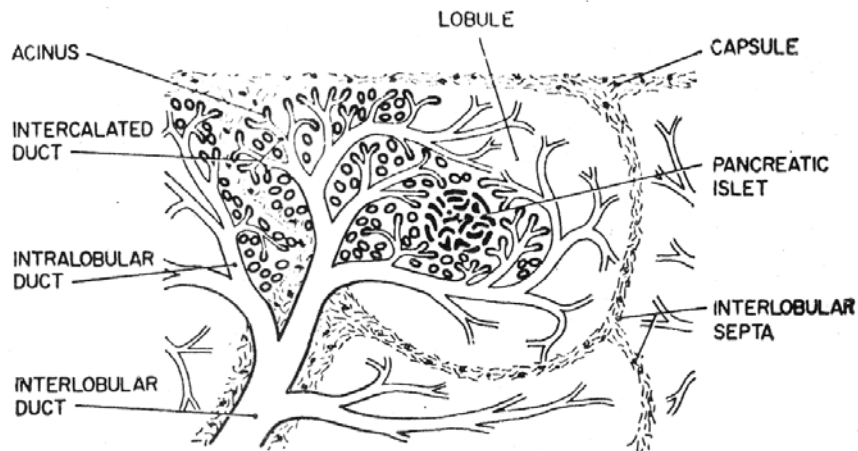


## INTRODUCTION

### A. Functional Anatomy



### B. Secretions

1. Acinar cells: exocrine functions – secrete digestive enzymes and electrolytes (especially bicarbonate) into the small intestine
2. Islet of Langerhan's cells: endocrine secretion
  - a. A (alpha) cells: Glucagon
  - b. B (beta) cells : Insulin
  - c. also D cells (secrete somatostatin) and F cells (secrete pancreatic polypeptide)

## INSULIN

### A. Synthesis and Distribution

1. Protein
2. Discharged into the blood, probably not protein bound
3. Rapid turnover, about 10 minutes

### B. Actions – occur when insulin binds to cell insulin receptors

1. Increase glucose entry into most cells by either facilitated diffusion or secondary active transport with Na ion

Note 1: insulin is not necessary for glucose uptake by nervous tissue

Note 2: glucose is the only metabolic substrate that is readily utilizable by brain neurons; in the absence of glucose, neuron activity is depressed (e.g. acute hypoglycemia => coma)

## INSULIN

### B. Actions (continued)

Note 3: ketones (products of fat breakdown) can support neuron metabolism but (1) adaptation to ketone metabolism takes time, and (2) brain neurons "prefer" glucose, and (3) production of ketones can lead to acidosis (keto acids)

Note 4: exercising muscles (but not resting muscles) can take up glucose even in the absence of insulin

2. Increase  $K^+$  entry into cells (partly due to stimulation of Na-K-ATPase active transport)
3. Promotes hepatic (liver) storage of glucose as glycogen
4. Inhibits breakdown of lipids in adipose tissue
5. Multiple other effects on metabolism

### C. Control of Insulin Secretion

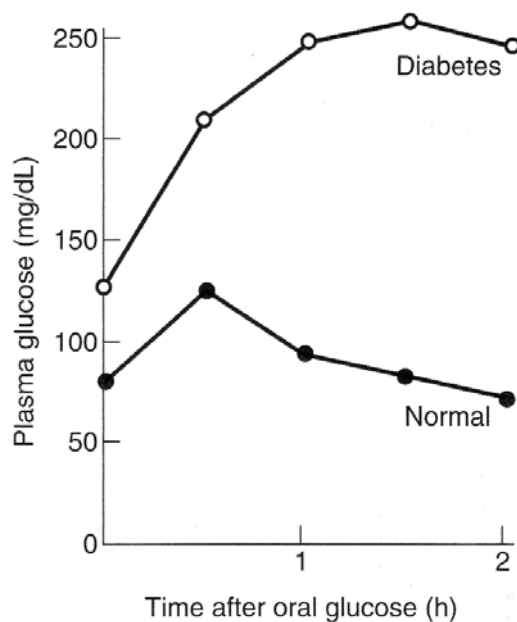
1. Direct effect on the pancreas of blood glucose level

blood glucose  $\uparrow$   $\Rightarrow$  pancreatic insulin release  $\uparrow$

2. Numerous other influences but the direct effect of blood glucose is the most important

### D. Test of Pancreatic Response

Glucose Tolerance Test: standard oral dose of glucose; follow blood and urine glucose levels over next 3-4 hours



## PATHOPHYSIOLOGY OF INSULIN

### A. Effects of Insulin Lack or Inability of Insulin to Activate Insulin Receptors

1. Hyperglycemia: inability of many cells to take up insulin and release of glucose by the liver
2. Glucosuria and polyuria (diabetes mellitus): more glucose filtered than can be reabsorbed (filtered glucose exceeds glucose tubular transport maximum)
3. Polydipsia (high water intake): thirst, partially due to increased plasma osmolality
4. Polyphagia (high food intake): due to glucose "starved" cells in the brain appetite centers
5. Weight loss: protein and fat breakdown
6. Acidosis (blood pH more acid than normal): consequence of breakdown of fat; can contribute to coma
7. Decreased resistance to infection: protein breakdown and hyperglycemia
8. Poor wound healing
9. Blood vessel damage (e.g. blindness due to damage to the retinal circulation – diabetic retinopathy)
10. Damage to peripheral nerves (diabetic neuropathy)

### B. Causes of Diabetes (major causes)

1. Type 1 diabetes
  - a. Also termed "insulin-dependent diabetes mellitus" as tissue responds to exogenous (administered) insulin, and "juvenile diabetes" as normal onset before age 40
  - b. Due to inability of pancreas B cells to synthesize and release insulin
2. Type 2 diabetes
  - a. Also termed "non-insulin-dependent diabetes mellitus" or "insulin-resistant" diabetes or "adult-onset diabetes" as generally develops after age 40.
  - b. More common than Type 1 diabetes
  - c. Less severe than Type 1 as pancreas B cells generally retain the ability to produce some insulin

## GLUCAGON

- A. Synthesis: Synthesized by A cells of the pancreas
- B. Action: Increase blood glucose level by its effect on the liver
  - 1. glycogen  $\Rightarrow$  glucose (glucose mobilization)
  - 2. protein  $\Rightarrow$  glucose (gluconeogenesis)
- C. Control of Glucagon Secretion
  - 1. Direct effect of blood glucose on pancreatic A cells  
blood glucose  $\Downarrow \Rightarrow$  glucagon secretion  $\Uparrow$
  - 2. Contributes, along with insulin regulation, to maintaining normal blood glucose levels