Insulin, glucagon and diabetes mellitus

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November 5, 2013

Lecture Outline

- Physiological regulation of blood glucose
- Insulin Signaling
- Glucagon Signaling
- Pathophysiology related to glucose control

Diabetes in the United States

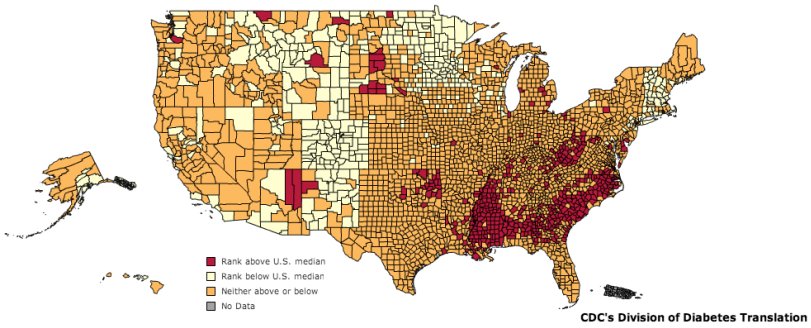

Figure 1: County Level Prevalence in Type II Diabetes

Acute regulation of circulating glucose

Glucose is maintained in a very narrow range

Primary control mechanisms

- postprandially regulated by insulin
- under starvation regulated by glucagon

Consequences of dysfunctional glucose homeostasis

Hyperglycemia

- Chronic hyperglycemia leads to glycation of membrane proteins. This leads to damaged nerves, kidneys, eyes, circulatory system (amputation) and Alzheimer's disease.
- Hyperglycemic hyperosmolar nonketotic syndrome.

Hypoglycemia

- Feinting, dizziness
- Diabetic ketoacidosis

Mechanisms of glucose control

- Glucose production
- Removal of glucose from the blood
- Synthesis of triglycerides and glycogen

Insulin Signaling

- Physiological effects of insulin
- Secretion of insulin
- Insulin signal transduction

Glucagon Signaling

- Physiological effects of glucagaon
- Regulation of glucagon release
- Effects of glucagon on the liver

Pathophysiology related to glucose control

Type I Diabetes Mellitus

- Loss of insulin producing cells
- Treatment options

Insulin Resistance and Type II Diabetes Mellitus

Mechanisms Underlying Insulin Resistance

- Inflammatory mediators of insulin resistance
- Mediation of insulin resistance by mTORC1

Adaptations to Insulin Resistance

- Hyperinsulinemia
- Pancreatic Failure

Other Control Circuits Related to Glucose Control

- Regulation of food intake
- Hypothalamic regulation of glucose release
- Counterinflammatory responses

Common Pharmacological Interventions for Insulin Resistance

- Primary intervention is diet and exercise alteration

Insulin sensitizers

- Thiazolidinediones
- Mechanism of action

Insulin secretagogues:

- Sulfonylureas

Glucose Utilization

- Metformin
- Mechanism of action

Potential Future Interventions for Insulin Resistance

Generation of Beige Fat

Anti-inflammatory Interventions

Further Reading