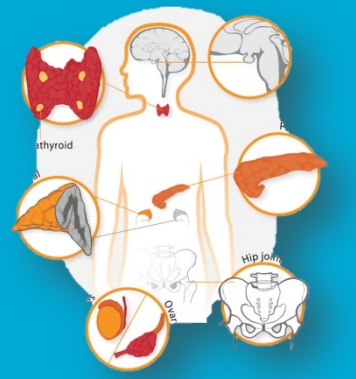
[lecture 5]

Glucose Homeostasis



Endocrine system

Biochemistry Team

Teams

The Objectives

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

Red = Import-ant

Blue = explain

Green = addition notes

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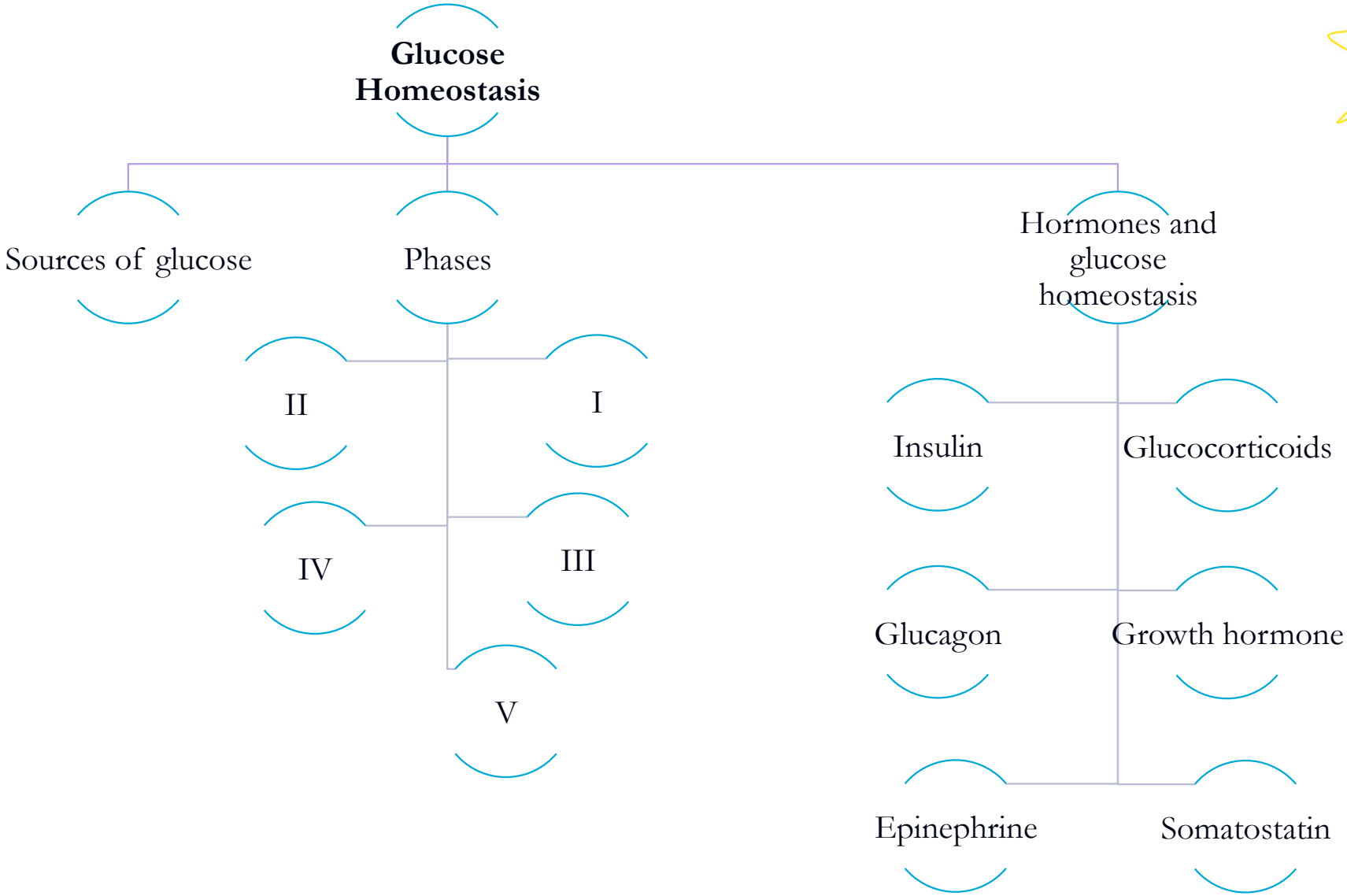
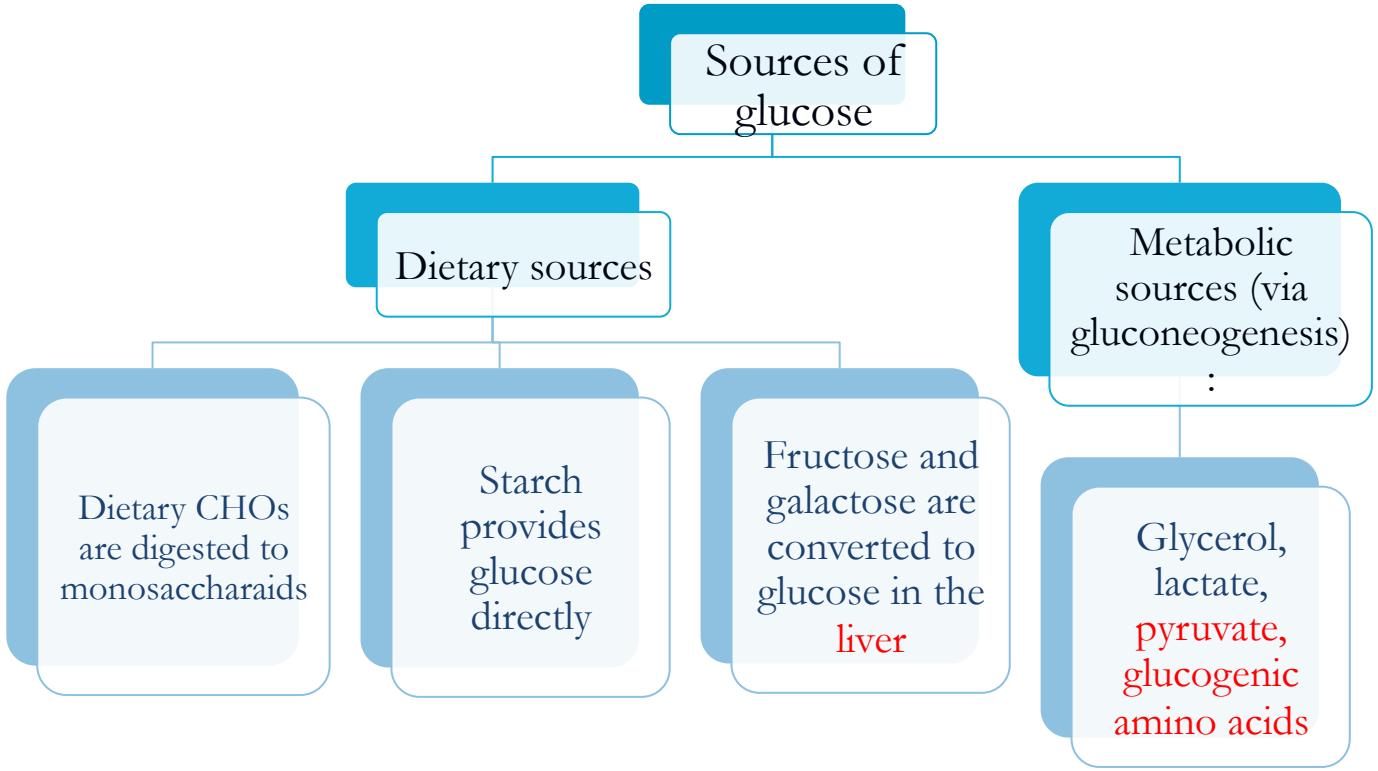
Mind Map


Glucose Homeostasis
Sources of glucose
Phases
II
I
IV
III
V
Hormones and glucose homeostasis
Insulin
Glucocorticoids
Glucagon
Growth hormone
Epinephrine
Somatostatin

