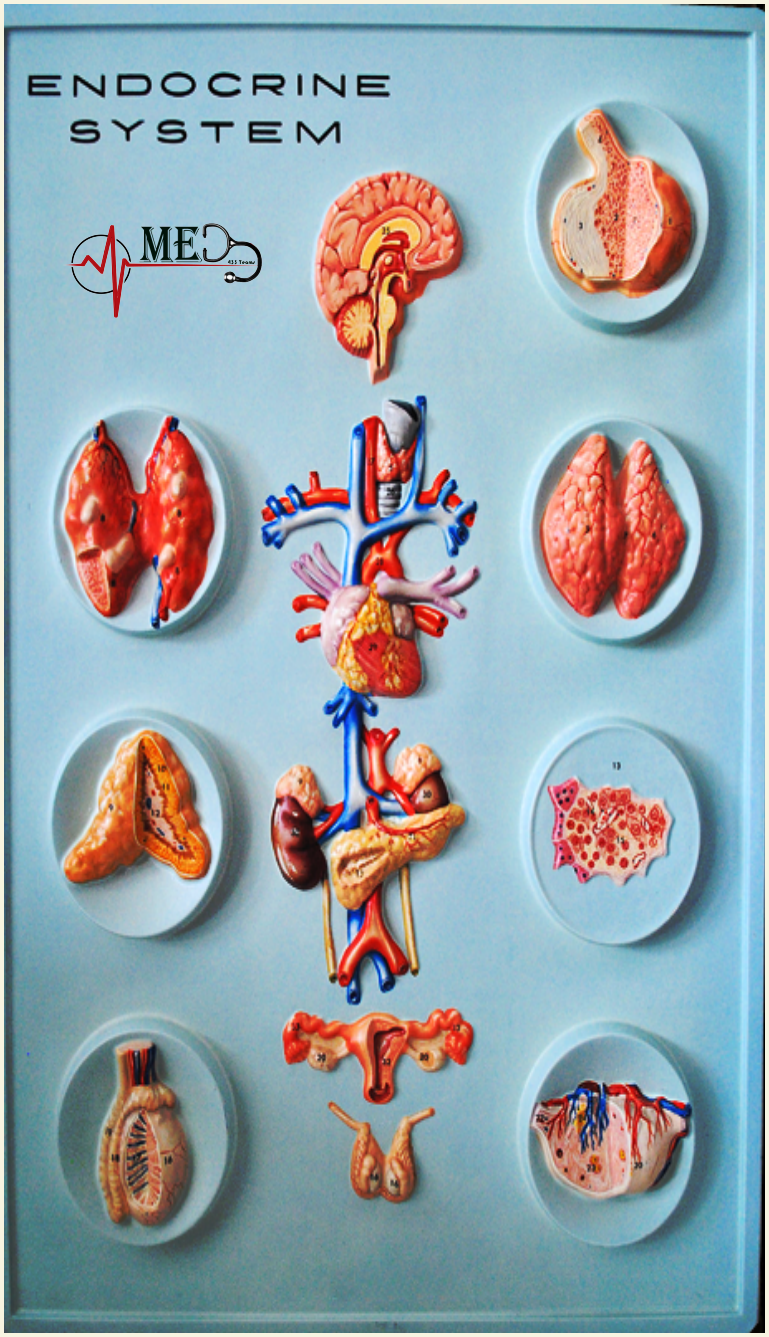


LECTURE 5 :

