النادي الطبي

HEMATOPOIETIC & LYMPHATIC SYSTEM

SUBJECT : _____

LEC NO. : 2

DONE BY : Tabark Aldaboubi

وَقُل رَّبِّ زِدْنِي عِلْمًا

Hemato-Lymphoid System HLS

DR. DUA ABUQUTEISH

iron Anemia of chronic → production of home بقللوا فنال] decresed production of Hb
Thlasemia → المشكلة فيه تكوين الجلوبين

لما يتم انتاج ال RBC بال bone marrow
وما يكون عندي Hb كافي نعشان bM تحاول
توزعه بالتساوي على ال RBC بتصغر حجم
ال RBC بعدها تتبطل قادرة تحافظ على
التركيز بصير Microcytic

THE RISK OF Iron Deficiency

IRON DEFICIENCY IS THE MOST COMMON NUTRIENT DEFICIENCY IN THE WORLD[1]

4 TO 5 BILLION

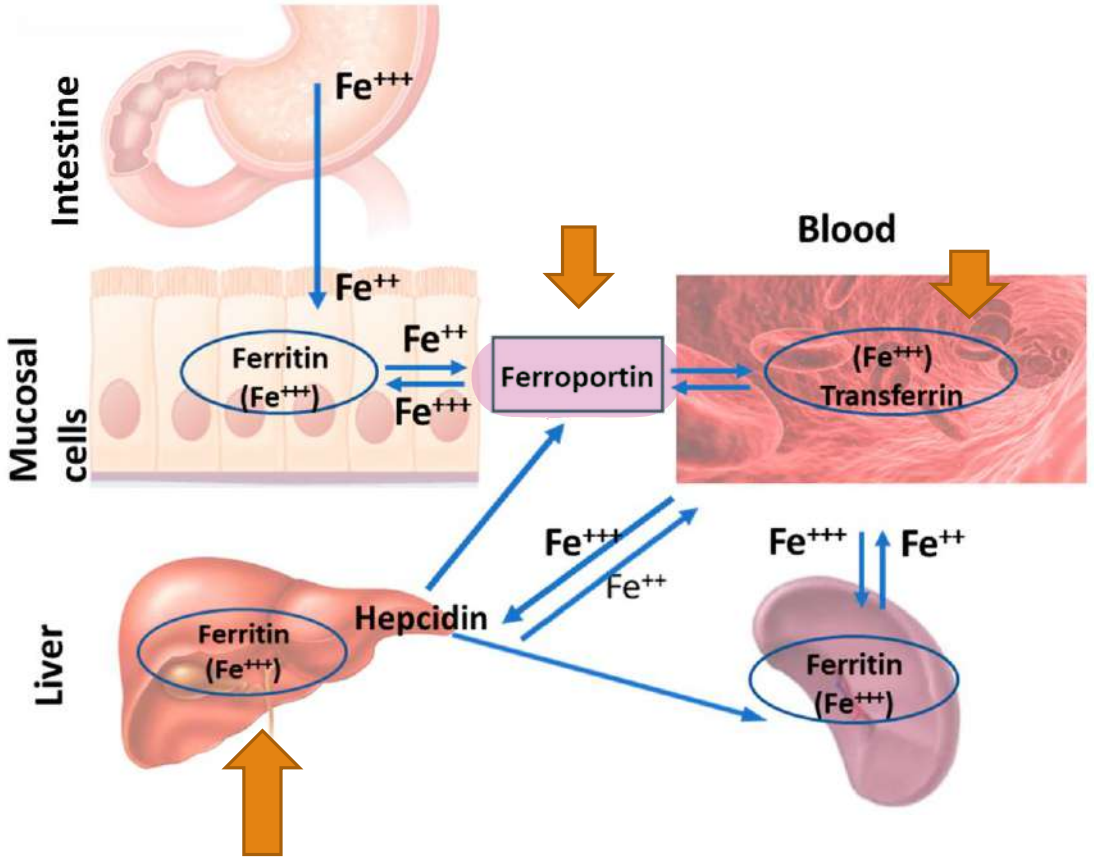
Up to 4 to 5 billion people may suffer from iron deficiency.[2]

Although prevalences can vary across communities, iron deficiency anaemia affects approximately 15% of the world population.[3]

111 MILLION

In the high developed countries, 9.1% of the population is affected resulting in 111 million affected people.[4]

Review of normal iron metabolism



- Fe is absorbed in **duodenum**. Protein called **FERROPORTIN -** transports Fe 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)**

يدخل الـ iron للجسم بختلط مع احماض المعدة وهو مهم جدًا لامتصاص الحديد يروح على (duodenum) يتم امتصاصه

يدخل على الدم عن طريق Ferroportin بلاقيه بروتين ناقل للحديد Transferrin كل 3 Transferrin يربطوا بـ 1 iron

بعيش بالدم لحد ما يوصل للكبد، الجسم بحتاج مخزون فيه الحديد (بتخزن بالـ hepatocyte macrophages) على شكل Ferritin

لما يوصل مخزون الحديد بالجسم للحد الكافي والمطلوب الكبد بتبطل تحتاج الحديد فبتفرز Hepcidin

