النادي الطبي MC

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&
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دعواتكم ✌️❤️

Q رح يجي سؤال على سيناريو وأعراضه ← غالبا بتجيب هاي الأعراض

Anemia Clinical cues

(إشارة)

Good luck

- Fainting, pallor, tachycardia...**anemia in general**
- Jaundice, gallbladder stones, red urine...**anemia due to hemolysis** (→ due to bile not obesity)
- Hx: Age of presentation, gender, past medical history, family history (→ thalassemia) (بعض الأمراض بتصيب ال males > females مثل الثقول.)
- Anemia workup: **CBC and blood smear,....among others**

ويجيب معاها مفتاح عادةً بحدد نوع ال Anemia مثلا تقول أنه عنده نقص B12 وأعطاه تعابه و.... بكون الجواب Macrocytic – M. -- Anemia وهكذا

tachycardia

cause the brain is very sensitive to O_2 levels.

* بالأغلب الدكتورة بتجيب clinical scenarios ..

لما يجي مريض عنده كل هاي الأعراض فشو الخطوة اللي رح اخذها

Reticulocyte Index (RI)

$$\text{Corrected Reticulocyte Count} = \text{Reticulocyte \%} \times \frac{\text{Actual Hct}}{\text{Normal Hct}}$$ (Hematocrit)

Normal Hct ≈ 45

* RI should be between 0.5-2.5% in healthy patients

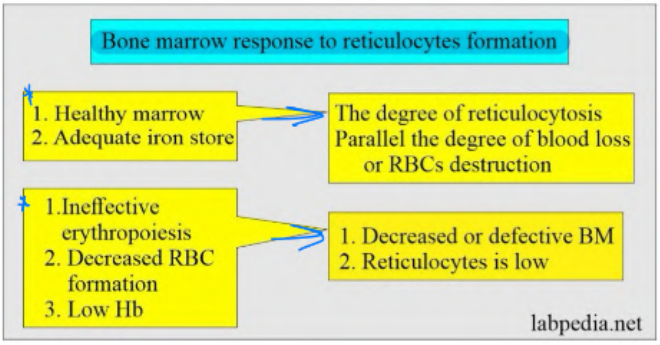
RI < 2% with anemia = inadequate response to correct anemia

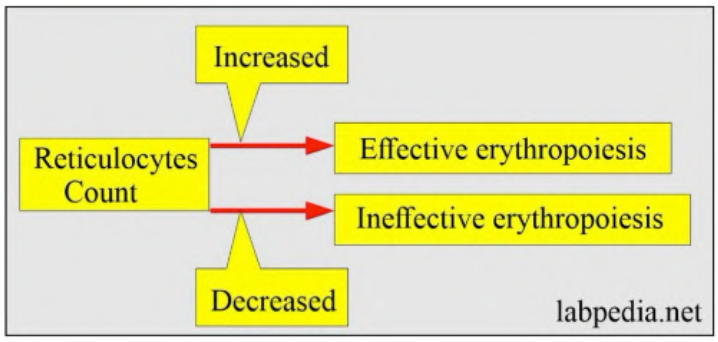
RI > 3% with anemia = compensatory production of reticulocytes

مشكلة بال BM ← BM ال عم تتعوض وعم تشتغل

P - 1

Reticulocytosis reflects marrow response to anemia





تفريغ مها الخريشا

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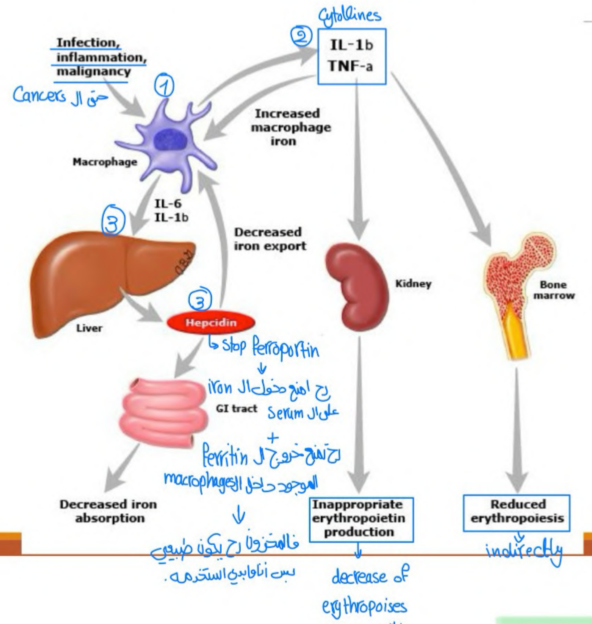
ترتيب السلايدات غير هيك - بس الدكتورة بلشت شرح من هون