GLUCOSE HOMEOSTASIS

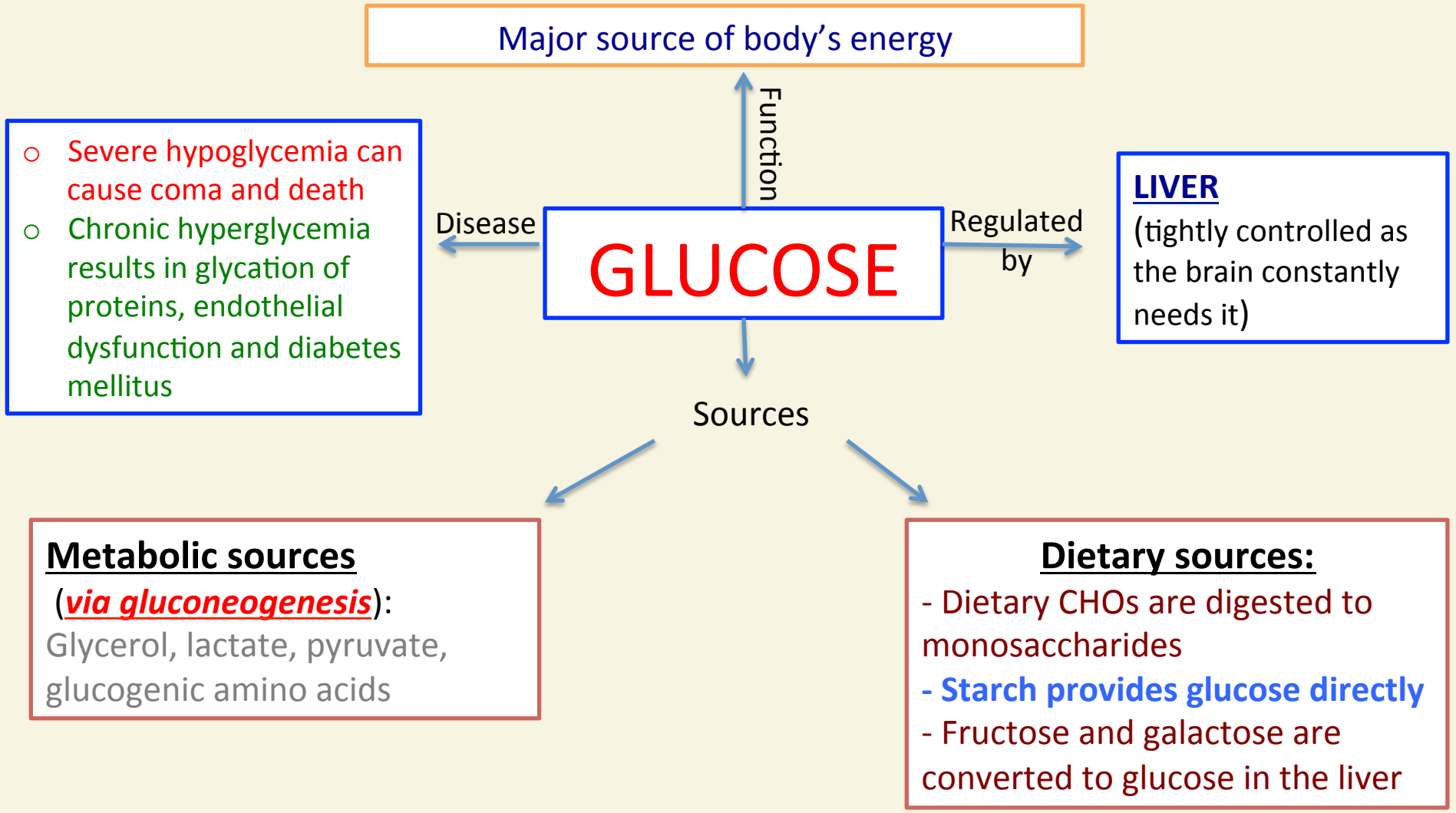
OVERVEIW:

- Sources of glucose
- Phases of glucose homeostasis
- Hormones in glucose homeostasis (actions, role in CHO metabolism)
- Insulin
- Glucagon
- Somatostatin
- Cortisol
- Growth hormone
- Epinephrine

GLUCOSE HOMEOSTASIS

A process that :

- ❑ Controls glucose metabolism and
- ❑ Maintains normal blood glucose level in the body



Phases of glucose homeostasis

Phase I (Well-fed state)

Phase II (Glycogenolysis)

Phase III (Gluconeogenesis)

Phase IV (Glucose, ketone bodies (KB) oxidation)