الـ Hepcidin وظيفتين

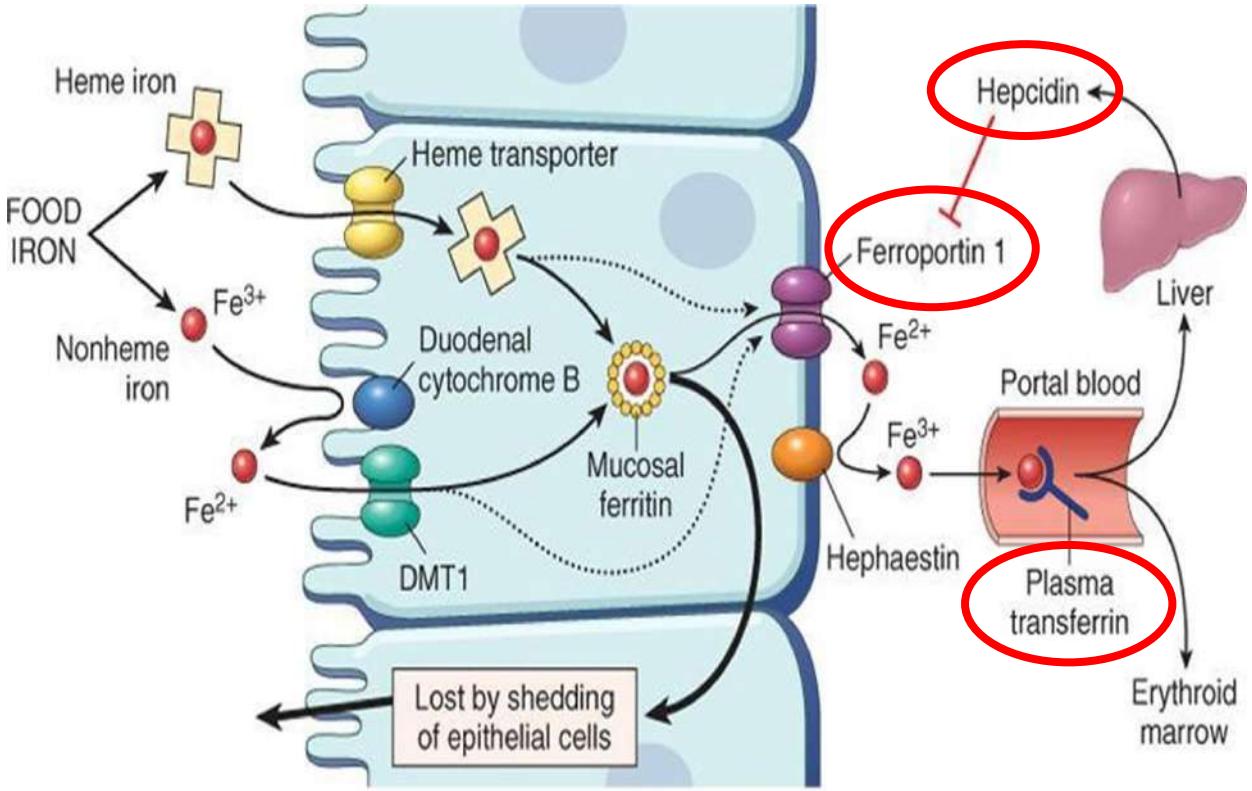
- يمنع خروج الحديد من الـ macrophage
- يمنع عمل الـ Ferroportin [دخول الحديد من الـ interocyte للدم]

Review of normal iron metabolism

➢Normally, **1 in every 3 transferrin in blood is bound to Fe.**

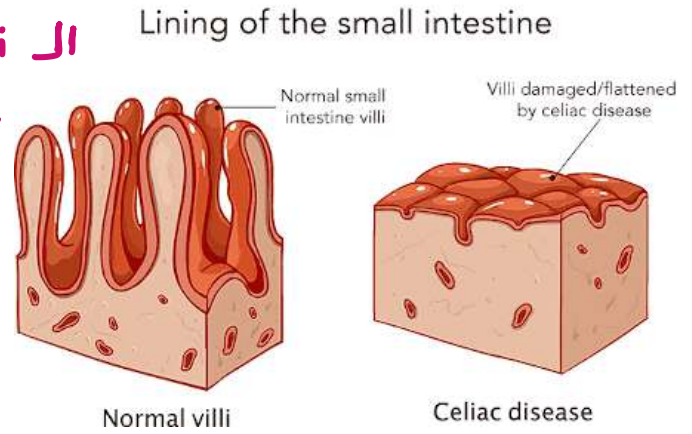
➢There is no real way to get rid of Iron from body. So, absorption by enterocytes is regulated (some by shedding and menstruation)

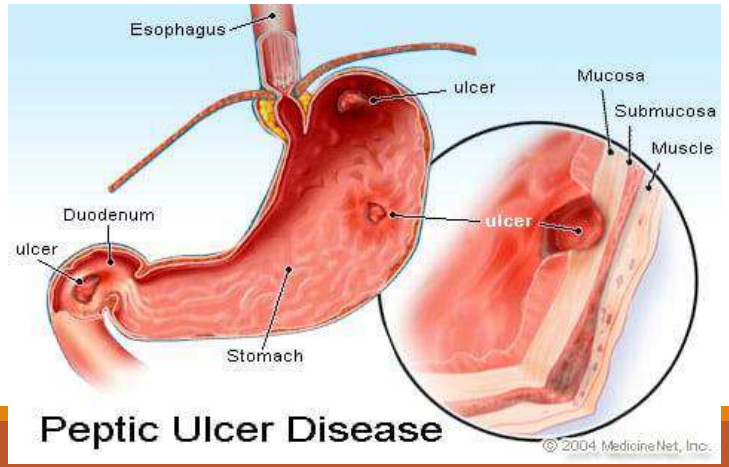
➢To regulate iron absorption, **Hepcidin** is produced from the liver, it interacts with ferroportin, and inhibits iron absorption from the gastrointestinal tract.



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)





Iron deficiency anemia Pathophysiology

- Iron is essential for hemoglobin synthesis during erythropoiesis
  - Impaired delivery of iron to erythroid precursors results in decreased erythropoiesis

الجسم رح يستخدم المخزون بحيث يعوض النقص الي عنده بخلص المخزون وما في حديد بدخل بالتالي بنقص الهيموغلوبين

- 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

اجا مريض (Anemic, weakness, Pallor) عملنا له CBC ← (↓Hb و ↓MCV, ↓MCH) وطلعت عنده (hypochromic microcytes)

Anemic of chronic desease, Thlasemia, iron deficiency ← بفكر بـ

Fe lab measurement:

كونه الـ most common ← هاي الشغلات ← iron pofile بطلب فيه

- **Serum Fe** – measures Fe in blood (most of it is bound to transferrin) ← قديش فيه iron بالدم
- **TIBC (total iron binding capacity)** – tells total transferrin in blood. Normally, 1 in every 3 transferrin in blood is bound to Fe. قديش Tranferrin رح تترتبط بالـ blood

↓
- **% saturation** – % saturation of transferrin by Fe ← نسبة اشباع الـ Transferrin بالـ iron
- **Serum ferritin** – indication of how much Fe is in storage sites

↓ ferritin ← الكبد بعرف انه فاضي حديد كافي يرجع

Transferrin يفرز (بروتين بيتم صناعته بالكبد) يرجع يفرز Transferrin وصيلك بزيد Transferrin الـ

