Diabetis Mellitus

→ It is a grp of metabolic disorders sharing the common feature of hyperglycemia.

→ In DM patient's body has trouble in moving glucose from blood to cells.

↓

1. ↑se glu in blood (hyperglycemia)
2. ↓se glu in cells.

↓

1. Chronic hyperglycemia may cause 2° damage in multiple organ systems
2. Cells starve for energy despite having glucose right on doorsteps.

Classification

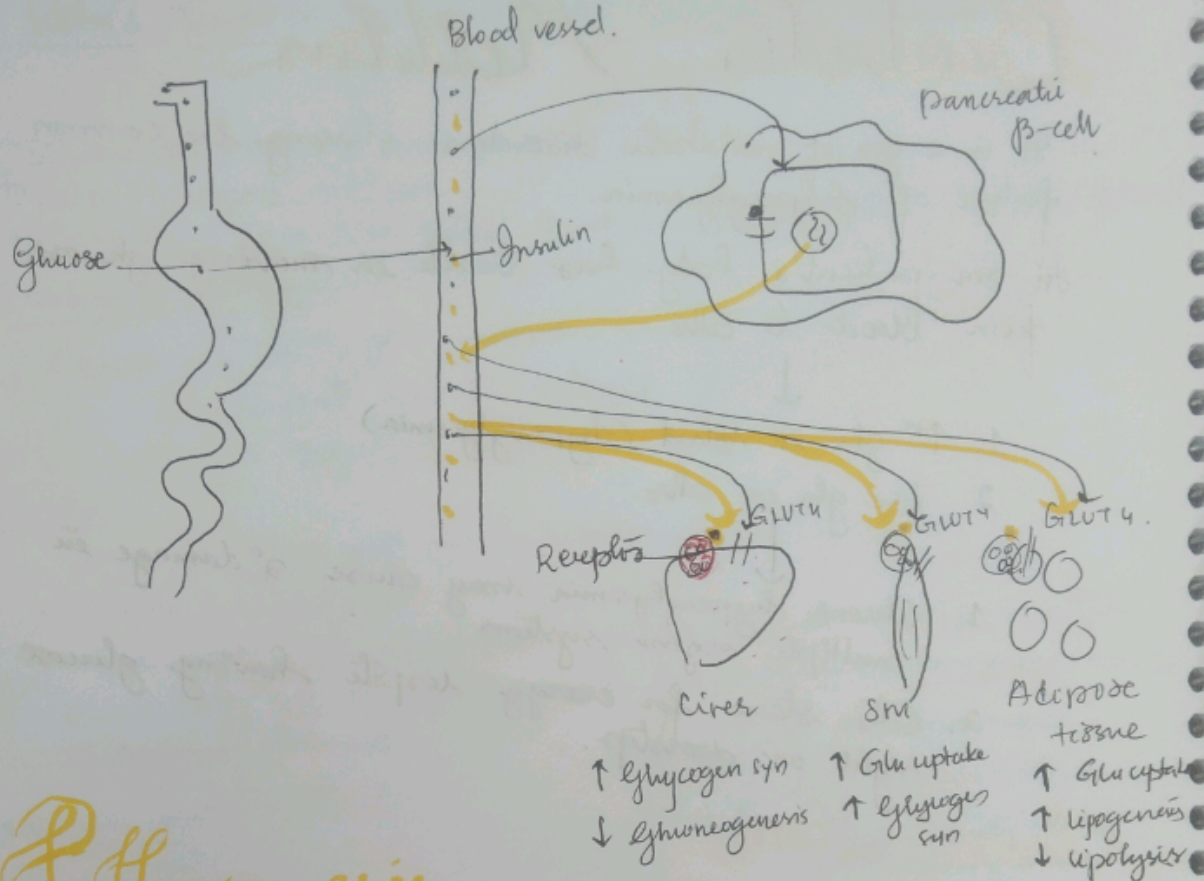
Type 1.

- 10% cases.
- Juvenile onset Diabetes (JODM)
- Insulin dependent DM (IDDM)

Tx: Insulin replacement.

Type 2.