Phase V (Fatty acid (FA), KB oxidation)

Phases of glucose homeostasis

	Phase I	Phase II	Phase III	Phase IV	Phase V
Source of glucose	Exogenous (CHO)	**Glycogen** Hepatic gluconeogenesis	**Hepatic gluconeogenesis** Glycogen	Hepatic and renal gluconeogenesis	Hepatic and renal gluconeogenesis
Tissues using glucose	ALL (Liver removes about 70% of glucose load after a CHO meal)	ALL (EXCEPT liver, muscle, adipose tissue at low rates)	ALL (EXCEPT liver, muscle, adipose tissue at low rates)	Brain RBCs Renal medulla Muscles (small amount)	Brain (low rates) RBCS Renal medulla
Major fuel of brain	GLUCOSE	GLUCOSE	GLUCOSE	**GLUCOSE** Ketone bodies	**Ketone bodies** GLUCOSE
When does it start ?	Food intake	During early fasting (when dietary glucose supply is exhausted)	When glycogen stores in liver are exhausted (< 20 hours)	Several days of fasting	Prolonged fasting

Phase I (Well-fed state)

- Some glucose is converted to glycogen for storage in the liver (glycogenesis)

- Excess glucose is converted to fatty acids and triglycerides in the liver

- Which are transported via VLDL to adipose tissue for storage

- Gluconeogenesis is inhibited in this phase

(Cori and glucose-alanine cycles are inhibited)

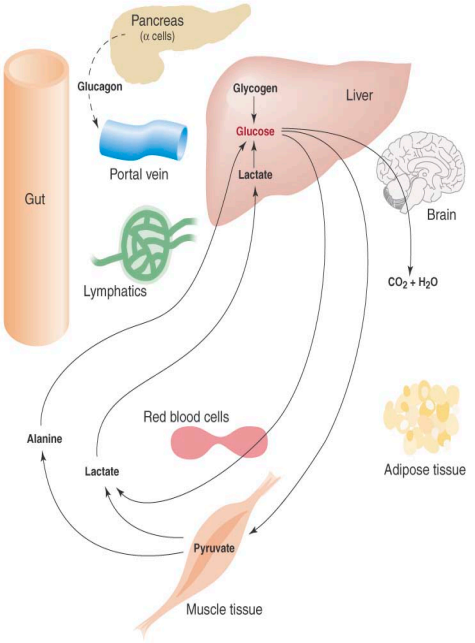


Figure 22.3. Metabolic interrelationships of major tissues in early fasting state.

Phase II (Glycogenolysis)

Hepatic **Glycogenolysis** and gluconeogenesis maintain blood glucose level in this phase

Phase III (Gluconeogenesis)

Its duration depends on:

1- Feeding status

2- Hepatic glycogen stores

3- Physical activity

Hepatic gluconeogenesis from lactate, pyruvate, glycerol and alanine maintains blood glucose level

Phase IV (Glucose and KB oxidation)

- Gluconeogenesis starts to decrease
- FA oxidation increases KB accumulation
- KBs enter the brain and muscle for energy production
- Brain uses both glucose and KB for energy

Phase V (FA and KB oxidation)

- Less dependence on gluconeogenesis
- All body tissues mainly use FA and KB oxidation for energy production
- High KB conc. and glucose levels inhibit proteolysis in muscle (conservation of muscle)
- When all fat and KBs are used up

=> Body uses muscle protein to maintain blood glucose level (the last stage)

