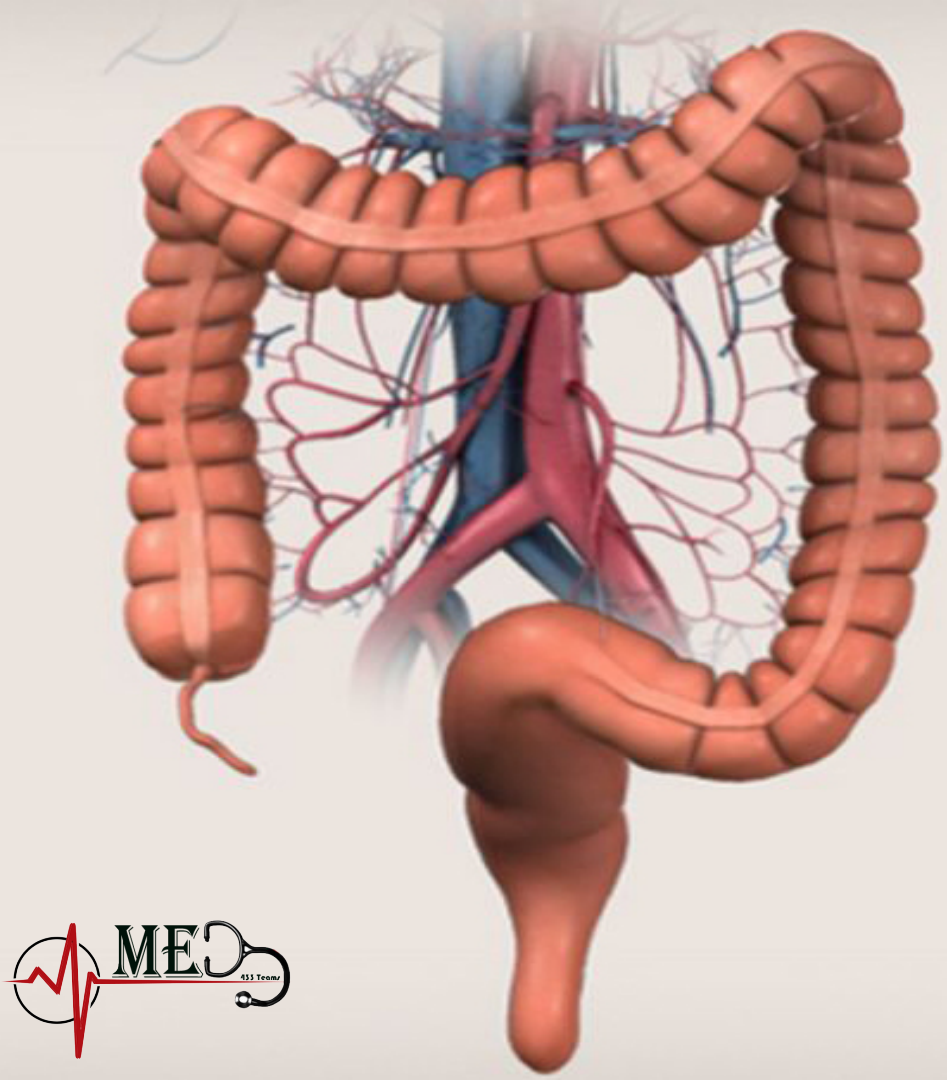


NOTE: The pictures in this lecture are important

Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency Anemia

OBJECTIVES:

- By the end of this lecture, the student should be able to understand:
- The biochemical basis of G6PD deficiency anemia
- The precipitating factors for G6PD deficiency anemia
- Classes of G6PD deficiency anemia (variant enzyme)
- Diagnosis of G6PD deficiency anemia

Biochemistry433@hotmail.com

Note **Cellular glucose selectively undergoes one of three Pathways : Glycolysis – Glycogenesis - PPP**

Background

Hexose Monophosphate Pathway (HMP) or Pentose Phosphate Pathway (PPP)

