

#### Q4 Describe the body's mechanisms for regulating blood glucose (Sept 2009)

Blood glucose levels (BGL) are maintained within a tight range (4-7mmol/L). Control is via a feedback system which controls the balance of insulin (anabolic actions) and glucagon (catabolism).

- Sensor: Islets of Langerhan cells
- Integrator: endocrine pancreas (and SNS)
- Effectors: endocrine pancreas, adrenaline, anterior pituitary cells (ACTH and growth hormone), liver (functions as 'Glycostat' – maintains BGL within a strict range)

#### Hormonal control

- Insulin: released from pancreatic beta islet cells when BGL >5 and acts via a tyrosine kinase second messenger receptor. Actions:

CHO →

- Stimulates GLUT 4 receptors to move to the surface of muscle and adipose tissue cells to increase glucose uptake (this does not happen in RBC, brain tissue, intestinal mucosal cells or renal tubule cells).
- Upregulates Glycogen Synthase to increase glycogen production
- Upregulates glucokinase in hepatocytes to trap glucose in cells by phosphorylating it
- Decreases gluconeogenesis and glycogenolysis (by inhibiting glucose-6-phosphatase)

Proteins →

- Upregulates amino acid uptake, enhances protein synthesis, and inhibits protein degradation in muscle and other tissues, thereby decreasing the plasma concentrations of most amino acids

Lipids →

- Upregulates Pyruvate Dehydrogenase, Lipoprotein Lipase and Fatty Acid Synthase to facilitate the breakdown of TAGs to fatty acids for uptake by adipose tissue cells
- Inhibits Hormone Sensitive lipase to decrease the hydrolysis of triglycerides stored in the adipocyte

- Glucagon: released from pancreatic alpha cells and acts via G protein coupled receptors. Actions:

CHO →

- Acts in the liver to stimulate breakdown of stored glycogen deposits to G-6-P and then glucose
- Acts in peripheral skeletal muscle and adipose tissue to breakdown peripheral glycogen deposits to pyruvate and lactate, using the pyruvate for the Krebs cycle and transporting the lactate to the liver for gluconeogenesis via the Cori cycle
- Inhibits cellular utilization of glucose during hypoglycaemia, causing most cells to use fatty acids or ketone bodies as their primary source of energy

Lipids →

- Stimulates hormone sensitive lipase to break down adipose tissue to free fatty acids and glycerol, providing substrates for Acetyl CoA production (can then enter the Krebs cycle or produce ketone bodies)
- Growth hormone and ACTH released from anterior pituitary → ACTH stimulates cortisol release from adrenal cortex. Cortisol and GH inhibit glucose uptake by reducing the number of GLUT4 receptors in the cell membrane
- Thyroxine → released from thyroid in response to TSH from anterior pituitary. Increases GIT absorption of glucose.
- Oestrogen and progesterone → cause mild insulin resistance

#### Neural control

- Adrenaline → released from adrenal cortex and sympathetic nerve terminals. Enhances the breakdown of glycogen and gluconeogenesis; acts on hormone sensitive lipases to increase adipose tissue breakdown; causes hunger, nausea, agitation, tachycardia