Blood Glucose Homeostasis

Medical Biochemistry Department

2015

Blood Glucose Concentration

- Fasting blood glucose (8-12 hrs)

  70-110 mg/dL

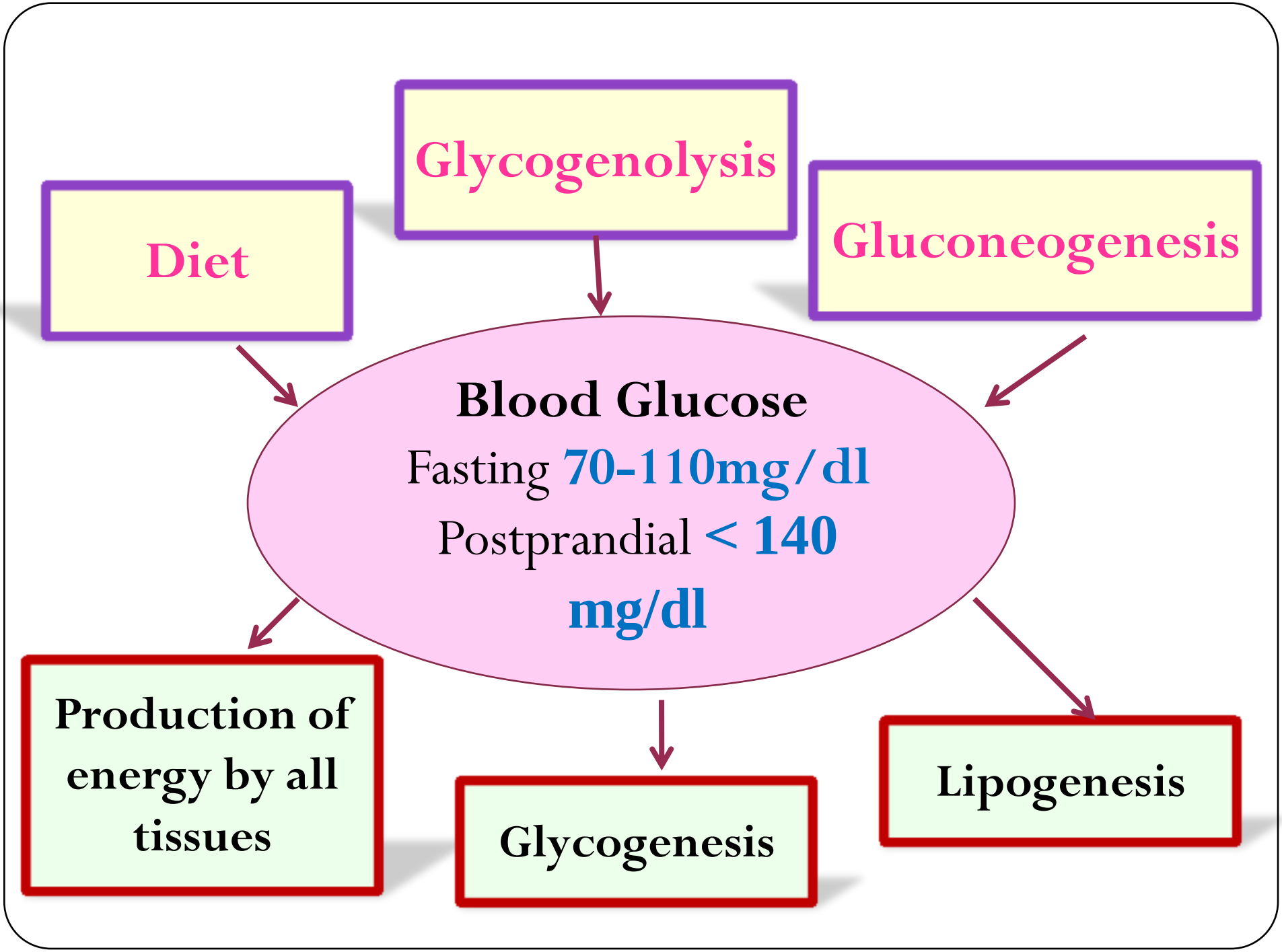
- It rises to 140 mg/dl after meal (post prandial).

