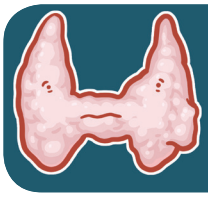

NOTES
PANCREATIC HORMONES

GLUCAGON

osms.it/glucagon

- Peptide hormone secreted by pancreatic alpha cells
- Important for blood glucose regulation, along with insulin
- Synthesis
  - Preproglucagon → proglucagon → glucagon

Secretion regulated mainly by glucose

- ↓ glucose levels between meals or while sleeping → ↓ insulin → glucagon secretion stimulation → hepatic glycogenolysis, gluconeogenesis → ↑ blood glucose levels

Other factors that regulate glucagon secretion

- Sympathetic nervous system
  - Adrenaline (α_2 receptors)
- Parasympathetic nervous system
  - Acetylcholine (M_3 receptors)
- Alanine, arginine
  - E.g. from high protein meal
- Cholecystokinin, somatostatin
- Exercise

GLUCAGON SIGNALING PATHWAY

- Glucagon receptor is a heterotrimer
  - G-protein coupled receptor that contains α, β, γ subunits
- Glucagon binds to receptor → activates G_s protein → α subunit released → activates adenylate cyclase → ↑ cAMP → activates protein kinase A → phosphorylation cascade → transcription factor activation → effects

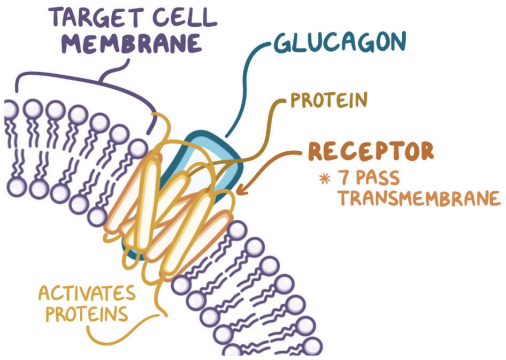

Figure 34.1 Glucagon exerts its effects by binding to G-protein coupled receptors on the membranes of liver and adipose cells.

EFFECTS OF GLUCAGON

- Primary action is to increase blood glucose when it falls below normal range
- *Carbohydrates:* ↑ blood glucose levels
  - Stimulates glycogenolysis in liver, muscle
  - Stimulates gluconeogenesis in liver, kidney
  - Inhibits hepatic glycolysis
- *Fats:* ↑ fatty acids, keto acid levels in blood
  - Inhibits fatty acid synthesis, oxidation in liver
  - Inhibits fat deposition in adipose tissue
  - Stimulates lipolysis
  - Stimulates keto acid production