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

* هسا الفكرة هون مواني عم ازيد مصايب المريض كمان مصيبة وا عملة

anemia بس لما يكون هو عنده .Chronic di أو عدوى مخصوصة لأنه يصير معه bacterial infection فالجسم بده يحمي حاله منها فبنزل من ال serum iron عشان ال bacteria ما تتغذى وتصير flourishing



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

ملاحظة مهمة: بهذا المرض رح يزيد ال (ferritin) مع إنه في (Anemia)

- الأحمر يعبّر عن الطفرة
- الأزرق يعبّر عن الوضع الطبيعي

α-thalassemia: 4 types

تفريغ مي صالحريشا

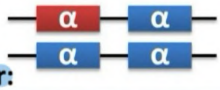
P-2

Alpha-thalassemia Genetics and Clinical Consequences

Normal — 2 chromosomes (1 من الأب + 1 من الأم)

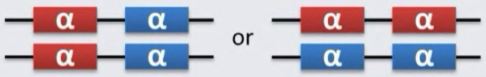
Carrier: Asymptomatic
No abnormalities

α-thalassemia silent carrier:



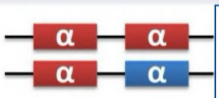
α-thal minor: Asymptomatic
Mild microcytic anemia

α-thalassemia trait:



Hb H Disease: Symptomatic
Hemolytic and Microcytic anemia
Splenomegaly

HbH disease:



- 3 genes deleted · Have just 1 for making α
- this one is enough for baby → فبيولدعادي
- جزء من الـ Hb فيه 2β، 2α وجزء فيه 4β ← anemia ← hemo ← نقص دم

Incompatible with Life
Hydrops Fetalis

Hb Bart's hydrops fetalis syndrome:

- 4 genes → all of them are mutated (deleted)
- The fetus have HbF (2α, 2γ) $\xrightarrow{\times\alpha}$ Hb have 4γ → Hb barts

لا يستطيع الطفل العيش، عند affinity عالية الـ O_2 فما بنقل يعطيها release و exchange

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

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β-Thalassemia; types

Types	Alleles	Description
Thalassemia minor	β^+/β or β^o/β	Only one of β globin alleles has a mutation. Patients will have microcytic anemia (MCV <80 fL) Heterozygous: One normal & One mutated
Thalassemia intermedia	β^+/β^+ β^o/β^+	Patients can have a normal life, but may need occasional transfusions, example at times of increase demand (illness or pregnancy) Homozygous: both of them are mutated → ↑ HbA_2
Thalassemia major	β^o/β^o -Homozygous -β لا يوجد	Severe microcytic, hypochromic anemia. Untreated, causes anemia, splenomegaly and severe bone deformities, and death before age 20. Treatment is blood transfusion; splenectomy for splenomegaly and chelation for iron overload + extramedullary hepatopoieses

Mutations as (βo) means no formation of β globin - mutations (β+) means some β globin chain is formed

deletion

secondary hemochromatosis due to increased iron overload.

("hair on end" & Chipmunk appearance of face)

P-3

Folic acid or vit. B12 → بتشبهوا الحمض كثير بس ال B12 بيجوا ب neurological manifestations واتبجي فيها الهامة

immature cell ←

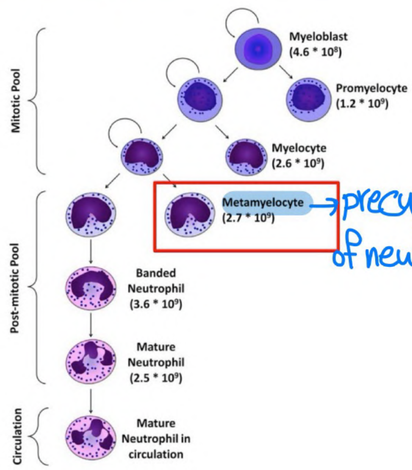
Megaloblastic Anemia
Diagnosis and morphology

CBC: anemia with high MCV. Also, might have leukopenia, and thrombocytopenia (pancytopenia). Low retic count (ineffective erythropoiesis)

