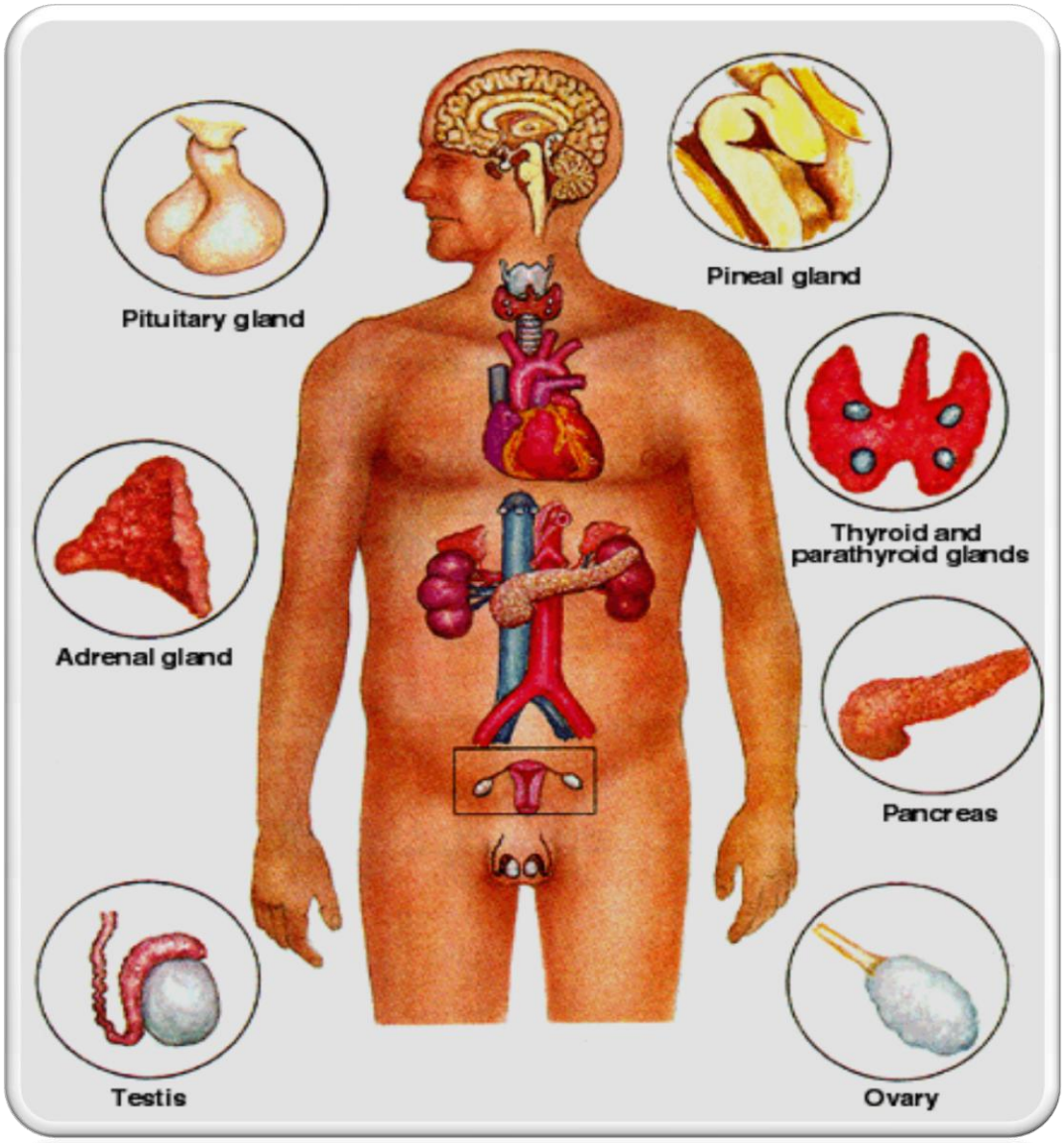
ENDOCRINE BLOCK

PHYSIOLOGY TEAM 431



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Pink : Team notes

Red : important

Physiology of Pancreas and Insulin – part I

A triangular gland, which has both exocrine and endocrine cells, located behind the stomach (Strategic location).