Glucose Homeostasis

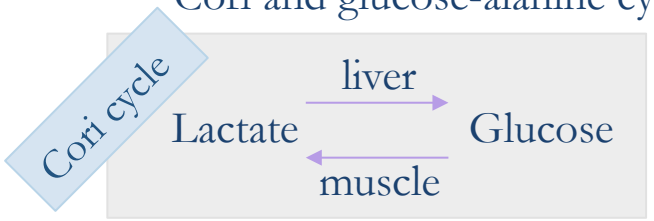
- It is a process that:
  - Controls glucose metabolism and
  - Maintains normal blood glucose level in the body
- Glucose is a major source of body's energy
- The liver plays a key role in maintaining blood glucose level
- It is tightly controlled as the brain constantly needs glucose
- Severe hypoglycemia can cause coma and death
- Chronic hyperglycemia results in glycation of proteins, endothelial dysfunction and diabetes mellitus

(Glycation of proteins: is the bonding between protein and glucose (in case of hyperglycemia) without the help of an enzyme (e.g hemoglobin A1c)



Phase I (Well-fed state): (5-6 hours after a meal)

- Glucose is mainly supplied by dietary CHOs
- Liver removes about 70% of glucose load after a CHO meal
- All body tissues use dietary glucose for energy in this phase
- Some glucose is converted to glycogen for storage in the liver (glycogenesis)
- Excess glucose is converted to fatty acids & Glycogen and triglycerides in the liver
- These are transported via VLDL (very low density lipoproteins) to adipose tissue for storage
- Gluconeogenesis is inhibited in this phase
  - Cori and glucose-alanine cycles are inhibited



Phase II (Glycogenolysis):

- Phase II starts during early fasting when dietary glucose supply is exhausted
- Hepatic glycogenolysis and gluconeogenesis maintain blood glucose level in this phase
- Major sources of blood glucose in this phase:
  - Glycogenolysis and gluconeogenesis

Phase III (Gluconeogenesis):

- Phase III starts when glycogen stores in liver are exhausted (< 20 hours)
- Duration of phase III (various) depends on
  1. Feeding status
  2. Hepatic glycogen stores
  3. Physical activity
- Hepatic gluconeogenesis from lactate, pyruvate, glycerol and alanine maintains blood glucose level
- Major source of blood glucose in this phase:
  - Gluconeogenesis