Regulation of blood glucose

The concentration of blood glucose level is maintained constant by

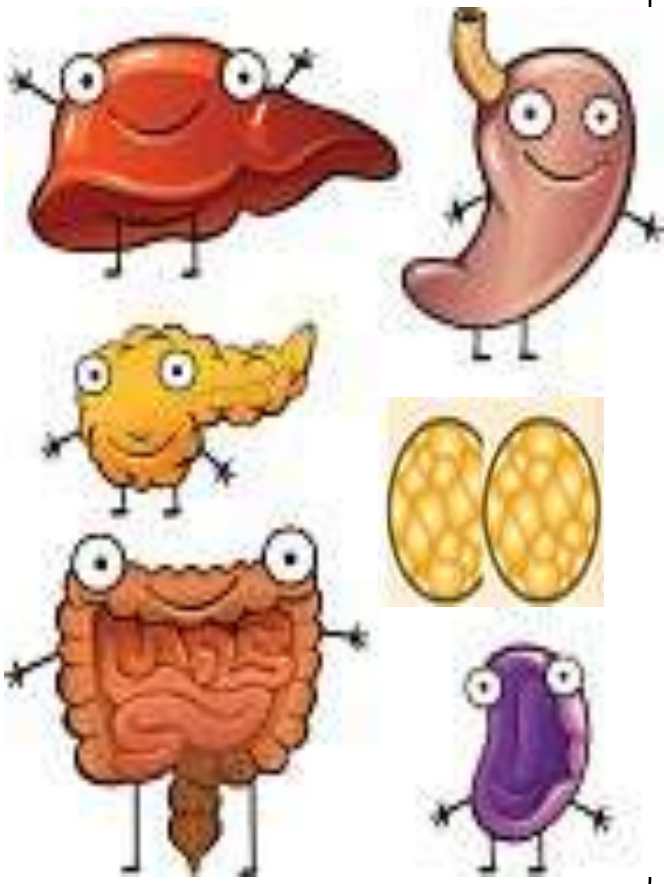
the action of two general opposing factors:

- **The rate of glucose enterance to the blood**
- **Rate of removal of blood glucose**


Glycogenolysis
Diet
Gluconeogenesis
Blood Glucose
Fasting 70-110mg/dl
Postprandial < 140
mg/dl
Production of energy by all tissues
Glycogenesis
Lipogenesis

Regulation of Blood Glucose

Several factors are important for regulating blood glucose level:



I. Regulation by different tissues and organs

Liver and Extrahepatic tissue

(Kidney, Gastrointestinal tract, Skeletal muscle, adipose tissue)

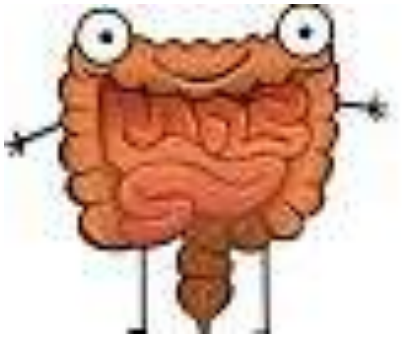
II. Hormones

Gastrointestinal tract

- It controls the rate of glucose absorption

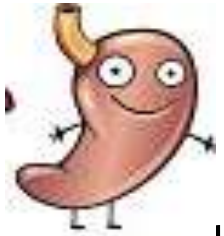
- It protects the body from sudden and excessive increase in blood glucose

by different ways:



- **The gradual evacuation** of gastric contents allows **good time** for absorption and utilization of glucose.

- The **secretion of gastro-intestinal hormones**, stimulate **insulin secretion** by B-cells of pancrease.



- **Insulin** is secreted to portal blood before absorption of glucose, **So, Glucose given orally stimulates more insulin than intravenous glucose.**

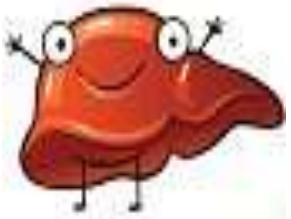
Glucose uptake by different tissues

This is mediated through different protein transporter (GLUT4) which is insulin dependent in skeletal muscles, heart and adipose tissues.

Liver

- The liver is the **main organ** **responsible for glucose homeostatic mechanisms.**

- The uptake or output of glucose by liver cells is directly related to blood glucose level.

