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Islet Cell Hormones

And

Hormonal Regulation of Fuel Metabolism

M2-Endocrine Sequence
Arno K. Kumagai, M.D
Dept. of Internal Medicine

Winter 2009
Normal Physiology

ISLET CELL HORMONES

Alpha Cells: GLUCAGON

Beta Cells: INSULIN (AND AMYLIN)
Normal Physiology

ISLET CELL HORMONES

Alpha Cells: GLUCAGON

Beta Cells: INSULIN
(AND AMYLIN)
Islet hormone secretion varies with circulating glucose levels.

Meal increases:

**Glucose**
- increased **insulin**
- decreased **glucagon**

**Amino acids, FA**
- increased **insulin**
Normal Insulin Physiology

STIMULI FOR INSULIN SECRETION:

GLUCOSE
Amino Acids
Fatty Acids

INSULIN
Insulin Action
Insulin Actions

Insulin stores stuff...
Insulin Action

- **SKELETAL MUSCLE**
  - Increases glucose transport
  - Increases glycogen synthesis
  - Inhibits gluconeogenesis

- **FAT**
  - Increases glucose transport
  - Increases lipogenesis
  - Inhibits lipolysis

- **LIVER**
  - Increases glycogen synthesis
  - Increases glycolysis
  - Inhibits gluconeogenesis

- **INSULIN**
  - Increases glucose transport
  - Increases lipogenesis
  - Inhibits lipolysis

A. Kumagai
Normal Glucose Metabolism

**GLUCOSE SUPPLY**

- DIET (Coke)

**BLOOD GLUCOSE**

70-120 mg/dL

**GLUCOSE DEMAND**

- BRAIN
- Insulin-independent tissues
- MUSCLE
- Insulin-dependent tissues

- Hepatic glucose production

- Insulin (-)
- Insulin (+)

A. Kumagai
Normal Glucose Metabolism: The Fasting State or “Feeding the Head”

GLUCOSE SUPPLY

GLUCOSE DEMAND

BLOOD GLUCOSE
70-120 mg/dL

DIET

BRAIN
Insulin-independent tissues

Liver
Hepatic glucose production

(-) INSULIN

INSULIN

MUSCLE
Insulin-dependent tissues

FAT CELL

A. Kumagai
The adult brain is completely dependent on glucose for normal metabolism until >5 days into a fast.
Normal Glucose Metabolism: The Fed State

**GLUCOSE SUPPLY**
- **DIET**
  - COKE
  - Liver
  - Hepatic glucose production

**BLOOD GLUCOSE**
- 70-120 mg/dL

**GLUCOSE DEMAND**
- **BRAIN**
- Insulin-independent tissues
- **MUSCLE**
- **FAT CELL**

**INSULIN**
- (-)
- (+)
INSULIN-GLUCAGON RELATIONSHIPS

STORAGE

INSULIN

Glycogenesis and decreased blood glucose

MOBILIZATION

GLUCAGON

Glucoenogenesis and increased blood glucose
Insulin Action

**Liver**
- Increases glycogen synthesis
- Increases glycolysis
- Inhibits gluconeogenesis

**FAT**
- Increases glucose transport
- Increases lipogenesis
- Inhibits lipolysis

**SKELETAL MUSCLE**
- Increases glucose transport
- Increases glycogen synthesis
- Inhibits gluconeogenesis
Insulin-regulated steps in muscle carbohydrate metabolism

- **I → = insulin-sensitive**
- **Facilitated glucose transport**
  - GLUT4

- **Glycogen synthase**
  - Inactive
  - Active

- **Glucose-FA cycle**
- **PFK**
- **Glycogen**
  - (Citrate inhib PKF → accum hexose P → reduce conc gradient for glucose entry)

- **Amino acids → AA → Protein**
- **(-)**

**Source:** Undetermined
Insulin Action

- Increases glycogen synthesis
- Increases glycolysis
- Inhibits gluconeogenesis

Liver

Fat
- Increases glucose transport
- Increases lipogenesis
- Inhibits lipolysis

Skeletal Muscle
- Increases glucose transport
- Increases glycogen synthesis
- Inhibits gluconeogenesis

Pancreas
Carbohydrate Metabolism in Hepatocytes

Insulin inhibits glucose production

Insulin stimulates glycogen storage

Insulin inhibits glycogen breakdown
Insulin Action

- Increases glycogen synthesis
- Increases glycolysis
- Inhibits gluconeogenesis

Liver

- Increases glucose transport
- Increases lipogenesis
- Inhibits lipolysis

FAT

- Increases glucose transport
- Increases glycogen synthesis
- Inhibits gluconeogenesis

SKELETAL MUSCLE

- Increases glucose transport
- Increases glycogen synthesis
- Inhibits gluconeogenesis
Insulin-regulated carbohydrate metabolism: adipocyte

Insulin inhibits lipolysis by stimulating lipoprotein lipase (LPL) and inhibiting hormone-sensitive lipase (HSL)

Facilitated glucose transport

GLUT4

† Lipogenesis

↓ Lipolysis

(+) LPL

(-) HSL

Source Undetermined
Fuel Metabolism: Take-Home Points

Understand:

1. That insulin binding to its receptor initiates a cascade of signaling pathways that results in translocation of the insulin-sensitive GLUT4 to the plasma membrane and increased glucose uptake.

2. The changes in insulin secretion in fasting and fed states and the physiologic “rationale” for preserving brain glucose uptake.
Fuel Metabolism: Take-Home Points

Understand:

3. The actions of insulin on skeletal muscle, liver, and fat.

4. The biochemistry: understand that insulin stores (e.g., stimulates glycogen synthase and lipoprotein lipase) and inhibits catabolism (e.g., inhibits HSL).
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