- **When ferritin↓, TIBC ↑ and vice versa**

Iron deficiency anemia
Clinical presentation

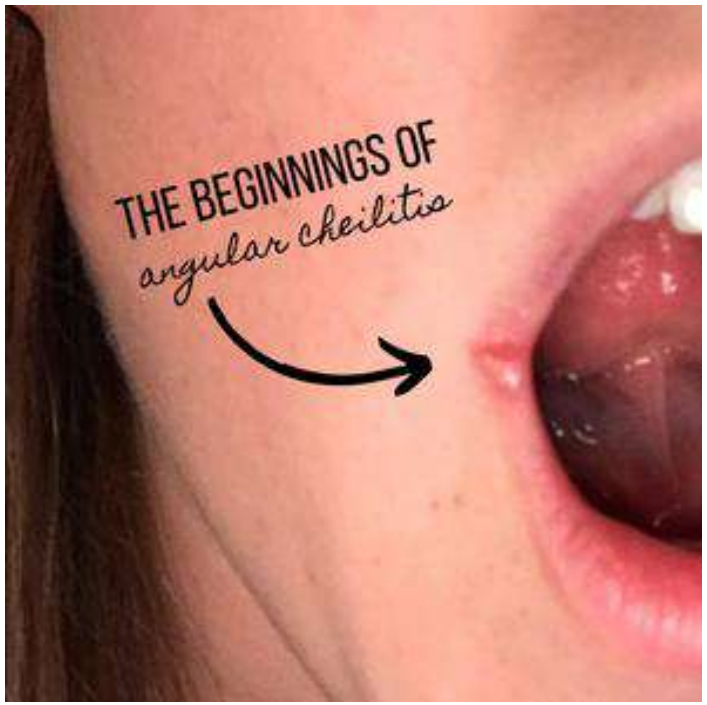
- In most cases iron deficiency anemia is asymptomatic.
- Anemia symptoms “**weakness** and **pallor"** may be present in severe cases
- With long-standing severe anemia, thinning, flattening, and eventually **"spooning" of the fingernails** sometimes appears. Also called **Koilonychia** (spoon shaped nails)

↳ خصوصا بالاطفال

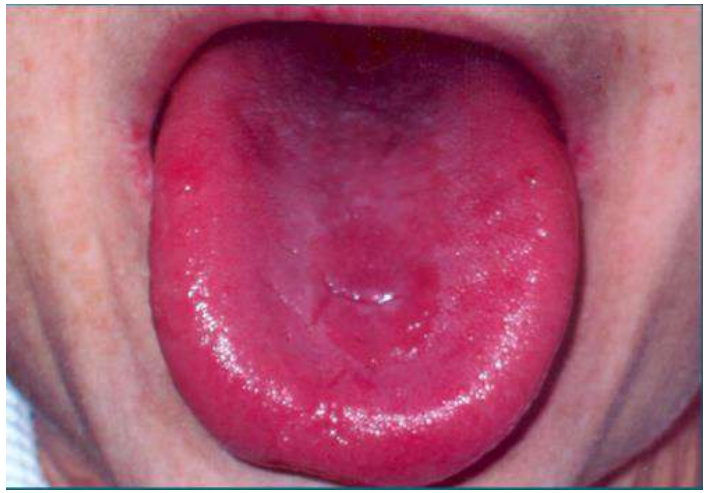
- Sometimes Pica (psychological drive to eat dirt – perhaps to get Fe) may develop with long standing anemia
- Glossitis and angular stomatitis (cheilitis)

inflammation
باللسان

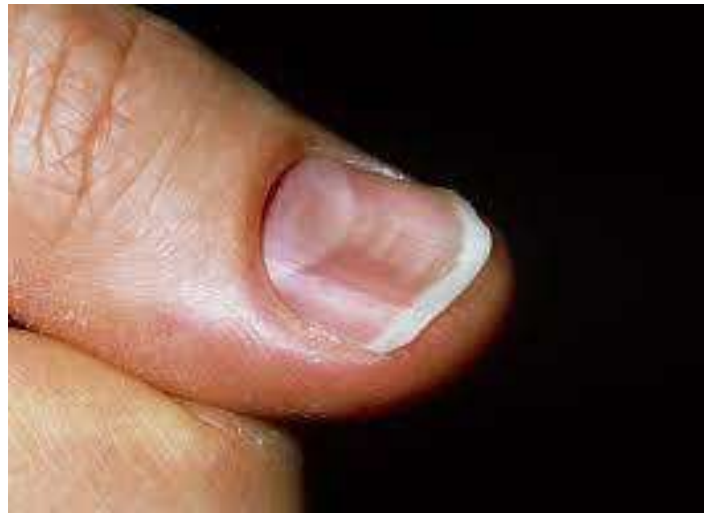
↳ angle
تاعت
mouth ال



stomatitis



Glossitis



(spoon shaped nails)

Iron deficiency anemia
Clinical presentation

Iron deficiency anemia
Lab findings

CBC

Variation in Size

- **Microcytic, hypochromic anemia** with ↑RDW

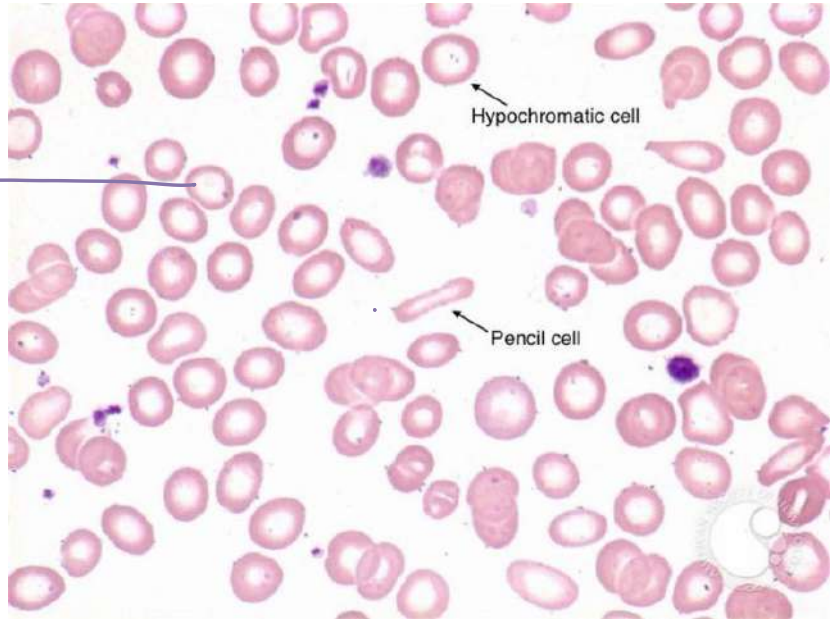
(RDW is like standard deviation of size of RBC; larger the variation in RBC sizes, larger the RDW)

لونها فاتح

بسبب نقصان Hb الـ

- ↓ferritin, ↑TIBC
- ↓serum iron, ↓%saturation
- **Blood smear**: Microcytic anemia with:

Poikilocytosis (variable shapes), anisocytosis (variable size), cigarette-shaped RBC or pencil cell



Blood smear – Iron def. anemia

Iron deficiency anemia Treatment

- It is easy to treat (iron supplementation) and saves unnecessary tests/treatments.