- Glucose is only metabolized in  cells when its level in blood is increased.
- Due to low affinity of glucokinase to glucose, and its induction by insulin.

- **If blood glucose level increases**, the 

  controls this elevation and decreases it through:

  - ⬆ **Oxidation of glucose.**
  - ⬆ **Glycogenesis.**
  - ⬆ **Lipogenesis.**
  - ⬇ **Glycogenolysis.**
  - ⬇ **Gluconeogenesis.**

- **If blood glucose level decreases**, the liver controls

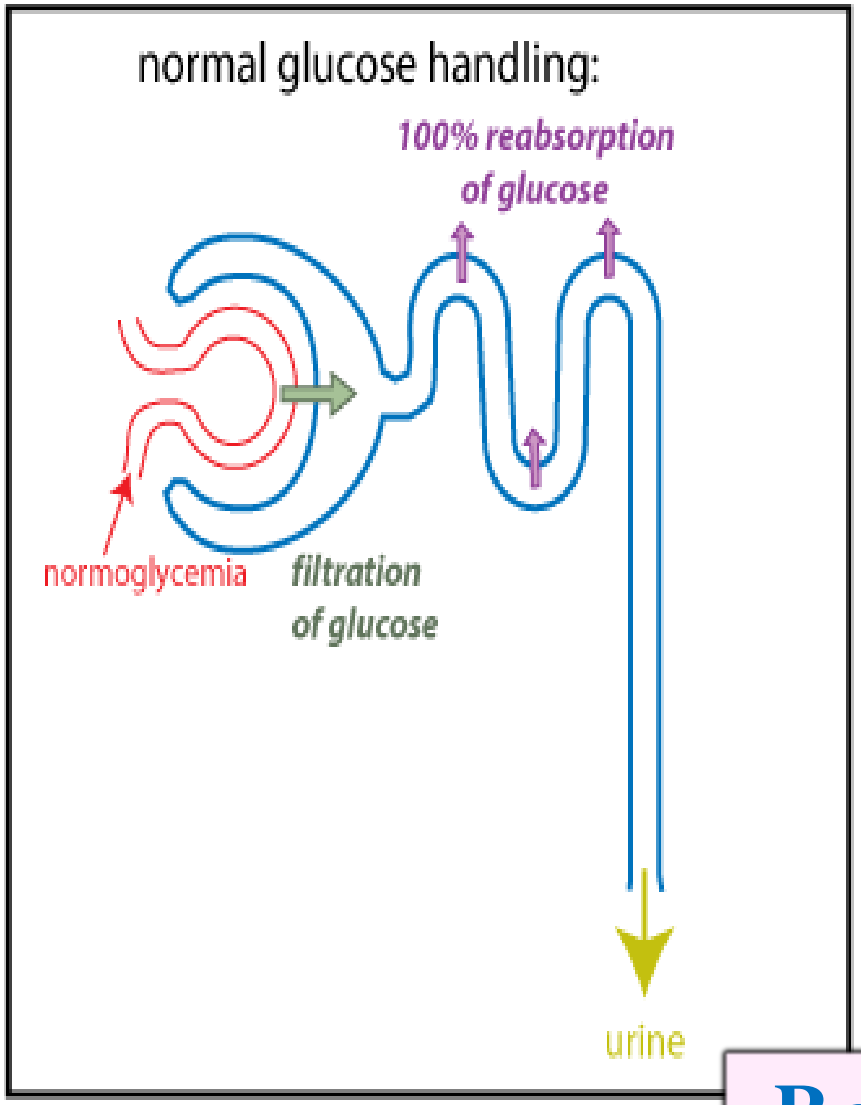
  this drop and increases it

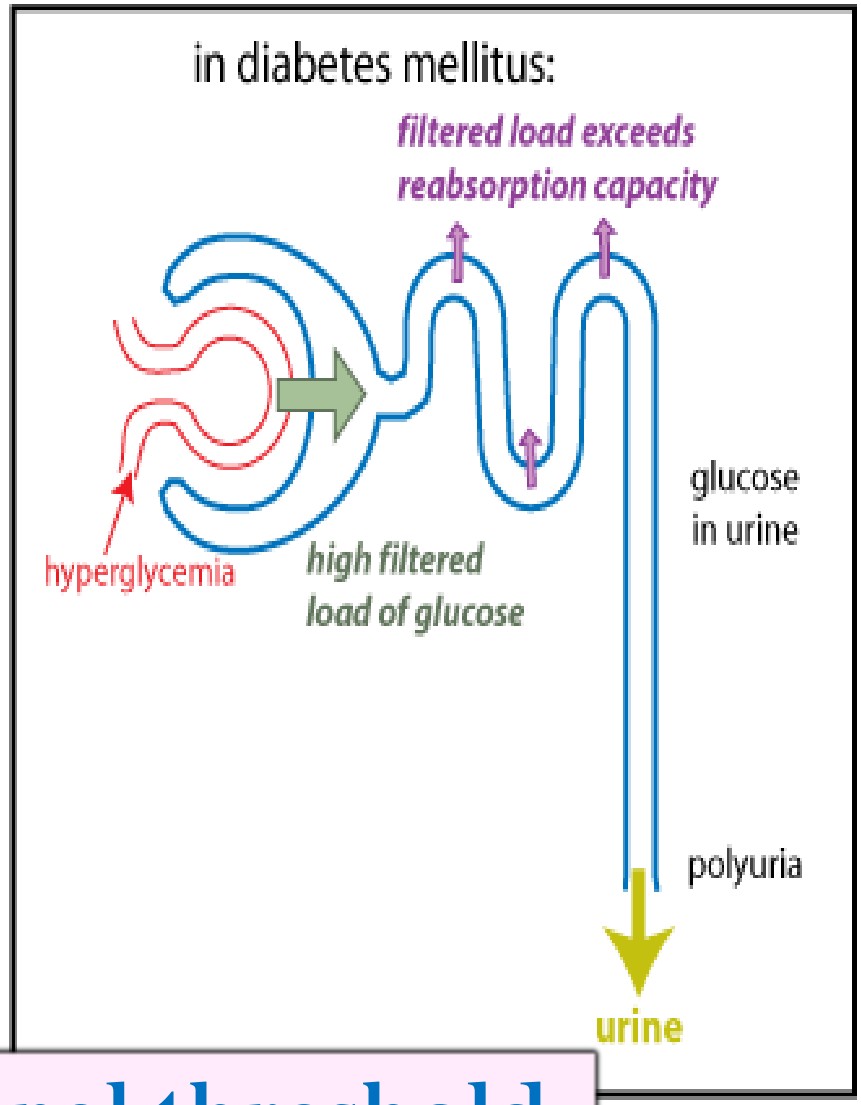
  The reverse occurs

Kidney

- All glucose in blood is filtered through the kidneys, it then completely returns to the blood by tubular **reabsorption**.

So, Normally urine is free from Glucose





Renal threshold

> 180 mg/dL

- If blood glucose **exceeds** a certain limit (**renal threshold**) or if the **renal threshold is abnormally low (renal glucosuria)**, it will pass in urine causing **glucosuria**.
- **Renal threshold**: it is the maximum rate of reabsorption of glucose by the renal tubules.
- Normally the renal threshold for glucose is **180 mg/dL.**

Adipose Tissue

They play an important role in glucose homeostatic mechanisms.

If blood glucose level increases, decreases it through

- ⬆ **The uptake of glucose by tissues**
- ⬆ **Glucose oxidation**
- ⬆ **Lipogensis.**

During fasting or carbohydrate deficiency,

⬇ Glucose uptake and utilization

⬆ Lipolysis → FFA

FFA are utilized by different tissues for production of energy (spare blood glucose)

Increase oxidation of fatty acids in 

++gluconeogenesis and --- glycolysis.

