Done By :

Maha Al-Balharith

Arwa Al-Madani

Sarah Bin-Hussain

Bedoor Al-Qadrah

Reham Al-Henaki

- Team notes are in Blue ;)

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
- Chronic hyperglycemia results in glycation of proteins, endothelial dysfunction and diabetes

Sources of glucose

Dietary sources:

- — 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

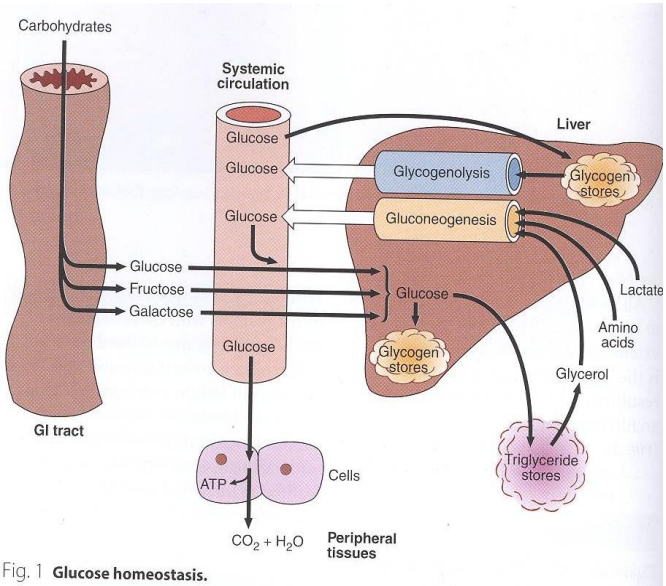


Fig. 1 **Glucose homeostasis.**

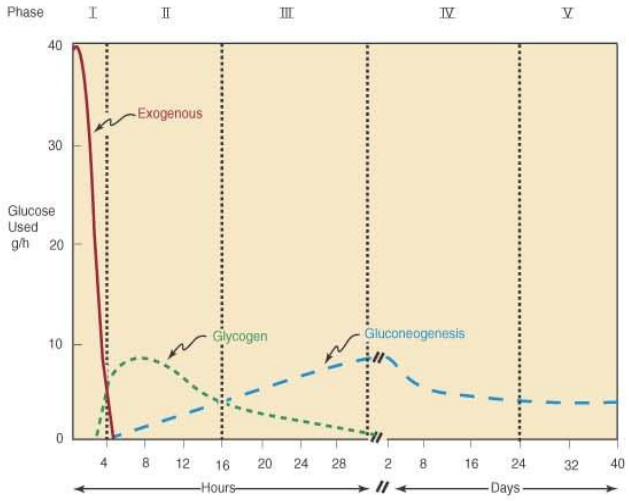
Metabolic sources are Gluconeogenesis and glycogenolysis

← the figer is what u have after you are feeded (postprandial)

- So you taking the CHO as glucose , fructose , glactose
- It's taking up by the liver in the glactose and fructose are converted to glucose and it's converted to glycogen so it will be in the glycogen storage and the excess goes to adipose tissue and stored as triglyceride
- And whenever you take a male your peripheral tissue use it as an energy and the rest goes to the liver
- When you finish the glucose that you have taken within your diet your body will break down the glycogen in your liver after it's finish you will depend on the non-carbohydrate source , gluconeogenesis .

Phases of glucose homeostasis

- Five phases:
  - Phase I (Well-fed state) → if u finish your dietry from 4-6 hours
  - Phase II (Glycogenolysis)→ then you start to break your glycogen stores 16-20 hours
  - Phase III (Gluconeogenesis)
  - Phase IV (Glucose, ketone bodies (KB) oxidation) ketone bodies are when you are starving they are products of fatty acid
  - Phase V (Fatty acid (FA), KB oxidation)



the graph shows :

exogenous = food

the Y access →the amount of glucose that's used

the X access → the time

and this is a period after a long starvation

Phase	ORIGIN OF BLOOD GLUCOSE	TISSUES USING GLUCOSE	MAJOR FUEL OF BRAIN
I	Exogenous	All	Glucose
II	Glycogen Hepatic gluco–neogenesis	All except liver. ★1 Muscle and adipose tissue at diminished rates	Glucose
III	Hepatic gluconeogenesis ★2 Glycogen	All except liver. Muscle and adipose tissue at rates intermediate between II and IV	Glucose
IV	Gluconeogenesis, hepatic and renal	Brain, RBCs, renal medulla. Small amount by muscle	Glucose, ketone bodies
V	Gluconeogenesis, hepatic and renal ★3	Brain at a diminished rate, RBCs, renal medulla	Ketone bodies, glucose