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

Peptic ulcer desease

Anemia of chronic disease/anemia of inflammation (ACD/AI)

Anemia of chronic disease/anemia of inflammation (ACD/AI)

- Anemia of chronic disease (ACD) is the most common anemia in hospitalized patients

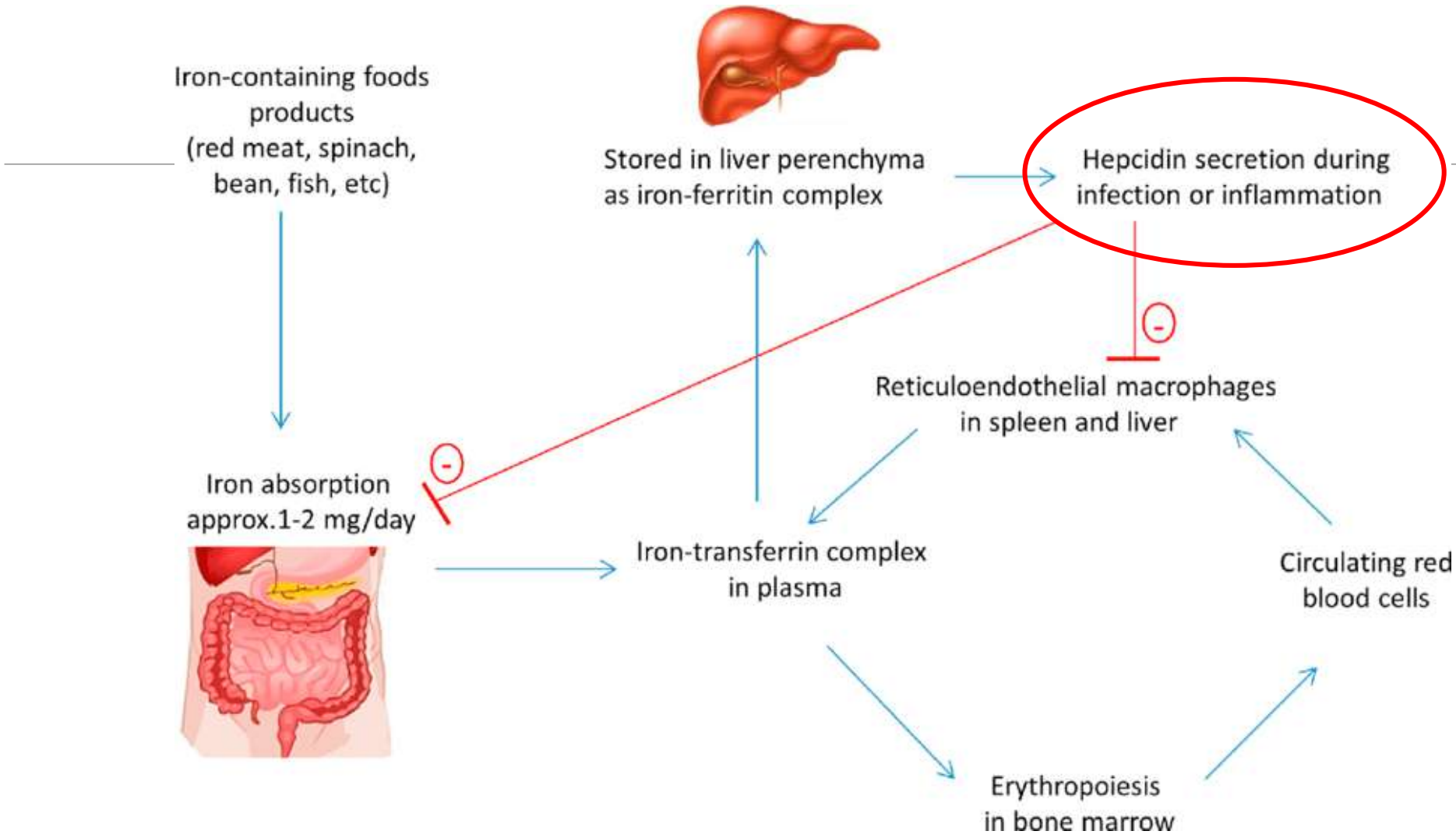
Pathophysiology: during acute/chronic inflammation, acute phase proteins are produced (an example is Hepcidin).