→ Glycerol

Substrate for gluconeogenesis

Skeletal muscle

- **During carbohydrate feeding,**
  - ⬆ **the uptake of glucose.**
  - ⬆ **glucose oxidation**
  - ⬆ **glycogensis.**

During fasting,

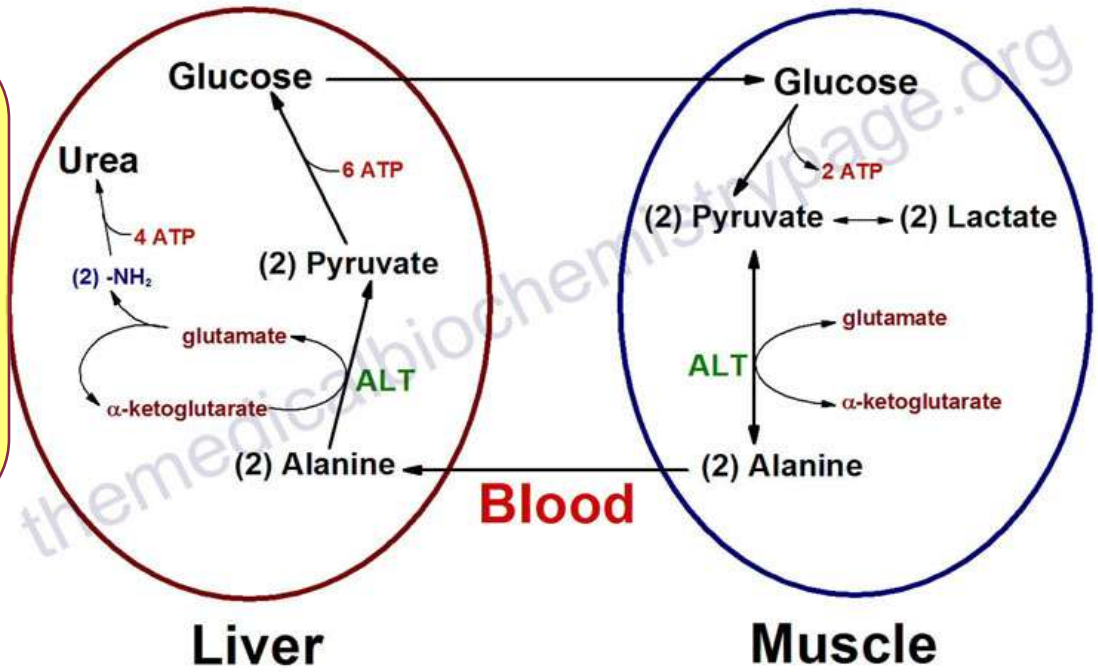
- The 

can oxidize fatty acids and ketone bodies instead of glucose for production of energy.