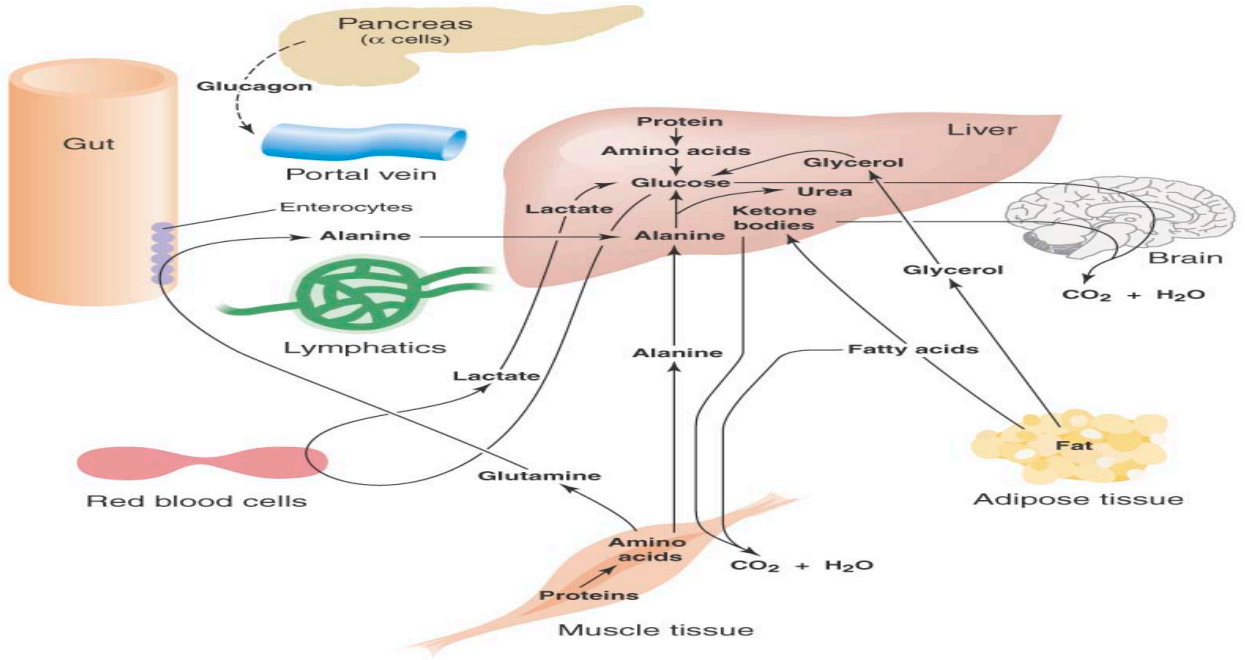


Figure 22.4. Metabolic interrelationships of major tissues in fasting state.

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Hormones and glucose homeostasis

Hormones that regulate glucose metabolism:

- ✓ Insulin (lowers blood glucose level)
- ✓ Glucagon
- ✓ Somatostatin
- ✓ Cortisol
- ✓ Growth hormone
- ✓ Epinephrine

