Diabetic emergencies

1- Diabetic Ketoacidosis

Triad of **hyperglycemia**, **high anion gap metabolic acidosis**, and **ketonemia.**
Characteristically **associated with T1DM** (may be the first presentation of it).
It has become increasingly common in T2DM (in severe stress).

Ketone Bodies
Products of fatty acid metabolism.

Ketone bodies are: 1-Acetoacetate 2-Acetone
3-β-Hydroxybutyrate
produced by **hepatocyte mitochondria** (ketogenesis) and **utilized for energy** by peripheral tissues (Ketolysis)

Normally, glucose is the **primary fuel for the brain** If glucose is **not available** for the brain, the brain can utilize plasma ketone bodies, , that can penetrate the blood brain barrier, and serve as fuel molecules (The brain's GLUT is: insulin-independent).

Ketone Bodies Synthesis

In uncontrolled DM there is ↑lipolysis in adipose tissue → ↑ [FFA] mobilization to liver.
1- ↑hepatic FA oxidation →↑ acetyl CoA which will be channeled into KB synthesis
2-Acetyl CoA→Acetoacetyl CoA→HMG CoA through: **HMG CoA synthase** "rate limiting enzyme"
3-HMG CoA → **acetoacetate** "The first KB to be synthesized"
4- Acetoacetate can be:
reduced to β-Hydroxybutyrate ,
or
spontaneously decarboxylated to acetone
- Acetyl CoA + oxaloacetate (OAA) → Krebs cycle.
- ↑ Acetyl CoA production activates **pyruvate carboxylas** → Converts **pyruvic acid into OAA** →OAA is used for **gluconeogenesis** (rather than Krebs cycle).

Ketone Bodies Utilization

Occurs in the mitochondria (so cannot occur in RBCs)
Does not occur in the liver (as the liver lacks the **thiophorase enzyme** required for ketolysis).
β-Hydroxybutyrate —oxidation→ acetoacetate.
Acetoacetate is converted to acetoacetyl CoA (catalyzed by thiophorase).
Acetoacetyl CoA is converted to acetyl CoAs.

In uncontrolled DM there is ↑lipolysis in adipose tissue → ↑ [FFA] → ↑ mobilization of FFA to liver → ↑hepatic FA oxidation → ↑ hepatic acetyl CoA which will be utilized in KB synthesis (ketogenesis) → ketoacidosis
In uncontrolled DM the rate of ketogenesis is > the rate of ketolysis → ketonemia (↑[KB] in blood)→ ketonuria (↑[KB] in urine).

Manifestations of DKA

1- Fruity odor of breath (because of acetone)
2-Acidosis (low pH of blood because KBs are acids)
3-Dehydration (due to glucosuria)

Precipitating factors for DKA
Infection (30-40%).
Inadequate insulin treatment or non-compliance (20%).
Severe illness (e.g. Myocardial infarction), Trauma, Drugs: e.g., steroids.

2- Hyperosmolar Hyperglycemic state (HHS)

insulin levels are insufficient to allow appropriate glucose utilization but are adequate to prevent lipolysis and subsequent ketogenesis. (also called Hyperosmolar Non-ketotic acidosis (HONK).

Characteristic

1- Little or NO accumulation of ketone bodies 2- Serum glucose is often >50 mmol/L
3-Plasma osmolality could reach 380 mosmol/Kg (Normal range 275-295)
4- Usually occurs in elderly with T2DM 5- Neurological abnormalities

3-hypoglaycemia

It is a **common complication** of treatment with insulin or oral hypoglycemics.
More common in patients with **T1DM**.

Hypoglycemia is a medical emergency
Because the brain has absolute requirement for a **continuous** supply of glucose.
Transient hypoglycemia → cerebral dysfunction
Severe, prolonged hypoglycemia → brain death

manifestations of hypoglycemia CNS Symptoms Low blood glucose conc	Symptoms resolved within minutes following the administration of glucose

Hypoglycemia occurs due to impaired protective responses to hypoglycemia:
1- Insulin is supplied exogenously and its release cannot be turned off
2- Glucagon & adrenaline response to hypoglycemia becomes impaired later in the course of DM

Clinical presentation:
1- Symptoms of **sympathetic overactivity** (plasma [glucose] **<3.6 mmol/L**, abrupt fall):
anxiety, tremors, sweating & palpitation

2- Symptoms **of neuroglycopenia** (plasma [glucose] **<2.6 mmol/L**, gradual fall):
headache, confusion, drowsiness.
3- ultimately loss of consciousness or seizures (at plasma [glucose] <1.5 mmol/L)

Hormonal mechanisms to prevent or correct hypoglycemia:
↓ Production of: insulin
↑production of: Epinephrine, glucagon, Growth hormone & Cortisol

Metabolic changes in DM & DKA

CHO	↓ glucose uptake by certain tissues (adipose tissue & muscle) ↑ glycogenolysis ↑ gluconeogenesis	DM
Lipid	↑ Lipolysis ↑ fatty acid oxidation ↑ production of Ketone bodies	
Protein	↓ protein synthesis ↑ protein degradation	
K+, Water & pH	↓ entry of K+ into the cells. Water loss secondary to glycosuria Acidosis due to ↑ production of ketone bodies	DKA