- An Alternative Oxidative Pathway for Glucose
- **No ATP Production**
- Produces Ribose-5-Phosphate for Nucleotide synthesis (Other than DNA)
- **MAJOR PATHWAY FOR NADPH PRODUCTION**

Uses of NADPH

- Reductive Biosynthesis (FA biosynthesis)
- Oxygen-Dependent Phagocytosis by WBCs (Oxidative burst)
- Synthesis of Nitric Oxide (NO)
- **ANTIOXIDANT** (Part of Glutathione System*)

Reactive Oxygen Species (ROS)

- Oxygen-Derived Free Radicals: Superoxide & Hydroxyl Radicals
- Non-Free Radicals; Hydrogen Peroxide (H_2O_2)

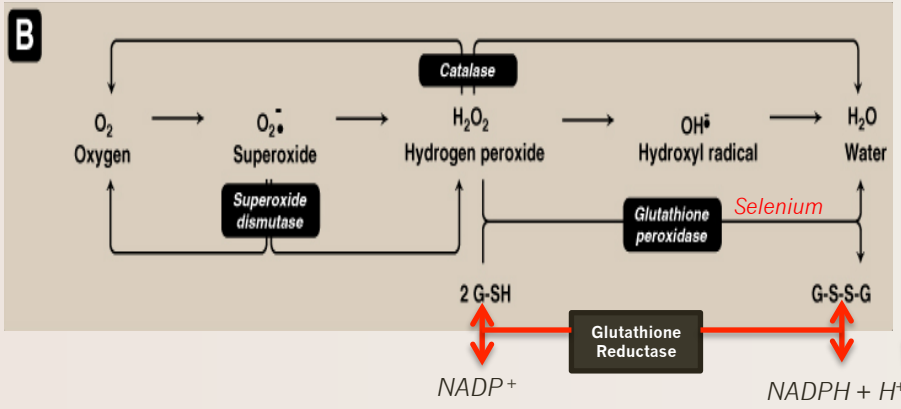
Oxidative Stress:

Imbalance Between Oxidant Production & Antioxidant Mechanisms

Oxidative Damage to :
- DNA
- Proteins
- Lipids (Unsaturated FA)

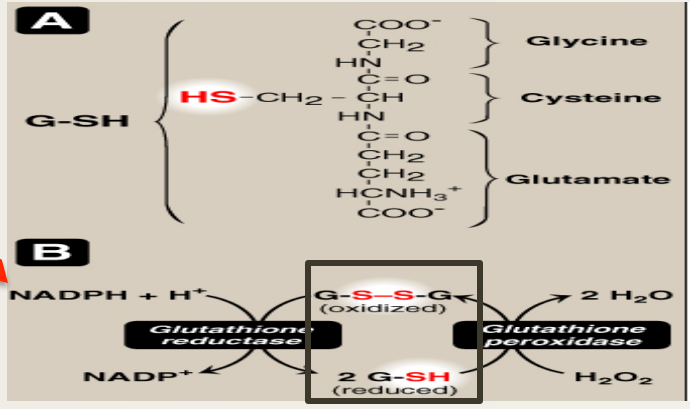
Oxidative Stress & Disease
- Inflammatory Conditions
- Obesity
- Cancer
- G6PD Deficiency Hemolytic Anemia

Antioxidant Mechanisms



HMP (PPP)

Glutathione System



G6PD Deficiency Hemolytic Anemia

- ❑ Inherited X-linked recessive disease, the most common enzyme-related Hemolytic Anemia
- ❑ Highest prevalence in Middle East & Tropical Africa Asia & Mediterranean ~400 different mutations affect G6PD gene, but only some can cause clinical Hemolytic Anemia
- ❑ G6PD deficient patients have increased resistance to infestation by Falciparum Malaria (Are not infected with malaria)

Precipitating factors that will lead to Hemolytic attacks in G6PD Deficient patients

1- Intake of Oxidant Drugs (AAA)

- **Antibiotics**; Sulfa preparation
- **Antimalarial**; Primaquine
- **Antipyretics**

