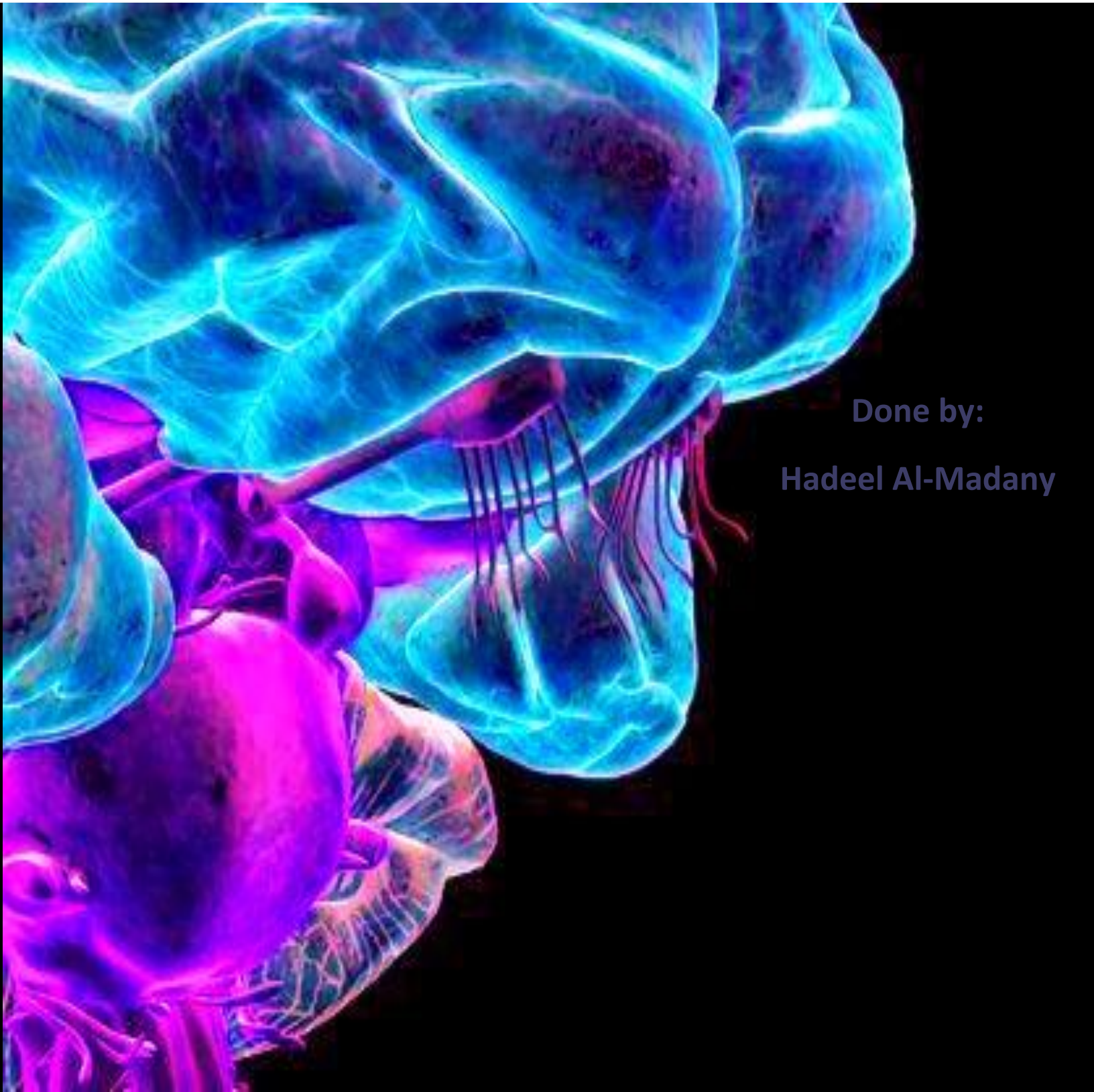
Diabetes Mellitus and Estimation of glucose



Done by:

Hadeel Al-Madany

Pre-diabetes: ths state beween being a normal and a diabetic state, a medical student should know the prediapetic state because in this case, diabetes may be prevented by life style modification or so.

Glucose Homeostasis

- The blood glucose is normally maintained within a narrow range under various conditions by hormones, such as **insulin**, and **anti-insulin** e.g., **glucagon,or epinephrine.**
- **Measurement of blood glucose** is one of the most commonly performed tests in hospital clinical chemistry laboratories.
- The most frequent disorder of carbohydrate metabolism is high level of blood glucose caused by Diabetes Mellitus.