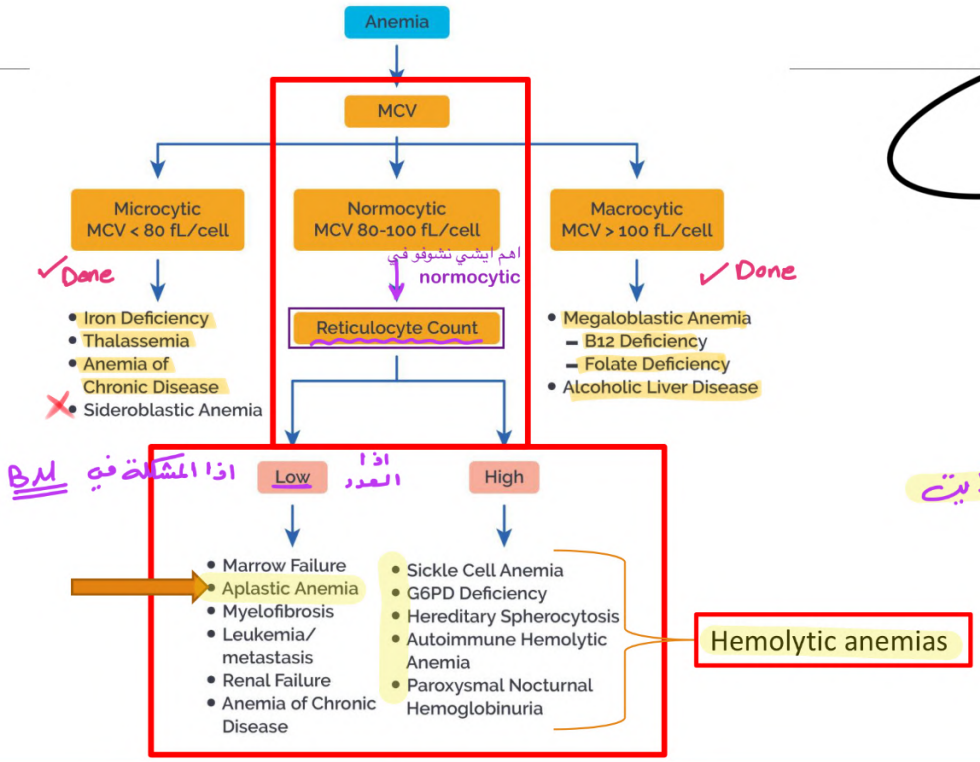
(Like Aplastic Anemia) (B.M) مشكلة بال

Peripheral smear: Macrocytes. Anisocytosis (variation in RBC size) and poikilocytosis (variation in RBC shape). Nucleated red cells are seen with immature nucleus. Neutrophils show hypersegmentation.

→ like β thalassemia major and SCA (Sickle Cell Anemia) and hereditary spherocytosis



→ precursor of neutrophils



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#اليرموك ندرس عنهم بالهايلايت

أسبابو

Aplastic anemia; etiology

P-4

Acquired aplastic anemia (most common)

- Infectious agents: parvovirus B19, HIV, EBV, Hepatitis C virus (Liver)
- Toxins such as benzene ممكن لعلاج كا نسو
- Drugs, chemicals, or radiations (example of drugs: chloramphenicol)
- Autoimmune disease - most common SLE
- Idiopathic → ما فيه سبب الذئبة الحمراء

Constitutional "congenital" aplastic anemia; example "Fanconi anemia"

بنولد فيه الطفل عندو مشكلة بعمل Aplastic anemia

تفريغ رنيم الحرّام

P - 4

Hemolytic anemia

هون في تداخل بينهم ما في واحد فيهم بصير **totally** بشكل كامل

intravascular or extravascular في واحد فيهم راح يكون **predominant** اكثر من الثاني

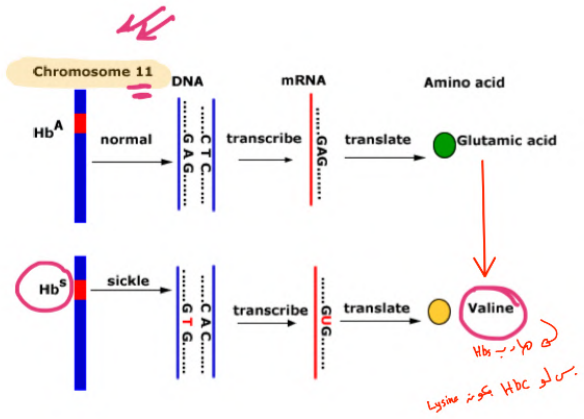
Test	Intravascular hemolysis	Extravascular hemolysis
Serum Haptoglobin (free haptoglobin)	⬇⬇	Normal or ⬇
Plasma Hb	Present	Absent لأنه رح يتكسر
Hemoglobinuria	Present	Absent
Hemosiderinuria	Present	Absent
Serum lactate dehydrogenase LDH (بطلع لما تتكسر الـ RBC)	⬆	⬆
Serum unconjugated bilirubin	Normal or ⬆	⬆

