SAWA UNIVERSITY

اسم المادة و الكورس

G6PD DEFICIENCY ANEMIA

جامعـــــــة ســـــــــاوة الاهلية

Sawa University

كليـــــة التقنيـــات الصحيـة والطبيـة

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المرحلـــــــــــــة .....الثالثة..

. .....third ..... Stage

محاضرة رقم 11

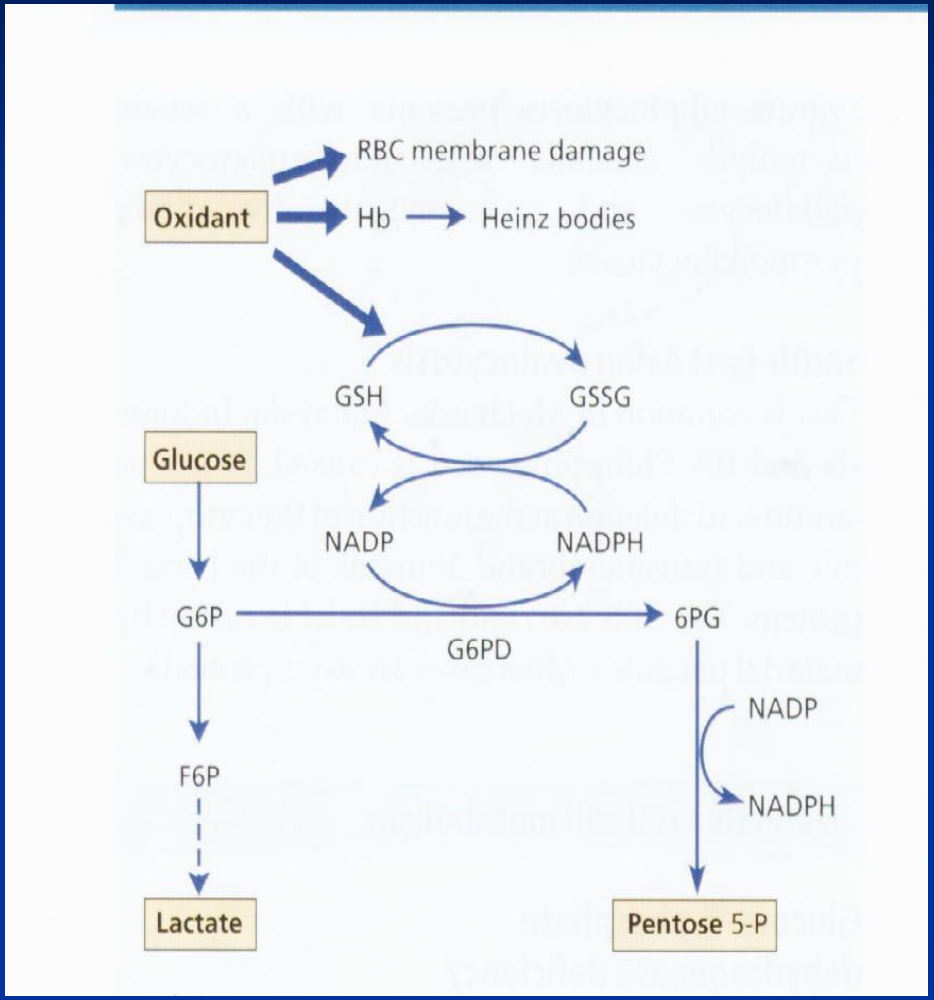
Lecture No. …11…..

الجانب النظري

Theoretical

... تدريسي المادة : ...د. وضاح علي

Red cell enzymopathies



G6PD functions to reduce nicotinamide adenine dinucleotide phosphate (NADPH) while oxidizing .glucose-6-phosphate

NADPH is needed for the production of reduced glutathione (GSH) which is important to defend the red .cells against oxidant stress

Red cell enzymopathies

Anaerobic glycolysis via;

the Embden–Meyerhof pathway generates ATP, and

the hexose monophosphate shunt; produces nicotinamide adenine dinucleotide phosphate (NADPH) and glutathione to protect against oxidative stress.

In general, defects in the hexose monophosphate shunt pathway result in periodic haemolysis precipitated by episodic oxidative stress,

whilst those in the Embden–Meyerhof pathway result

in shortened red cell survival and chronic haemolysis.

