Pancreatic Hormones

Aims
- Pancreatic hormones
  - Insulin
  - Glucagon
- Describe the fundamental physiological mechanisms controlling the secretion of insulin and glucagon into the blood stream.
- Understand the effects of insulin and glucagon on glucose, fatty acid, and amino acid metabolism in the various body tissues.

Anatomy and histological of pancreas

Islet of Langerhans

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Insulin
**Insulin processing**

- Rough ER
- Vesicle
- Golgi
- Processing in vesicles
- Cleavage of proinsulin
- Insulin secretion

**Factor affecting insulin secretion**

- Diabetogenic H
- Parasympathetic
- Sympathetic
- Insulin
- Somatostatin

**Glucose-stimulated insulin secretion mechanism**

- Glucose
- Glucose-6-P
- GK
- Hexokinase
- Pyruvate
- Electron transport chain
- Mitochondria
- Acetyl Co A
- ATP
- [ATP]/[ADP]

**Normal blood glucose**

- Normal blood glucose
  - Basal plasma insulin concentration

**Insulin secretion**

- ATP dependent
- Non ATP dependent
**Insulin transport**

Insulin (peptide hormone) 

Dissolve in blood plasma 

Half life of insulin is less than 10 minutes

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**Insulin Action on Cells:**

**Dominates in Fed State Metabolism**

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**Insulin signaling**

- Glucose transport
- Protein synthesis
- Lipid synthesis
- Glycogen synthesis
- Growth and Gene expression

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**Insulin actions**

**Metabolic effect**

**Carbohydrate**

- Facilitates glucose transport into muscle, adipose and many other tissues but not brain
- Stimulates glycogen production (glycogen synthesis) and inhibits glycogen breakdown (glycogenolysis) in liver and skeletal muscle

**Protein**

- Facilitates amino acids into muscle and other tissues
- Stimulates protein synthesis and inhibits protein breakdown

**Lipid**

- Facilitates free fatty acids into cells (lipoprotein lipase)
- Promotes formation of fatty acids and glycerol from glucose
- Promotes synthesis of triglyceride and inhibits their breakdown (hormone sensitive lipase)
**Insulin actions**

**Growth**

- Promotes growth of the fetus
- Promotes postnatal growth by inhibiting protein degradation
- Needed for promotion of IGFs

**Insulin deficit ➔ Diabetes Mellitus**

- **Absolute:** Insulin dependent diabetes mellitus (IDDM)/ Type I ~ 5-10%
- **Relative:** Non insulin dependent diabetes mellitus (NIDDM)/ Type II ~ 90-95%
  - Defect in insulin secretion
  - Insulin resistance
    - Receptor
    - Postreceptor

**Diagnosis Diabetes Mellitus**

- A casual plasma glucose level (taken at any time of day) of 200 mg/dL or greater when the symptoms of diabetes are present.
- A fasting plasma glucose value of 126 mg/dL or greater.
- An OGTT value in the blood of 200 mg/dL or greater measured at the 2-hour interval.

**Insulin deficiency**

- Glucose uptake
- Glycogenolysis
- Gluconeogenesis
- Protein breakdown

- Change in blood
- Plasma glucose (hyperglycemia)

- Change in urine
- Glucose in urine (glycosuria)
- Osmotic diuresis
- Frequency of urination (polyuria)
- Dehydration, Thirst (polydipsia)
- Food consumption (polyphagia)
- Weight loss

- Sign and symptoms

- Change in blood
- Plasma lipid used as fuel
  - Ketosis

- Change in urine
  - Ketones in the urine (ketonuria)
**Signs and symptoms of diabetes mellitus**

- Hyperglycemia
- Glucosuria (Osmotic diuresis)
- Hyperlipidemia
- Ketonemia
- Protein wasting
- Weight loss

**Insulin excess**

- Overdose insulin
- Insulinoma
  - Hypoglycemia
    - Neuroglycopenia
      - Hunger
      - Dizziness
      - Coma
    - Cathecolamine: anxiety, sweating, tachycardia

**Glucagon**

- 29 amino acids identical to enteroglucagon
- Glucagon act by binding to its receptor and activated G protein which cause an increase in cAMP.
- Glucagon has the effect of increasing blood glucose levels (opposite effect of insulin)

**Enteroglucagon**

Processing of pro-glucagon in intestinal L-cells

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<th>GRPP</th>
<th>Glucagon</th>
<th>IP-1</th>
<th>GLP-1</th>
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Factor affecting glucagon secretion

- Sympathetic activity
- Secretin
- CCK
- Parasympathetic activity
- Amino Acids
- Insulin
- Glucose

Glucagon secretion
Glucagon actions

**Metabolic effect**

- Stimulates breakdown of glycogen stored in the liver and inhibits glycogen synthesis
- Stimulates gluconeogenesis in the liver

**Carbohydrate**

- Stimulates amino acids uptake in the liver
- Stimulates protein breakdown and inhibits protein synthesis

**Protein**

- Stimulates lipolysis in fat and liver
- Stimulates ketone formation in the liver

**Lipid**

- Stimulates lipolysis in fat and liver
- Stimulates ketone formation in the liver

Insulin & Glucagon Regulate Metabolism

**Fed state** insulin dominates

- Glucose oxidation
- Glucose synthesis
- Lipid synthesis
- Protein synthesis

**Fast state** glucagon dominates

- Glucose oxidation
- Glucose production
- Lipogenesis
- Ketogenesis
**High blood glucose**

Insulin released by B cells of pancreas

Fat cells take in glucose from blood

Achieve Normal blood Glucose levels

**Low blood glucose**

Glucagon released by A cells of pancreas

Liver releases Glucose into blood

**Insulin and glucagon cause the tight control of blood glucose concentration**

Glucagon excess and deficit are rare

- **Glucagon excess**: cancer of alpha cells (glucagonomas)
- There is no report of glucagon deficit.

**Somatostatin**

- Somatotrophin-release inhibiting factor (SRIF)
- Also found in nerve terminals and other tissues.
- Somatostatin is a local inhibitor of insulin and glucagon secretion.
- Also function as a neurotransmitter/neuromodulator in the control of motor activity and cognitive functions.

**Pancreatic polypeptide (PP)**

- 36 amino acids
- Secretion of PP is mainly under autonomic control.
- PP is released following feeding or during hypoglycaemia
- Role of PP is still not understood.