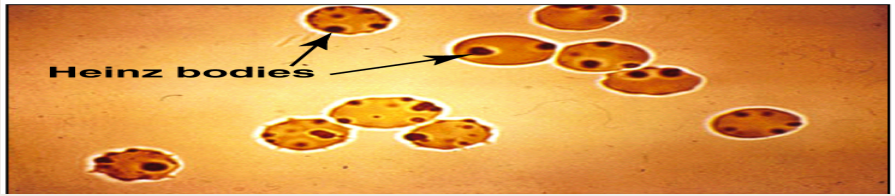
2- Ingestion of Fava Beans من أنواع الفول

- **Favism**
- **Mediterranean Variant**

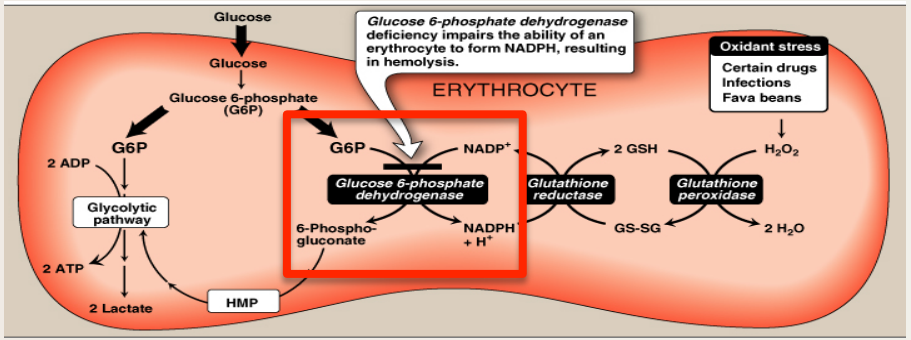
3- Exposure to Infections

**** Chronic nonspherocytic anemia **:**
Hemolytic attacks occurring in absence of the precipitating factors mentioned above, this is a severe form and is due to Class I mutation

Biochemical Basis



Oxidation of sulfhydryl (SH) groups of proteins inside **RBCs** causes **protein denaturation and formation of insoluble masses (Heinz bodies)** that attach to RBCs membranes



- ❑ G6PD Deficiency affects all cells, but is more severe in **RBCs because G6PD in the RBC is the only source of NADPH.**
- ❑ Other sources for NADPH production:
  e.g.,Malic enzyme that converts malate into pyruvate

Diagnosis

Diagnosis of Hemolytic Anemia	•CBC & Reticulocytic Count
Screening	•Qualitative Assessment of G6PD Enzymatic Activity (UV-Based Test)
Confirmatory Test	•Quantitative Measurement of G6PD Enzymatic Activity
Molecular Test	•Detection of G6PD Gene Mutation

Different Classes

There are 4 different classes

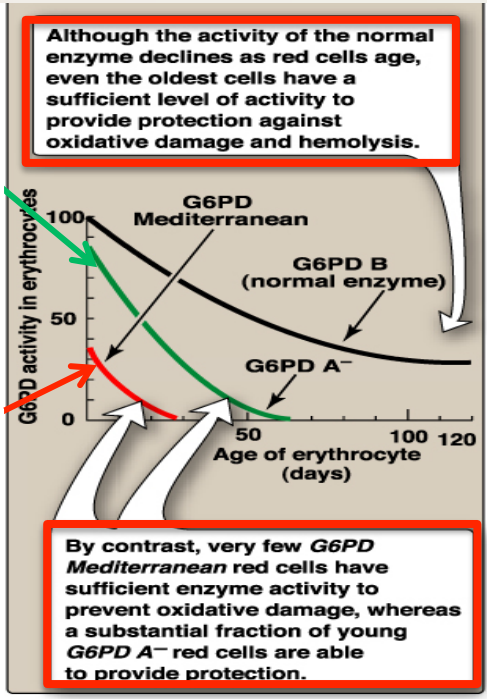
1. **I (Very severe)**
2. **II (Severe e.g. Mediterranean)**
3. **III (Moderate G6PD A-)**
4. **IV (Normal)**