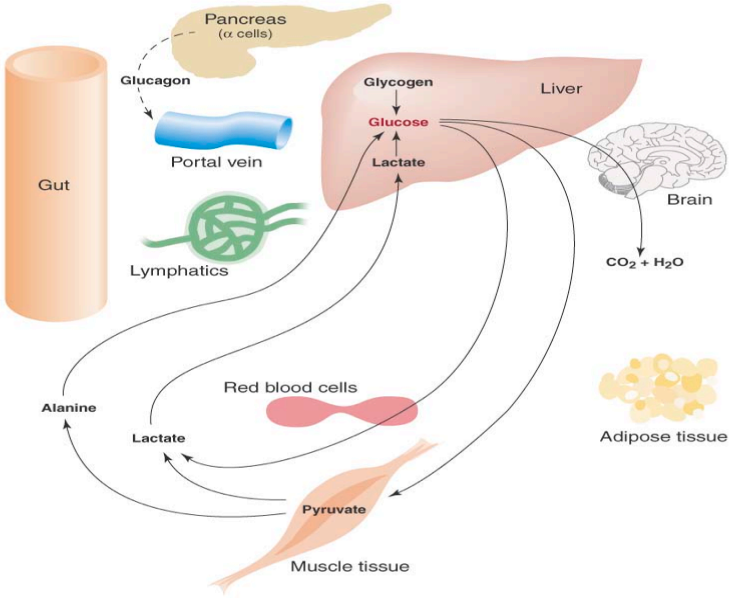


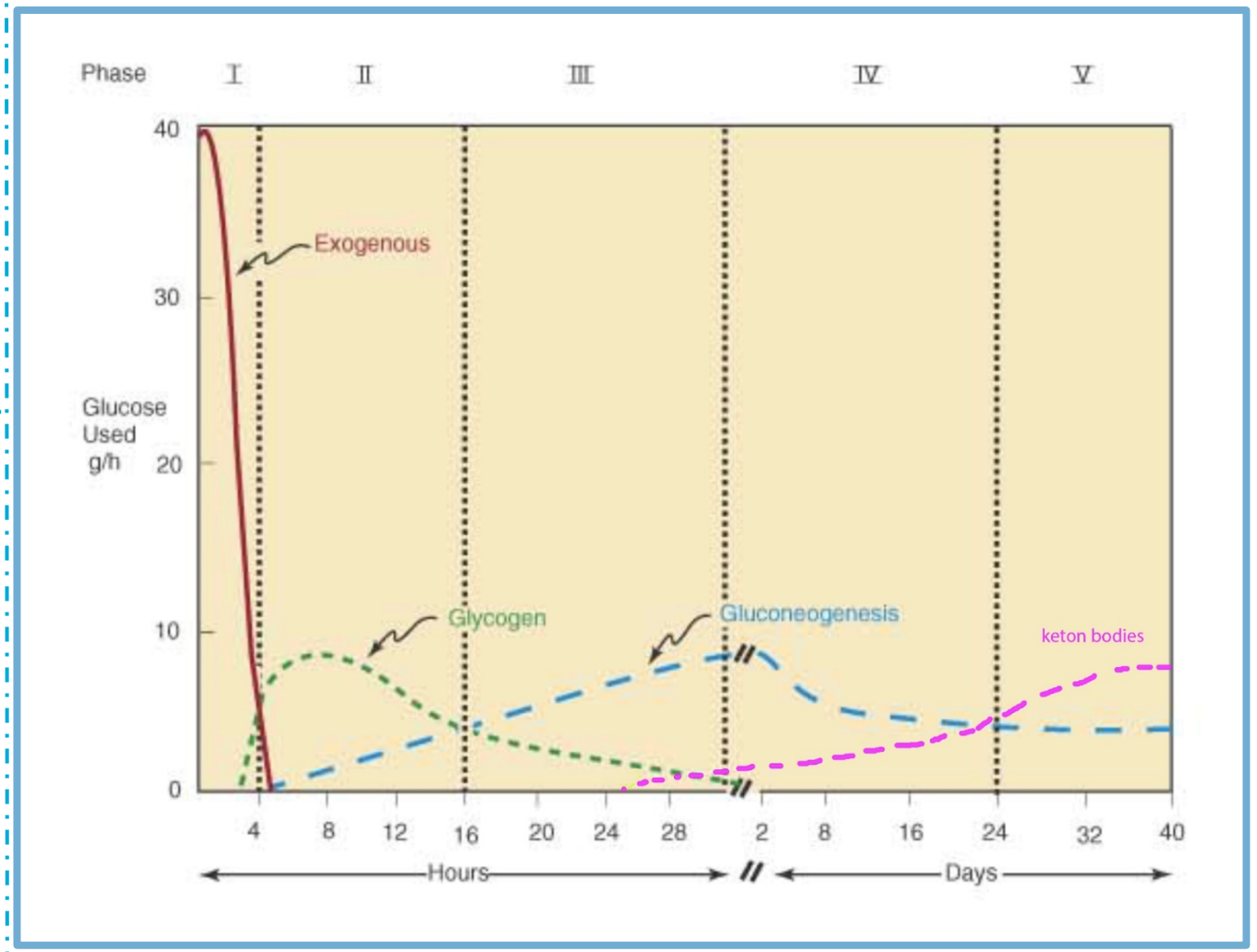
Figure 22.3. Metabolic interrelationships of major tissues in early fasting state.

Phase IV (Glucose and KB oxidation):

- Several days of fasting leads to phase IV
- 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):

- Prolonged fasting(more than week) leads to phase V
- Less dependence on gluconeogenesis
- All body tissues mainly use FA and KB oxidation for energy production
- Gluconeogenesis somewhat maintains blood glucose level in this phase
- High KB conc. and glucose levels inhibit proteolysis in muscle (conservation of muscle).
- When all fat and KBs are used up
    I. Body uses muscle protein to maintain blood glucose level (protein sparing effect)



