University of Fallujah
College of Medicine

Carbohydrates Disorders

Lecture : 6&7

Stage : 2nd Stage

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Learn Objectives

-What is Glucose 6-P dehydrogenase deficiency diseases?

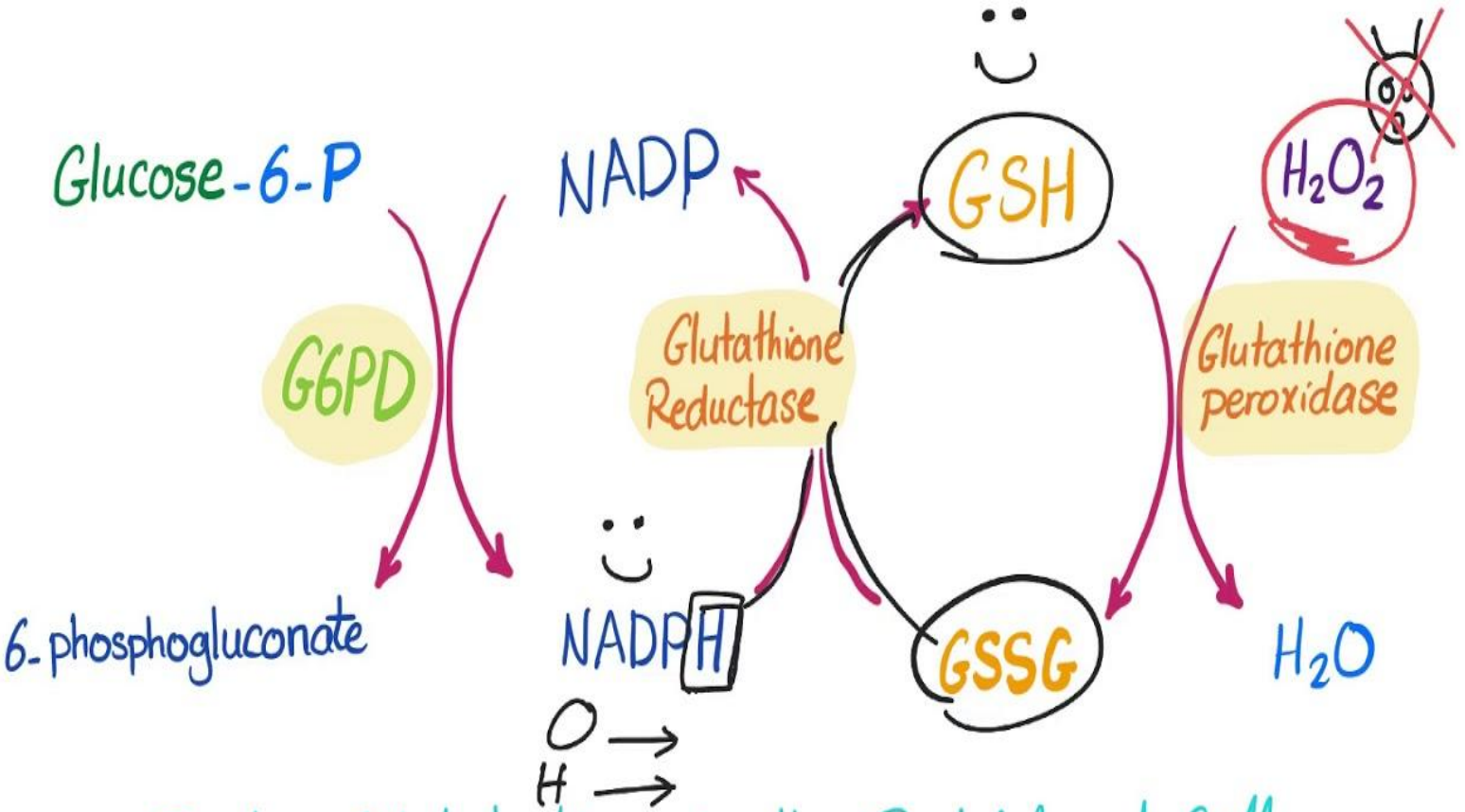
-Diabetes mellitus causes , diagnosis in Lab.

Glucose 6-P dehydrogenase deficiency

It is an **inherited disease** characterized by **hemolytic anemia**, by the **inability to detoxify oxidizing agents**.