Acinar cells produce an enzyme-rich juice used for digestion (exocrine product) ➔ NOT IMPORTANT .

Pancreatic islets (**islets of Langerhans**) (mainly in the tail of Pancreas) produce hormones involved in regulating fuel storage and use .

Hormones are:

Insulin , glucagon, somatostatin, Pancreatic polypeptide

Islets of Langerhans:

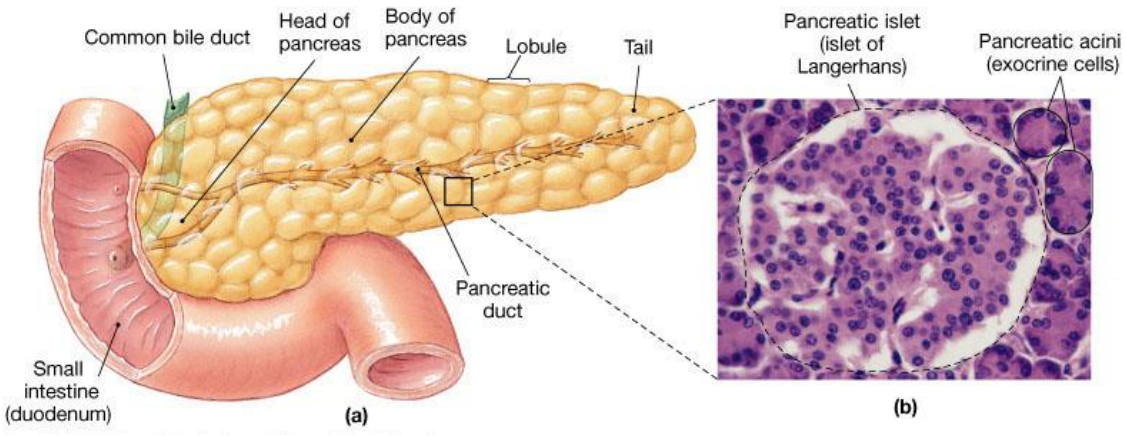
1-2 million islets

Beta (β) cells produce insulin (70%) present in the center and get stimulated by any source of energy + by glucagon.

Alpha (α) cells produce glucagon (20%) in the periphery.

Delta (δ) cells produce somatostatin (5%) scattered everywhere and inhibit insulin + glucagon .

F cells produce pancreatic polypeptide (5%).



Insulin: (Hormone of abundance):

Insulin =Stimulates the anabolism + inhibit the catabolism

Hormone of nutrient abundance

A protein hormone consisting of two amino acid chains linked by disulfide bonds ➔ the active form

Synthesized as part of proinsulin (86 AA) and then excised by enzymes, releasing functional insulin (51 AA) and C peptide (29 AA).

Has a plasma half-life of 6 minutes.

Insulin Synthesis:

DNA (chromosome 11) in β cells

↓

mRNA

↓

Preproinsulin (signal peptide, A chain, B chain, and peptide C)

↓

Proinsulin attached with C- peptide

↓

Insulin

Benefit of C-peptide in proinsulin is to make the molecule folded for easier attachment with disulfide

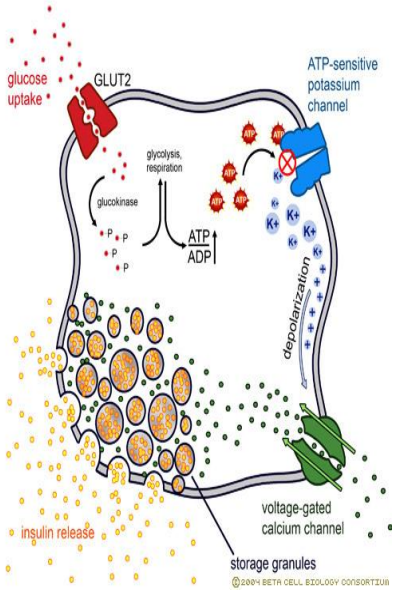
The active form get out from Golgi apparatus in vesicles in addition to c – peptide

