**Exocrine Pancreas**

- Acini - Pancreatic juice
- (1°)
- (2°)
- Secretions- neuronal and hormonal mechanisms
  1) Secretin - bicarbonate rich
  2) Cholecystokinin - enzyme rich

**Endocrine Pancreas**

- Islets of Langerhans (contain 4 cell types)
  - Alpha cells (α)- produce Glucagon (20-25%)
  - Beta cells (β)- produce Insulin (60-70%)
  - Delta cells (δ)- produce Somatostatin (10%)
  - F-cells- produce pancreatic polypeptide (few)

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**EMBRYOLOGY**

1st- Islets of Langerhans
2nd- Acinar cells

**History of Investigation**

- Aristotle
- Von Mering and Minkowski
- Schultze
- Banting and Best

**Insulin Synthesis**

- Ribosomes
- Rough ER (proinsulin)
- Golgi Apparatus
- B cell- Islet of Langerhans secretes insulin
- Endocrine- Insulin to Bloodstream

**GENERAL STATEMENT**

INSULIN SECRETION IS STIMULATED UNDER CIRCUMSTANCES OF FUEL EXCESS AND INHIBITED UNDER CIRCUMSTANCES OF FUEL DEFICIENCY
Factors Influencing Insulin Secretion

- Elevated Plasma Glucose
  - most profound stimulus
  - biphasic response by pancreas

- Elevated Plasma Amino Acids
- Elevated Plasma Fatty Acids
- Gastrointestinal hormones (anticipatory)
  - Glucagon-like Peptide (GLP-1)
  - Gastric Inhibitory Peptide

- Autonomic Nervous System
  - Parasympathetic stimulation increases secretion
  - Sympathetic decreases insulin secretion

- Somatostatin (GHIH)
  - Inhibits insulin secretion

Actions of Insulin

Carbohydrate Metabolism
Acts to decrease plasma glucose
- initiates or enhances glucose transport into most cells (muscle*, fat, not liver, brain) by increasing the availability of the carrier molecule (GLUT-4)
- Stimulates activity of glucokinase
- stimulates glycogenesis especially of liver and skeletal muscle
- inhibits glycolysis
- inhibits gluconeogenesis

*Not required in exercising skeletal muscle.

Fat Metabolism
Acts to stimulate the production and storage of fat
- enhances transport of glucose into adipocytes
- converts glucose derivatives into fatty acids
- enhances transport of fatty acids into adipocytes
- inhibits hormone sensitive lipase which hydrolyses fats (lipoprotein lipase)
- inhibits β-oxidation of fatty acids

Protein Metabolism
Acts much like Growth Hormone
- enhances ribosomal protein synthesis (anabolic action)
- enhances active transport of amino acids into cells
- decreases protein catabolism
**Actions of Insulin**
Other Actions

- Increases movement of potassium from extracellular fluid to intracellular fluid.
- Decreases activity of neuropeptide-Y.

**GLUCAGON**

- Major site of action is liver.
- Antagonistic to insulin.

**Actions of Glucagon**

**Carbohydrates**
- Enhances glycogenolysis.
- Enhances gluconeogenesis.

**Fats**
- Enhances biolysis and beta oxidation.

**Proteins**
- Enhances uptake of Gluconeogenesis precursors in liver.

**Glucagon Regulation**

- Decreased plasma glucose concentration.
- Elevated plasma amino acids.
- Sympathetic nervous system.
- Somatostatin and insulin (as paracrine secretions) decrease glucagon secretion.

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**Other Pancreatic Hormones**

1) Somatostatin
- Stimuli—same as insulin.
- Actions
  - Decrease gut motility and secretions.
  - Decrease insulin and glucagon secretions.
  - Puts "break" on rate at which meal is being digested and absorbed.

2) Pancreatic Polypeptide
- Stimuli
  - Ingestion of protein-rich meal, hypoglycemia. Exercise.
- Actions
  - Inhibit gall bladder and exocrine pancreas.

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Diabetes Mellitus

**Type I (IDDM)**
- 10-20%
- juvenile onset
- rapid progression
- not obesity related
- result of viral disease which causes T-cells to destroy β-cells
- insulin level = 0
- ketosis

**Type II (NIDDM)**
- 80-90%
- adult onset
- slow progression
- typically obese
- not well known possibly due to down-regulation of insulin receptors
- insulin high, low, normal
- no ketosis

**Symptoms**
- hyperglycemia
- polyuria
- polydipsia
- polyphagia
- ketoacidosis
- hyperlipemia

**Pathologies**
- neuropathies
- nephropathies
- microangiopathies
- macroangiopathies
- decreased bld vol
- retinopathies
- other visual problems
**PHARMACOLOGY**

- Simulate increased production
  - GLUCOTROL

- Decrease hepatic output
  - GLUCOPHAGE

- Drugs which increase insulin sensitivity
  - AVANDIA

- Mimics Incretins (g.i hormones which dec bld glucose)
  - BYETTA

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**PHARMACOLOGY**

- Insulin
  - HUMALOG (insulin lispro)
  - NOVOLOG (insulin aspart)
  - LANTUS (insulin glargine)
  - EXUBERA (human insulin)