RBCs become small and microcytic anemia occurs.

Iron absorption in small intestine:

- Fe is absorbed in duodenum. Protein called FERROPORTIN plays a key role in Fe transport from lumen to enterocyte to blood.
- TRANSFERRIN transports iron in blood and takes it to liver and bone marrow macrophages for storage
- Stored intracellular iron is bound to FERRITIN (high is a good indicator of the adequacy of body iron stores)
- There is no real way to get rid af Iron from body. So, absorption by enterocytes is regulated (some by shedding and menstruation)
- Iron is always bound ta something because free Fe generates free radicals

(1) lumen to enterocyte

* ferric +3 to ferrous +2 (reductase)
* DMT1 via apical membrane.

(2) enterocyte to blood

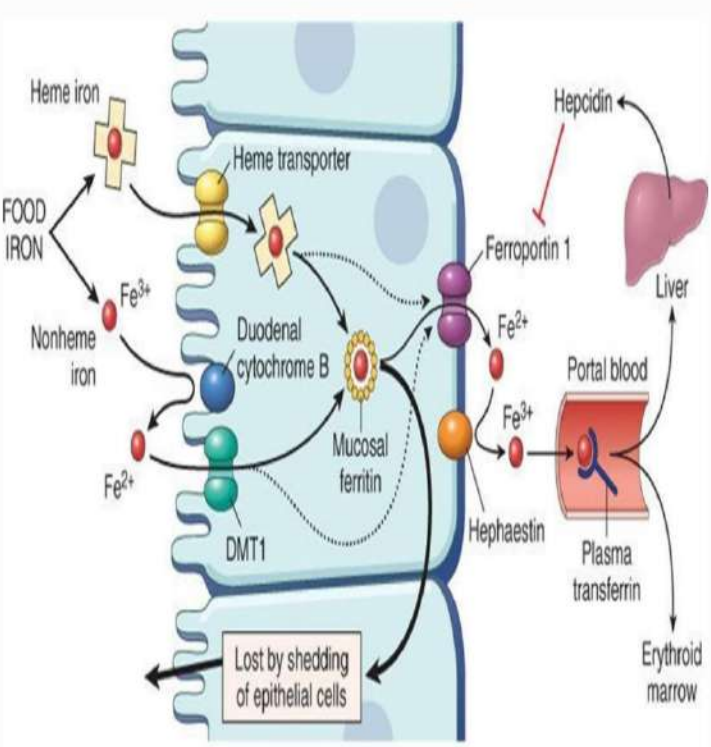
*via ferroportin1
* ferrous to ferric (oxidase)

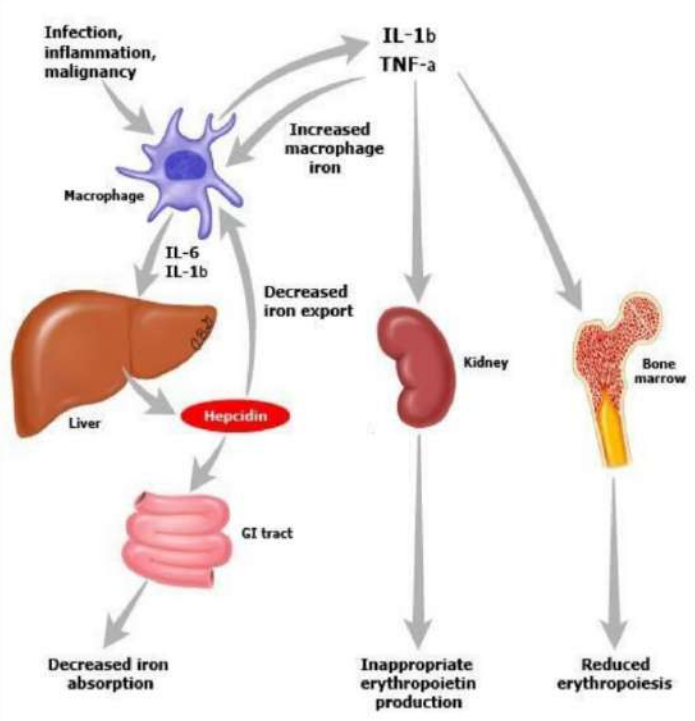
In plasma via transferrin to the LIVER

In liver :

* Hepcidin produced by liver that's Induced by IL-6.

inhibits Ferroportin...
High Hepcidin...
Low ferroportin..
Low iron absorption...





Causes of iron deficiency anemia:

- Malnutrition (vegetarian diet)
- Malabsorption as in celiac disease, or after gastrectomy (acid is needed for Fe absorption)
- Increased demands as in pregnancy, labor & infancy.
- chronic blood loss such as gynecological bleeding (menorrhagia) and GIT bleeding (peptic ulcer, cancer, polyps, inflammatory bowel disease and others)

IDA pathohysiology:

- Iron is essential for hemoglobin synthesis during erythropoiesis
- Impaired delivery of iron to erythroid precursors results in decreased erythropoiesis
- Iron deficiency leading to IDA is a chronic process
- Initially normal RBCs are produced
- Later, decreased iron transport to bone marrow results in microcytic hypochromic RBCs

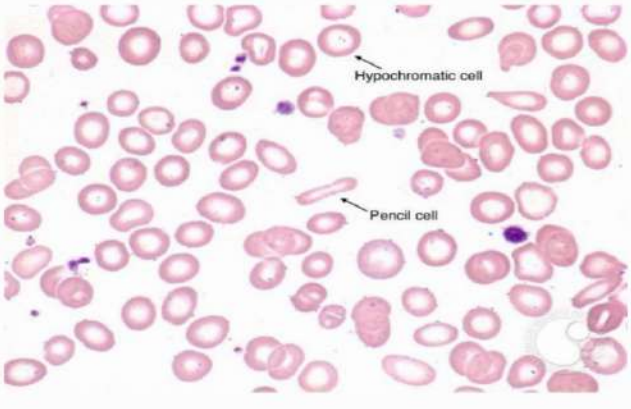
Iron deficiency anemia Fe lab measurments:

- Serum Fe - measures Fe in blood (most of it is bound to transferrin)
- TIBC (total iron binding capacity) - tells total transferrin in blood. Normally, I in every 3 transferrin in blood is bound to Fe.
- % saturation - % saturation of transferrin by Fe
- Serum ferritin - indication of how much Fe is in storage sites.