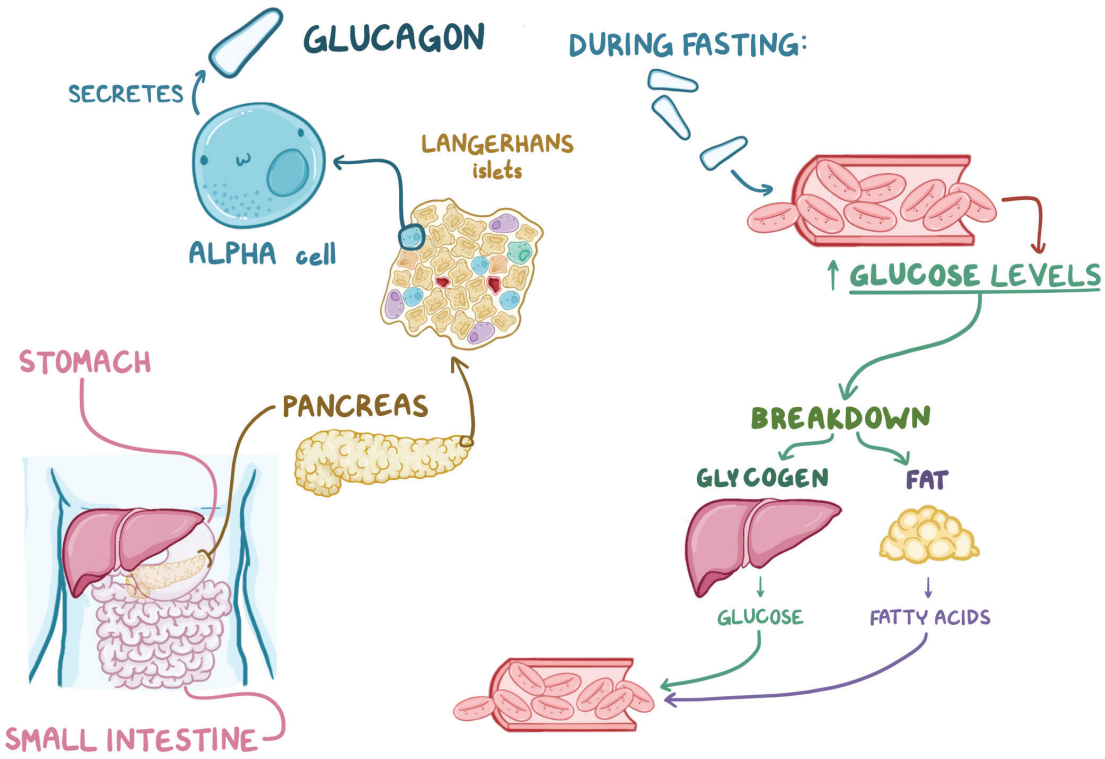

Figure 34.2 Glucagon is secreted by pancreatic alpha cells when glucose levels are low. It increases glucose levels in the bloodstream by inducing the breakdown of storage molecules in the liver and adipose cells.

INSULIN

osms.it/insulin

- Peptide hormone secreted by pancreatic beta cells
- Important for blood glucose regulation
- Consists of A and B amino acid chains connected with two disulfide (-S-S-) bonds

SYNTHESIS

- Preproinsulin → proinsulin → insulin
- During insulin synthesis, protein called C-peptide cleaved off, secreted together with insulin in equimolar amounts within secretory vesicles → C-peptide used to measure insulin levels

SECRETION

Secretion regulated mainly by glucose

- Carbohydrates consumption → ↑ glucose → passive diffusion into beta cells through GLUT2 transporters → stimulation of insulin secretion

Other factors that stimulate insulin secretion

- ↑ fatty acid, amino acid levels in blood
- Parasympathetic nervous system
  - Acetylcholine (M_3 receptors)
- Sympathetic nervous system
  - Adrenaline (β_2 receptors)
- Growth hormone (GH), adrenal corticotropic hormone (ACTH)

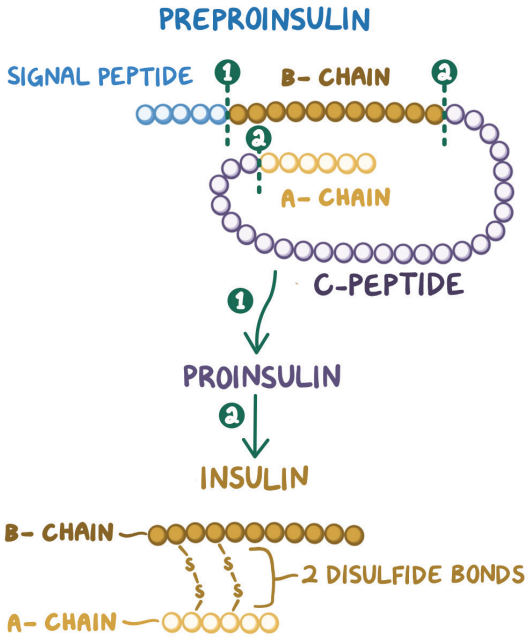

Figure 34.3 Insulin synthesis.

PHASES OF INSULIN RELEASE

- Two phases

First phase

- Involves L-type Ca^{2+} channels
- Rapidly triggered release of preformed secretory vesicles
- Lasts 10 minutes

Second phase

- Involves R-type Ca^{2+} channels
- Slow release of newly formed secretory vesicles
- Lasts 2–3 hours

INSULIN SIGNALING PATHWAY

- Insulin receptor is a tetramer
  - Contains two extracellular α subunits connected by disulfide bonds, two intracellular β subunits connected to each α subunit
- Insulin binds to α subunits → activates tyrosine kinase activity in β subunits → β subunit autophosphorylation → insulin receptor substrates (IRS) phosphorylation cascade → transcription factor activation → effects

EFFECTS OF INSULIN

- The primary action of insulin is lowering blood glucose levels when above normal range
- *Carbohydrates:* ↓ blood glucose levels
  - Translocates GLUT4 transporters to muscle, adipose cell membranes → facilitates cell uptake of glucose
  - Activates glycogen synthesis in liver, muscles
  - Inhibits hepatic glycogenolysis, gluconeogenesis
- *Fats:* ↓ fatty acids, keto acid levels in blood
  - Inhibits fatty acids mobilization, oxidation
  - Stimulates fat deposition in adipose tissue
  - Inhibits lipolysis
  - Inhibits keto acid formation in liver
- *Proteins:* anabolic effect
  - Stimulates amino acid, protein uptake
  - Stimulates protein synthesis
  - Inhibits proteolysis
- *Other:* ↓ K^+ levels in blood
  - Increases potassium uptake
  - Stimulation of cell growth, gene expression