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Red cell housekeeping enzymes :

1. The embden-Meyerhof Pathway :

for glycolysis provides energy for :

a. Na+, K+ and Ca+2 pumps in the cell membrane.

b. phosphorylation of membrane components and synthesis of glutathione for protection from oxidative damage.

c. reduction of NAD to NADH which is important in reducing met-hemoglobin to hemoglobin.

2.The pentose-phosphate shunt :

maintains levels of NADH which is important in the *reduction* of oxidized glutathione (GSSH) to reduced glutathione (GSH).

GSH is important in :
a. destroying the oxidant hydrogen peroxide with glutathione peroxidase.

b. maintaining sulphhydryl group in Hb. and in various enzymes and within the cell membrane.

Oxidant hemolysis (enzymopathy)

1. Glucose – 6- phosphate dehydrogenase (G6PD) deficiency :

X-linked disorder.
G6PD is important for generation of both NAD and NADH as well as glutathione, which is required for reduction or protection of sulfhydroxyl groups.
Enzyme variants :
Normal forms: Two forms of G6PD have normal activity, B form and A form or (A+) & (B+).

Deficiency forms:

(A-) isoenzyme & Mediterranean isoenzyme.

***Enzyme may exist at normal intracellular levels but have decrease activity.**

***May be unstable lead to increased break down in red cells.**

Pathophysiology

the daily destruction of RBC, Hb is being constantly oxidized to ***met Hb.*** **but a special protective mechanism that uses the E.M pathway reduces it back to Hb this is important because; Met-hemoglobin dissociates into heme and globin and then precipitates as an insoluble mass (Heinz body) in the RBCs.**

These red cells with Heinz body are *non deformable* and have difficulty passing through the spleen.

Splenic removal of Heinz bodies damages RBCs membrane, forming spherocytes and causing hemolysis.

Precipitating factors

1.oxidant drugs : (antimalarial, antipyretic, sulfonamide and related group, nitrofurantion,)
(moth ball)
***2.fava beans(Favism*).**
3.Infection (resp. viruses, hepatitis, infectious mononucleosis , bacterial preumonia, and septicemia).
4.Stressful conditions: diabetic ketoacidosis,uraemia

Clinical manifestations

1. General features, patient with G6PD deficiency display signs and symptoms of IV hemolysis.
The deficiency usually is episodic and occasionally is chronic.
2. patient with the common (A-)form of G6PD deficiency generally have mild hemolysis only when stressed.*hemolysis is self-limited,reticulocyte have high levels of the enzyme thus, compensating for the decreased activity.

3. patients with the rare *Mediterranean* form of G6PD deficiency :- severe hemolysis when exposed to oxidants or stressed by surgery or infection the hemolysis persist as long as the stress or oxidant persists.

