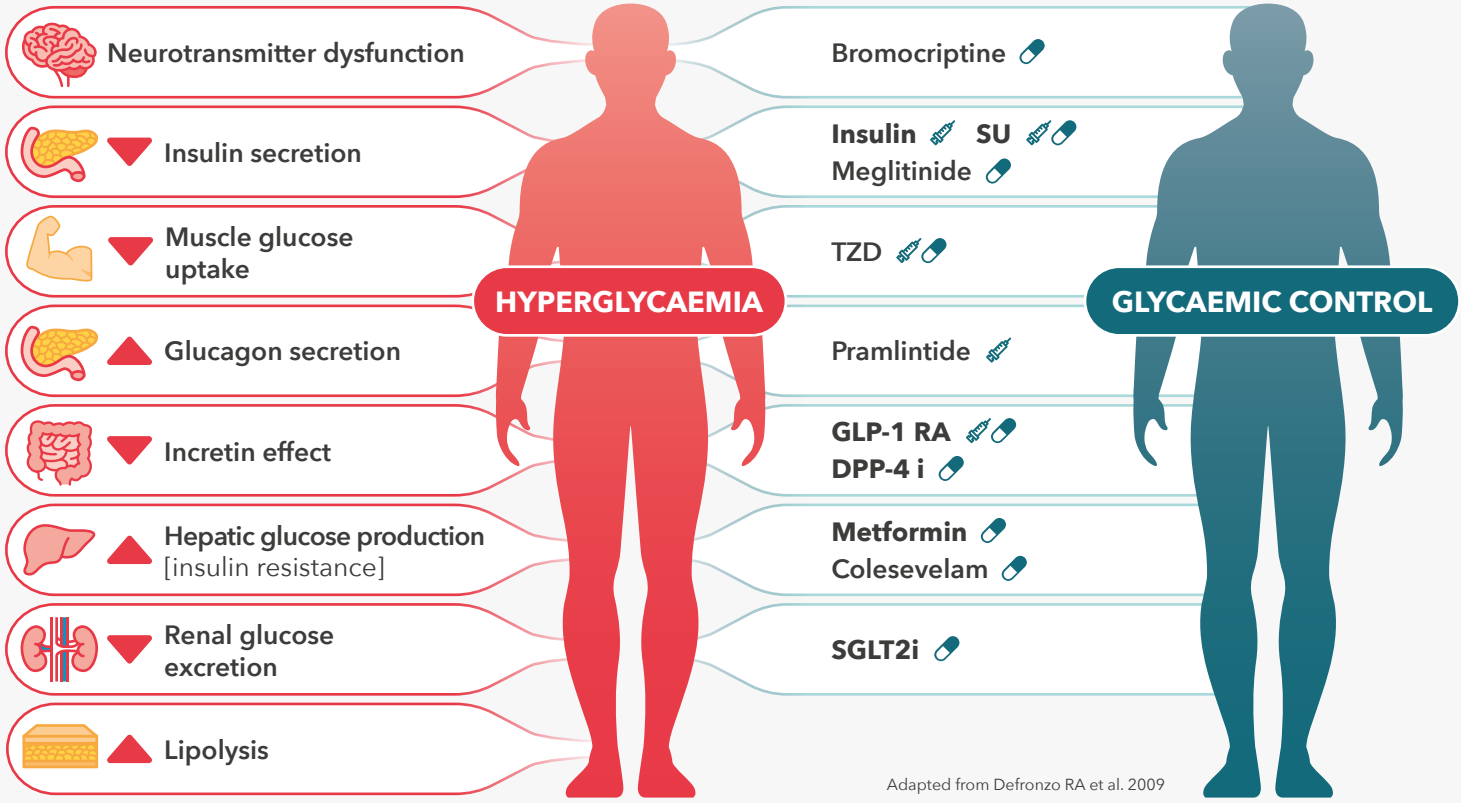
Diabetes Pathophysiology

Radcliffe Medical Education
Supported by an educational grant from Novo Nordisk A/S

8 pathophysiologic abnormalities, collectively referred to as the "**Ominous Octet**" lead to T2DM[1]

Several **pathophysiologically-based therapies** have been developed that lead to improved glucose control in T2DM

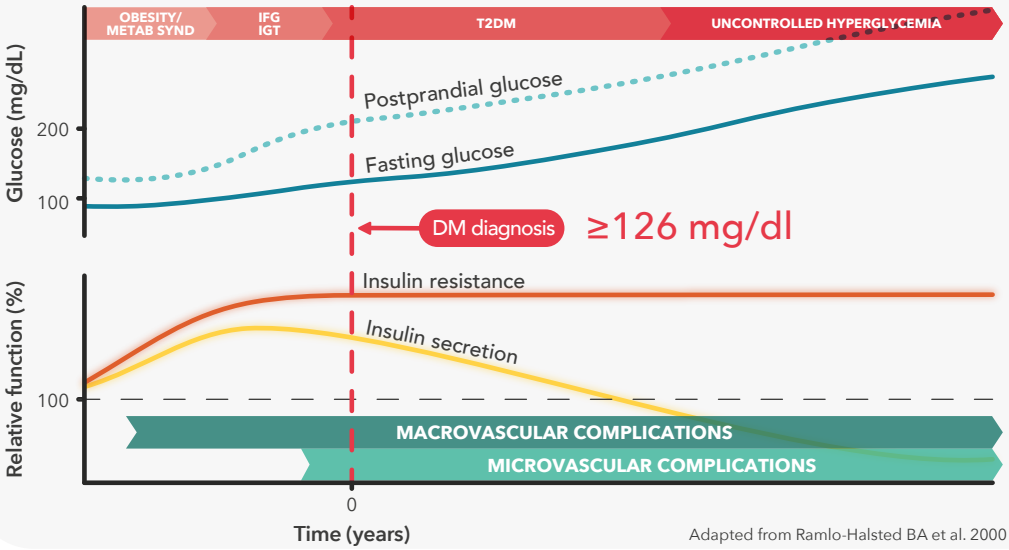


Adapted from Defronzo RA et al. 2009

The **incretin effect** is due to gut hormones, **GLP-1** and **GIP** which are secreted in response to meal ingestion and are served to increase insulin secretion and supress glucagon secretion.

Reduced incretin effect result in hyperglycaemia and eventually in T2DM

T2DM progression over time[2]



Adapted from Ramlo-Halsted BA et al. 2000

Postprandial glucose and **fasting glucose** increase when the ability of pancreas to produce insulin is reduced. This leads to IGT in "pre-diabetes" stage and eventually leads to T2DM

Insulin resistance occurs due to aging, increased body weight, and reduced physical activity. At early stages **insulin secretion** keeps in step with insulin resistance, hence normal glucose tolerance is sustained

Microvascular complications occur due to further decrease in ß-cell function and further increase in hypoglycaemia. **Macrovascular complications** may start during any point of disease span

Abbreviations: CVD, cardiovascular disease; DM, diabetes mellitus; DPP-4i, dipeptidyl peptidase-4 inhibitor; GIP, gastric inhibitory polypeptide ; GLP-1, glucagon-like peptide-1; GLP-1 RAs, glucagon-like peptide-1 receptor agonists; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; SGLT2i, sodium-glucose co-transporter-2 inhibitors; SU, sulfonylureas; TZD, thiazolidinediones; T2DM, type 2 diabetes mellitus

References: **1.** Defronzo RA. *Diabetes Care* 2009;58(4):773-795. **2.** Ramlo-Halsted BA et al. *Clin Diabetes* 2000;18:80-84.