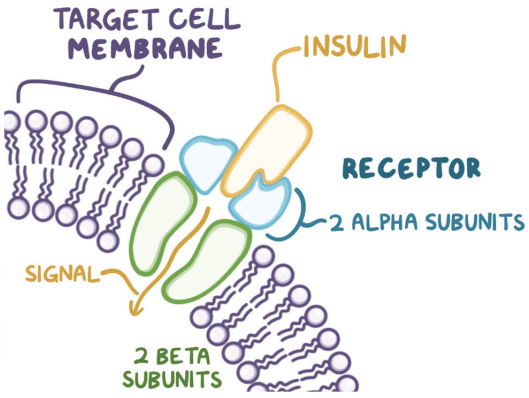

Figure 34.4 Insulin exerts its effects by binding to alpha subunits of insulin receptor, which leads to signal transduction within cell.

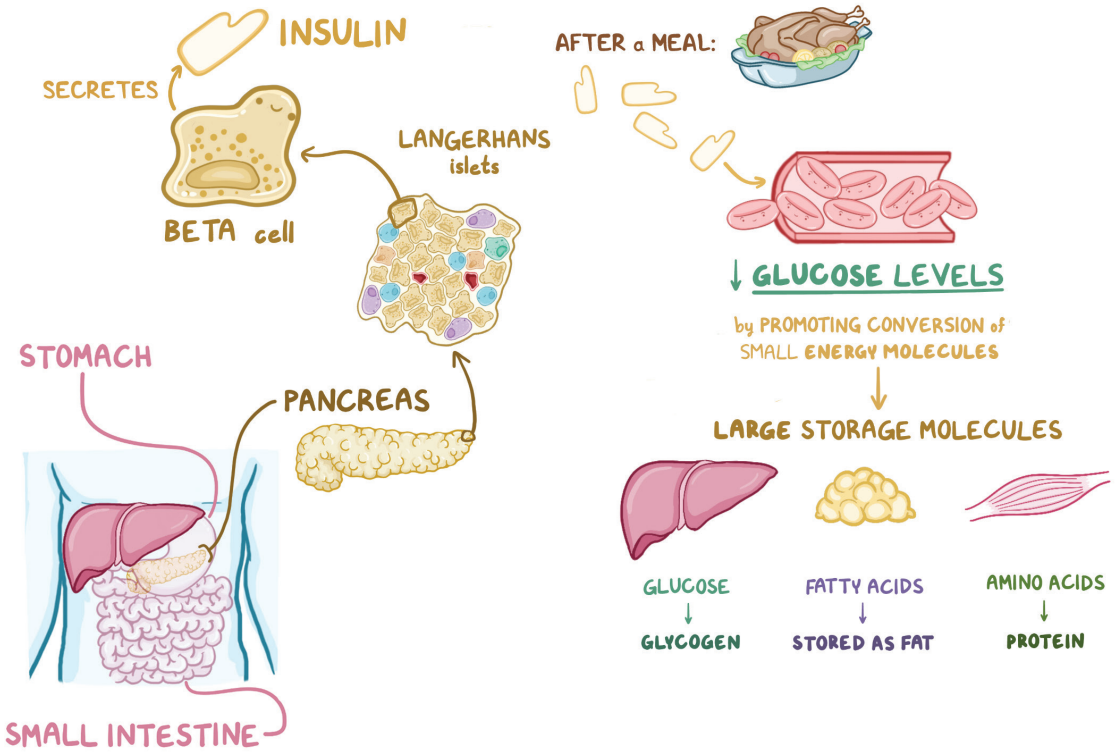

Figure 34.5 Insulin is secreted by pancreatic beta cells when glucose levels are high. It promotes conversion of glucose → glycogen in liver, fatty acids → fat, and amino acids → protein.

SOMATOSTATIN

osms.it/growth-hormone-and-somatostatin

- Peptide hormone secreted by pancreatic delta cells

Factors that regulate somatostatin secretion

- Ingestion of glucose, fatty acids, amino acids
- Glucagon
- Sympathetic nervous system
  - β-adrenergic agonists

SOMATOSTATIN SIGNALING PATHWAY

- Somatostatin receptor is a G-protein coupled receptor
- Somatostatin binds to receptor → activates G_i protein → inhibits adenylate cyclase → ↓ cAMP → ↓ Ca^{2+} → inhibitory effect

EFFECTS OF SOMATOSTATIN

- Inhibits secretion of insulin, glucagon
- Inhibits pancreatic exocrine secretion
- Inhibits secretion of all gastrointestinal hormones (gastrin, cholecystokinin, secretin, motilin etc.)
- Decreases gastrointestinal motility, blood flow, gastric emptying