PHY2032 Notes

Module 1: Hormonal Regulation of Organic Metabolism

Absorptive and post-absorptive states

Absorptive state: entry of nutrients into the blood from the gastrointestinal tract after a meal (storing energy).
Post-absorptive state: gastrointestinal tract is empty of nutrients, and the body's own stores must supply energy (releasing energy).

The main function of the post-absorptive state is to ensure that blood glucose levels are maintained. The sources of blood glucose during the post-absorptive state are glycogenolysis, lipolysis, protein catabolism and gluconeogenesis. Glucose sparing also takes place. The liver can also convert fatty acids to ketones, which provide an energy source during prolonged fasting for many tissues, including the nervous system.

Key terms:
Glycogenolysis: The breakdown of glycogen in the liver and skeletal muscle. First line of defence against falling blood glucose levels.

Lipolysis: The catabolism of triglycerides in adipose tissue results in glycerol and fatty acids, which then enter the bloodstream via diffusion → glycerol enters the liver and is used to synthesise glucose.

Protein catabolism: The breakdown of proteins which supply large quantities of amino acids which enter the blood and are then taken up by the liver. Some amino acids can be metabolised to glucose by the α-keto pathway, which is then released into the blood. Protein catabolism is an important source of glucose a few hours into the post-absorptive state.

Gluconeogenesis: The synthesis of glucose from precursors other than carbohydrates, such as amino acids and glycerol.

Glucose sparing: Ensures that the glucose produced by the liver in the post-absorptive state is spared for the brain. During the post-absorptive state, most organs and tissues other than the central nervous system, significantly decrease their glucose catabolism and switch to fat as their main source of energy.

Hormonal control of the absorptive and post-absorptive states

Pancreas

- Secretes the main endocrine hormones: insulin and glucagon.
- Insulin and glucagon are secreted by the **islets of Langerhans.**

The pancreas:

- Is usually 100-200 microns in diameter.
- Contains approximately 1000 endocrine cells

Islets of Langerhans
Beta cells (70%) secrete insulin.

Alpha cells (20%) secrete glucagon.
Delta cells (<10%) secrete somatostatin (a paracrine factor that regulates insulin and glucagon secretions).
PP cells (<5%) secrete pancreatic polypeptide (function is unknown).

- Beta cells form intimate contact with the vasculature which enables them to sense nutritional state. Beta cells receive 10x the amount of blood than surrounding cells.
- Islets in the pancreas have a rich supply of capillaries, into which they secrete their hormones.
- Sympathetic and parasympathetic neurons terminate on the islets, allowing the nervous system to influence the secretion of the islet hormones.

Synthesis of insulin

1. In beta cells, insulin is produced from a proinsulin (a precursor).
2. Proinsulin is packaged into vesicles in the Golgi apparatus, and is cleaved and modified inside the vesicles to produce insulin and C-peptide (C-peptide has no known function).
3. Insulin has 51 amino acids, C-peptide has 31 amino acids.

Secretion of insulin

1. Beta cell responds to increase in blood glucose levels. GLUT2 on the surface of beta cells transports glucose into the cell, where it is converted to glucose-6-phosphate and can be used for ATP production in cellular respiration.
2. Increased glycolysis and ATP production closes the K+ channels, causing depolarisation of the cell membrane.
3. Depolarisation results in Ca^{2+} channels opening, leading to insulin secretion.
4. Insulin is metabolised by the kidney and liver, its half-life is 5 minutes.

Pattern of insulin secretion

- After a meal, the rise in plasma glucose levels are mirrored by an increase in insulin.
- Insulin stimulates the uptake of glucose by cells (primarily muscle and adipose cells) which decreases plasma glucose levels and, via negative feedback, inhibits the secretion of insulin by β-cells.

NOTE: there are two units used for glucose concentration. In Australia, mmol/L is used (approximately 5 mmol is normal). In the US, mm/dL is used (approximately 90 mmol/dL is normal).

Control of insulin secretion
Plasma glucose is the major regulator of insulin secretion, but other factors are also involved:
AMINO ACIDS

- Increased amino acid concentration increases intracellular Ca^{2+} in beta cells, which enhances insulin secretion. Insulin stimulates the uptake of amino acids by muscle and other cells.
- *Negative feedback control*: amino acid concentration in blood increases after ingestion of a protein-rich meal → increased plasma insulin stimulates uptake of