هي عادة بتكون نورمال بس شوية **intravascular** ترتفع شوي **elements**

عادة بتكون نورمال بس لو صار شوي **extravascular elements** ممكن ترتفع **شوي**

P - 4

SICKLE CELL DISEASE



Is more common than thalassemia

- Sickling increases with **hypoxemia, dehydration** and **acidosis.**

- Molecular basis: single point mutation (A to T substitution) in the first exon of the β globin gene, converting glutamic acid into valine.
  Hydrophilic — Hydrophobic

- It is an **autosomal recessive** inheritance

Treatment:

- ✓ Prophylactic treatment with penicillin to prevent pneumococcal infection .
- ✓ Adequate hydration and pain relief
- ✓ Use the hydroxyurea therapy "increase HbF"
- ✓ In severe cases, exchange transfusion to reduce the Hgb S

GDPD Deficiency aka favism

Hemolysis due to oxidant stress:

قعدنا نحكي انه بتعرض الجسم لoxitadive stress
طب شو بخلي الجسم يتعرضلهم ؟

- Drugs: eg. Antimalarials, sulfonamides, furantoins,…etc.
- Favism: chickpeas (الحمص) , green peas (فاصوليا خضراء) , all types of beans should be avoided (وبرضو البقوليات كلها)
- Infections: produces free radicals

اي infection ممكن ينتج عنه free radicals

Oxidation leads to denaturation of globin chains, and precipitation at membranes forming **Heinz bodies.**

RBCs: Bite cells and Heinz bodies

Features of Extra/Intravascular hemolysis

كمحصلة من الطريقتين للspleen بتصير عنا الextra والintra

تفريغ ضياء عبد الهادي

Causes of autoimmune-IHA
IgG or IgM mediated destruction of RBC

P-5

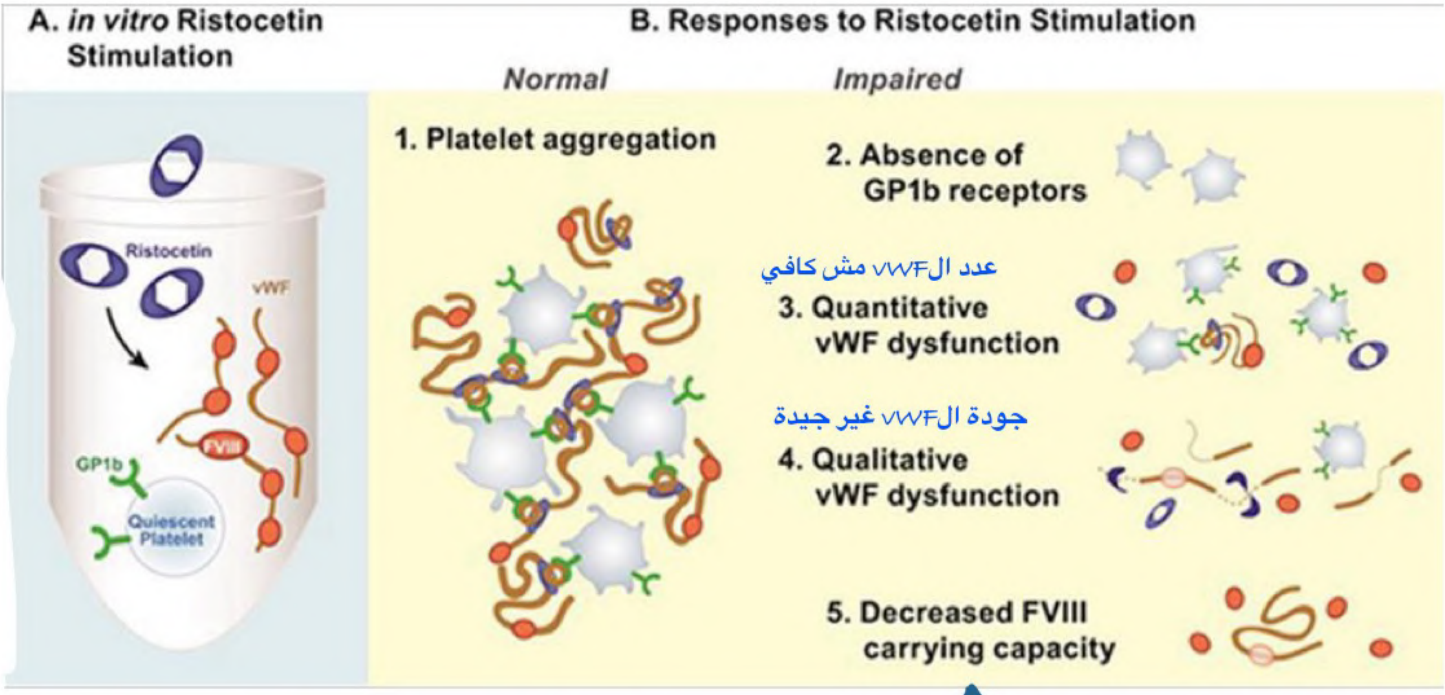
Warm Antibody: IgG/IgA type لانها تنشط بحرارة الجسم	Cold Antibody: IgM type تعتبر كبيرة فيها خمس اماكن للارتباط
Activated at body temp. (37 c)	Active at 0-4°C بدرجة الحرارة الباردة، يكون باطراف الجسم اكيد IgM binds to RBC in cold temp (extremities)
IgG-coated RBC lysis in spleen (predominantly extravascular)	Clumping and complement fixation causes lysis in blood vessels and liver (intra- and extravascular) لما يرتبط بهذا الantibody خمس RBCs بتاكلهم الspleen فهيك extravascular hemolysis
Morphology: spherocytes (splenic macrophage phagocytose tagged RBC leading to formation of spherocytes) ممكن الspleen بدل ما تاكل كل الRBC، تروح تاكل الantibody فقط، الRBC يكون عليها اكثر من antibody، فكل مرة تاكل antibody بتفقد جزء من الRBC وبتصير اصغر وشكلها كروي	IgM agglutination (hemolysis occurs in the hands & feet in cold weather) برضو الIgM عنده القدرة لينشط ال MAC (تذكروا انه بثقب الخلية بالتالي
80% of immune hemolytic anemias: Primary (50-70%) يعني ما بنعرف السبب الحقيقي Secondary: يعني بنعرف السبب - Lymphoproliferative disorders - Autoimmune diseases (SLE) - Drugs (penicillin and cephalosporins) لانه ممكن يغطوا الRBC زي ما حكينا فوق	• Infectious mononucleosis (EBV) → IgM • Mycoplasma infection • Lymphoproliferative disorders الدكتورة ركزت انه نعرف اسباب الحدوث

