Diabetes Mellitus

Pathophysiology and Laboratory Diagnosis

Prof. Dr. Talat Tariq Khalil
Nano-Biochemistry&Clinical biochemistry

Dr. Ammar Hatem Abdullateef
MBChB - F.B.M.S Path. (Chemical pathology)

Dr. Widad Hamaza Shekair

Senior Specialist pediatrician

Introduction

- **Diabetes mellitus (DM):** is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both.
- It's a major global health issue associated with **obesity, sedentary lifestyle,** and aging population.
- It is one of the leading causes of **blindness**, **kidney failure**, and **cardiovascular disease**.

DIABETES MELLITUS

The term is derived from the Greek words dia (=through), bainein (=to go) and diabetes literally means pass through. The disease causes loss of weight as if the body mass is passed through the urine. The Greek word, mellitus, means sweet, as it is known to early workers, that the urine of the patient contains sugar.

Diabetes mellitus is a disease known from very ancient times. Charaka in his treatise (circa 400 BC) gives a very elaborate clinical description of *madhumeha* (= sweet urine). He had the vision that carbohydrate and fat metabolisms are altered in this disease.

Pathophysiology

- Normal glucose regulation involves insulin and counter-regulatory hormones.
- In DM, insulin deficiency or resistance reduces glucose uptake by cells, leading to hyperglycemia, glucosuria, and dehydration.
- Chronic hyperglycemia causes protein glycation and vascular damage.

Classification of Diabetes Mellitus

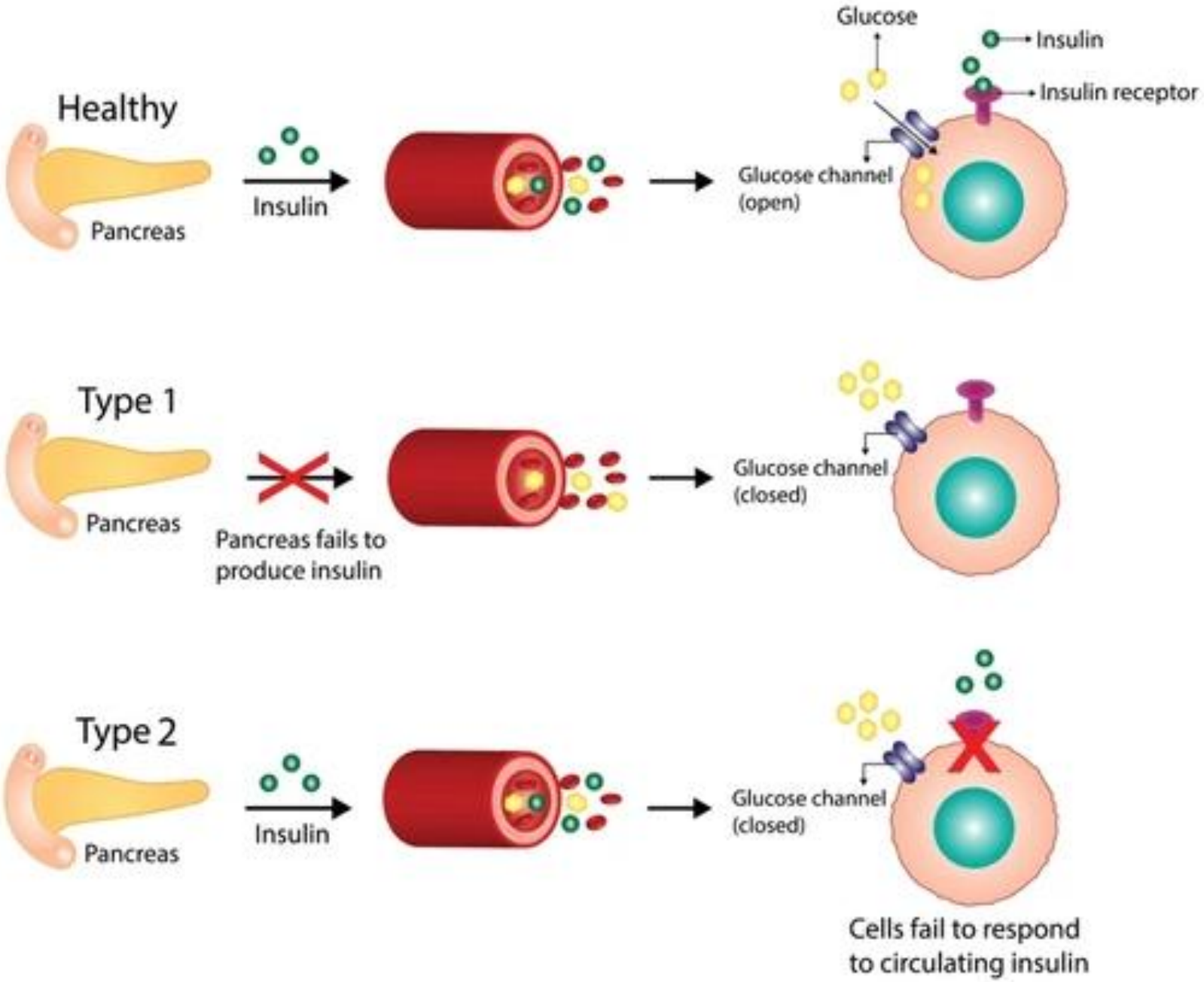
- **Type 1 DM:** Autoimmune destruction of pancreatic β-cells → absolute insulin deficiency.
- **Type 2 DM:** Insulin resistance with relative insulin deficiency.
- **Gestational DM:** Glucose intolerance during pregnancy.
- **Other Specific Types:** pancreatic diseases, endocrinopathies, drug-induced.