such as: C reactive protein

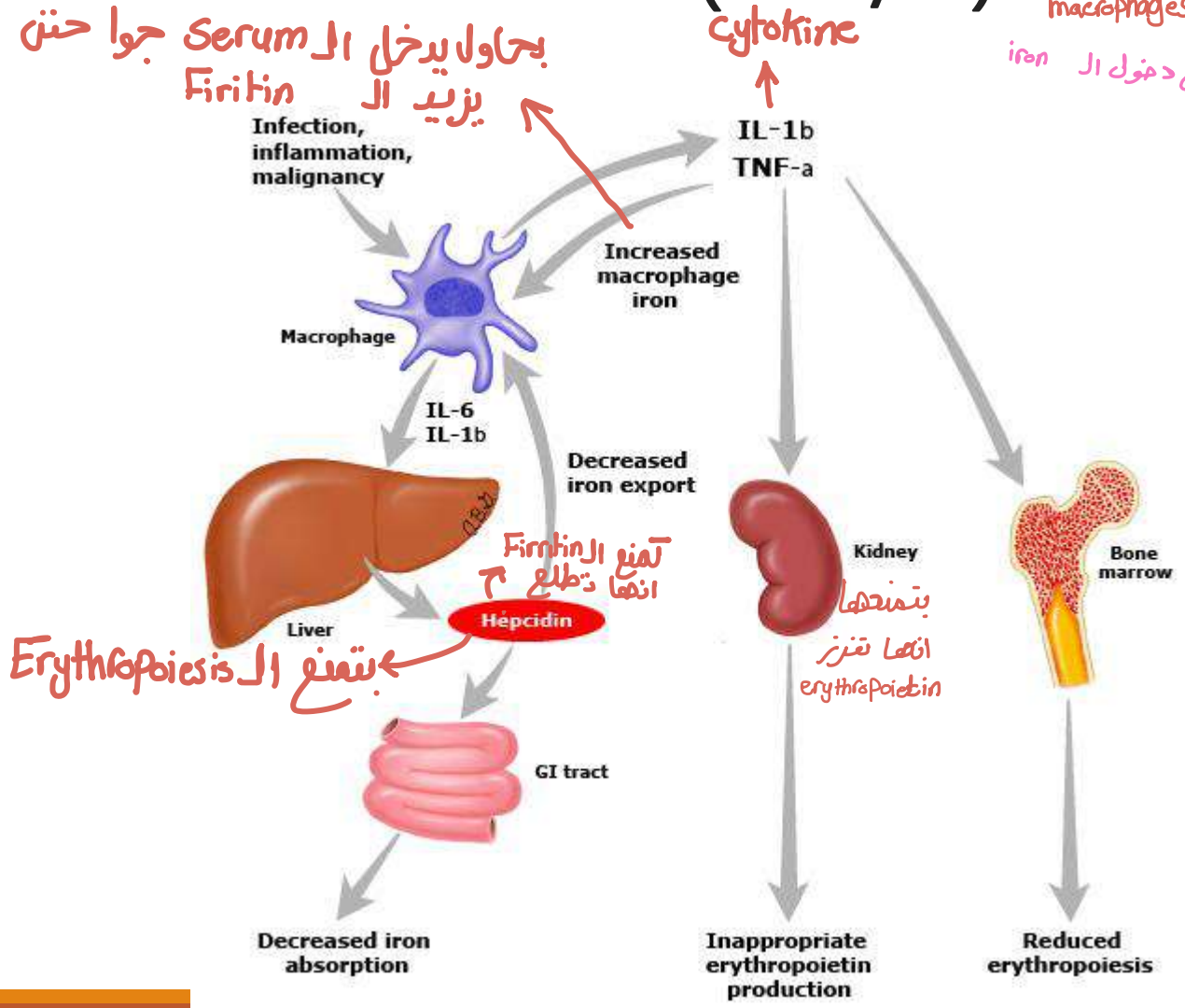
Hepcidin causes anemia by:

1. ↓Erythropoietin production (indirectly by IL-1b 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.


Iron-containing foods products (red meat, spinach, bean, fish, etc)
Stored in liver perenchyma as iron-ferritin complex
Hepcidin secretion during infection or inflammation
Reticuloendothelial macrophages in spleen and liver
Iron absorption approx.1-2 mg/day
Iron-transferrin complex in plasma
Circulating red blood cells
Erythropoiesis in bone marrow

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

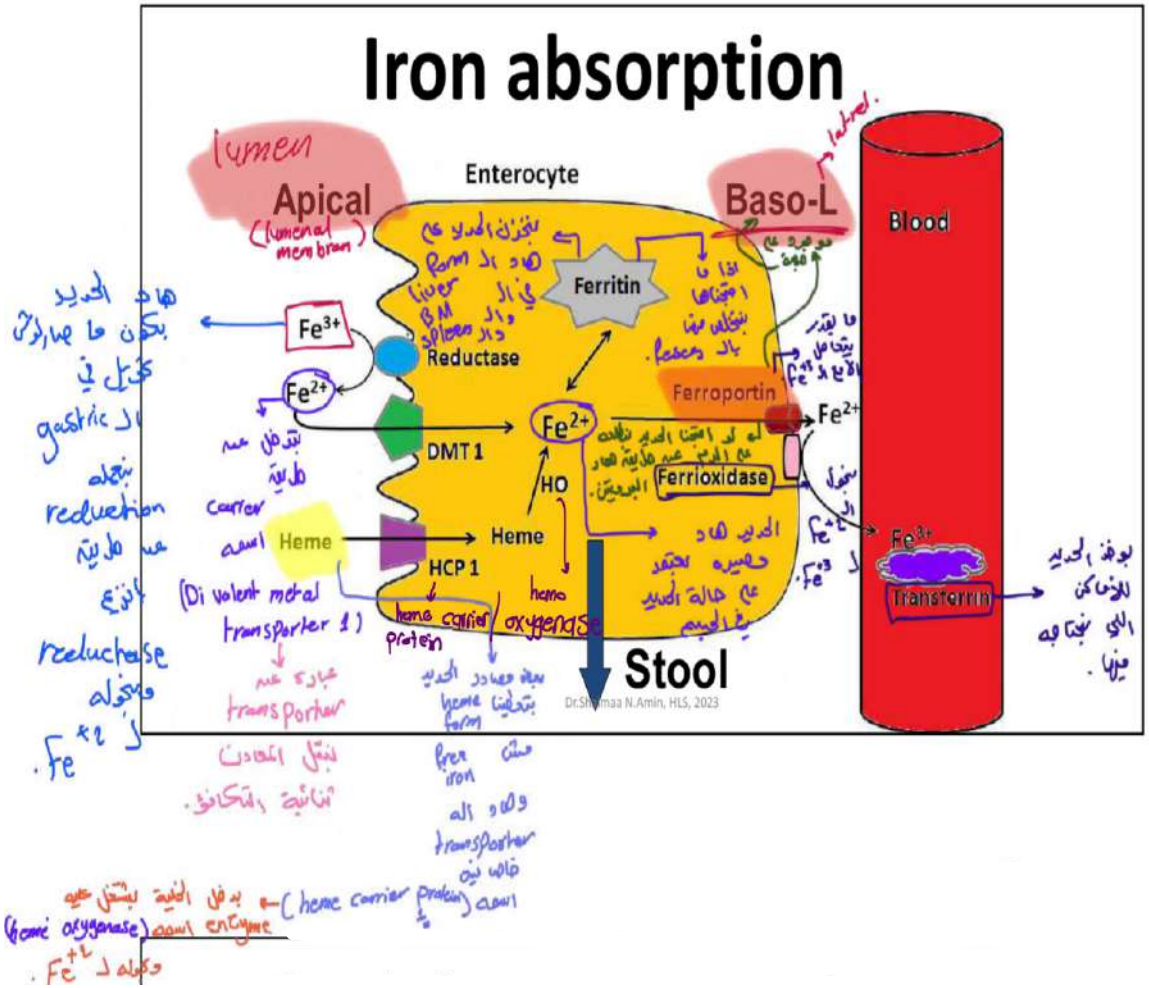


A proposed mechanism for ACD/AI is shown here. In the presence of infection, inflammation, or malignancy, the **macrophage is stimulated to produce IL-6 and IL-1b**, which **induce the production of hepcidin by the liver.**

Hepcidin reduces plasma iron levels characteristic of ACD/AI.