#note:When ferritin ↓, TIBC ↑and vice versa.

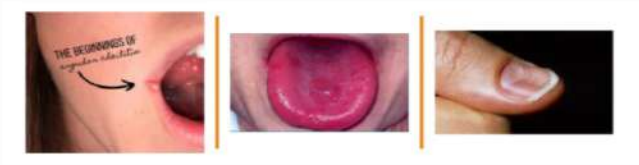
Iron deficiency anemia Lab findings:

- Microcytic, hypochromic anemia with RDW ↑
- ↓ferritin↑ TIBC
- ↓serum iron,↓ %saturation
- Blood smear: Microcytic anemia with:
  1) Poikilocytosis (variable shapes),
  2) anisocytosis (variable size),
  3)cigarette- shaped RBC or pencil cell.



IDA clinical presentation:

- in most cases iron deficiency anemia is asymptomatic.
- Anemia symptoms "weakness and pallor" may be present in severe cases
- With long-standing severe anemia, thinning, flattening, and eventually "spooning" of the fingernails sometimes appears. Also called Koilonychia (spoon shaped nails)
- Sometimes Pica (psychological drive to eat dirt - perhaps to get Fe) may develop with long standing anemia.
- Glossitis and angular stamatitis (cheilitis)



IDA treatment:

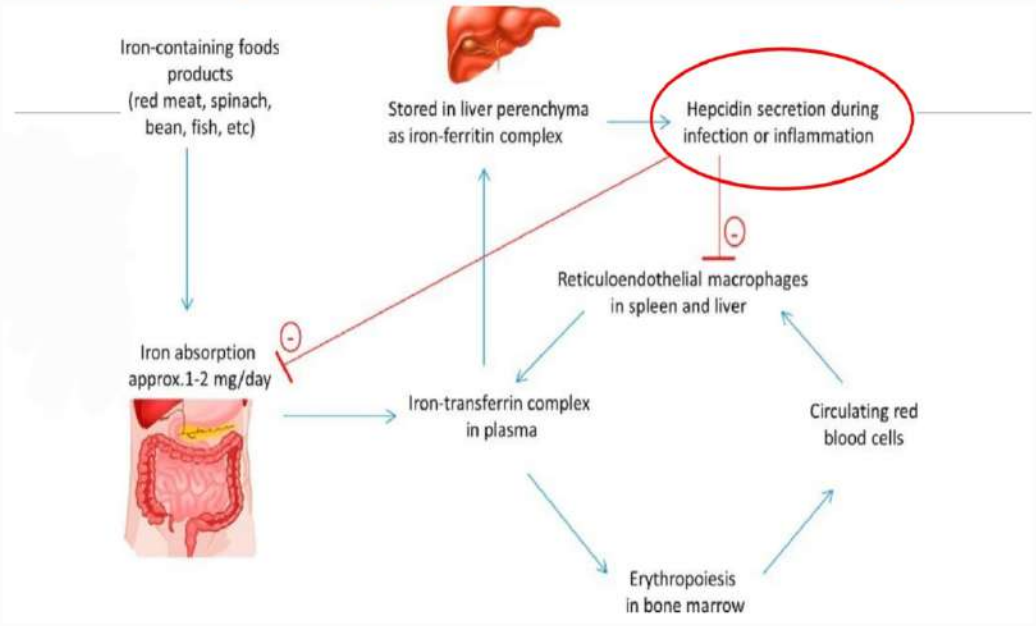
- It is easy to treat (iron supplementation).
- It may be the earliest manifestation of a serious underlying diseases (10-20% of iron deficient patients have cancer, up to 50% have GER/PUD).

Anemia of chronic disease/anmia of inflammatiom:

- Anemia of chronic disease (ACD) is the most common anemia in hospitalized patients. Pathophysiology: during acute/chronic inflammation, acute phase proteins are produced (an example is Hepcidin).
- Hepcidin causes anemia by:

1 . Erythropoietin production (indirectly by IL-l b and TNF-a)
2.Hepcidin interacts with iron export protein ferroportin, thus inhibiting iron absorption from the gastrointestinal tract.
3. Decreases release of iron from macrophages.

Note: advantage of Hepcidin is that bacteria need Fe to grow and flourish.



Mechanism for anemia of chronic disease/anemia of inflammation(ACD/AI)

- In thepresence of infection, inflammation, or malignancy, the macrophage produceS IL-6 and IL- I b, which induce the production of hepcidin by the liver.
- Hepcidin reduces plasma iron levels [characteristic of ACD/AI Inflammatory cytokines such as IL-I b and TNF-a] reduce erythropoietin production

Anemia of chronic disease/anemia of inflammation lab findings:

- ↑ ferritin, ↓TIBC
- ↓ serum iron (bone marrow takes Fe From serum as macrophage isn't giving it)
- ↓ % saturation

Treatment of ACD:

- Treat underlying cause of chronic disease (to reduce hepcidin)
- Exogenous erythropoietin (especially helpful in cancer patients)

	Fe deficiency anemia	Anemia of chronic disease
Serum Fe	↓	↓
Transferrin/TIBC	↑	↓
Ferretin	↓	↑