This classification is based on the **Residual enzyme activity (Least in class I, and Highest in class IV)**

Variant Enzymes

G6PD A- (class III):
Moderate, young RBCs contain enzymatic activity. Unstable enzyme, but kinetically normal

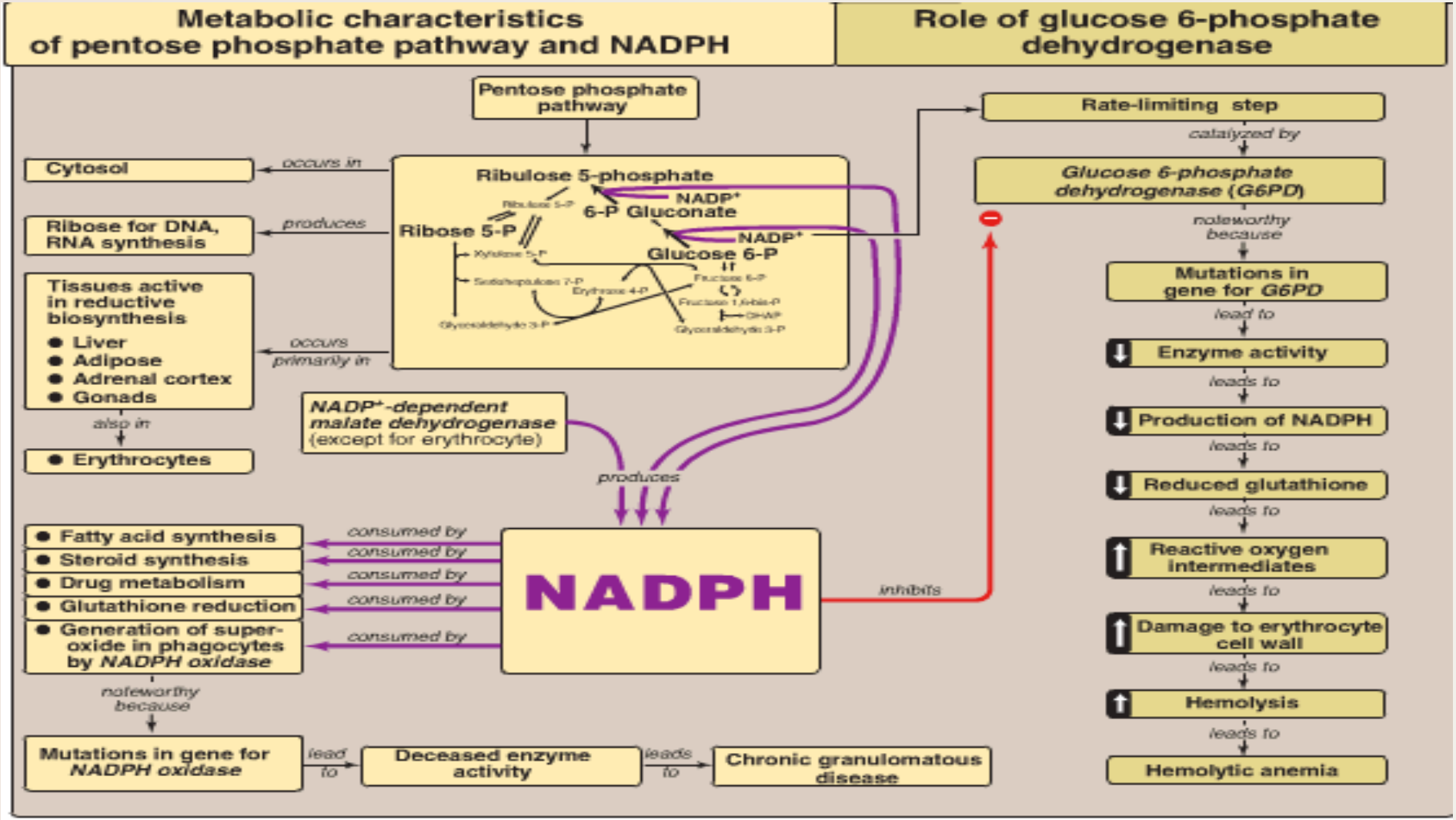
G6PD Mediterranean (II)
Enzyme with normal stability but low activity (severe). Affect all RBCs (both young and old)



