Diabetes Mellitus

PROFESSOR DOCTOR
SAAD HASAN MOHAMMED ALI

2024 / 2025

Learning Objectives:

1. Describe pathophysiology of diabetes mellitus [DM].
2. Describe etiology of DM.
3. Outline types of DM
4. Outline epidemiology and risk factors of DM.
5. Reviewing & Illustration figures of the common general and oral complications of DM
6. Reviewing general medical management [diagnosis and treatment] of patients with DM=.

Diabetes Mellitus (DM):

- **A metabolic disease = characterized by an elevations of blood glucose levels (= Hyperglycemia) .**

- Diabetes is due to either the pancreas not producing enough insulin or the cells of the body not responding properly to the insulin produced.

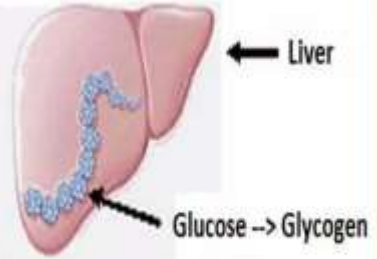
❑ Need Glucose→ Obtained *In the fasting state from:*

- ❑ ***1. Intestinal Absorption of Glucose***
- ❑ **2. Glycogenolysis: → this process in the liver → breaks down glycogen → releases glucose into the bloodstream.**
- ❑ **3. Gluconeogenesis: → this process in the liver → produces glucose from non-carbohydrate sources → → → such as amino acids + fatty acids → releases glucose into the bloodstream.**

PATHOPHYSIOLOGY

- The body obtains glucose from three main places:
  - The intestinal absorption of food

  - The breakdown of glycogen, the storage form of glucose found in the liver



  - Gluconeogenesis, the generation of glucose from non-carbohydrate substrates in the body.

"Normal Physiology"

- ***During digestion:*** most foods are broken down into glucose, then enters blood and used by cells for energy and growth.
- **Most cells:** **Except** central nervous system, Require the presence of insulin to allow glucose entry.

Insulin:

- **Produced** by the ***β cells*** ***of the islets of Langerhans of the pancreas*** and increased insulin secretion occurs in response to increased blood glucose concentrations.
- **Binds** to specific cellular **receptors** to exert its effects.
- **Suppresses** gluconeogenesis and promotes protein synthesis and lipogenesis.