★1 Phase 2 : all body tissue use the glycogen except liver but the muscle , adipose tissue use it in a reduced rate. Obviously when you're starving you're moving less

★2 Phase 3 : main source of CHO and glycogen store basically finished so the amount of glycogen is less here

Phase 5 : day 24 to 40 of starvation so it's a really a prolonged starvation

Phase I (Well-fed state)	Phase II (Glycogenolysis)	Phase III (Gluconeogenesis)	Phase IV (Glucose and KB oxidation)	Phase V (FA and KB oxidation)
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 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 starts during early fasting when dietary glucose supply is exhausted **like after 6 hours** -Hepatic glycogenolysis maintains blood glucose level in this phase -**Glycogenolysis** is the major source of blood glucose in this phase	-here the glucose taken from the non-carbohydrate sources -Phase III starts when glycogen stores in liver are exhausted (within 20 hours) -Duration of phase III depends on *Feeding status How the person was fed before the starvation period . *-Hepatic glycogen stores If he has enough glycogen store or not *Physical activity -Hepatic gluconeogenesis from lactate, pyruvate, glycerol and alanine maintains blood glucose level -**Gluconeogenesis** is the major source of blood glucose in this phase	-Several days of fasting 24 days for almost a month leads to phase IV -Gluconeogenesis starts to decrease -KB accumulation increases which enter the brain for energy production -Brain uses both glucose and KB for energy - **glucose from Gluconeogenesis & KB oxidation** are the major sources of blood glucose in this phase	-Prolonged fasting leads to phase V -Less dependence on gluconeogenesis -All body tissues 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 *Body uses muscle protein to maintain blood glucose level

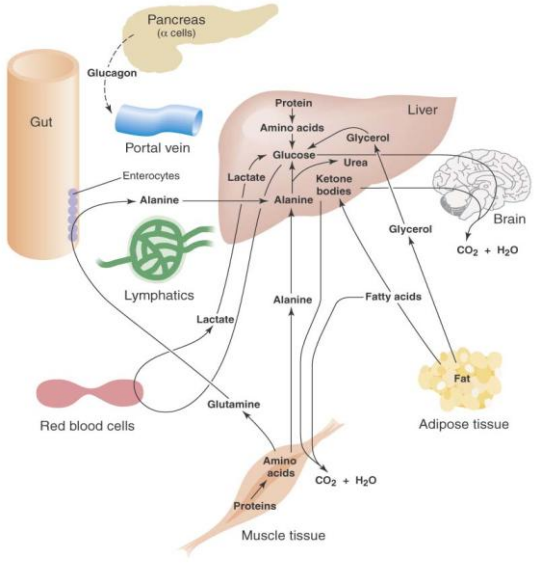


Figure 22.4. Metabolic interrelationships of major tissues in fasting state.

Textbook of Biochemistry With Clinical Correlations, Sixth Edition, Edited by Thomas M. Devlin. Copyright © 2006 John Wiley & Sons, Inc.

Phase2 :

-glycogen is breaking down to→ glucose →breaks down to CO_2 + H_2O and nothing is going to adipose tissue

-from muscle we have pyrovate some goes to RBC where it's converted to lactate , pyrovate and there's some breakdown of muscle protein so that's provide the alanine which goes to the liver and converted to glucose .

Phase 5 :

Fat breaks down to provide glycerol that goes to the liver and converted to glucose

Fatty acid provide KB to the liver and other tissue

And in the muscle tissue what's happening is you have protein break down which comes the last converted to glutamine goes to enterocyte converted to alanine which goes to the liver and finally converts to glucose and also the protein within the liver breaks down .