A family of deficiencies caused by more than **400 different mutations in the gene coding for G6PD**. Only some of these mutations cause clinical symptoms

Diminished G6PD activity impairs the ability of the cell to form the NADPH that is essential for the maintenance of the reduced glutathione pool



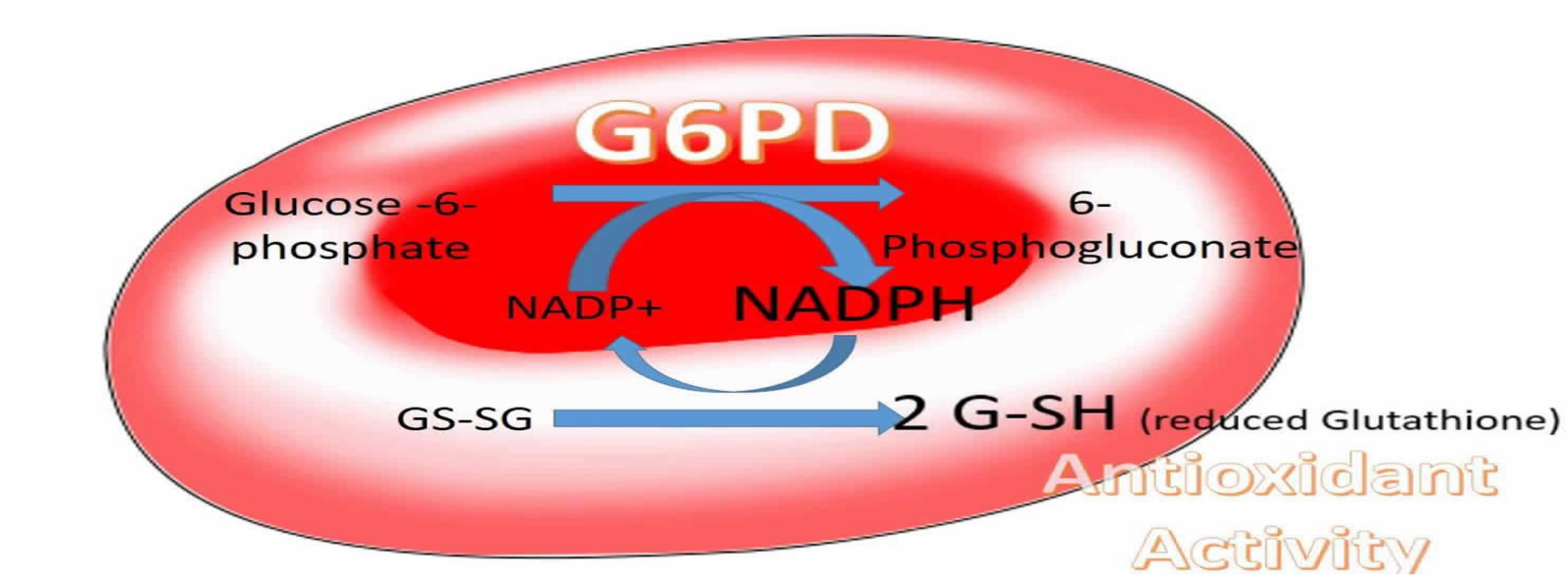
Redox Metabolism in the Red blood Cell

Diminished G6PD activity impairs the ability of the cell to form the NADPH that is essential for the maintenance of the reduced glutathione pool

These results in a decrease in the cellular detoxification of free radicals and peroxides formed within the cell. Although G6PD deficiency occurs in all cells of the affected individual, it is most severe in erythrocytes, where the pentose phosphate pathway provides the only means of generating NADPH.

Class	Clinical Symptoms	Residual enzyme activity
I	Very severe	< 2%
II	Severe	< 10%
III	Moderate	10-50%
IV	None	≥ 60 %

The erythrocyte has no nucleus or ribosomes and cannot renew its supply of the enzyme



However, some patients with G6PD deficiency develop hemolytic anemia if they are **treated with**:

1- **An oxidant drugs***:* Commonly used drugs that produce hemolytic anemia in patients with G6PD deficiency are: **Antibiotics**, Antimalarials, and Antipyretics

2- **Favism**

3- **Infection**: is the most common precipitating factor of hemolysis in G6PD deficiency. **The inflammatory response to infection results in the generation of free radicals in macrophages, which can diffuse into the red blood cells and cause oxidative damage**.

4- **Neonatal Jaundice***:* Babies with G6PD deficiency may experience neonatal jaundice appearing one to four days after birth. The jaundice which may be sever, results from impaired hepatic catabolism of heme or increased production of bilirubin.

Diabetes mellitus

Diabetes mellitus refers to the group of diseases that lead to high blood glucose levels, due to defects in either insulin secretion or insulin action in the body. Diabetes develops due to a diminished production of insulin (type 1) or a resistance to its effects (type 2), including gestational diabetes. This can lead to hyperglycemia, which is largely responsible for the acute signs of diabetes, namely:

- Excessive urine production (**polyuria**)
- Thirst and increased fluid intake (**polydipsia**)
- **Blurred vision**
- **weight loss** (in type 1)
- Lethargy
- Changes in energy metabolism.