Hormones Increase Blood Glucose=

1. Glucagon
2. Catecholamines
3. Growth hormones
4. Thyroid hormones
5. Glucocorticoids.

Diabetes Mellitus/// Etiology

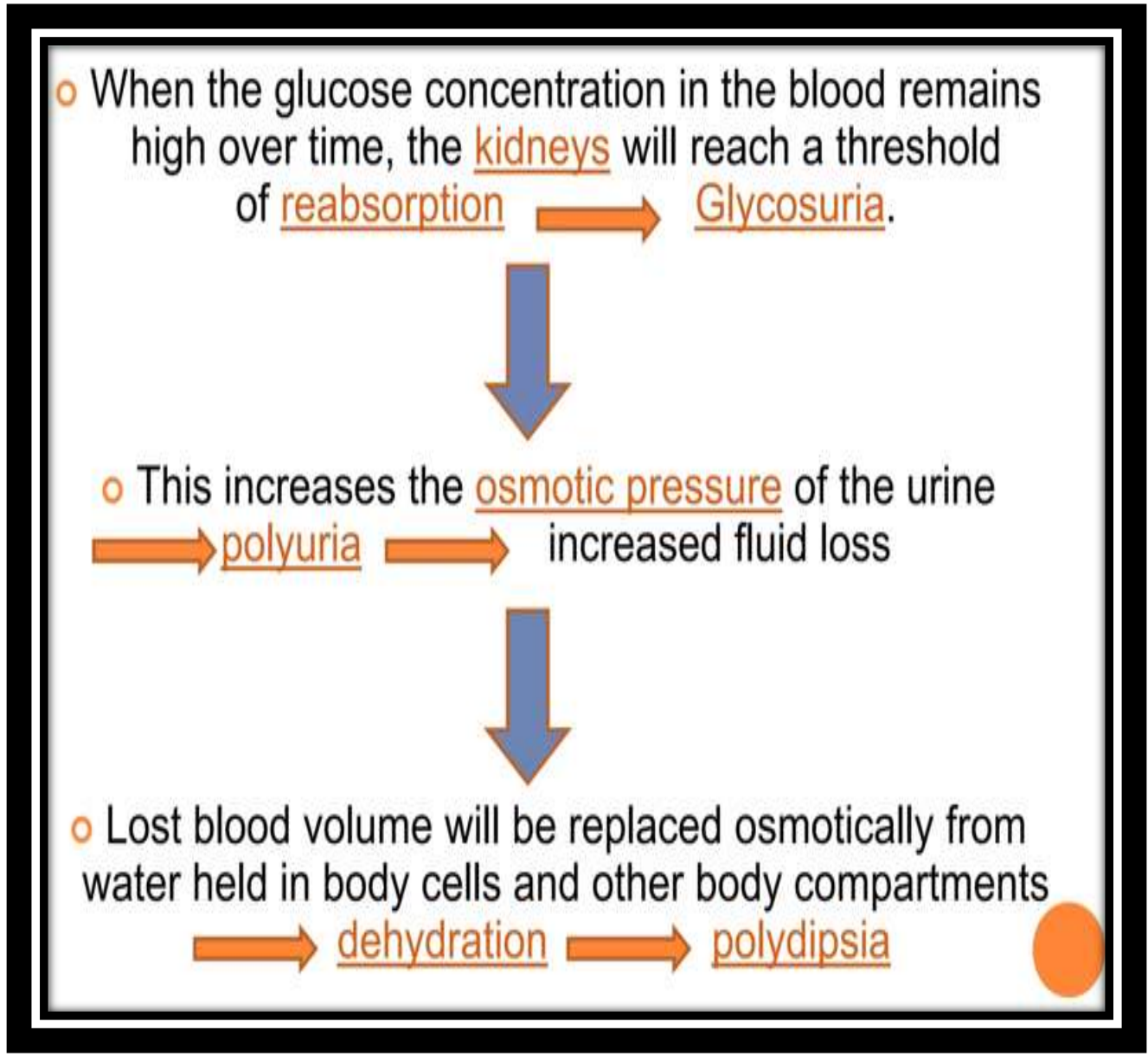
1) In islets of Langerhans of pancreas = two main endocrine cells= insulin-producing beta cells + glucagon secreting alpha cells.
2) Beta and alpha cells are continually changing their hormonal levels based on =glucose environment.
3) Without the balance between insulin and glucagon= the glucose levels become Abnormally + Un-Controlled [+ OR -]

[بدون توازن الهورمونين= انحراف خطير بمستويات سكر الدم]

1) In DM= insulin = is either absent and/or has impaired its action (insulin resistance)= leads to hyperglycemia.

Cardinal Signs of Diabetes Mellitus (DM) :-

- Polydipsia
- Polyuria
- Polyphagia
- Weigh loss= Type 1 DM
- Obesity= Type 2 DM
- Weakness
- Poor wound healing
- Severe infection



"American Diabetes Association Classification of Diabetes Mellitus / DM "