→ **Antagonize insulin action**

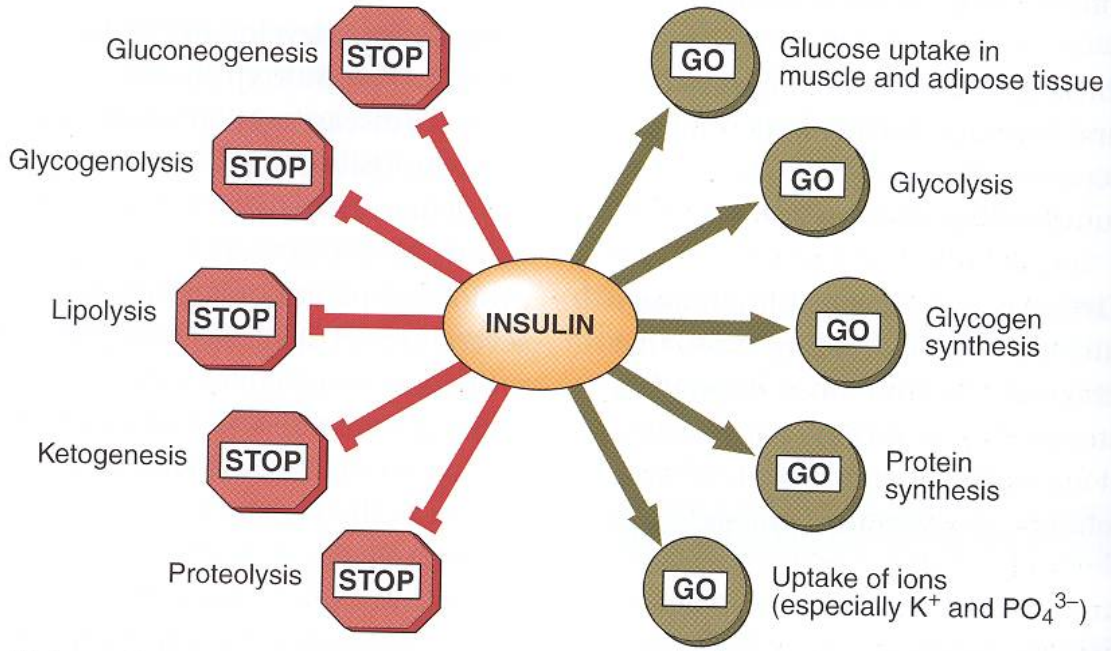


Fig. 2 **The actions of insulin.**

INSULIN :

small protein composed of two chains, plays major role in glucose homeostasis.

Synthesized by:

β-cells of islets of Langerhans of pancreas

Stimulated by:

Rise in blood glucose level

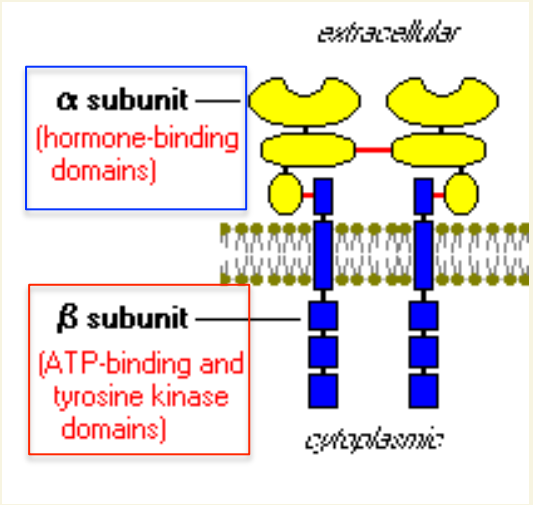
Promote:

entry of glucose into cells

Mechanism of action of insulin

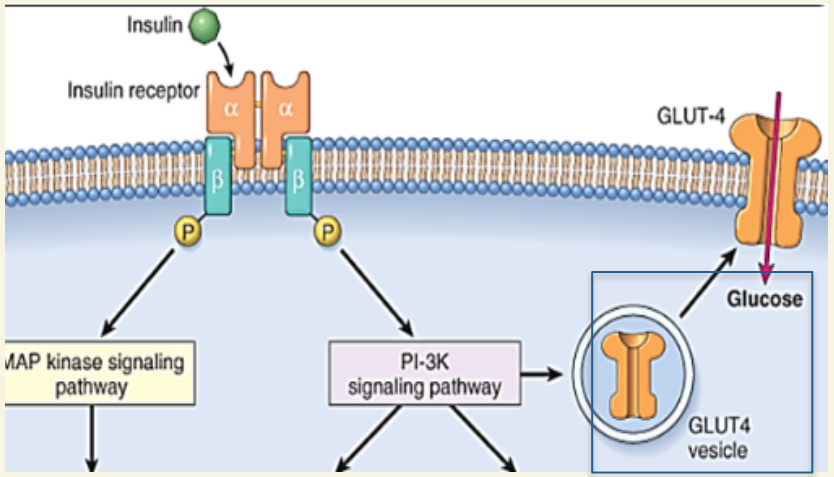
The insulin receptor is present **on the plasma membrane** of cell
Composed of:

- α-subunit (extracellular)
- β-subunit (cytoplasmic)