Type 1 Diabetes Mellitus

- represent about less than **10%** of total diabetes cases
- Age at presentation: **Childhood or adolescence**
- Onset: Sudden
- Cause: **Autoimmune destruction** of β-cells → no insulin
- treatment: **needs lifelong insulin**
- Ketoacidosis: **Common**
- Family history: **Less common**

Type 2 Diabetes Mellitus

- Represent about **90**% of total diabetes cases
- Age at presentation: **Adults (often >40 yrs)**
- Onset: Gradual
- Cause: **Insulin resistance** related to obesity & sedentary lifestyle then relative insulin deficiency
- Body type: **Overweight / Obese**
- treatment: **lifestyle modification and drugs increase insulin sensitivity**
- Ketoacidosis: not presented
- Family history: **Strongly positive**


Healthy
Pancreas
Insulin
Glucose
Insulin
Insulin receptor
Glucose channel
(open)
Type 1
Pancreas
Pancreas fails to
produce insulin
Glucose channel
(closed)
Type 2
Pancreas
Insulin
Glucose channel
(closed)
Cells fail to respond
to circulating insulin

	Type 1 Diabetes	Type 2 Diabetes
1	Most often diagnosed in childhood.	Usually diagnosed in over 30 year old's.
2	Not linked to increased body weight.	In most cases associated with increased body.
3	Often associated with higher than normal ketone levels at diagnosis.	It is related to high blood pressure and / or cholesterol levels in the diagnosis.
4	Insulin injections or insulin pumps are treated.	It can treat initially without medication or with tablets.
5	Episodes of low blood sugar level (hypoglycemia) are common.	There are no episodes of low blood sugar level, unless the person is taking insulin or certain diabetes medicines.
6	It can't be controlled without injecting insulin.	Sometimes possible to come off diabetes medication.

Gestational Diabetes Mellitus (GDM)

- **Definition:** Glucose intolerance first recognized during pregnancy (**in the 2nd or 3rd trimester**). with increased risk of
- -future Type 2 DM (for the mother)
- -fetal (Macrosomia, hypoglycemia after birth)

- Cause: Placental hormones (like human placental lactogen, estrogen, and progesterone) cause insulin resistance → high blood glucose.