<<5 general types (Determined by the Underlying Mechanism)>>

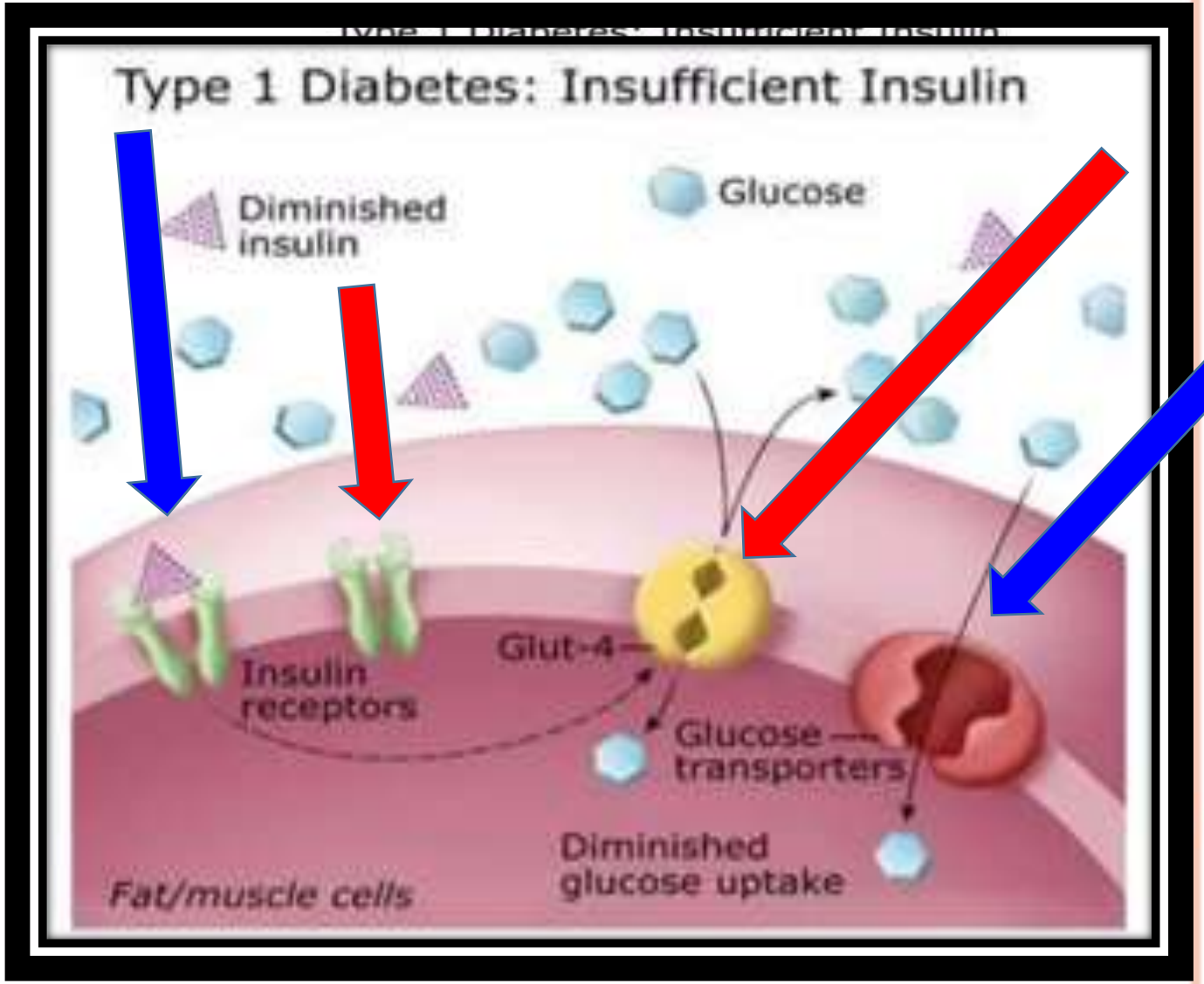
1. Type 1 diabetes: (due to **autoimmune β-cell destruction**➔ leading to absolute insulin deficiency [[**including LADA=** latent autoimmune diabetes of adulthood]]. **autoimmune type 1 diabetes rarely occurs before 6 months of age.**

Type 1 DM

- Results from the pancreas's failure to produce enough insulin.

- This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes".

- **Genetic predisposition factors = 1/3th susceptibility to Type 1 DM.**
- **Environmental predisposition factors = Could trigger:**
- Direct toxicity to β cells
- Autoimmune reaction against β cells.



