Biochemistry Bandits 434

MED 434 ICINE

GLUCOSE HOMEOSTASIS

❖ Important ❖ Extra ❖ Biochemistry Edit

ENDOCRINE BLOCK

GLUCOSE HOMEOSTASIS

A process that controls glucose metabolism and maintains blood glucose level in the body.

- Glucose is a major source of body's energy.
- The liver plays a key role in maintaining blood glucose level.
- Blood glucose level is tightly controlled because the brain constantly needs glucose.
- Severe hypoglycemia can cause coma and death. because of acidosis.
- Chronic hyperglycemia results in glycation of proteins, endothelial dysfunction and diabetes.

Sources of glucose

- Dietary CHO is digested in the GI to monosaccharides
- Starch provides glucose **directly**
- Fructose and galactose are converted to glucose in the liver

Metabolic sources (via gluconeogenesis) :

Glycerol, lactate, pyruvate, glucogenic amino acids

Note

* in Hyperglycemia we have too much glucose In blood it leads to glycation, which means glucose attached non enzymatically to protein " hemoglobin " and that will form A1c but this is not only protein get glycation , increase amount of glucose > glycation of addition glucose > when protein in blood start binding to glucose > become large in size > cause occlusion of smaller capillaries , this can be seen in diabetic foot

1- Glucose, fractose and glactose “monosaccharides” going into blood stream
2- From blood to periphral tissue to provide energy and it goes to liver “Liver removes about 70% of glucose load after a CHO meal”
3- When it goes to liver some of glucose used to make glycogen “ glycogenesis” (for storage)
4-Excess glucose is converted to fatty acids and triglycerides in the liver
These are transported via VLDL (very low density lipoproteins) to adipose tissue for storage
*All these happen when you have enough glucose
5- when you are starving the gluconeogenesis will start .

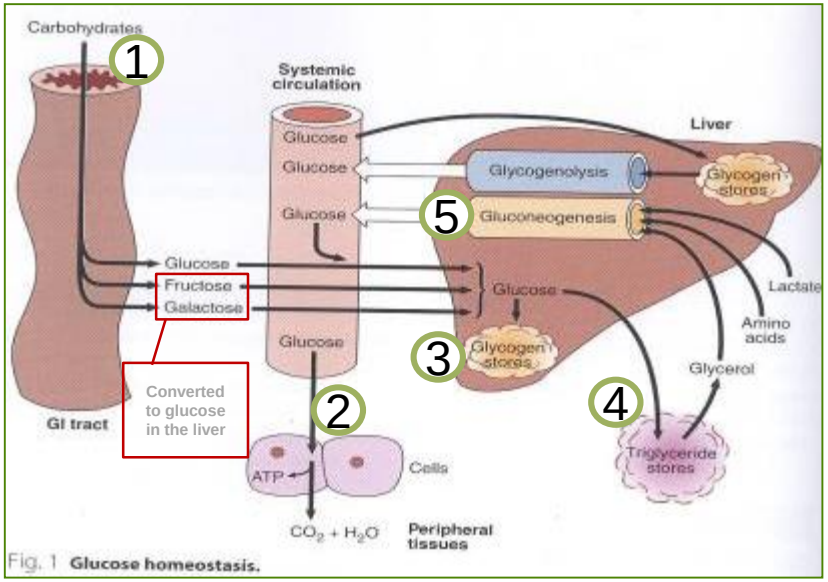


Fig. 1 **Glucose homeostasis.**

First there is a lot of glucose used from exogenous sources

Time 0 start after you have had meal , then the starving period start

By 4 to 5 hours glucose supply will be limited “ fasting phase” at this time you start to break down your glycogen you can survive up to 15 to 16 hours.