Causes

Causes

P-5

Restocetin test: بنفحص فيه الـ(vwf) المفروض أنه بس نضيفه يصير تفاعل وتجلط حليه لو ضفناه وماصار؟!! بكون مشكلة بواحد مدهدول



Treatment: Desmopressin

لو عملنا الRistocetin test وكانت استجابته سيئة معناته واحد من هذول

P-5

MICROANGIOPATHIC HEMOLYTIC ANEMIA (MAHA)

Signs of hemolysis: intravascular hemolysis نفس ال
Increase LDH
Increase indirect bilirubin
Decrease Haptoglobin

بالوضع الطبيعي لما يتكون primary hemostatic plug، ال vWF بتتجمع
هسا لما الجسم يشوف انه حجم ال primary صار كويس وبكفي منه وبدنا نبلش بال secondary مين بكون المسؤول ؟ ADAMTS 13
شو بعمل ؟ بكسر ال vWF
بهذا المرض بكون عنا antibodies ضد ADAMTS 13 وبكسروه، فهيك ال vWF بتضل شغالة وفش اشي بوقفها فبتزيد

TTP (Thrombotic thrombocytopenic purpura)
بشبهوا بعض ← Hyaline thrombi (Platelet rich)

HUS (Hemolytic Uremic Syndrome) (E.Coli O157:H7) سببها ← (منه أعراضها المميزة أنه رح يصير دم بالبول يعني رح يصير (Renal failer) يعني رح يغسلكل وكمان بتصير أكثر بال (Pediatrics))

Another name → **DIC** (disseminated Intravascular Coagulation) → **consumptive coagulopathy**,

بدايته انه في كثير thrombosis ويستهلك فيها ال platelets وال coagulation
وبعد ما نستهلكهم بكمية كبيرة بصير في bleeding

TTP and HUS: platelet activation (coagulation pathway not activated)

DIC: activation of coagulation pathway (prolonged PT, PTT and TT)
platelets، primary and secondary hemostasis :هون نشاط كلشي