- The amino acids released from 

(especially alanine) are utilized as substrarte for gluconeogenesis in 

glucose-alanine cycle

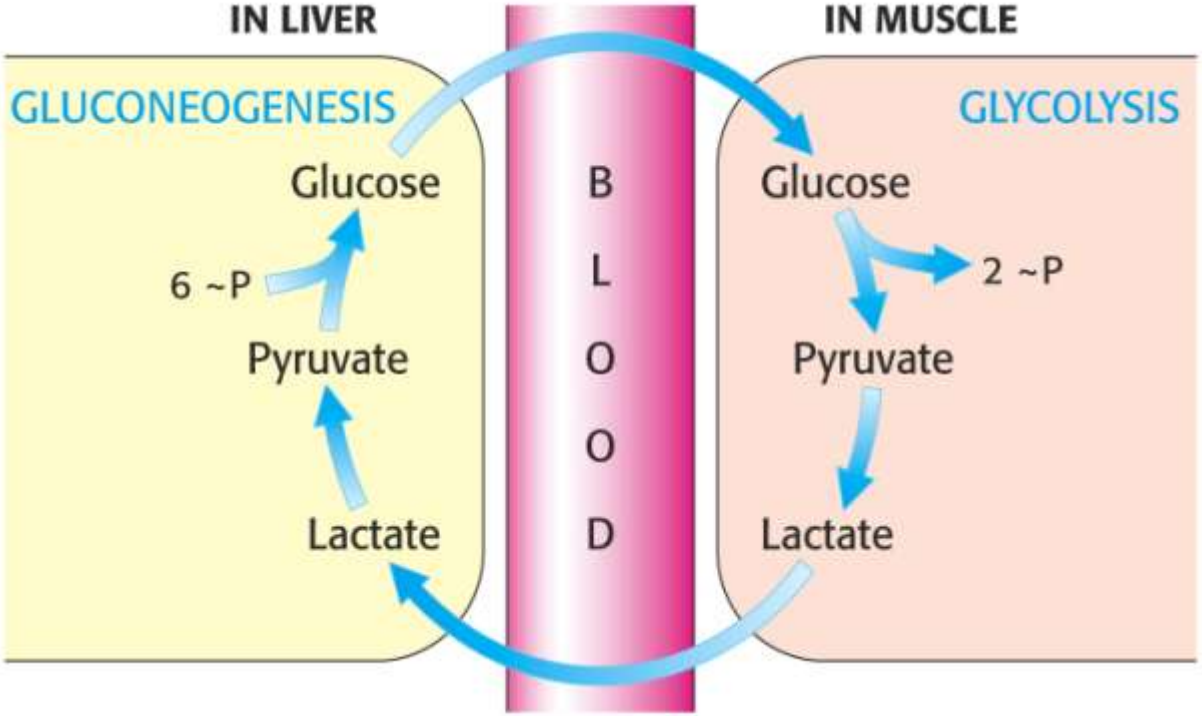


- **Lactate** produced during severe muscular exercise is used as **substrarte for gluconeogenesis** in 