Phases of glucose homeostasis

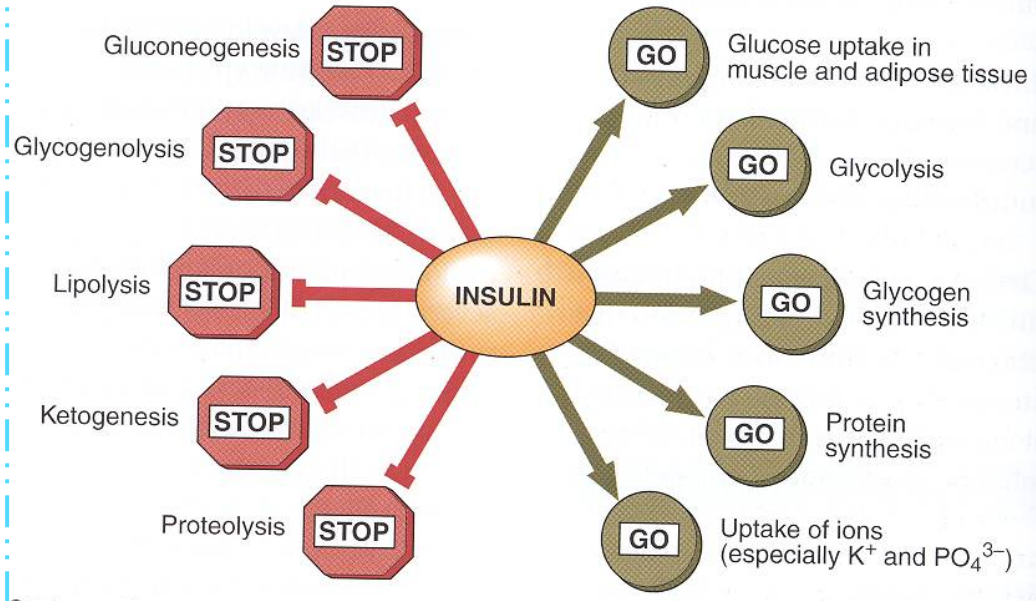
Phase	Origin of Blood Glucose	Tissues Using Glucose	Major Fuel of Brain
I	Exogenous	All	Glucose (transported by $GLUT_3$)
II	1. Glycogen 2. Hepatic Gluconeogenesis	All except liver. Muscle & adipose tissue at diminished rates	Glucose
III	1. Hepatic Gluconeogenesis 2. Glycogen	All except liver. Muscle & adipose tissue at rates intermediate between II &IV	Glucose
IV	Hepatic & Renal Gluconeogenesis	Brain, RBCs, Renal Medulla, muscles.	Glucose, ketone bodies
V	Hepatic & Renal Gluconeogenesis	Brain, RBCs, Renal Medulla.	Glucose, ketone bodies

Hormones that regulate glucose metabolism:

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

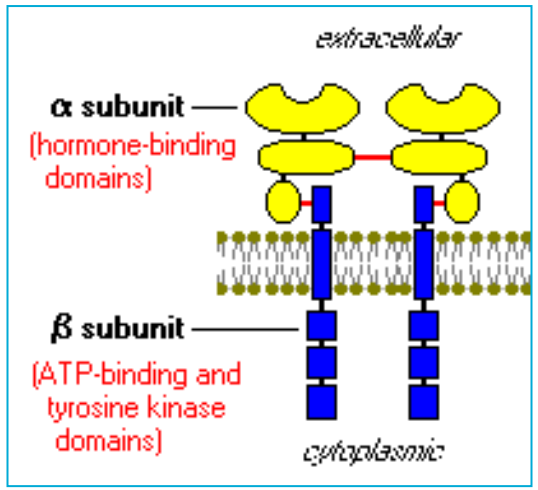
Antagonize insulin action

Insulin actions



❖Insulin

- Plays a major role in glucose homeostasis
- Synthesized by the β-cells of islets of Langerhans of pancreas
- A small protein composed of two chains
- Rise in blood glucose level stimulates insulin secretion
- Promotes entry of glucose into cells