Hormones and glucose homeostasis :

Hormones that regulate glucose metabolism:

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

Antagonize insulin action basically they are helping to increase the blood glucose level

Insulin: produced when the glucose in the blood is high

- 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 (2 tails the C peptide and the insulin)
- Formed as prepro-insulin and converted to pro-insulin upon secretion
- Rise in blood glucose level stimulates insulin secretion
- Promotes entry of glucose from the blood into the cells so the idea is to lower the blood glucose level

Insulin actions:

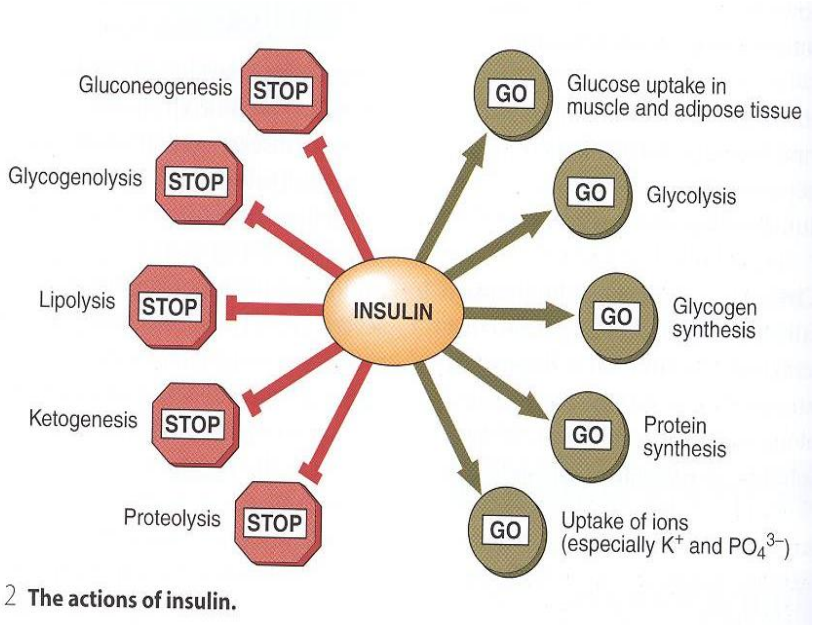


Fig. 2 **The actions of insulin.**

Mechanism of action:

- The insulin receptor is present on the plasma membrane of cell
- Composed of
    - 2a-subunit (extracellular)
    - 2b-subunit (cytoplasmic) intracellular
- Binding of insulin to a-subunit causes phosphorylation of b-subunit and leads to signaling cascade
- This activates the receptor
- The activated receptor then phosphorylates intracellular proteins generating a biological response

The insulin binds to insulin Rs on the cells and there will be a vesicles (bags) which have the glucose transporters .when activates the Rs on the cell surface it start the signaling cascade that leads to those vesicles to comes to the membrane and fuse with it , so now the glucose transporter are on the membrane and take the glucose from the blood inside the cell .

Insulin and CHO metabolism:

Promotes glucose uptake into cell:

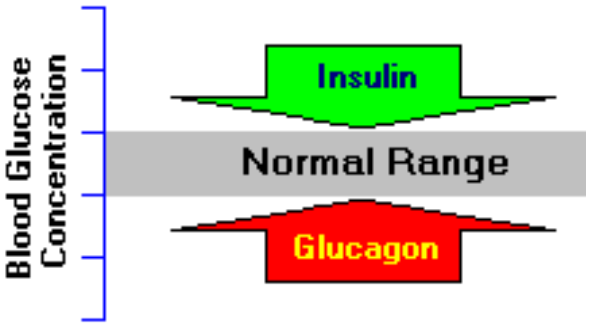
- Glucose is diffused into cells through hexose transporters such as GLUT4
- GLUT4 is present in cytoplasmic vesicles
- Insulin binding to its receptor causes vesicles to diffuse into plasma membrane
- GLUT4 is inserted into the membrane
- Allowing glucose transport into the cell
- Brain and liver have non-insulin dependent glucose transporter
- Stimulates glycogen synthesis
- Decreases blood glucose levels
- Increases glycolysis
- 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 a-cells of pancreatic islets
- Secreted in response to hypoglycemia during starvation in the fasting state
- It's function is to Increase 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 & growth hormone
- Affects glucose homeostasis indirectly

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
- Inhibits glucose uptake by cells
- Stimulates fat breakdown in adipose tissue

Growth hormone:

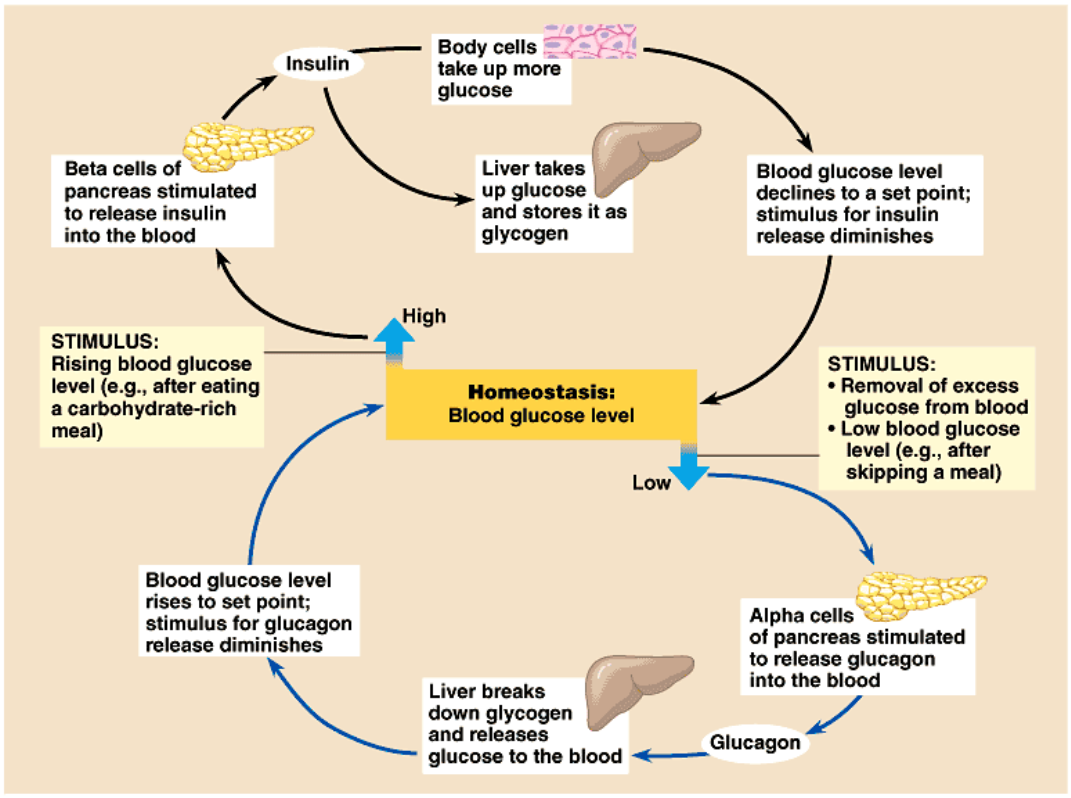
- A protein hormone secreted by anterior pituitary gland
- Maintains blood glucose levels by:
    - Inhibiting insulin action
    - Stimulating gluconeogenesis in the liver

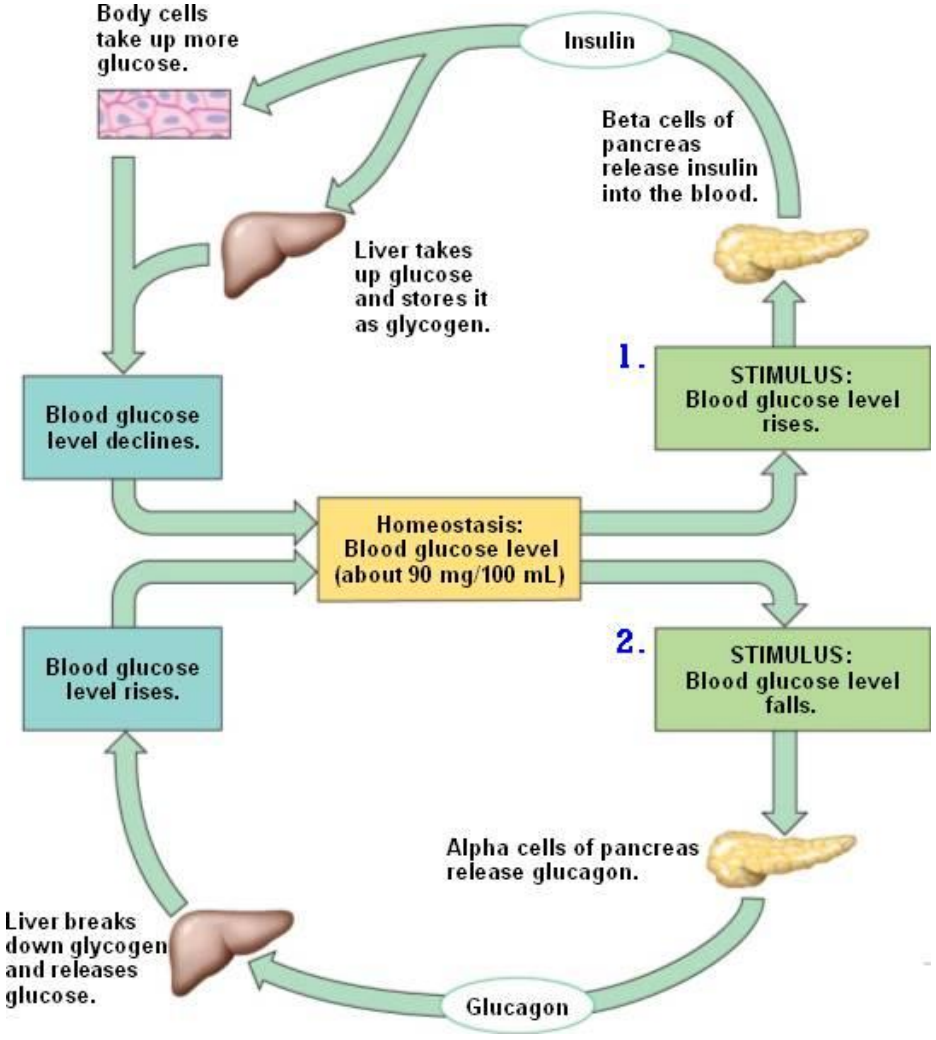
Epinephrine:

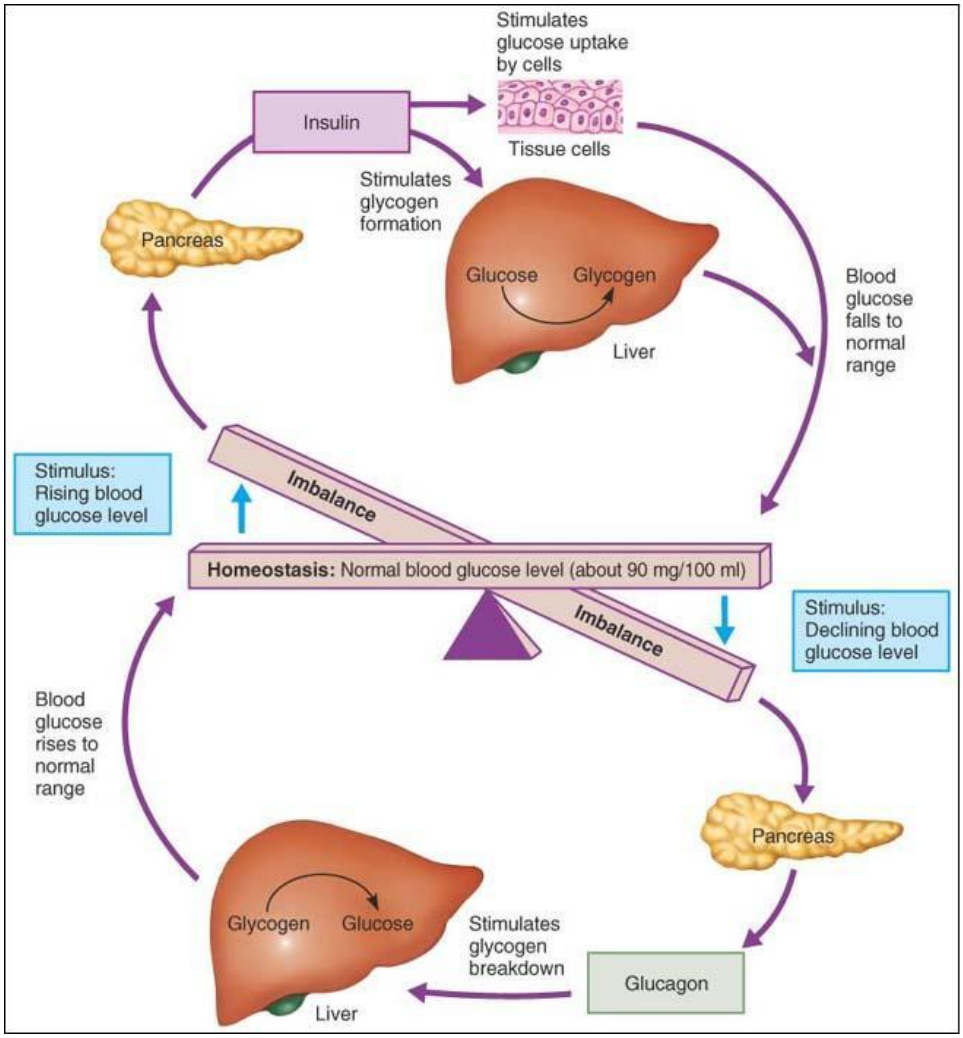
- A catecholamine hormone secreted by adrenal gland
- Stimulates lipolysis in adipose tissue when glucose blood levels fall
- Promotes glycogenolysis in skeletal muscle , Increase the release of glucagon & insulin