Inflammatory cytokines such as IL-1b and TNF-a reduce erythropoietin production

ربط مع الفسيو👈



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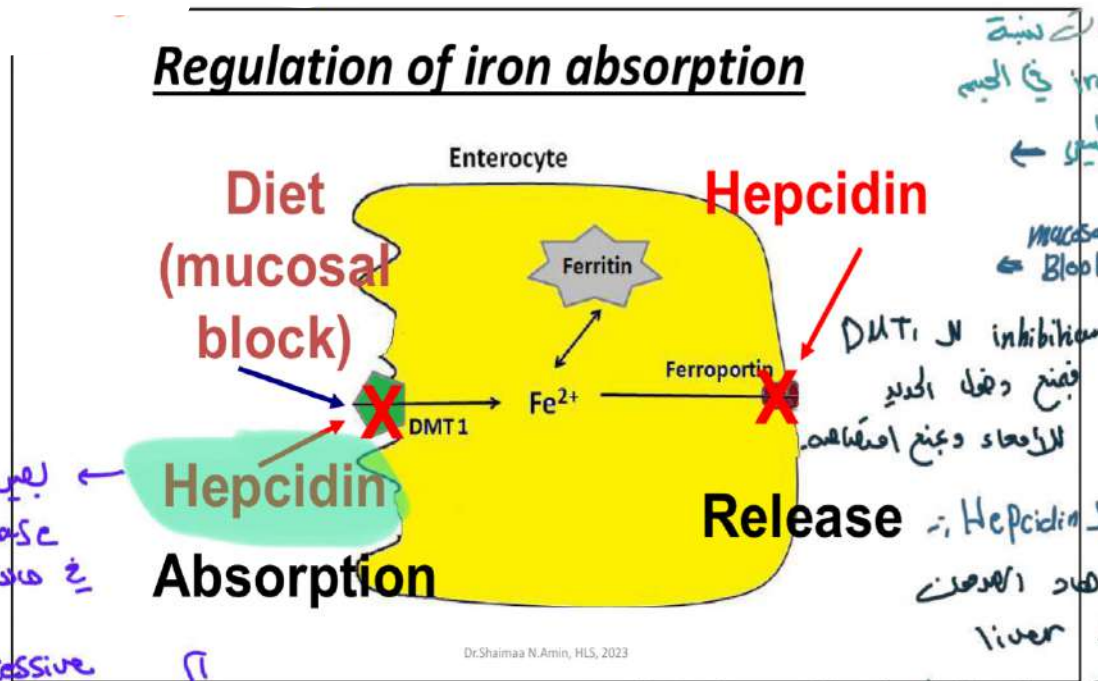


Anemia of chronic disease/anemia of inflammation (ACD/AI)

Lab findings in ACD:

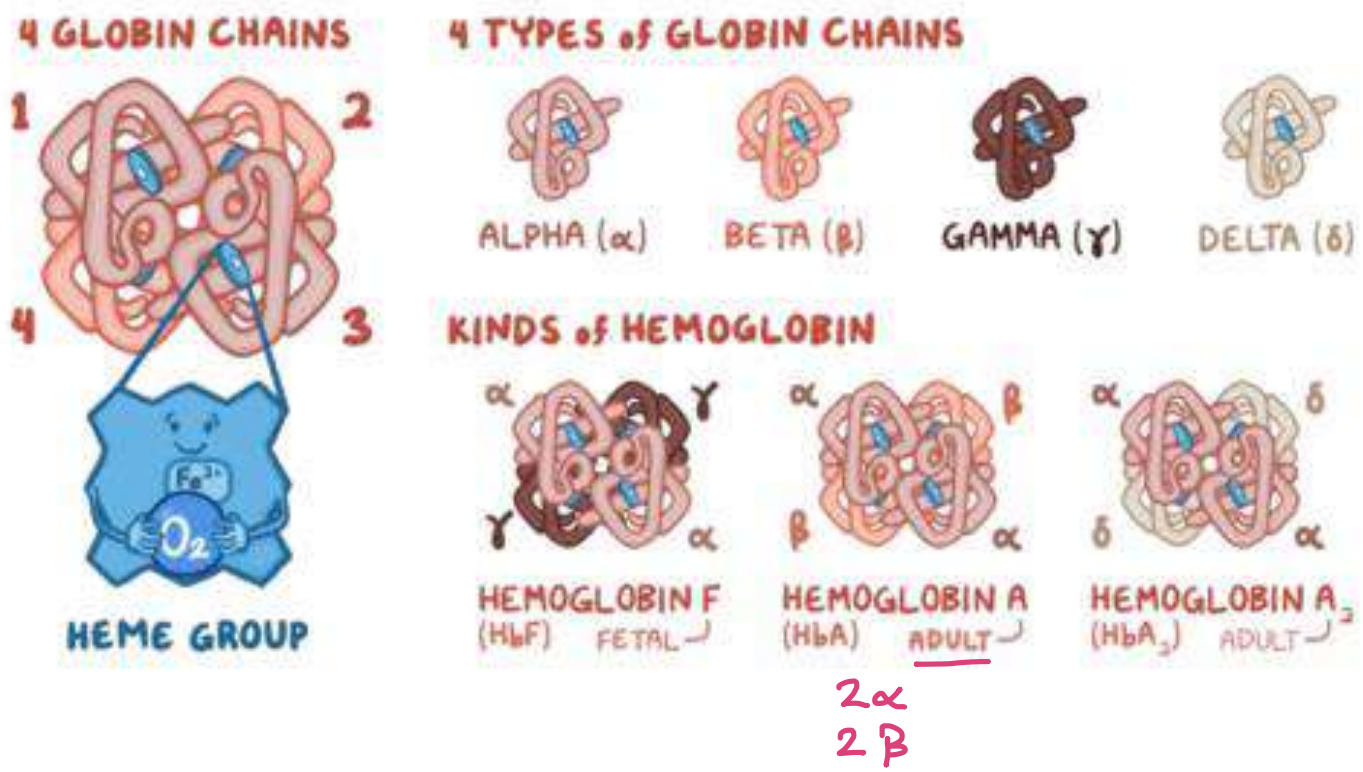
- ↑ferritin, ↓TIBC الكبد ما بدها حديد بتروح ترفع الـ hepcidin وبتنزل الـ Transferrin من الـ
- ↓serum iron (bone marrow takes Fe from serum as macrophage isn't giving it)
- ↓% saturation الـ bone marrow بحاول يعمل erythropoiesis بضل يوخذ زيادة من الـ Serum مع هيك بقدرش يعمل الانيميا .