Diabetes Mellitus: Common signs, symptoms & Lab results

- All due to Hyperglycemia
- Polyuria and glucosuria
- Polydipsia
- Polyphagia

Laboratory tests for glucose

- FPG "Fasting plasma glucose": is measurement of plasma glucose after 8-12 hours of fasting (no caloric intake)
    - Normal level: ***3.9-5.6 mmol/l*** (70-100 mg/dL).
- OGTT and 2-hours post prandial (2-hours PP): "Oral glucose tolerance test" is performed by serial measurement of plasma glucose before and after a specific amount of glucose given orally (75g glucose).
- So the patient comes fasting for 8-12 hours, we take a blood sample, measure his plasma glucose. Then, we give the patient 75g glucose orally, and we measure his blood glucose every 30 minutes for 2 hours and we use the finding to make a curve and measure the area under the curve. OGTT is very important to know if the patient is pre-diabetic. The difference between OGTT and the 2-hours post prandial test is that in the 2nd we don't measure in between (every 3o minutes).

Impaired glucose tolerance

IFG/IGT collectively known as pre-diabetes: "Impaired fasting glucose" (IFG) or "impaired glucose tolerance" (IGT) when FPG or 2-hours PP is in the range **above normal but below diabetic criteria**

Criteria for Diagnosis of DM

Categories of increased risk for diabetes*

FPG 100-125 mg/dL (5.6-6.9 mmol/L) [IFG]	Pre-diabetic
2-h PG on the 75-g OGTT 140-199 mg/dL (7.8-11.0 mmol/L) [IGT]	Pre-diabetic
A1C 5.7-6.4 percent	Pre-diabetic

FPG: fasting plasma glucose; IFG: impaired fasting glucose; PG: post glucose; OGTT: oral glucose tolerance test; IGT: impaired glucose tolerance; A1C: glycated hemoglobin.

You MUST memorize the numbers

Criteria for the diagnosis of diabetes

1. A1C ≥6.5 percent. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay.* **OR**	Diabetic
2. FPG ≥126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h.* **OR**	Diabetic
3. Two-hour plasma glucose ≥200 mg/dL (11.1 mmol/L) during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water.* **OR**	Diabetic
4. In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥200 mg/dL (11.1 mmol/L).	Diabetic

A1C: glycated hemoglobin; NGSP: National glycohemoglobin standardization program; DCCT: Diabetes control and complications trial; FPG: fasting plasma glucose; OGTT: oral glucose tolerance test.
* In the absence of unequivocal hyperglycemia, criteria 1-3 should be confirmed by repeat testing.
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***American Diabetes Association (ADA), 2011**

HEMOGLOBIN A1C

- Hemoglobin A1C (A1C) is the result of non-enzymatic covalent glycosylation of hemoglobin
- It is used to estimate glycemic control in the last 1-2 months
- **Recently, A1C is recommended for the detection of T2DM "type 2 diabetes mellitus"**

- A1C and fasting plasma glucose (FPG) were found to **be similarly effective** in diagnosing diabetes.
- **A1C cut-off point of ≥ 6.5 % is used to diagnose diabetes.**

Comparison of type 1 and type 2 DM

	Type 1 Diabetes	Type 2 Diabetes
Age of onset	Usually during **childhood or puberty**	Frequently after age 35
Prevalence %	10% of diagnosed diabetics	90% of diagnosed diabetics
Defect or deficiency	β cells are destroyed, eliminating insulin production	Insulin resistance combined with inability of β cells to produce appropriate quantities of insulin
Ketoacidosis	Common	rare
Treatment	**Insulin** is always necessary	Diet, exercise, oral hypoglycemic drugs, **+/- insulin**

Ketone Bodies

- Acetone (excreted by lungs, **characteristic smell** in diabetic ketoacidotic patients)
- Acetoacetate
- β-Hydroxybutyrate
- the last two are metabolically functional

They are produced by the liver and utilized for energy production by peripheral tissues

Blood glucose Assay

- Blood glucose is detected by a series of enzymatic reactions that ultimately form **a colored product**.
- The ***intensity of color is proportional to the amount of glucose present in blood***
- Color intensity is determined **spectrophotometerically** by measuring the absorbance of the colored solution at a wavelength of 546nm

Procedure

	Test	Standard	Blank
Reagent	**2.5 ml**	**2.5 ml**	**2.5 ml**
sample	**25 µl**	**-**	**-**
Standard	**-**	**25 µl**	**-**
H_2O	**-**	**-**	**25 µl**

- Mix and incubate for 10 minutes at room temperature
- Measure absorbance at 546 nm

Calculation

$$\text{Glucose conc (mmol/l)} = \frac{\text{Abs of sample}}{\text{Abs of standard}} \times \text{Conc of standard (5.6 mmol/l)}$$

Normal Range

Normal reference values for serum glucose: **3.9-5.6 mmol/L** (70-100 mg/dL)

Urine analysis using dipstick: used to detect:

Protein (to assess diabetic nephropathy)
Glucose (to detect glucosuria)
Ketones (to detect ketonuria)
pH

Principle:

- Dipsticks are plastic strips impregnated with chemical reagents which react with specific substances in the urine to produce color-coded visual results.
- They provide quick determination of pH, protein, glucose and ketones. The depth of color produced relates to the concentration of the substance in urine.
- Color controls are provided against which the actual color produced by the urine sample can be compared.

Procedure:

- Dip the dipstick in the urine sample provided then remove it immediately.
- Remove the excess urine
- Read the color produced within 60 seconds
- Match the color changes to the control charts