Clinical Features of DM

Classic Symptoms:

- These are known as the **“3 Ps”** — classic features of hyperglycemia:
- **Polyuria** (excessive urination)
- **Polydipsia** (excessive thirst)
- **Polyphagia** (excessive hunger)

Other symptoms:

Weight loss (especially in type I), Fatigue, blurred vision, recurrent infections, slow wound healing.

Features of acute complications of DM

- **Diabetic Ketoacidosis (DKA)**
- Polyuria, polydipsia, dehydration
- Nausea, vomiting, abdominal pain
- Kussmaul breathing (deep, rapid)
- Fruity (acetone) breath odor
- Drowsiness → coma
- Blood glucose > 250 mg/dL, Ketones positive, metabolic acidosis

- **Hypoglycemia**
- **Autonomic (Adrenergic) Symptoms – Early Warning Signs:**
- Sweating, tremor, palpitations, hunger, anxiety, tingling.
- **Neuroglycopenic Symptoms – Occur Later (Low Brain Glucose):**
- Headache, confusion, blurred vision, weakness, seizures, coma.
- Blood glucose < 70 mg/dl

Diagnostic Criteria

- Fasting Plasma Glucose ≥126 mg/dL
- 2-hour OGTT ≥200 mg/dL
- HbA1c ≥6.5%
- Random Plasma Glucose ≥200 mg/dL with classic symptoms.

- Diagnosis should be **confirmed** on another day testing unless symptoms are clear.

Clinical interpretation of laboratory results

Normal	Pre-Diabetes	Diabetes
Fasting glucose < 100 mg/dl	Impaired fasting glucose ≥ 100 - 125 mg/dl	Fasting glucose ≥ 126 mg/dl
2-h PG < 140 mg/dl	Impaired glucose tolerance 2-h PG ≥ 140 - 199 mg/dl	2-h post meal glucose ≥ 200 mg Random PG ≥ 200 + symptoms
A1C < 5.7%	5.7% to 6.4%	≥ 6.5%

Oral Glucose Tolerance Test (OGTT)

- Performed after 8–12 hours over night fasting.
- 75 g glucose dissolved in 300ml water and given orally.
- Samples collected at fasting and 2 hours.
- OGTT is less used nowadays because it is time-consuming, inconvenient, and requires special preparations, so it is mainly reserved for: **gestational diabetes (GDM)** and **borderline** cases.

- **Note:** in GDM need at least 3 readings (0,1,2 hrs) and specific cut values for diagnosis and the test done at 24 to 28 weeks of gestations.

Glycated Hemoglobin (HbA1c)

- **Definition:**
- Glycated hemoglobin is formed by a non-enzymatic, irreversible reaction between glucose and the N-terminal valine of the β-chain of hemoglobin A (HbA) in red blood cells
- Because the average red blood cell lives approximately 120 days, the glycosylated hemoglobin level at any one time reflects the average blood glucose level over the **last 2 to 3 months.**
- **Reference Ranges:**
- < 5.7 % – Normal
- 5.7 – 6.4 % – Prediabetes
- ≥ 6.5 % – Diagnostic for Diabetes Mellitus
- **Clinical Importance:**
- Used for diagnosis of diabetes
- Useful for long-term monitoring because it Reflects average glucose over past 2–3 months.
- Not affected by short-term glucose changes so **no fasting required**.

May be unreliable in anemia or hemoglobinopathies.

Urine Tests

- **Glucosuria** appears when plasma glucose >180 mg/dL. It is supportive **not diagnostic** test
- Ketonuria suggests (insulin deficiency-type I DM as in DKA).
- **Microalbuminuria** : urinary albumin(30–300 mg/day) is an early sign of nephropathy.

Complications

- **Acute:**
- Diabetic Ketoacidosis (type I), Hyperosmolar Hyperglycemic State(type II), lactic acidosis and Hypoglycemia.
- **Chronic:**
- Retinopathy, Nephropathy, Neuropathy, Coronary artery disease, Stroke, Diabetic foot ulcers.

Good luck