Type 1 Diabetes Mellitus

3 main Environmental categories:

1) **Viruses:** Mumps, cytomegalovirus and Epstein–Barr viruses.
2) **Specific drugs or chemicals.**
3) **Dietary constituents:** [= **diabetogenic toxins**]

A. Nitrosamines:

(smoked and cured meats + coffee)

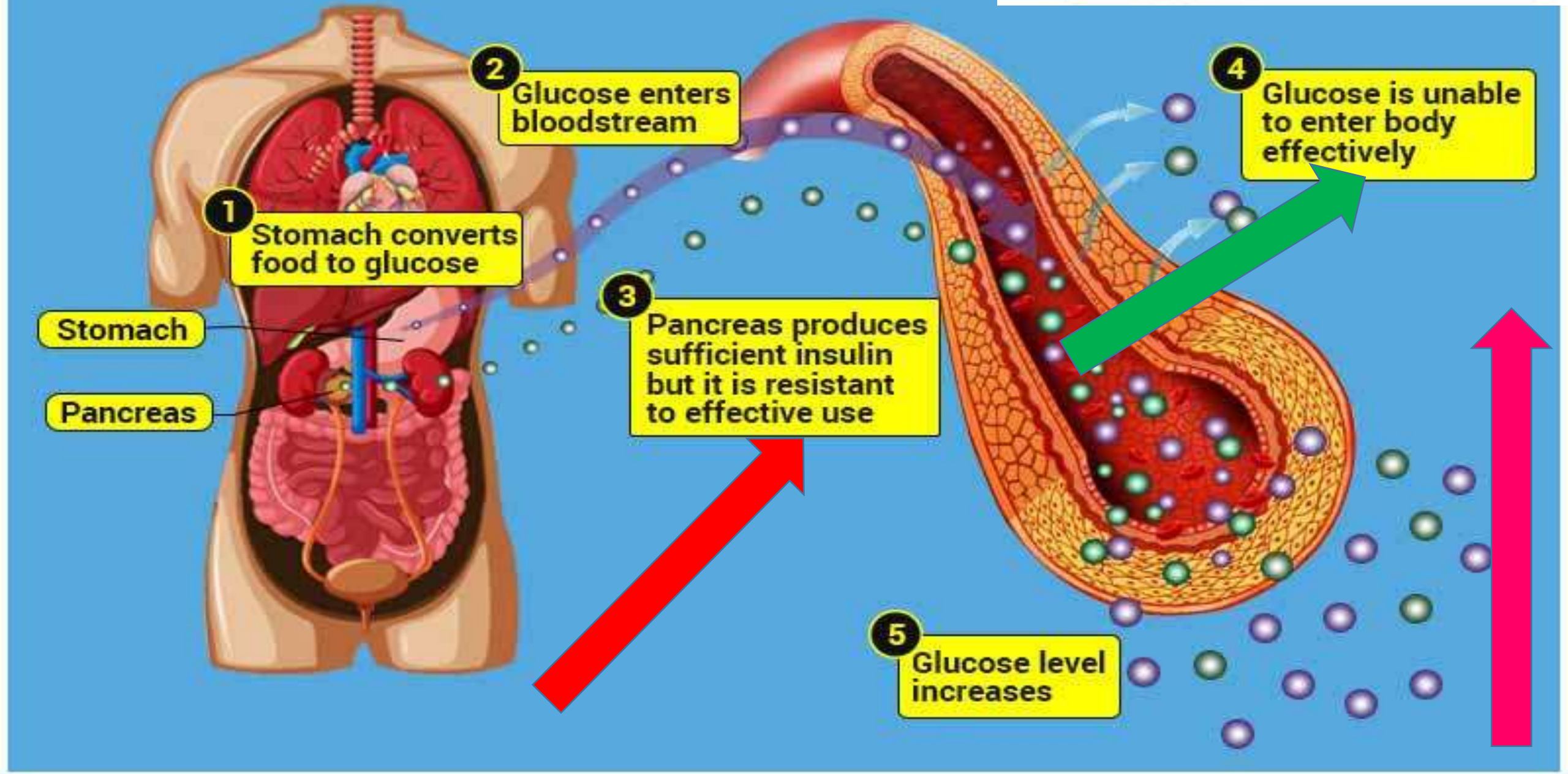
B. Bovine serum albumin (cow's milk)

2. Type 2 diabetes:

(due to a **progressive loss of adequate β-cell insulin secretion** on **background of insulin resistance**)

DIABETES

Type 2 DM



Type 2 DM

- Begins with insulin resistance, a condition in which cells fail to respond to insulin properly.