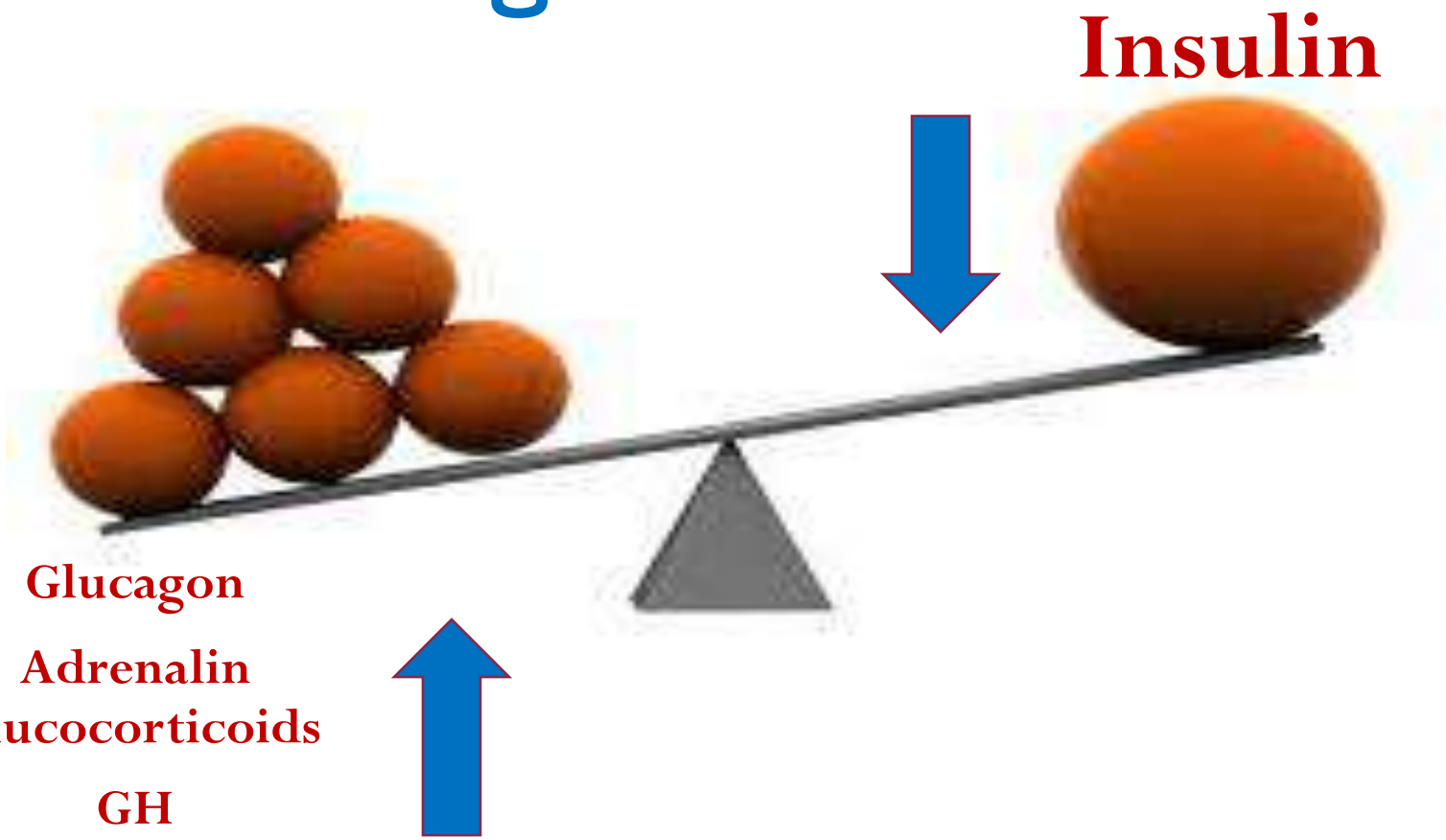
Cori cycle

Or

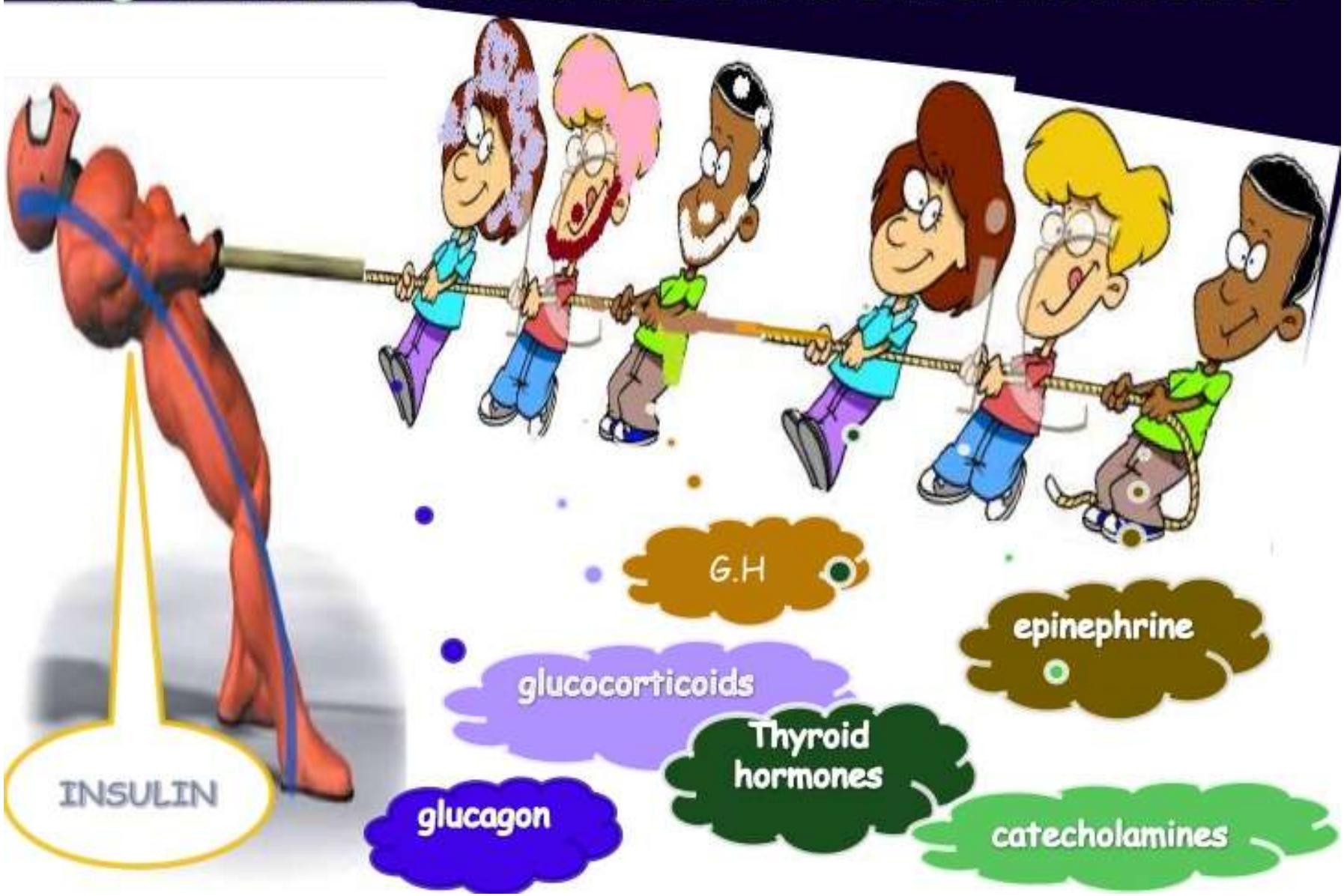
glucose – lactate cycle



Hormonal regulating of blood glucose



Tug of war between Insulin & other hormones



Hormonal regulating of blood glucose

Insulin: leads to decrease of blood glucose level

⬇ **Gluconeogenesis**

⬆ **Glucose entrance to the cells and oxidation.**

⬆ **glycogenesis(ms & liver)---** ⬇ **Glycogenolysis**

⬆ **Lipogenesis ----------** ⬇ **lipolysis**

⬆ **Protein synthesis**

⬇ **Ketogenesis**

Adrenaline

- ⬆ Gluconeogenesis
- ⬆ Glycogenolysis ---------- ⬇ glycogenesis
- ⬇ Insulin secretion.

Glucagon

- ⬆ Gluconeogenesis(in the liver only)
- ⬆ Glycogenolysis -------- ⬇ glycogenesis

Glucocorticoids

- ↑ Gluconeogenesis
- Facilitate the action of glucagons, adrenaline and growth H.

Growth hormone

- ↓Glucose uptake by the tissues.
- ↑ Lipolysis which ↑FFA leading to ↓ glucose utilization (glucose sparing effect)

Variations in normal blood glucose

Hyperglycemia
> 110 mg/dl

Hypoglycemia
< 70mg/dl

Hyperglycemia

- *Def.*

It is the rise of blood glucose level above the normal level.

- *Causes*

  - **Deficiency of insulin:**
    - Diabetes mellitus.
    - Pancreatictomy (total or subtotal).

- **Increase of anti-insulin hormones:**
  - **Adrenaline as in emotion or in case of pheochromocytoma**
  - **Glucocorticoids as in adrenal tumors and Cushing syndrome.**
  - **Thyroxin as in hyperthyroidism.**
  - **Pituitary growth hormone as in acromegally.**

Hypoglycaemia

- ***Def.***

It is the decrease in blood glucose level below the fasting level.

- **Classified into**

  - **Fasting Hypoglycaemia** (occurs as a response to fasting for 12 – 16 hr).