Elevated D dimers and other fibrin degradation products

Intravascular

I. Microangiopathy (MAHA)

II. Acute hemolytic transfusion reaction (ABO mismatch)

III. Paroxysmal nocturnal hemoglobinuria (PNH)

IV. Paroxysmal cold hemoglobinuria (PCH)

V. Infections

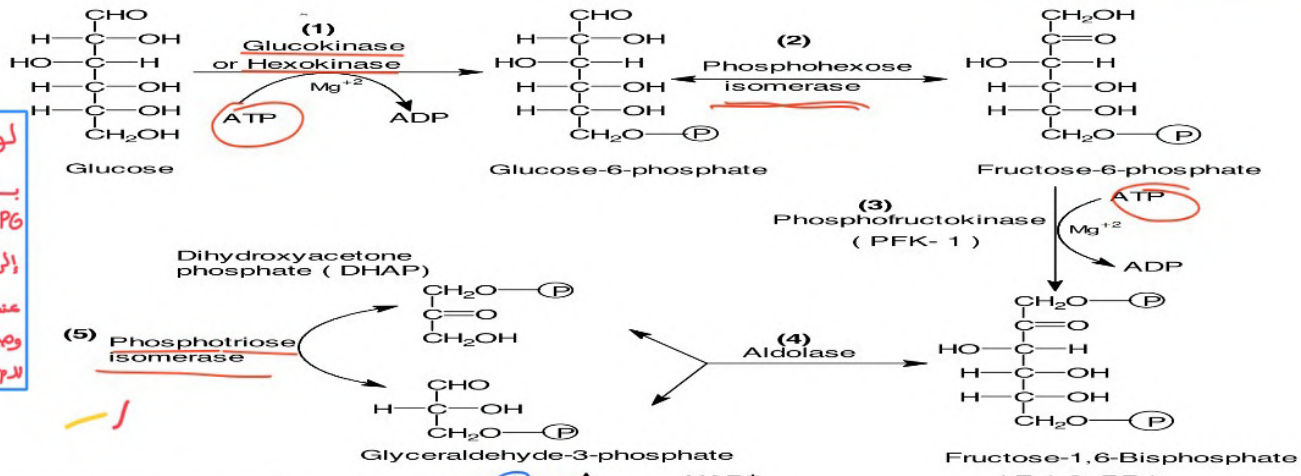
VI. Snake bites/venoms

Extravascular

I. Intrinsic RBC defects
- A. Hemoglobinopathies
  - i. Sickle cell
  - ii. Thalassemias
- B. Membrane defects
  - i. Hereditary spherocytosis
  - ii. Hereditary elliptocytosis
- C. Enzyme deficiencies
  - i. G6PD deficiency
  - ii. Pyruvate kinase deficiency

II. Extracorpuscular defects
- A. Immune-mediated hemolytic anemia
  - i. Autoimmune
  - ii. Drug-induced
- B. Liver disease
- C. Infections
- D. Toxins

B - 1



لو رحنا (unAerobic)
بس لما وصلنا عند
1,3 BPG وحولناها
الـ 1,3BPG لـ 2 ثم لـ
3PG عشان مارح نكسب
ATP وطبيعي بكونه ناتج Glycolysis
لـ ATP صفر
Zero

شو مصدر الطاقة؟

Aerobic : 2
unaerobic : 8

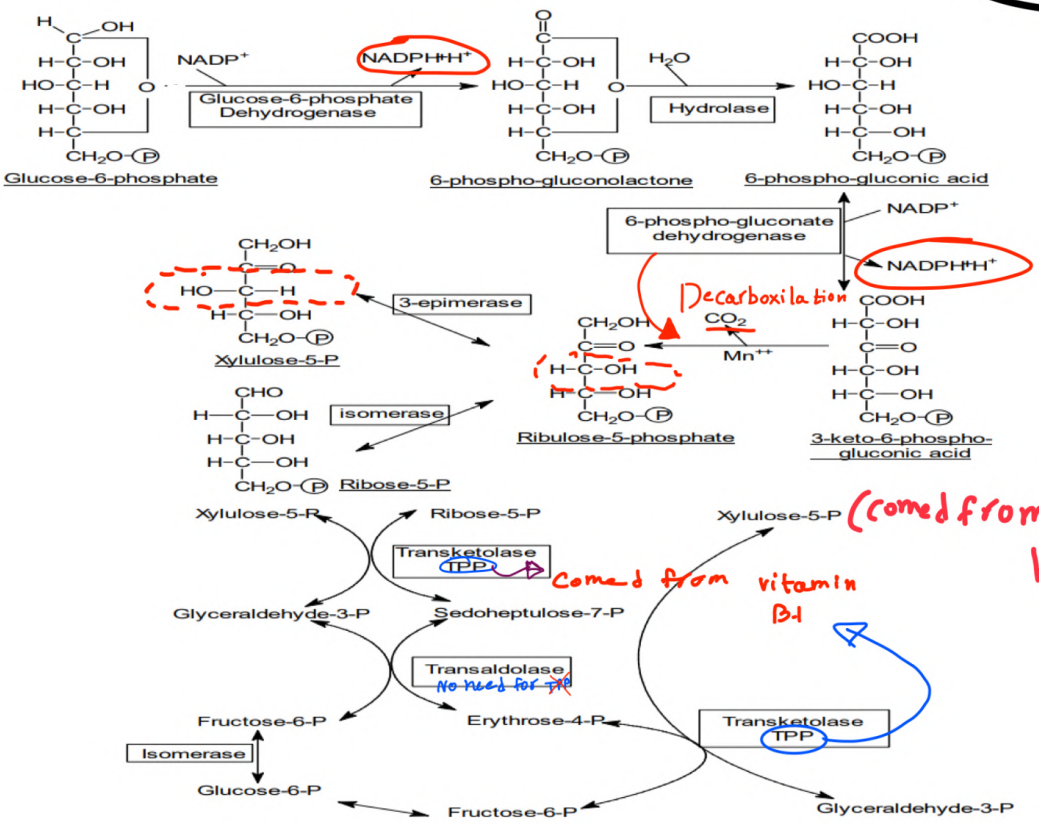
لو بلشنا من Glycogen
بزيدوا (1) ليش؟
عشان صار بتحول عطول لـ F-6-P
وبنطلعه أول خارة لـ (ATP)