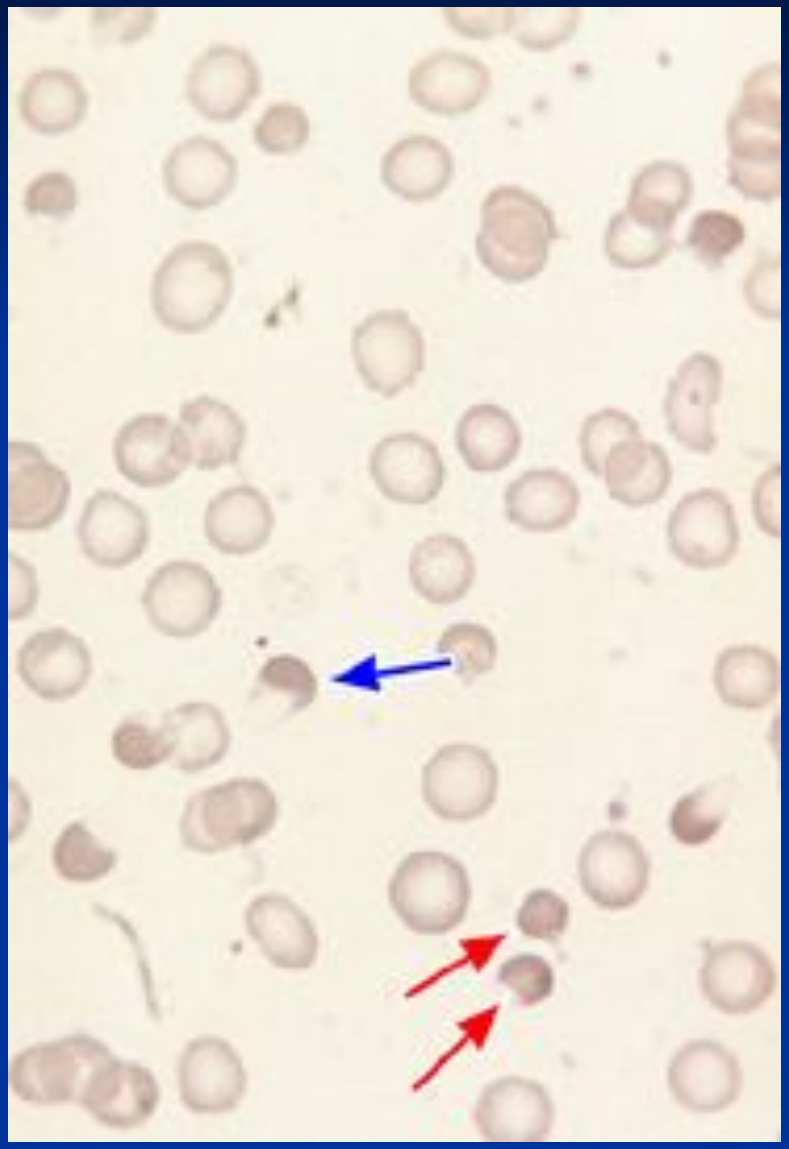
Diagnosis

1. red cell enzyme levels measured by electrophoresis show very low activities in severe disease and low to normal activity in mild disease depending on when the test is performed.

measurement should not be taken at the time of hemolysis and reticulocytosis

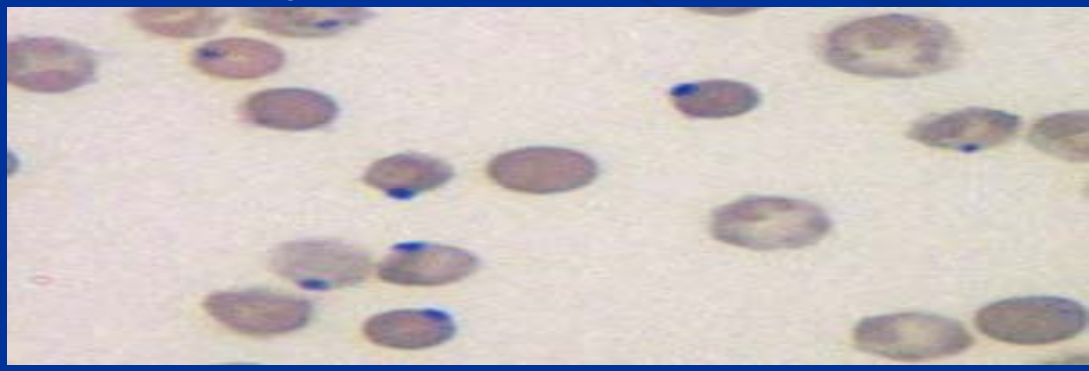
2. Heinz bodies can be demonstrated only during early phase of G6PD deficiency. characteristic of IV hemolysis.

Diagnosis



The blood film shows *irregularly contracted cells* [deep red arrows] and sometimes *hemighosts* [deep blue arrow] in which all the haemoglobin appears to have retracted to one side of the erythrocyte

Heinz bodies



Treatment

1.primary therapy is to avoid oxidative agents.
2.recovery is rapid , but if the anaemia is severe transfusion of red cells with normal enzyme complement may be required.
3.Splenectomy is without value.

Pyruvate kinase(PK) deficiency

***Congenital non-spherocytic hemolytic anaemia(CNSHA).**
***Autosomal recessive.**
***Characterized by decreased generation of ATP.**
***Impairement of glycolysis lead to increased 2,3 DPG level.**

Clinical manifestation

1.-chronic hemolytic syndrome of variable severity.
2.severe deficient may be apparent in neonatal stage.
3.-may be a symptomatic.
4.-manifestation (reticulocytosis, marrow hyperplasia, splenomegaly, jaundice, gall stone).

Diagnosis

*measuring PK enzyme level in red cells

Treatment :

1.depend on severity of anaemia. folate supplements,

2.Splenectomy

Q1 Laboratory finding for patient with favism

Q2 timing of G6PD enzyme assay for patient with G6PD enzyme deficiency

Q3 enumerate 3 precipitating factors of hemolysis in patient with G6PD enzyme deficiency