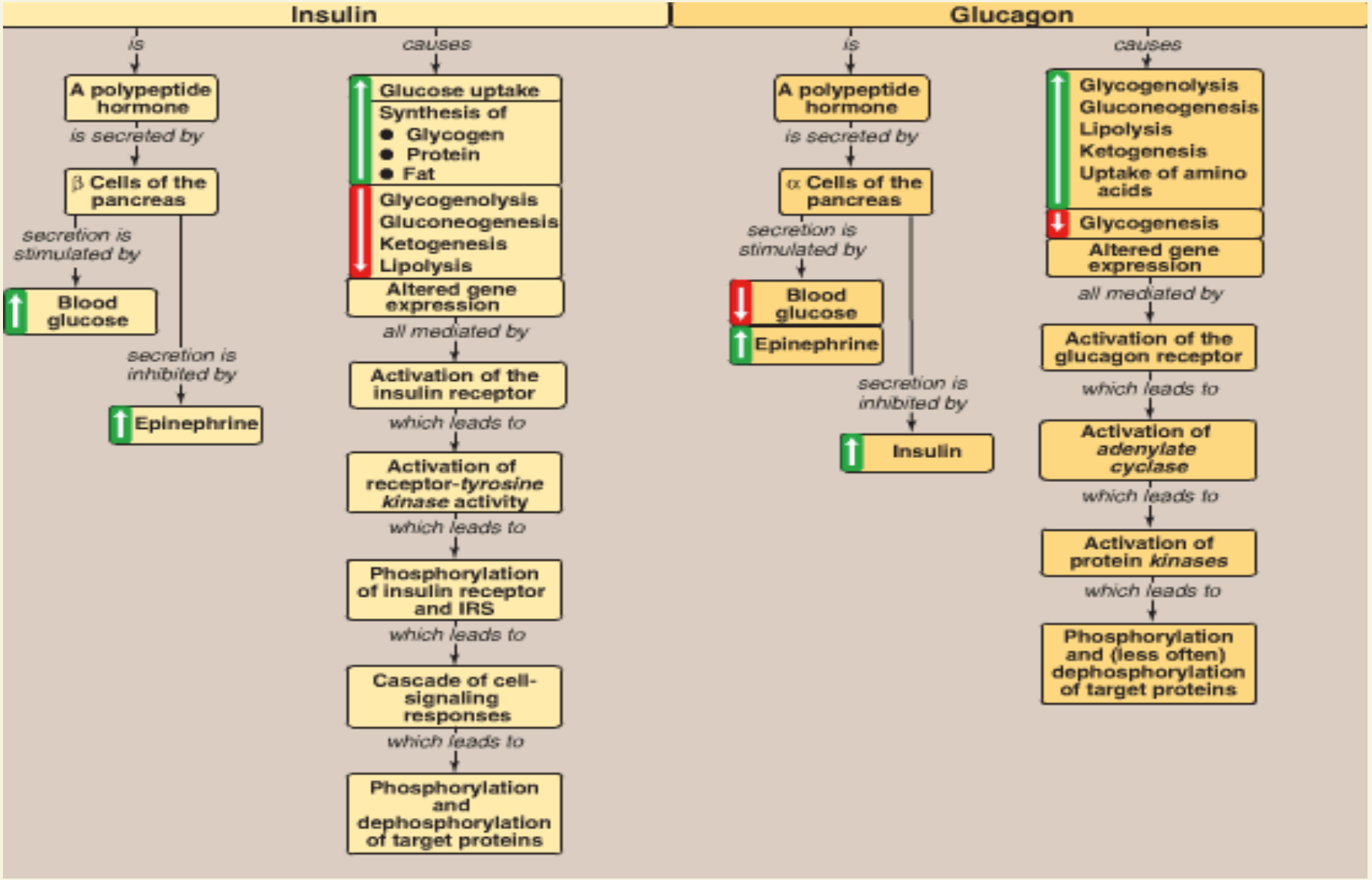
Binding of insulin to α-subunit causes phosphorylation of β-subunit => This activates the receptor
=> The activated receptor then phosphorylates intracellular proteins generating a biological response

Glucose is diffused into cells through hexose transporters such as GLUT4
GLUT4 is present in cytoplasmic vesicles