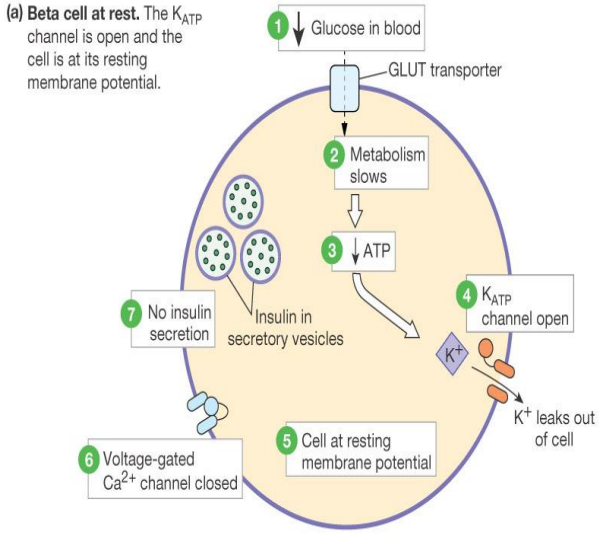
Insulin Synthesis:

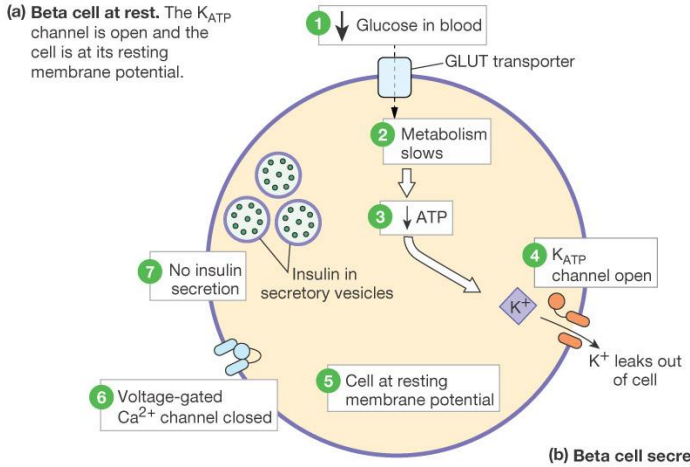
Insulin synthesis is stimulated by glucose or feeding and decreased by fasting

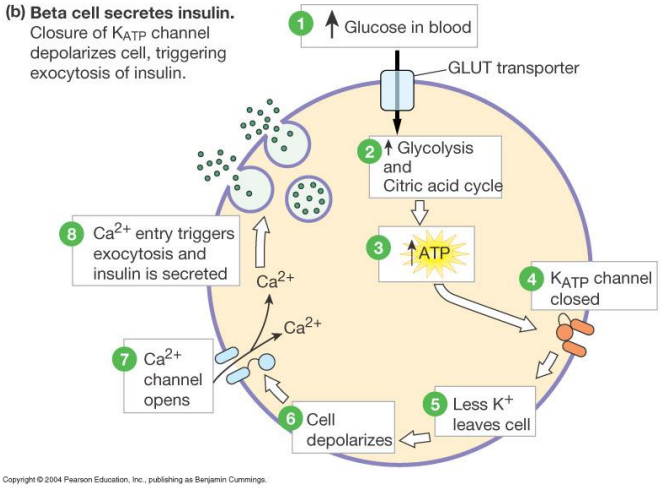
Threshold of glucose-stimulated insulin secretion is 100 mg/dl. **Glucose is the primary stimulator of insulin secretion**

Glucose rapidly increase the translation of the insulin mRNA and slowly increases transcription of the insulin gene.