By the time your glycogen stores are finishing up “ exhausted” , your body start gluconeogenesis phase

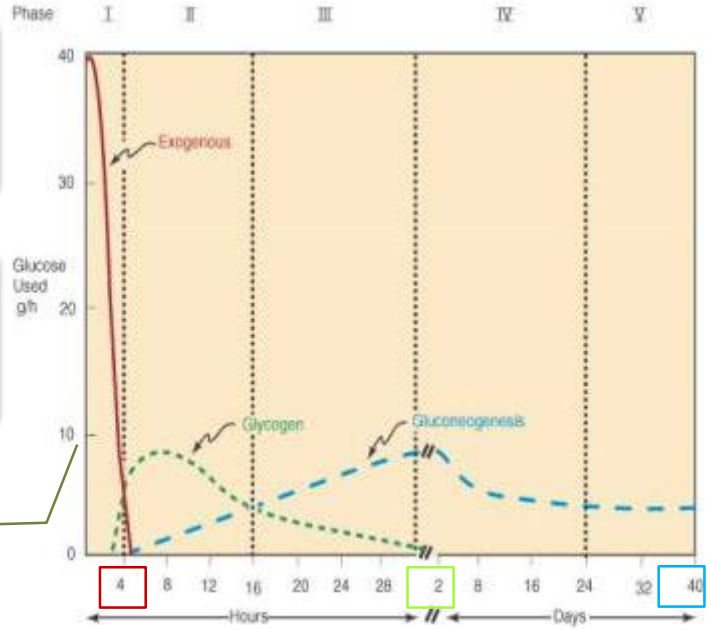
There is no clear demarcation between phase 3 and 4 the difference is in the gluconeogenesis

mainly is hepatic gluconeogenesis in phase 3 while the renal gluconeogenesis will start in phase 4

In phase 4 basically start breaking fat stores , so ketone bodies are produced and used by cells

In phase 5 the fatty acid stores are kind of exhausted and then will go for the last thing “ protein”

notice each source and when it starts .
For example:
Glycogenolysis starts in the early hours of fasting



PHASES OF GLUCOSE HOMEOSTASIS

Phase	Origin of blood glucose	Tissue using glucose	Major fuel for brain	Notes
Phase I (Well-fed state)	Exogenous "dietary CHOs"	All body tissues	Glucose	• Some glucose is converted to glycogen for storage in the liver (glycogenesis) • Gluconeogenesis is inhibited in this phase • Cori and glucose-alanine cycles are inhibited
Phase II (Glycogenolysis)	Glycogenolysis is the major source of blood glucose in this phase & Hepatic gluconeogenesis	All except liver . Muscle and adipose tissue. At diminished rate	Glucose	Phase II starts during early fasting when dietary glucose supply is exhausted
Phase III (Gluconeogenesis)	Gluconeogenesis is the major source of blood glucose in this phase *Hepatic gluconeogenesis from lactate, pyruvate, glycerol and alanine maintains blood glucose level	All except liver . Muscle and adipose tissue. At moderate rate	Glucose	• Phase III starts when glycogen stores in liver are exhausted (within 20 hours) • Duration of phase III depends on : Feeding status , Hepatic glycogen stores , Physical activity
Phase IV (Glucose and KB oxidation)	Hepatic & Renal gluconeogenesis	Brain , RBCS ,Adrenal medulla . Small amount by muscle	Glucose & ketone bodies	• Several days of fasting leads to phase IV • Gluconeogenesis starts to decrease • KB accumulation increases which enter the brain for energy production
Phase V (FA and KB oxidation)	Hepatic & Renal gluconeogenesis *Gluconeogenesis somewhat maintains blood glucose level in this phase	All body tissues use FA and KB oxidation for energy production	Glucose & ketone bodies	• Prolonged fasting leads to phase V • 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

HORMONES AND GLUCOSE HOMEOSTASIS

Hormones That Regulate Glucose Metabolism:

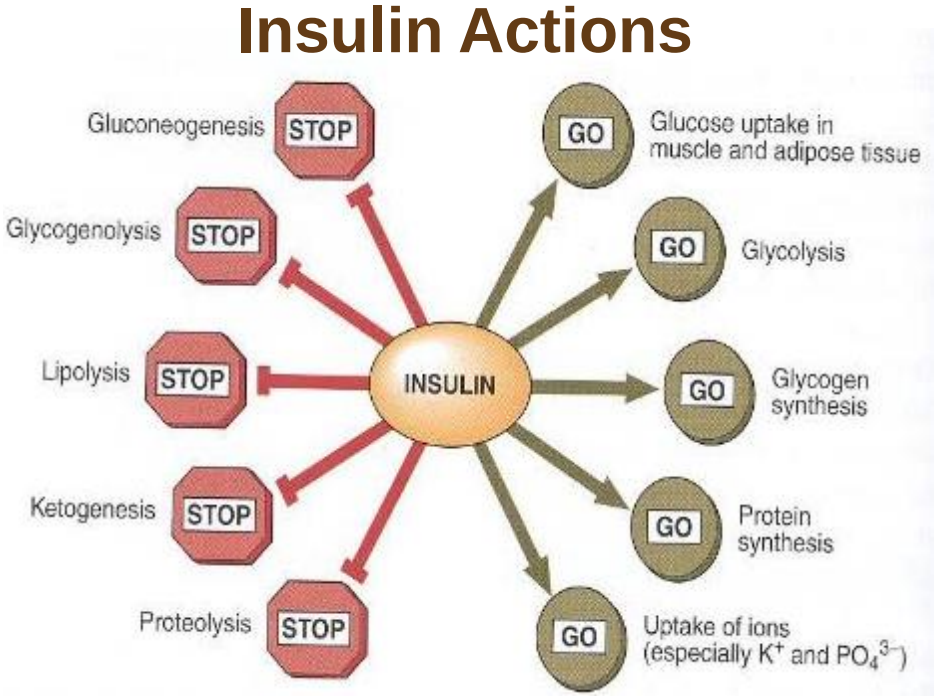
- **Insulin (Lowers Blood Glucose Level)**
- **Glucagon**
- Cortisol
- Growth Hormone
- Adrenaline

} Antagonize insulin action

❖ INSULIN:

Is a small protein composed of *two chains*, plays a major role in *glucose homeostasis,*

- Formed as **prepro-insulin** and converted to **pro-insulin** upon secretion.
- **Synthesized by:**
  B-cells of islets of Langerhans of pancreas.
- **Stimulated by:**
  Rise in blood glucose level.
- **Promotes entry of glucose into cells.**

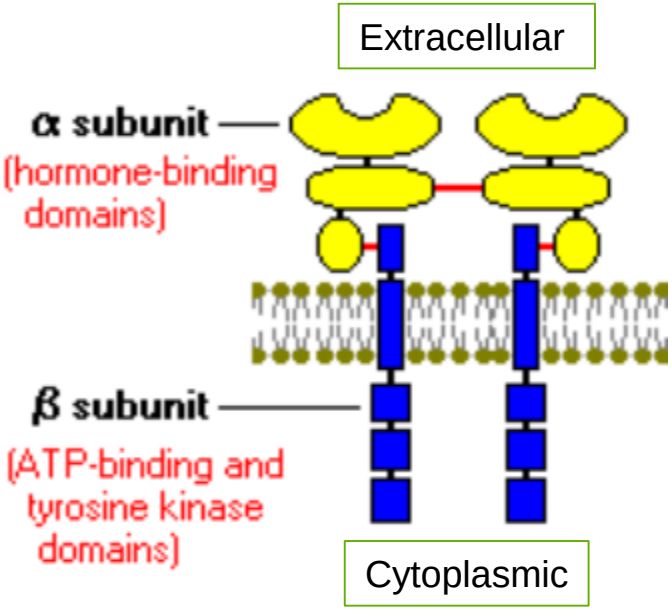


MECHANISM OF ACTION

The insulin receptor is present on the plasma membrane of cell.