B - 1

* When ferrous iron is oxidized, it is converted to ferric iron.
* Hemoglobin that carries the ferric iron is called methemoglobin
* Methemoglobin cannot transport oxygen because ferric iron cannot carry O_2.
* NADH cytochrome b5 methemoglobin reductase system reduces Fe^{+3} back to Fe^{+2}

حطيب منه و ينك بنجيب (NADH) جاهز يدوّ !؟؟ أكيد منه ال (Glycolysis)

B-1


Glucose-6-phosphate
NADP+
NADPH+H+
Glucose-6-phosphate Dehydrogenase
6-phospho-gluconolactone
H2O
Hydrolase
6-phospho-gluconic acid
6-phospho-gluconate dehydrogenase
NADP+
NADPH+H+
Decarboxilation
CO2
Mn++
3-keto-6-phospho-gluconic acid
Ribulose-5-phosphate
3-epimerase
Xylulose-5-P
isomerase
Ribose-5-P
Xylulose-5-P
Ribose-5-P
Transketolase
TPP
Comed from vitamin B-1
Glyceraldehyde-3-P
Sedoheptulose-7-P
Transaldolase
No need for TPP
Fructose-6-P
Erythrose-4-P
Isomerase
Glucose-6-P
Fructose-6-P
Xylulose-5-P
Transketolase
TPP
Glyceraldehyde-3-P
(comed from another HMP shunt)

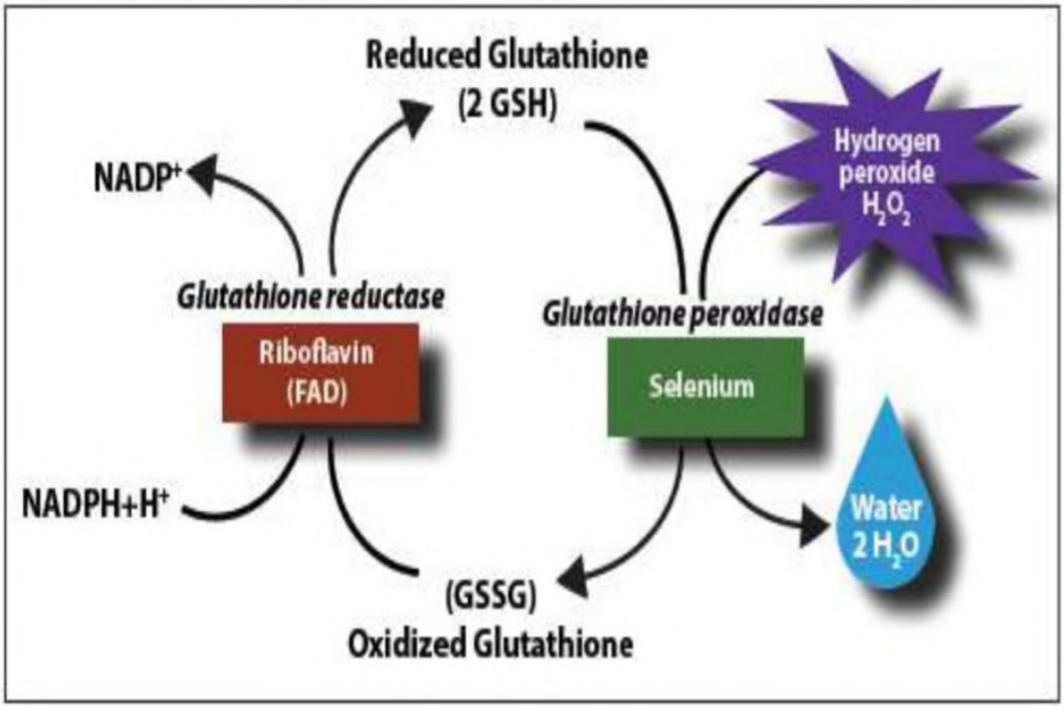
B-2

Glutathione (GSH) is a tripeptide γ-glutamyl-cysteinyl-glycine.