Note:
As RBCs get older, their G6PD activity decreases
X-axis is the activity of G6PD in RBC
Y-Axis is the age of the RBC

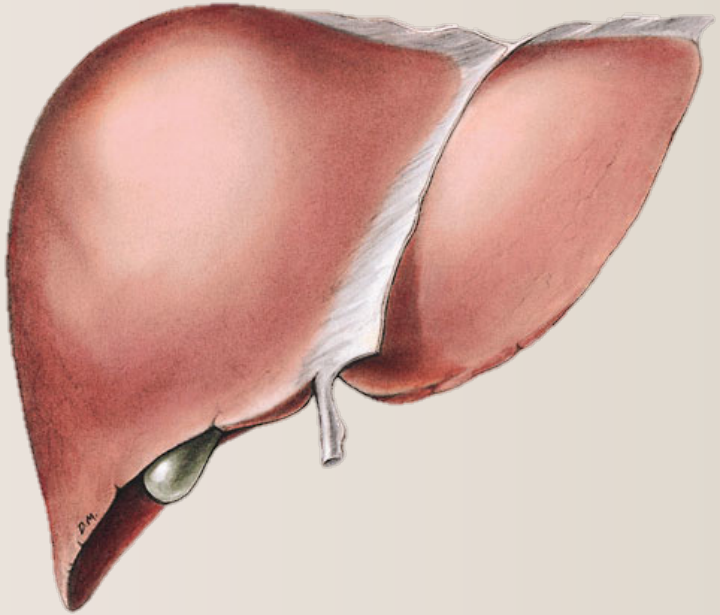
Metabolic characteristics of pentose phosphate pathway and NADPH

Role of glucose 6-phosphate dehydrogenase



1. Which one of the following is one of (ROS) and NOT free radical?
   A. Superoxide
   B. Hydroxyl Radical
   C. Hydrogen Peroxide
   D. PO4
2. Which one of the following enzymes converts H2O2 to H2O :
   A. Glutathione Peroxidase
   B. Glutathione Reductase
   C. Glutathione Synthetase
   D. G6PD
3. G6PD Deficiency Hemolytic Anemia is :
   A. Autosomal recessive
   B. X-linked recessive
   C. X-linked dominant
   D. Y-linked recessive
4. Q5/ 4years old boy, in the emergency he looks pale, fever with dark urine. his mother give him antipyretic CBC show hemolytic anemia. which one of these is the cause of his anemia?
   A. G6PD deficiency
   B. Pyruvate kinase deficiency
   C. sickle cell anemia
   D. Thalassemia major
5. The mechanism by which RBCs are being the most affected cells due to G6PD deficiency is that they:
   A. Don't have a nucleus
   B. Have a Fragile Cell Membrane
   C. Don't have extra NADPH-production pathway
   D. Have High Oxygen Content
6. Which of the following is a Precipitating Factor for G6PD Deficiency Hemolytic Anemia?
   A. Captopril
   B. Mediterranean variant ingestion
   C. Wheat Ingestion
   D. Anti-Epileptic Drugs
7. Oxidation of sulfhydryl groups of proteins inside RBCs causes protein denaturation and formation of insoluble masses called :
   A. Ketone Bodies
   B. Mamillary Bodies
   C. Psommama Bodies
   D. Heinz bodies
8. Which of the following best describes biochemical consequences of G6PD deficiency that leads to hemolytic anemia ?
   A. Low RBC Hemoglobin
   B. Low NADPH
   C. Low Glucose 6-Phosphate

Answers: 1-C 2- A 3-B 4-A 5-C 6-B 7-D 8-B



Thank You!

Done by:

Basmah AlDeghaither
Mohammed AlNafisah