✧ Mechanism of its action

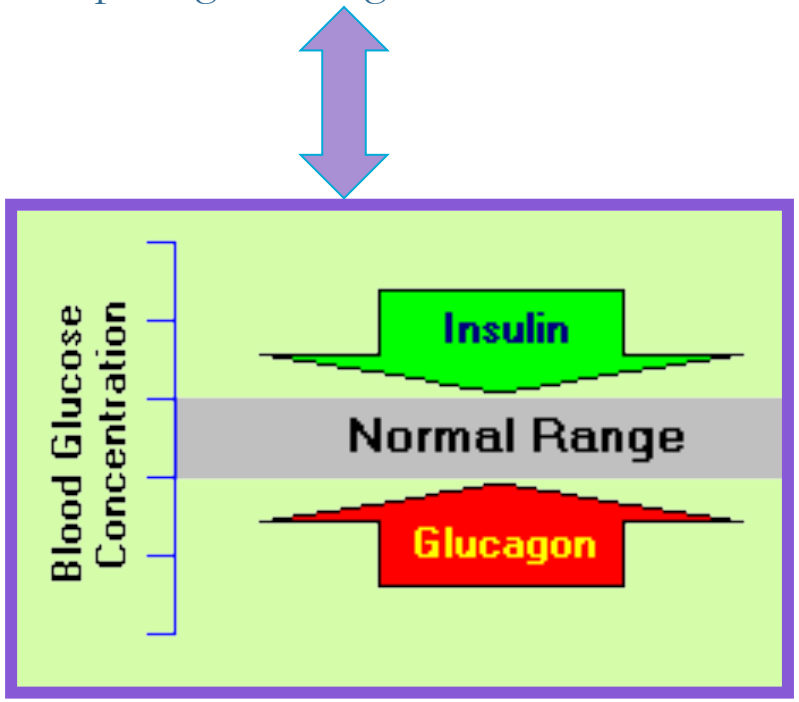
- The insulin receptor is present on the plasma membrane of cell
- Composed of
  - a-subunit (extracellular)
  - b-subunit (cytoplasmic)
- Binding of insulin to a-subunit causes phosphorylation of b-subunit
- This activates the receptor
- The activated receptor then phosphorylates intracellular proteins generating a biological response

✧ Insulin and CHO metabolism:

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

❖Glucagon

- A peptide hormone secreted by α-cells of pancreatic islets
- Secreted in response to hypoglycemia
- Increases glucose levels
- Stimulates glycogenolysis
- Activates hepatic gluconeogenesis



♣ Somatostatin

- A peptide hormone secreted by δ-cells of pancreatic islets, stomach and intestine
- An inhibitory hormone
- Inhibits secretion of both insulin and glucagon
- Affects glucose homeostasis indirectly

♣ Growth hormone

- A protein hormone secreted by anterior pituitary gland
- Maintains blood glucose levels by:
  1. Inhibiting insulin action
  2. Stimulating gluconeogenesis in the liver

♣ Glucocorticoids (Cortisol)

- Cortisol is a steroid hormone secreted by adrenal gland
- Contributes to glucose homeostasis
- Maintains normal glucose levels in fasting
- Stimulates gluconeogenesis in the liver
- Mobilizes amino acids for gluconeogenesis
- Stimulates fat breakdown in adipose tissue

♣ Epinephrine

- A catecholamine hormone secreted by adrenal gland
- Stimulates lipolysis in adipose tissue when glucose blood levels fall
- 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).
- In Phase II Major sources of blood glucose is Glycogenolysis and gluconeogenesis.
- Phase III starts when glycogen stores in liver are exhausted. & Major source of blood glucose in this phase Gluconeogenesis.
- In Phase IV Brain uses both glucose and KB for energy.
- In Phase V All body tissues mainly use FA and KB oxidation for energy production
- Insulin Promotes entry of glucose into cells.
- 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

Extra Slide !

- Glycogenesis - FORMATION of GLYCOGEN from glucose. (Glyco - glycogen; genesis - creation)
- Gluconeogenesis - FORMATION of GLUCOSE from smaller molecules. (Gluco - glucose; genesis - creation)
- Glycogenolysis - BREAKDOWN of GLYCOGEN to form glucose. (Glyco - glycogen; lyse - destroy)
- Glycolysis - BREAKDOWN of GLUCOSE to form energy and smaller molecules. (Lyse - destroy; it is confusing because it is Gly not Glu, but it's just something you need to memorize!)

Test your knowledge ..!

Q1: Glucose uptake by liver cells is:

A. Energy-consuming
B. A saturable process
C. Insulin-dependent
D. Insulin-independent

Q2: The conversion of alanine to glucose is termed:

A. Glycolysis
B. Oxidative decarboxylation
C. Specific dynamic action
D. Gluconeogenesis

Q3: Which of following abundant sources is used in phase III of glucose homeostasis:

A. Glycogenolysis
B. Fatty acid oxidation
C. Gluconeogenesis
D. Diet

Q4. Which of the following is an action of insulin:

A. Simulate ketogenesis
B. inhibit glucose up take in muscle
C. stimulate glycogenolysis
D. Lipogenesis

Q5. Regarding the action of glucagon:

A. It stimulates glycogenolysis
B. It stimulates glycolysis
C. It inhibits glycogenolysis
D. It stimulates insulin activity

1. D
2. D
3. C
4. D
5. A

Biochemistry
Team

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