Treatment of ACD:

- Treat underlying cause of chronic disease (to reduce hepcidin)
- Exogenous erythropoietin (especially helpful in cancer patients) لأنو بضل فيه افراز للـ cytokine بتأثر على الكلية وبتمنعها من افراز الـ erythropoieses بعطيهم

Thalassemia

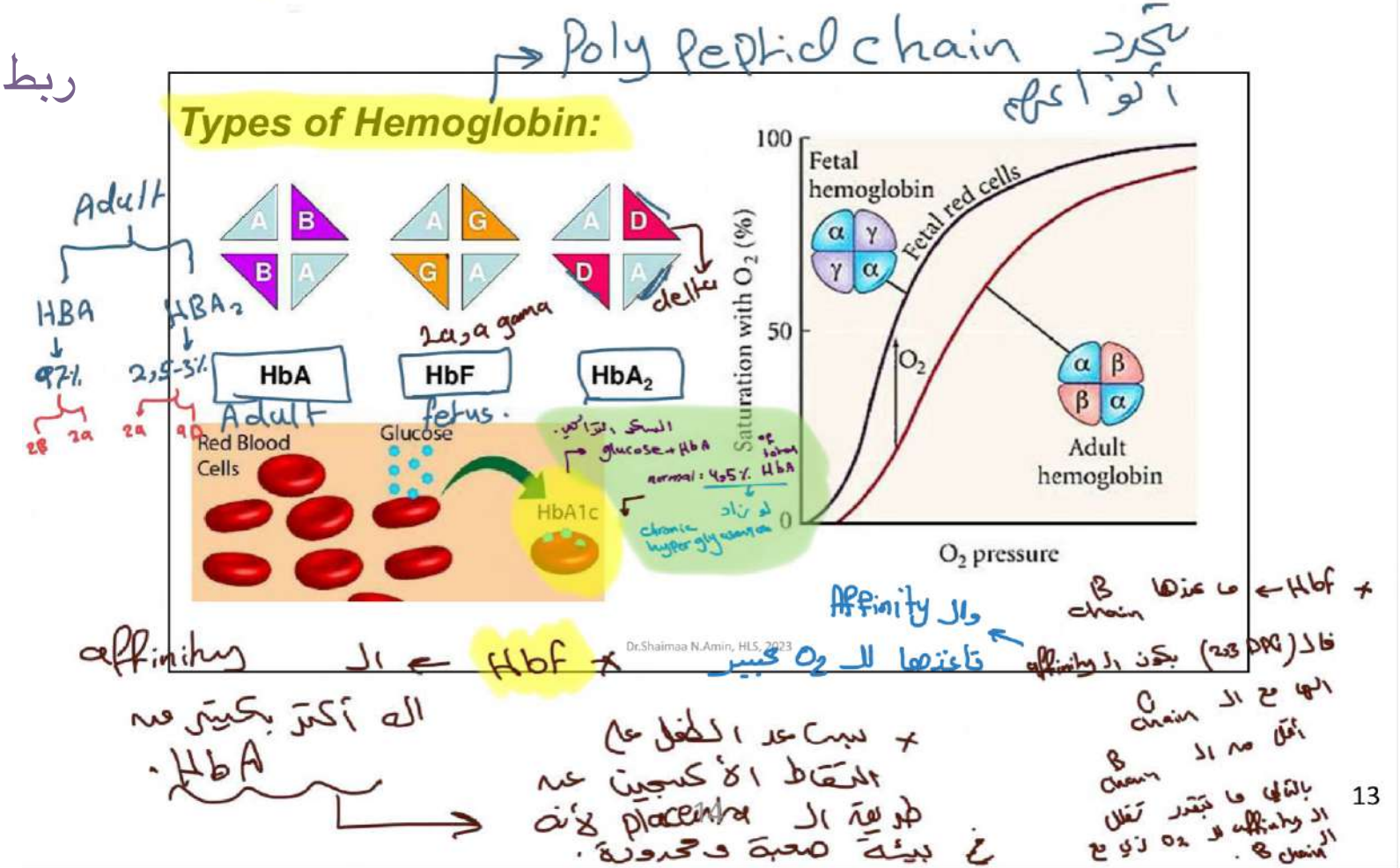
فحص ما قبل الزواج : اذا كانوا الطرفين عندهم low MCV و low MCH
بروحوا على خطوة ثانية بشوفوا فيه Iron deficiency ولا لا
اذا ما كان هيك بروحوا بعملوا electrophoresis عشان يشوفوا في
ثلاسيميا او لا .



Normal globin molecule in hemoglobin

In adults, HbA is the major hemoglobin (97%), composed of ($\alpha_2\beta_2$) with minor amount of HbA2 (1.5 - 3.5%; α2δ2) and HbF (< 1%; α2γ2)

ربط مع الفسيو



Thalassemia

مشكلتها في تكوين الغلوبين

متوارثة

A heterogeneous group of inherited disorders caused by mutations that decrease the rate of synthesis of α- or β-globin chains.

طفرات بالجينات المسؤولة عن انتاج α او β

- Can be of two types :

- **α-thalassemia** : characterized by deficient synthesis of α-globin chains
- **β-thalassemia** : caused by deficient synthesis of β-globin chains

So, there is a deficiency of hemoglobin, with additional secondary red cell abnormalities caused by the relative excess of the other unaffected globin chain.