- This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes".
- The primary cause is excessive body weight and not enough exercise.

Insulin → **uptake of glucose**

from the blood into the cells

Normal Pathophysiology:-

Pancreas

(Beta cells found In islets of Langerhans)

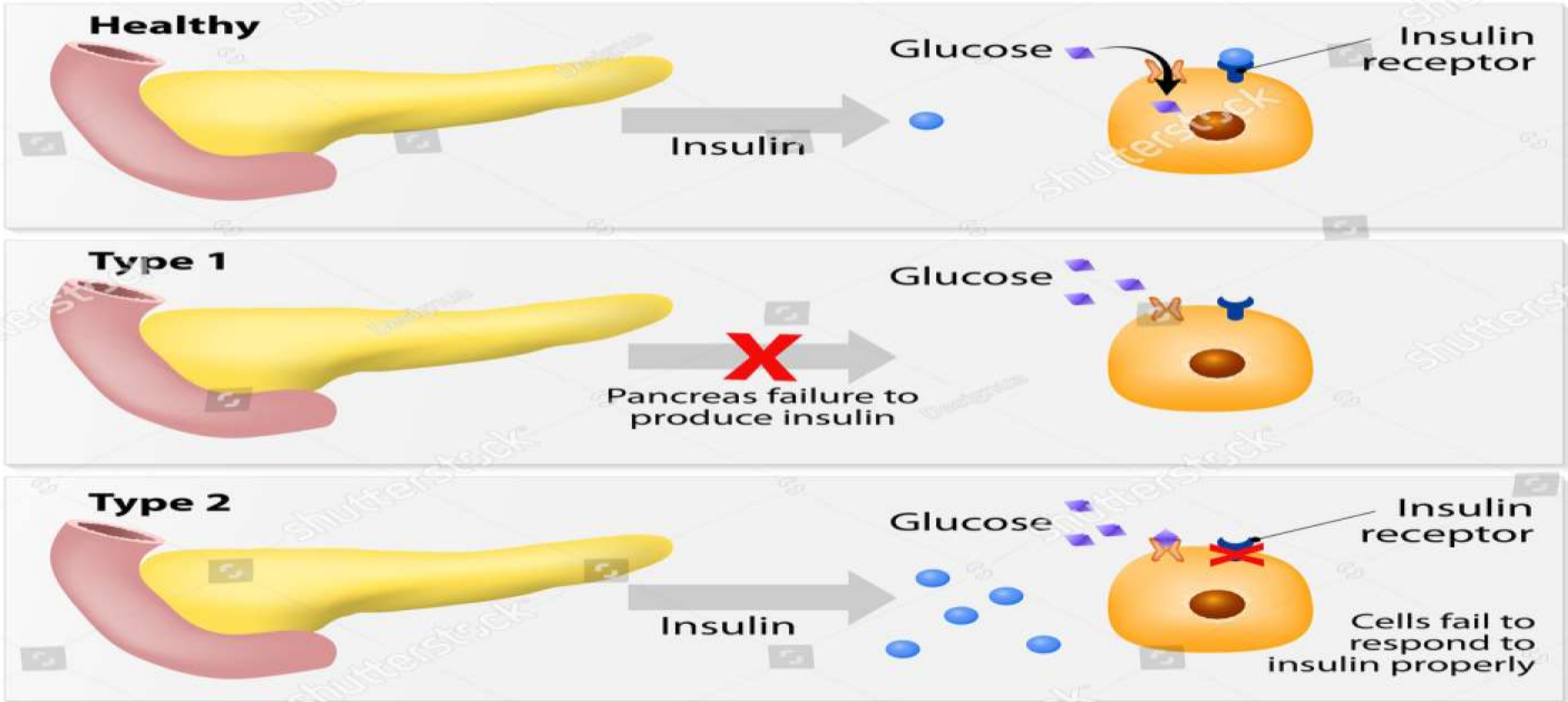
in response to **rising level of blood glucose**