Composed of:

- 2α-subunit (extracellular)
- 2β-subunit (cytoplasmic)



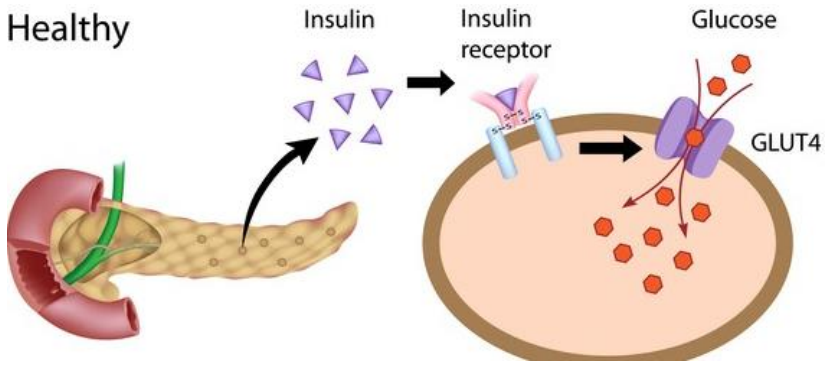
Binding of insulin to α-subunit causes phosphorylation of β-subunit → This activates the receptor → The activated receptor then phosphorylates intracellular proteins generating a biological response

INSULIN AND CHO METABOLISM

- Promotes glucose uptake into cell
- Stimulates glycogen synthesis.
- Decreases blood glucose levels
- Increases glycolysis.
- Stimulates protein synthesis.
- Insulin deficiency causes diabetes mellitus.
- Hyperinsulinemia is due to insulin resistance in:
  - Diabetes mellitus.
  - Metabolic syndrome.

- 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.



HORMONES AND GLUCOSE HOMEOSTASIS

	GLUCAGON	CORTISOL	GROWTH HORMONE	EPINEPHRINE
nature	peptide	steroid	protein	catecholamine
Secreted by	α-cells of pancreatic islets	adrenal gland	anterior pituitary gland	adrenal gland
Functions	▪ Secreted in response to hypoglycemia. ▪ Increases glucose levels. ▪ Stimulates glycogenolysis ▪ Activates hepatic gluconeogenesis.	Contributes to glucose homeostasis ▪ Maintains normal glucose levels in fasting. ▪ Stimulates gluconeogenesis in the liver ▪ Mobilizes amino acids for gluconeogenesis ▪ Inhibits glucose uptake by cells ▪ Stimulates fat breakdown in adipose tissue.	Maintains blood glucose levels by: -Inhibiting insulin action -Stimulating gluconeogenesis in the liver	▪ Stimulates lipolysis in adipose tissue when glucose blood levels fall. ▪ Promotes glycogenolysis in skeletal muscle

MCQS&SAQS

1- Chronic hyperglycemia results in:

A-diabetes

B-dysfunction of endothelium

C- Dehydration

D- A&B

2- In which phase there will use glucose from the hepatic gluconeogenesis MAINLY:

A- phase 2

B- phase 3

C- phase 4

D- phase 5

3-which phase will start after prolonged fasting?

A- phase 2

B- phase 3

C- phase 5

4)Insulin receptor is present in:

A. Cytosol

B. Plasma membrane

C. Nucleus

5)Growth hormone maintain blood glucose level by:

A. Mobilizes amino acids for gluconeogenesis

B. Stimulates fat breakdown in adipose tissue.

C. Stimulating gluconeogenesis in the liver

6)Which of the following is the binding site of insulin:

A. Beta-domain

B. Alpha-domain

C. both

1.D 2.B 3.C 4.B 5.C 6.B

1- Enumerate the 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)

2- How does hyperglycemia affect blood vessels ?

Once glucose increased in blood that leads to glycation of proteins which will make them large in size and that cause occlusion of blood vessels.

3) What stimulate insulin secretion?

Rise in blood glucose level.

Biochemistry Bandits 434

اللهم إني استودعك ما قرأت وما حفظت وما تعلمت
فرده عند حاجتي إنك على كل شيء قدير.

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