Regulators of insulin secretion

Stimulators of insulin secretion	Inhibitors of insulin secretion
Directly: ↑ Serum glucose	↓ Glucose
↑ Serum amino acids	↓ Amino acids
↑ Serum free fatty acids	↓ Free fatty acids
↑ Serum ketone bodies	
Hormones	Hormones
GIT hormones: Gastroinhibitory peptide (GIP)	Somatostatin
Glucagon	Epinephrine (α-receptor)
Gastrin	
Cholecystokinin (CCK)	
Secretin	
Vasoactive intestinal peptide (VIP)	
Epinephrine (β-receptor)	
Parasympathetic nervous system	Sympathetic nervous system stimulation
Ketone bodies	

Note:

Glucagon stimulates insulin but the insulin inhibit glucagon

Patient with ketone bodies is treated by giving him insulin

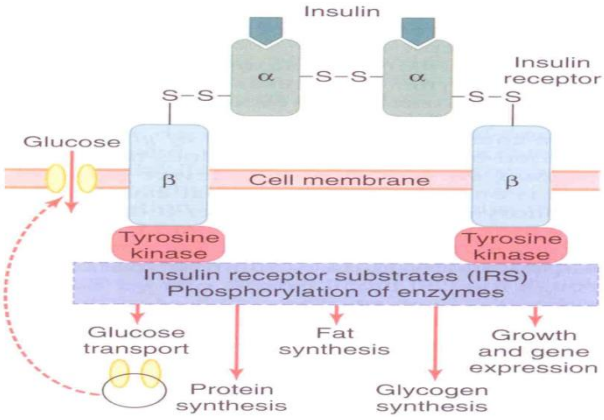
Question: if you give a patient oral glucose would it be faster in stimulating the insulin release than the IV glucose?
Yes, because the digestive enzymes will potentiate the release of insulin+ parasympathetic (rest and digest)

Insulin Receptor

the insulin receptor is a transmembrane receptor

belongs to the large class of **tyrosine kinase receptors** (very important)

Made of two alpha subunits and two beta subunits



Tyrosine kinase is inactive enzyme will be activated when binds to insulin ➔autophosphorylation➔ works on 5 enzymes (IRS)

1- PROTEIN SYNTHESIS

2-LIPID SYNTHESIS

3-GLYCOGEN SYNTHESIS

5- GROWTH= IT CONSIDER A GROWTH HORMONE SO A CHILD WITH TYPE 1 DIABETES MUST BE GIVEN INSULIN REPLACEMENT THERAPY

Actions of insulin Rapid (seconds)

(+) transport of glucose, amino acids, K+ into insulin-sensitive cells

Intermediate (minutes)

(+) protein synthesis

(-) protein degradation

(+) of glycolytic enzymes and glycogen synthase

(-) phosphorylase and gluconeogenic enzymes

Delayed (hours)

(+) mRNAs for lipogenic and other enzymes

Action of insulin on Adipose tissue:

(+) glucose entry

(+) fatty acid synthesis inhibit the lipase enzyme in adipose tissue = inhibit catabolism ➔ thin patient with diabetes.

(+) glycerol phosphate synthesis

(+) triglyceride dep0sition

(+)lipoprotein lipase ➔ formation of TAG obesity in increase glucose and insulin (fatty acid transported by VLDL in the blood to the adipose tissue.

(-) of hormone-sensitive lipase

(+) K uptake ➔ **VEREY IMPORTANT IN CLINICAL PRACTICAL patient with hyperkalemia (more dangerous than glucose level) ➔ treat the patient with intravenous insulin**

Action of insulin on Muscle:

(+) glucose entry

(+) glycogen synthesis

(+) amino acid uptake

(+) protein synthesis in ribosomes

(-) protein catabolism

(-) release of gluconeogenic aminco acids

(+) ketone uptake

(+) K uptake

In the liver glucose entry is not insulin sensitive

+

Brain does not depend on insulin

Action of insulin on Liver:

(-) ketogenesis

(+) protein synthesis

(+) lipid synthesis

(-)gluconogenesis, (+) glycogen synthesis, (+) glycolysis

General

(+) cell growth

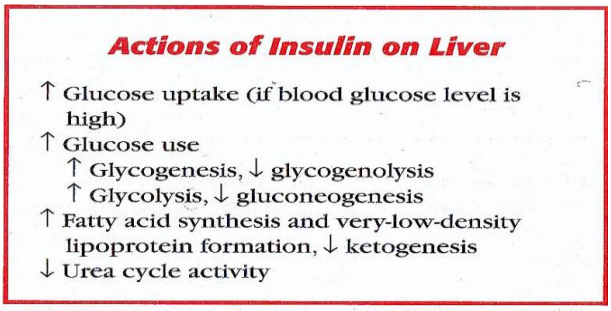
Glucose Transport

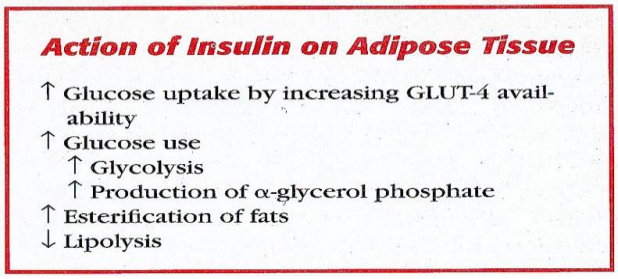
GLUT1 (erythrocytes, brain)

GLUT2 (liver, pancreas, small intestines)

GLUT3 (brain)

GLUT4, insulin sensitive transporter (muscle, adipose tissue)





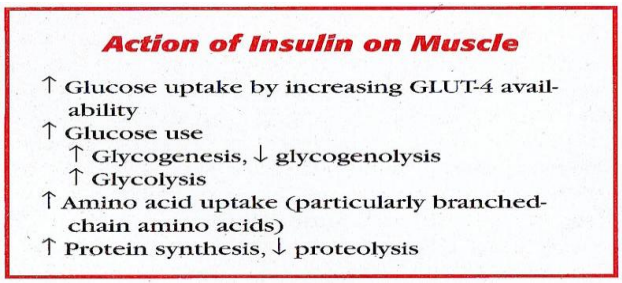


Table 22-3: Insulin

Cell of origin	Beta cells of pancreas
Chemical nature	51-amino acid peptide
Biosynthesis	Typical peptide
Transport in the circulation	Dissolved in plasma
Half-life	5 minutes
Factors affecting release	Plasma [glucose] > 100 mg/dL; ↑ blood amino acids; GI hormones (feedforward reflex) and parasympathetic amplify. Sympathetic inhibits.
Target cells or tissues	Liver, muscle, and adipose tissue primarily; brain, kidney, and intestine not insulin-dependent
Target receptor	Membrane receptor with tyrosine kinase activity; pathway with insulin-receptor substrates
Whole body or tissue action	↓ Plasma [glucose] by ↑ transport into cells or ↑ metabolic use of glucose
Action at cellular level	↑ Glycogen synthesis; ↑ aerobic metabolism of glucose; ↑ protein and triglyceride synthesis

Summary:

1-beta cells located in the center of the **islets of Langerhans**.
2- the insulin is form of 2 amino acids chains linked by 2 disulfide bonds.
3-DNA transcription located on chromosome number 11.
4- we can assess the function of bête cells measuring the c peptide in urine because for each molecule there is c peptide secrete with it.
4- primary stimulus of insulin is glucose.
5- parasympathetic will stimulate the insulin release and the opposite with the sympathetic.
6-oral glucose is more powerful than iv glucose because of GIT stimulation in addition to beta cells.
7- GLUT-4- is insulin sensitive transporter in muscle and adipose tissue.

Questions

1-Regarding insulin synthesis:
A-stimulated by fasting
B-stimulated by feeding
C-inhibited by FFAs
D-inhibited by glucagon

2-Regarding the insulin actions:
A-it decreases glycogen synthesis
B-it increases lipolysis
C-it has anabolic effect on proteins
D-it increases gluconeogenesis

3- The main glucose transporter in muscles and adipose tissues:
A-GLUT 1
B-GLUT2
C-GLUT3
D-GLUT4

1	2	3
B	C	D