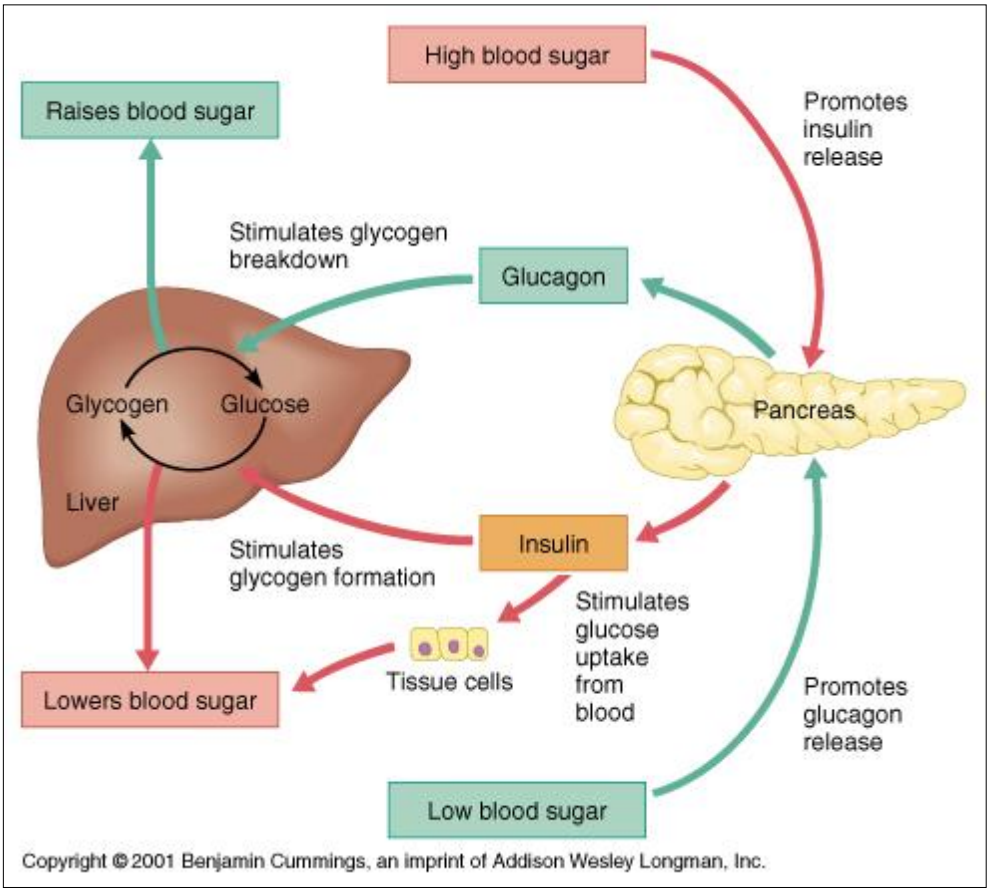
Good Luck

extra for revision *_^






Stimulates glucose uptake by cells
Insulin
Tissue cells
Stimulates glycogen formation
Pancreas
Glucose
Glycogen
Liver
Blood glucose falls to normal range
Stimulus: Rising blood glucose level
Imbalance
Homeostasis: Normal blood glucose level (about 90 mg/100 ml)
Imbalance
Stimulus: Declining blood glucose level
Blood glucose rises to normal range
Pancreas
Glycogen
Glucose
Stimulates glycogen breakdown
Glucagon
Liver


High blood sugar
Raises blood sugar
Promotes insulin release
Stimulates glycogen breakdown
Glucagon
Glycogen
Glucose
Pancreas
Liver
Insulin
Stimulates glycogen formation
Stimulates glucose uptake from blood
Tissue cells
Lowers blood sugar
Promotes glucagon release
Low blood sugar
Copyright © 2001 Benjamin Cummings, an imprint of Addison Wesley Longman, Inc.