INSULIN,GLUCAGON AND THYROID HORMONES

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Mechanisms Hormonal Regulate The Concentration of the Blood Glucose

- Source of blood glucose :
  - Digestion and absorption of carbohydrates
  - Glycogenolysis process
  - Gluconeogenesis process
- Several hormones play a part to maintenance of stable levels of glucose in the blood
- INSULIN
  - Plays a central role in regulating blood glucose
  - Secreted as a direct response to hyperglycemia
  - Stimulation of glucose transport at the plasma membrane

INSULIN
- Increase glucose utilization in a part by promoting glycogenesis
- inhibiting glycogenolysis
-cause lower of blood glucose

- Blood glucose maintained within normal limit by:
- Hormonal regulation of :
  - Peripheral glucose uptake
  - Hepatic glucose production.
- After a meal ⟶ blood glucose ↗ rapidly stimulates insulin secretion ⟶ ↗ glucose transport,metabolism,storage by muscles and adipocytes.
- -insulin inhibits glucagon synthesis ⟶ ↘ hepatic glucose production.

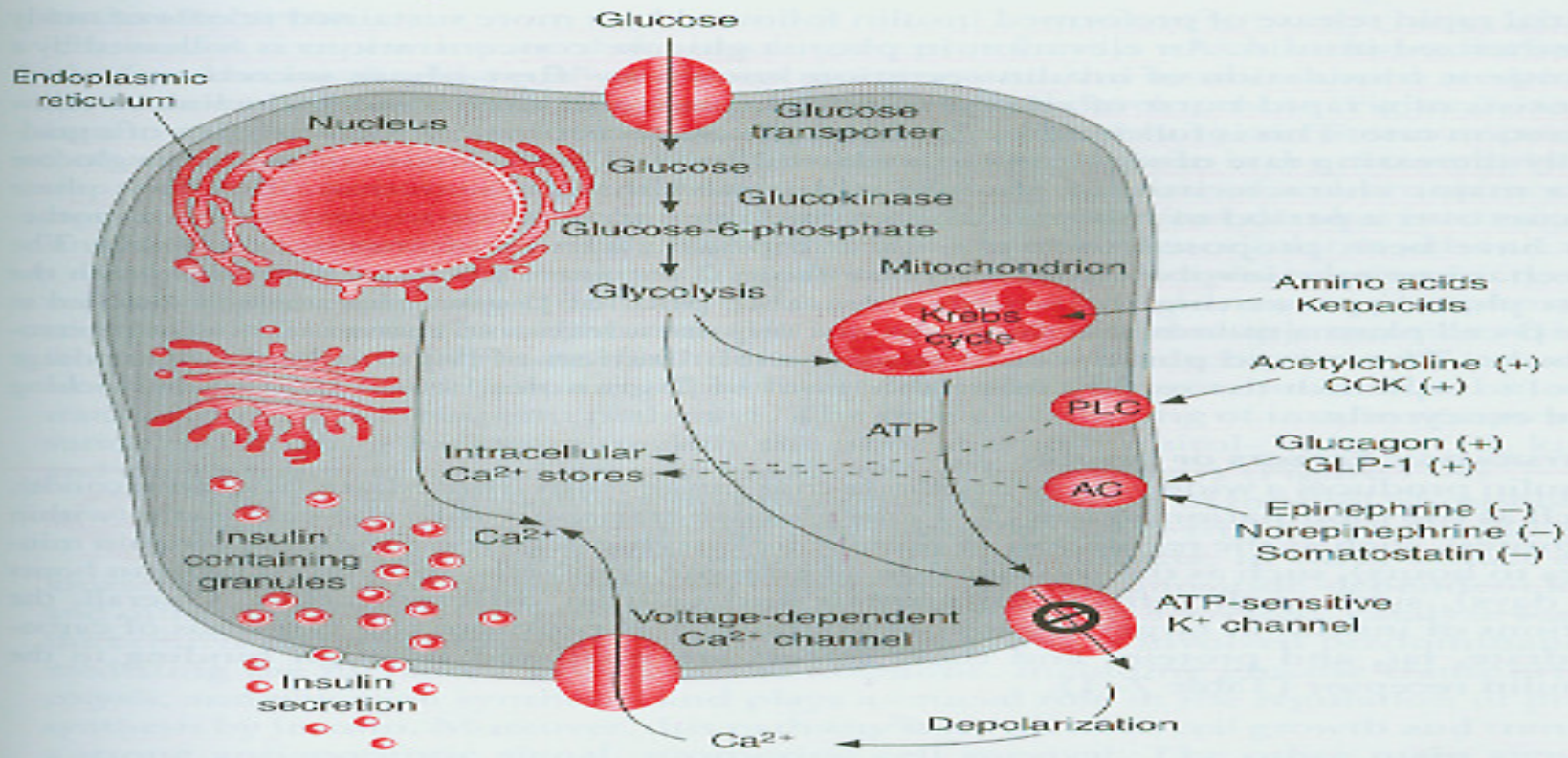

Figure 7–3. Regulation of insulin release. Glucose is transported into the β-cell by a specific glucose transporter protein (GLUT-2) on the cell surface. The glucokinase phosphorylates glucose, forming glucose-6-phosphate in the first step of glycolysis. The generation of adenosine triphosphate (ATP) by glycolysis and the Krebs cycle leads to inhibition and closure of the ATP-sensitive potassium channels (the target of sulfonylurea drugs), depolarization of the plasma membrane, and opening of the voltage-dependent calcium channels. The influx of extracellular calcium and mobilization of calcium from intracellular stores lead to the fusion of insulin-containing secretory granules with the plasma membrane and the release of insulin into the circulation. In addition to glucose, other factors can also stimulate insulin release from the β-cell, including hormones, neurotransmitters, and acetylcholine. Glucose enhances the response of the β-cell to these factors. PLC = phospholipase C; AC = adenylate cyclase; CCK = cholecystokinin; GLP-1 = glucagon-like peptide-1. (Modified, with permission, from Fajans SS et al. Mechanisms of disease: Molecular mechanisms and clinical pathophysiology of maturity-onset diabetes of the young. *N Engl J Med.* 2001;345:971.)

Table 7–1. Insulin effects on carbohydrate, fat, and protein metabolism

Metabolic effects	Insulin stimulates	Insulin inhibits