Insulin binding to its receptor causes vesicles to diffuse into plasma membrane
⇒ GLUT4 is inserted into the membrane allowing glucose transport into the cell

**** Brain and liver have non-insulin dependent glucose transporter**



- Insulin deficiency causes diabetes mellitus
- Hyperinsulinemia is due to insulin resistance in:

1. **Diabetes mellitus**
2. **Metabolic syndrome**

Hormones and glucose homeostasis

	GLUCAGON	Somatostatin (Inhibitory)	Cortisol	Growth hormone	Epinephrine
Nature	peptide	Peptide	steroid	Protein	Catecholamine
Secreted by	a-cells of pancreatic islets	d-cells of pancreatic islets, stomach and intestine	Adrenal gland	anterior pituitary gland	Adrenal gland
Functions	1. Increases glucose levels 2. Stimulates Glycogenolysis 3. Activates hepatic gluconeogenesis	1- Inhibits secretion of both insulin and glucagon 2- Affects glucose homeostasis indirectly	1- Maintains normal glucose levels in fasting 2- Stimulates gluconeogenesis in the liver 3- Mobilizes amino acids for gluconeogenesis 4- Stimulates fat breakdown in adipose tissue	Maintains blood glucose levels by: 1- Inhibiting insulin action 2- Stimulating gluconeogenesis in the liver	1- Stimulates lipolysis in adipose tissue when glucose blood levels fall 2- Promotes Glycogenolysis in skeletal muscle

Summary

- Glucose is a major source of body's energy.
- Sources of glucose is Dietary sources & Metabolic sources (via gluconeogenesis).
- In **Phase I** Glucose is mainly supplied by dietary CHOs (exogenous) and Gluconeogenesis is inhibited in this phase.
- **In Phase II** Major sources of blood glucose is Glycogenolysis and gluconeogenesis.
- **Phase III** starts when glycogen stores in liver are exhausted. The Major source of blood glucose in this phase Gluconeogenesis from lactate,pyruvate, alanine and glycerol .
- **In Phase IV** Brain uses both glucose and KB for energy. Gluconeogenesis also starts to decrease.
- In **Phase** V All body tissues mainly use FA and KB oxidation for energy production
- Insulin which is synthesized in the pancreatic beta cells, Promotes entry of glucose into cells. Its secretion depends on the glucose levels in the blood.
- Brain and liver have non-insulin dependent glucose transporter
- Glucagon Stimulates glycogenolysis
- Somatostatin Inhibits secretion of both insulin and glucagon
- Cortisol, GH, Epinephrine, Glucagon, & somatostatin are Antagonize insulin action

TEST YOURSELF!

Q1: Glucose uptake by liver cells is:
A. Energy-consuming
B. A saturable process
C. Insulin-dependent
D. Insulin-independent

Q2: Which of following abundant sources is used in phase III of glucose homeostasis:
A. Glycogenolysis
B. Fatty acid oxidation
C. Gluconeogenesis
D. Diet

Q3. Regarding the action of glucagon:
A. It stimulates glycogenolysis
B. It stimulates glycolysis
C. It inhibits glycogenolysis
D. It stimulates insulin activity

Q4. Which of the following is a direct glucose source:
A. starch
B. Fructose
C. galactose
D. None

Q5. which of the folling is the binding site for insulin:
A. Beta domain
B. Alpha domain
C. delta
D. Both alpha and beta

Q6: The conversion of alanine to glucose is termed:
A. Glycolysis
B. Oxidative decarboxylation
C. Specific dynamic action
D. Gluconeogenesis

Q7. Which of the following is an action of insulin:
A. Simulate ketogenesis
B. inhibit glucose up take in muscle
C. stimulate glycogenolysis
D. Lipogenesis

Q8. In which of the following are ketone bodies produced:
A. Phase I
B. Phase II
C. Phase III
D. Phase V

Ans:
1- D
2- C
3- A
4- A
5- B
6- D
7- D
8- D

THANK YOU ...

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