Types of diabetes mellitus:

1- **Genetic defects of b-cell function**

● Maturity-onset diabetes of the young (MODY):

– MODY 1: mutation of the hepatocyte nuclear factor (HNF4A) gene,

– MODY 2: mutation of the glucokinase gene.

, – MODY 3: mutation of the HNF1A gene.

● **Type A insulin resistance (insulin receptor defect).**

2- defects of insulin action receptor (insulin resistance (type 2)

3-Insulin deficiency due to pancreatic disease

● Chronic pancreatitis.

● Pancreatectomy.

4-Drugs

● Interferon-a.

● Glucocorticoids.

5-Infections

- Septicemia.
- Congenital rubella.

6-Genetic syndromes associated with diabetes

- Down‟s syndrome.
- Turner‟ssyndrome.
- Klinefelter‟s syndrome.

7-**Gestational diabetes mellitus** Resembles type 2 diabetes, but is transient, occurring in about 2–5% of pregnancies. While it is fully treatable, about 20–50% of affected women develop type 2 diabetes later in life.

Type 1 diabetes:

The cause of type 1 diabetes is not fully understood. An autoimmune attack (to the β- cells of the pancreas) may be triggered by reaction to an infection, for example by one of the viruses of the Coxsackie virus family or German measles, although the evidence is inconclusive. Individuals may display genetically; an observed inherited tendency to develop type 1 diabetes has been traced to particular human leukocyte antigen (HLA) genotypes (the major histocompatibility complex (MHC) in humans is known as the HLA system). Environmental factors can also strongly influence expression of type 1 diabetes. Type 1 diabetes is a polygenic disease (different genes contribute to its expression); it can be dominant, recessive or intermediate. The gene IDDM1, located in the MHC class II region on chromosome 6, is believed to be responsible for the histocompatibility disorder characteristic of type 1 diabetes. Insulin-producing pancreas cells (βcells) display improper antigens to T-cells, which lead to the production of antibodies that attack those β-cells..

Other associated genes are located on chromosomes 11 and 18. Pancreatic β-cells in the islets of Langerhans are destroyed or damaged sufficiently to effectively abolish endogenous insulin production. This an etiology distinguishes type 1 origin from type 2; that is, whether the patient is insulin resistant (type 2) or insulin deficient without insulin resistance (type 1). Type 1 diabetes, formerly known as „childhood", „juvenile" or „insulin-dependent" diabetes, is not exclusively a childhood problem. Type 1 diabetes is treated with insulin replacement therapy, usually by insulin injection or insulin pump, along with attention to dietary management and careful monitoring of blood glucose levels. The most definitive laboratory test to distinguish type 1 from type 2 diabetes is the C-peptide assay, which is a measure of endogenous insulin production

The presence of anti-islet antibodies or absence of insulin resistance (determined by a glucose tolerance test) is also suggestive of type 1. Homeostasis Model Assessment (HOMA) =F1* FG /405

Type 2 diabetes

Type 2 diabetes (non-insulin-dependent diabetes mellitus (NIDDM) or adult-onset diabetes) is a metabolic disorder characterized of two processes: a slowly developing resistance to insulin signaling and a compensatory increase in β-cell release of the hormone. With time β-cells no longer produce enough insulin to maintain control of metabolism and type 2 diabetes results. While the underlying cause of insulin resistance is unknown, there is see correlation between obesity, increased plasma lipids and resistance. Insulin resistance is generally „post receptor‟, meaning it is a problem with the cells that respond to insulin rather than a problem with production of insulin. Central obesity (fat concentrated around the waist in relation to abdominal organs, but not subcutaneous fat) is known to predispose individuals to insulin resistance.

Abdominal fat is especially active hormonally, secreting a group of hormones called adipokines, which may possibly impair glucose tolerance. Obesity is found in approximately 55% of patients diagnosed with type 2 diabetes. There is also a strong inheritable genetic connection in type 2 diabetes. Having relatives (especially first degree) with this disorder substantially increases the risk of developing type 2 diabetes. Environmental exposures may contribute to recent increases in the rate of type 2 diabetes.

A comparison and explanation of the common symptoms of types 1 and 2 diabetes

Symptom	Type 1 diabetes	Type 2 diabetes
Tiredness	Inefficient utilisation of fuels	Inefficient utilisation of fuels
Thirst/polyuria	High glucose (osmotic diuresis)	–
Very low insulin	Damage to insulin-producing β-cells	–
Raised insulin	–	Suggests insulin resistance – linked with obesity
Weight loss	Protein catabolism to provide amino acids for gluconeogenesis, and utilisation of fats for energy	–
Raised HbA1c	High – blood glucose constantly high	Moderate – blood glucose often higher than normal
Ketonuria	Increased metabolism of fats, raised acetyl CoA and increased ketogenesis	–