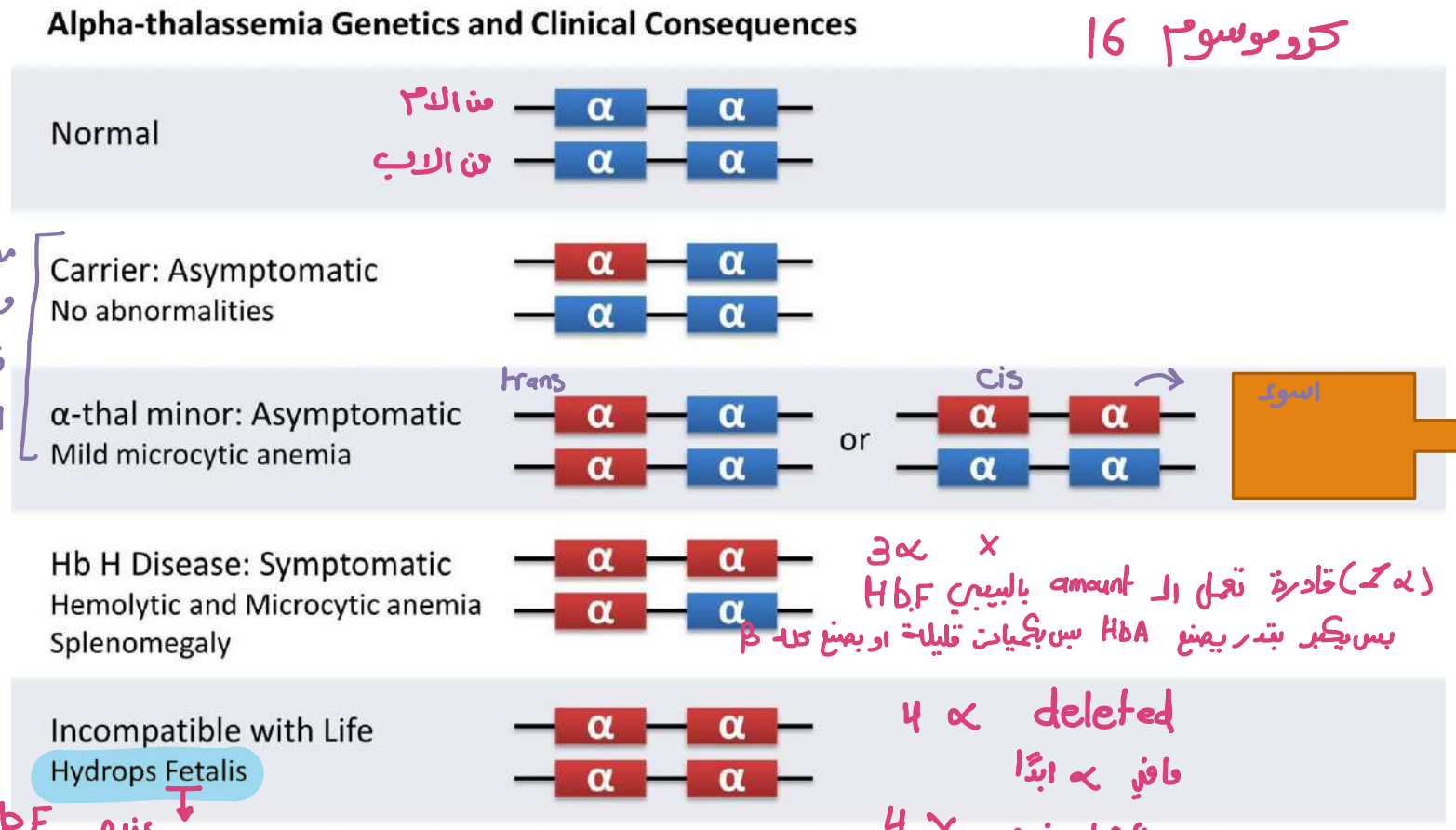
α بالـ excess يعني α الـ يكون unaffected الـ β في انتاج

α-thalassemia

نوع الطفرة

- ✓ **α-thalassemia is caused due to gene deletion of alpha chain of hemoglobin.**
- ✓Two α-globin genes are located on each **chromosome 16**, resulting in **4 α-gene loci (αα/αα)**
- ✓**Severity of α-thalassemia depends** on the **number of deleted alpha loci**
- ✓**α-thalassemia is usually inherited in an autosomal recessive manner**
- ✓**It results in low levels of hemoglobin, decreased mean corpuscular volume (MCV) and decreased mean corpuscular hemoglobin (MCH)**

α-thalassemia: 4 types



Cys deletion (deletion of both allele on same chromome) is worse than **trans deletion** (deletion of two allele on different chromosome)

Because cys is associated with increased risk of severe thalassemia in offspring

mutation ← الاحمر

α-thalassemia; 4 types

Severe

1. **Bart's hydrops fetalis syndrome:** complete absence of all 4 α chains (--/--)

- Because of the absence of α chains, **no HbA or HbF is present**
- There is excess production of gamma globin of the HbF which is called **Hb Barts (γ4)**.
- Hb Bart's have an extremely high oxygen affinity and are incapable of effective oxygen delivery
- **Incompatible with life**, fetuses are still born with severe anemia, marked edema and hepatosplenomegaly

اي يسبي بنولد ميت بعد ٣٤ اسبوع

لأنه بحاول الجسم يعمل erythropoises

α-thalassemia; 4 types

2. HbH disease: absence of 3 α chains (--/-α) → وحدة بتشتغل والباقي deleted

- There is excessive HbH (β4) hence called HbH disease .
- This HbH has a high affinity to oxygen (10 X the affinity of HbA) but it cannot transfer oxygen to the cells properly. → فا بقدر يعمل تبادل للغازات
- RBC have precipitated HbH and damaged walls, so they are phagocytosed in the spleen.
- Chronic hemolytic anemia, mild jaundice and hepatosplenomegaly → بسبب الـ bilirubin
- Most individuals clinically do well and survive; transfusion is rarely needed

هاي (α-α) قادرة تعمل الـ amount بالبيبي HbF
بس بكبر بقدر يصنع HbA بس بكميات قليلة ٥ اذا احتاج اكثر دم و HbA
الجسم وش قادر يطلع HbA فبتصير الـ β تتراكم مع بعض 4 β

بتصير تعمل aggregate ← β β
ويتجمعوا بتيجي الـ spleen
اللي وظيفتها تكسر الـ Abnormal RBC

α-thalassemia; 4 types

3. α-thalassemia trait: absence of 2 α chains either (--/αα) or (-α/-α)

- Benign condition with most patients diagnosed on routine screening
- Does not require treatment

4. α-thalassemia silent carrier: absence of 1 α chain (αα/-α)

- No clinical abnormalities

Diagnosis of thalassemia is done by CBC, electrophoresis, blood smear, family hx

history

α-thalassemia; lab findings

- **Hb Bart's hydrops fetalis syndrome:**
  - CBC: severe microcytic hypochromic anemia and reticulocytosis
  - Hb Bart's > 80%
- **HbH disease:**
  - CBC: decreased MCV and MCH, and reticulocytosis
- **α-thalassemia trait:**
  - CBC: may show mild hypochromic (low MCH), microcytic (low MCV) anemia
- **α-thalassemia silent carrier:**
  - CBC: either normal or mild reduction of MCV and MCH

كُلُّ يَوْمٍ هُوَ

فُرْصَةٌ

لِبِدَايَةٍ جَدِيدَةٍ