  - **Reactive hypoglycaemia** (Hypoglycaemia due to some other stimuli)

Causes of fasting hypoglycaemia

- Insulinoma
- Non-pancreatic tumours (usually mesodermal)
- Liver disease of various types
- Hypoadrenalism
- Hypopituitarism
- Glycogen storage diseases
- Neonatal hypoglycaemia
- Idilopathic hypoglycaemia of childhood.

Causes of reactive (or stimulative) hypoglycaemia

- **Drug-induced**, due to insulin, oral hypoglycaemic agents (e.g. tolbutamide), also to dietary constituents e.g. alcohol, L-leucine.
- **Essential reactive hypoglycaemia**, in which symptoms occur 2-4 hr after a meal, **probably** due to an exaggeration of the normal insulin response to carbohydrate ingestion.
- **Galactosaemia.**
- **Hyereditary fructose intolerance**.

Glucosuria

Def.

Presence of detectable amounts of glucose in urine (>30 mg/dL).

Causes:

A. **Hyperglycemic glocusuria**

B. **Normoglycemic or renal glucosuria**

Hyperglycemic Glucosuria

- Blood glucose exceeds the renal threshold **(180mg/dL).**
- It is **caused by**:

1. **Diabetes mellitus**.
2. **Emotional or stress glucosuria**

(epinephrine glucosuria)

1. **Alimentary glucosuria**;

It is due to increased rate of glucose absorption as in cases of gastrectomy or gastrojejunostomy.

Normoglycemic = renal glucosuria

1. **Congenital renal glucosuria:** due to congenital defect in renal tubular reabsorption of glucose.
2. **Acquired renal disease** (e.g. nephritis).
3. **Pregnancy**: due to decreased carbohydrate tolerance and renal threshold in the later months of pregnancy.
4. **Injection of phlorhizin** due to inhibition of the (SGLUT) in renal tubules.

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