Abnormal Pathophysiology:-

1. If **insufficient amount of insulin available**
   - Type 1 DM
2. If **insulin Resistance = respond poorly to** insulin
   - Type 2 DM

high level of blood glucose → [**Diabetes Mellitus**]

DIABETES MELLITUS



3. Gestational diabetes mellitus:

Gestational Diabetes Mellitus

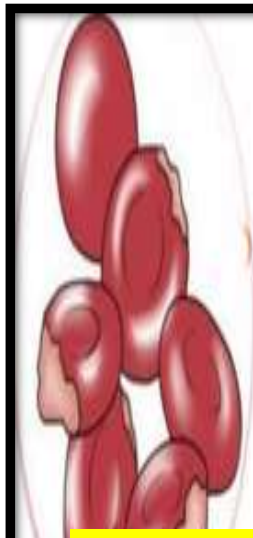
Is the third main form and occurs in pregnant women without a previous history of diabetes

(diagnosed in second or third trimester of pregnancy)

- Gestational diabetes mellitus (GDM) resembles type 2 DM in several aspects.
  - Involves a combination of relatively inadequate insulin secretion and responsiveness.
    - It occurs in about 2–10% of all pregnancies and may improve or disappear after delivery.

- Increased levels of insulin in a fetus's blood may inhibit fetal surfactant production and cause respiratory distress syndrome.

Respiratoy Distress



- A high blood bilirubin level may result from red blood cell destruction.

Jaundice

High blood glucose levels in mother

Brings extra glucose to baby

Increase weight

4. Specific DM

Types=Monogenic diabetes syndromes

(such as **neonatal diabetes** and **maturity-onset diabetes of the young**).

❑Maturity-onset diabetes of the young (MODY)

1) Autosomal dominant inheritance
   =mutated glucokinase (GK) gene=
   leading to increased glucose production
2) Child = have 50% chance to inherit DM
3) *subclinical at birth* >>>>
   clinically presented before age of 25 years

Diagnosis of MODY?

1) Onset before 25 years of age
2) DM in two consecutive family generations
3) Absence of autoantibodies to β-cell antigens
4) Pancreas produce endogenous insulin secretion + Preserved serum C-peptide= level of >200 pmol/L [while In type 1 DM insulin production is very low].

[C-peptide links the A and B chains of insulin]

Neonatal Diabetes=

Commonly due to Autosomal dominant mutations in the:

1.. chromosome 11 [30%] = *KCNJ11* and *ABCC8* genes encoding β-cell K_{ATP} channel = … lead to =

Overexpression of genes

OR

2.. chromosome 6 [20%]= Insulin gene (*INS*)= … lead to=

Decrease insulin production

➔ very high levels of blood glucose

5. Secondary Diabetes? Due to other causes / Other Conditions:

A. Diseases of the Pancreas: such as

1. **+cystic fibrosis**
2. **+ Pancreatitis**
3. **+ Pancreatic cancer**
4. **+ Glucagonoma**
5. **+ Hemochromatosis (=harmful levels of iron that damage pancreas)**

5. Secondary Diabetes? Due to other causes / Other Conditions:

B.. Drug- or chemical- induced diabetes (using them are known to increase the risk of diabetes :

1. Excess production of antagonists to insulin (= catecholamines)
2. glucocorticoid,
3. thiazide diuretics
4. some HIV medications
5. antipsychotics,

C.. Diseases-induced Diabetes

1. Viral infections = congenital rubella
2. Genetic syndromes =Down’s syndrome).

COMPLICATIONS OF DIABETES MELLITUS:

I. Acute complications:

1)diabetic ketoacidosis
2)diabetic coma

II. Chronic complications:

A. Microvascular :

1)Retinopathy
2)Nephropathy
3)Neuropathy
4)Diabetic Foot
5)Dermopathy

B. Macrovascular:

1)Cerbro-vascular Accidents.
2)Cardio-vascular Accidents.
3)Peripheral Vascular Disease.

Thank You For Your Attention

Any questions?