- Reduced glutathione (G-SH) is a coenzyme for the enzyme **glutathione peroxidase** (contains selenium) that reduces hydrogen peroxide to water, protecting cells from its toxic effects.

الدكتورة حكمت صرصم كتير

- During its function as a coenzyme for antioxidant activities, GSH is oxidized to the disulfide form, GSSG, which is then regenerated by the action of **glutathione reductase .**



Hb (α-β-γ-δ).

- α –chain → 141 amino acids

(α chain gene is on chromosome 16)

- β-γ-δ chains → 146 amino acids

(β-γ-δ chain genes are on chromosome 11)

- **Hb is composed of 2 α and 2 either β , γ or δ**

B-3

α chain

zeta-gene is expressed during embryonic life. It stops working by the end of the first 3 months of pregnancy, and replaced by the α- genes.

β chain

ε-gene, like the ζ- gene, is expressed during embryonic life. It stops working by the end of the first 3 months of pregnancy, its function being gradually replaced by the γ - genes. (HbF will start)

واللي بتتوقف بعد الولادة بـ (٦) أشهر وبتبدل بـ (β)

during the first 3 months of pregnancy: alpha, gamma and beta genes are turned off. Zeta and epsilon genes are turned on.

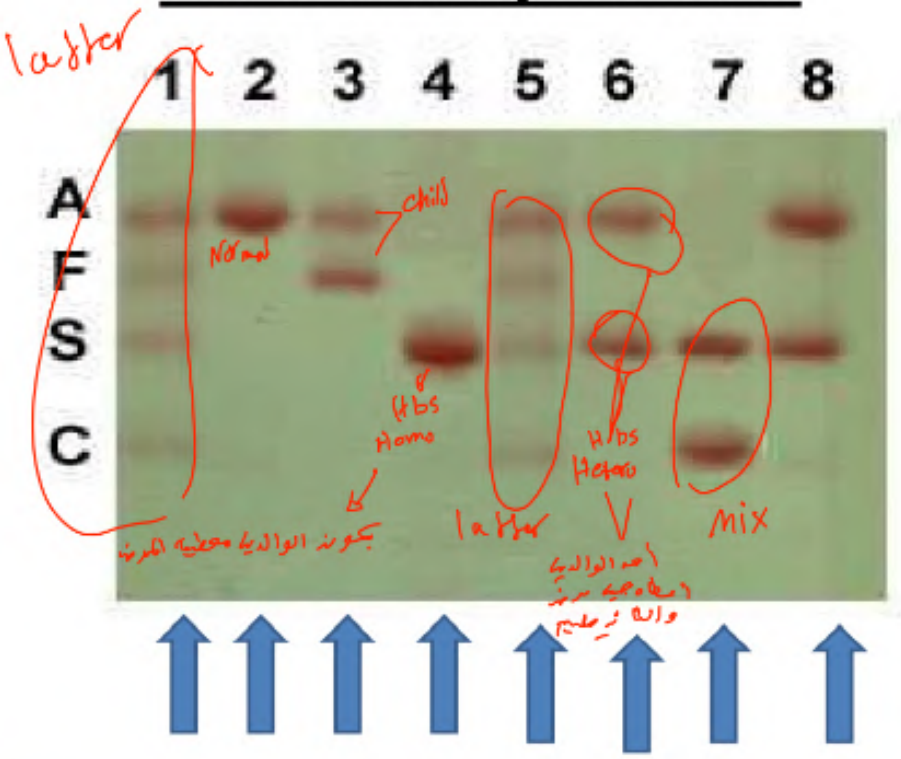
After 3 months of pregnancy: alpha and gamma genes are turned on to encode for alpha and gamma chains → HbF

Normal and abnormal hemoglobins can be identified by electrophoresis:

The arrangement of hemoglobins , fastest to slowest , is A, F, S and C. HbA_2 runs with HbC

B-3

Hb electrophoresis



1) the marker
2) ز
3) Normal child
4) Homozygous sickle cell anemia
5) .
6) Heterozygous sickle cell anemia
7) ده غريب جدا
8) Heterozygous sickle cell anemia