- 90% cases
- Maturity onset diabetes
- Non-insulin dependent DM (NIDDM)



Pathogenesis

TYPE 1 DM:

- Body cannot make enough insulin.
- It is an Autoimmune disorder / diseases - islet destruction caused by cytotoxic T cells → against endogenous β-cell antigens

↓

becomes abnormal & self reactive

↓

Self reactive cytotoxic T cells.

- They kills body's own antibody

Self + Autoimmunity.

In Diabetes Mellitus 1.

There is genetic abnormality & environmental trigger
↓
Loss of self tolerance
↓
Self reactive clonal T cells are not killed / deleted in thymus
↓
Attacks β-cells of pancreas (β-cells act as autoantigens)
↓
Dec in Insulin
↓
Inc glu. in blood (hyperglycemia)

TYPE 2 DM:

Insulin Resistance: failure of target tissues to respond normally to insulin.
↓
Main tissues → liver, skeletal ms, adipose tissue.

Genetic Component
Constitutional factors + such as obesity, hypertension & level of physical activity play contributory role.
↓
Insulin resistance on target organs
↓
Hyperglycemia

Clinical features

-> Classic triad - Polyuria, Polydipsia, Polyphagia (P's)
-> Weight loss.

Insulin def.

↓ Cellular glu uptake
↓
Hyperglycemia.
↓
Glycosuria.
↓
POLYURIA → Vol. & electrolyte depletion → ↓ Intracellular H_2O.
↓
Stimulation of osmoreceptors
↓
Intense thirst → Polydipsia

↑ lipolysis
↑ proteolysis in ms
↓
-Ve energy balance (wt loss)
↓
↑ Appetite
↓
POLYPHAGIA

Complications

I. Acute Metabolic Complications – Diabetic ketoacidosis (DKA)
– Hyperosmolar hyperglycemic non ketotic coma (HHS).

II Late Systemic Complications
1. ATHEROSCLEROSIS → resulting in ↑ed risk of MI, stroke, and lower extremity ischemia.
2. Diabetic Nephropathy
3. Diabetic neuropathy
4. Diabetic Retinopathy
5. Infections.

DIABETIC KETOACIDOSIS:

Insulin def. → stimulates lipoprotein lipase.
↓
Resultant breakdown of adipose stores.
↓
An ↑ in levels of free fatty acids.
↓
When these free fatty acids reach the liver, they are esterified to fatty acyl coenzyme A.
↓
Oxidn of fatty acyl Coenzyme A molecules with the hepatic mitochondria produce ketone bodies
↓
Ketonemia
↓
Ketonuria
↓
If the urinary excretion of ketones is compromised by dehydration, the result is a systemic metabolic ketoacidosis.

Diagnosis

1. Urine test.
   - → Glucosuria - Benedict's test
   - → Ketonuria - Rothera's test.
2. Blood test. (Revised criteria) ADA.

1) Random glucose	Fasting glucose (>8 hr).	2-hr after 75 gram glucose load.
≥ 200 mg/dL	≥ 126 mg/dl	≥ 200 mg/dL.
11.1 mmol/L	7.0 mmol/L	11.1 mmol/L.

→ ~~Gh~~ HbA1C - diabetic control (90-120 days).

Diabetic Nephropathy

3 types of lesions in DM.

Diabetic Glomerulosclerosis

2 forms - 1. Diffuse
2. Nodular.

1. Diffuse glomerulosclerosis
   - → Most common
   - → Hyaline deposition in 4 places.
     1) Mesangium (deposit)
     2) GBM (thickened) (earliest)
     3) capillary (fibrin cap)
     4) Bowman's capsule (capsular drop)

Vascular lesions

→ Hyaline arteriosclerosis affecting the afferent & efferent arterioles of the glomeruli

Tubular lesions (ARMANNI-EBSTEIN lesions)

↳ The epithelial cells of PCT → extensive glycogen deposits → appear as vacuoles

ii) Nodular glomerulosclerosis:-

→ Also called as Kimmelstiel - Wilson (KW) lesions or intercapillary glomerulosclerosis.
→ Pathognomonic (most specific)
→ Specific for type 1 DM.
→ Pathological changes consists of one or more nodules in a few glomeruli.