Carbohydrate metabolism	Transport of glucose across the cell membrane in adipose tissue and muscle Rate of glycolysis in muscle and adipose tissue Glycogen synthesis in adipose tissue, muscle, and liver	Glycogen breakdown in muscle and liver Rate of glycogenolysis and gluconeogenesis in the liver
Lipid metabolism	Fatty acid and triacylglycerol synthesis in tissues Uptake of triglycerides from the blood into adipose tissue and muscle Rate of cholesterol synthesis in the liver	Lipolysis in adipose tissue, lowering the plasma fatty acid level Fatty acid oxidation in muscle and liver Ketogenesis
Protein metabolism	Amino acid transport into tissues Protein synthesis in muscle, adipose tissue, liver, and other tissues	Protein degradation in muscle Urea formation

- Insulin receptor
  - PI 3 kinase pathway (metaboiic effect of insulin)
  - MAPK pathway. (proliferative effect of insulin)

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- Glucagon

  - A cell of pancreatic islets.

  - Principal target tissues : liver and adipose tissue.

  - Its secretion is stimulated by hypoglycemia.

  -In liver it stimulates glycogenolysis by activating phosphorylase.

  -Enhances gluconeogenesis from amino acid and lactate.

  - Glucagon acts via generation of cAMP.

  -Both hepatic glycogenolysis and gluconeogenesis contribute to hyperglycemic effect.

Table 7–3. Effects of glucagon on hepatic glucose metabolism

Effect on target enzyme	Metabolic response
Increased expression of glucose-6-phosphatase	Frees glucose to enter the circulation
Suppression of glucokinase	Decreases glucose entry into the glycolytic cascade
Phosphorylation (activation) of glycogen phosphorylase	Stimulates glycogenolysis
Inhibition of glycogen synthase	Inhibits glycogen synthesis
Stimulation of phosphoenolpyruvate carboxykinase expression	Stimulates gluconeogenesis
Inactivation of phosphofructokinase-2 (PFK-2) and activation of fructose-6-phosphatase. PFK-2 is the kinase activity and fructose-2,6-bisphosphatase (F-2,6-BPase) is the phosphatase activity of the bifunctional regulatory enzyme, phosphofructokinase-2/fructose-2,6-bisphosphatase (PFK-2/F-2,6-BPase).	Inhibits glycolysis Stimulates gluconeogenesis
Suppression of activity of the pyruvate kinase	Decreases glycolysis

Hormone Thyroid

- Important modulator or intermediary metabolism.
  - Hypothyroidism ⟶ hypercholesterolemia
  - Hyperthyroidism ⟶ weight loss.
- Thyroid hormone stimulates :
  - Lipogenesis ⟶ maintain fat stores.
  - Lipolysis.

THANK YOU