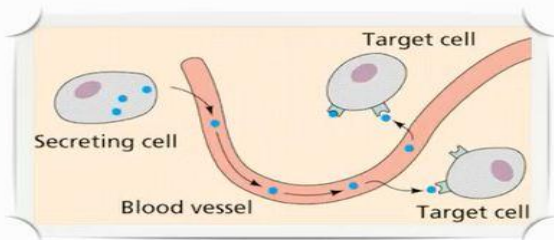
# NUTRITIONAL BIOCHEMISTRY

## UNIT: IV_HARMONES

## What are hormones?




- 'Chemical messengers'
- Secreted by glands
- Carried in the blood plasma to target cells
- Widespread and long-lasting effects

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- A model of hormone action where one hormone causes a new chemical pathway to be activated within a cell
- The hormone never actually enters the cell, it binds to a receptor on the cell's surface
- Hormone-receptor complex causes production of the 'second messenger'
- Second messenger causes chemical changes within the cell that results in the new pathway being activated

- A structure which makes hormones in the body is called endocrine glands.
- They are also called ductless glands because they do not have ducts to secrete their hormones.
- A group of endocrine glands which produces various hormones is called an endocrine system. It is also called hormonal system.
- Endocrine system helps in coordinating the activities of our body.

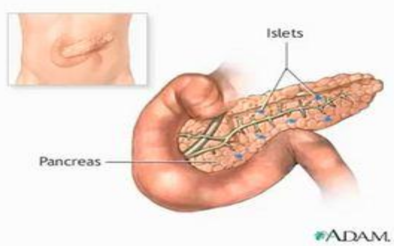
## Various Endocrine Glands

- Hypothalamus
- Pituitary gland
- Thyroid gland
- Parathyroid
- Thymus
- Pancreas
- Adrenal gland
- Testes
- Ovaries

# Pancreas

- The pancreas is unique in that it's both an endocrine and exocrine gland. In other words, the pancreas has the dual function of secreting hormones into blood (endocrine) and secreting enzymes through ducts (exocrine).
- The pancreas is a 6 inch-long flattened gland that lies deep within the abdomen, between the stomach and the spine. It is connected to the duodenum, which is part of the small intestine.
- It secretes insulin.

# The Pancreas

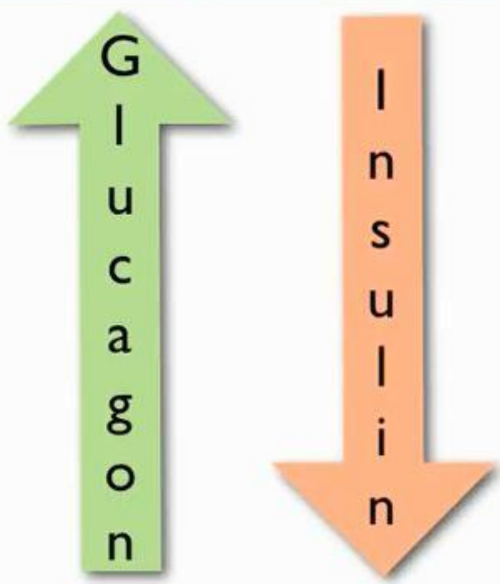



- The pancreas produces many useful substances, including digestive enzymes
- It also acts as a endocrine gland, releasing the hormones insulin and glucagon
- The hormones are released from areas of the pancreas known as the Islets of Langerhans

# Functions of Pancreas

- The pancreas maintains the body's blood glucose (sugar) balance.
- Primary hormones of the pancreas include insulin and glucagon, and both regulate blood glucose.
- Diabetes is the most common disorder associated with the pancreas.

# Glucagon & Insulin

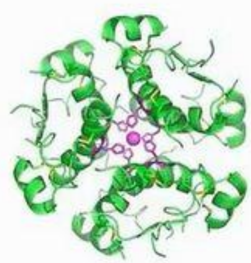



- Glucagon raises blood glucose levels
- Insulin lowers blood glucose levels

# Blood Glucose Level Variation

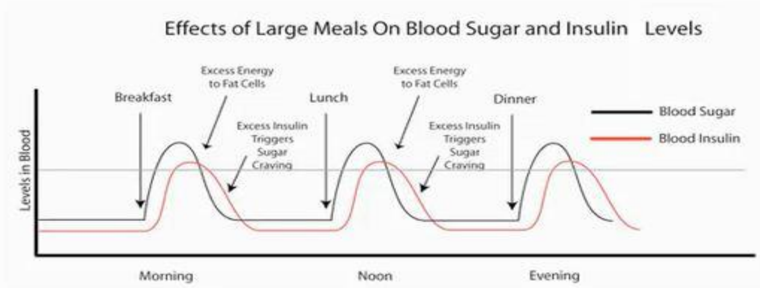
- Normal blood glucose level is 90mg /100cm$^3$ blood
- Blood glucose comes from:
  - Diet (digestion of carbohydrates)
  - Breakdown of glycogen (glycogenolysis)
  - Making new glucose (gluconeogenesis)
- Insulin, Glucagon and Adrenaline affect glucose levels

# Insulin



- Produced by β cells of the Islets of Langerhans
- Released in response to rising blood glucose
- Causes glucose to be taken up in cells by increase the number of transport proteins

# How Insulin Works




- Increased absorption of glucose into cells
- Increased respiratory rate
- Increased glycogen formation (muscles and liver)
- Increased fat formation

## Insulin and its metabolic effects

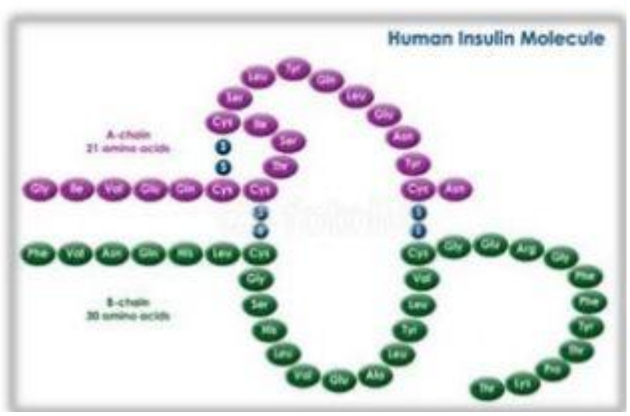
| | Normal insulin action | Insulin-resistance state |
|---|---|---|
| Carbohydrates | ↓ Hepatic glucose production<br>↑ Glucose utilization<br>↑ Glycogenesis | Hyperglycemia<br>Hyperinsulinemia |
| Lipids | ↓ Lipolysis<br>↓ Free fatty acids and glycerol<br>↑ Lipogenesis<br>↑ HDL<br>↓ Triglycerides | ↑ Lipolysis<br>↑ Free fatty acids and glycerol<br>↑ Hepatic triglyceride and apoB synthesis<br>↓ HDL<br>Hypertriglyceridemia<br>↑ Small dense LDL |
| Proteins | ↓ Gluconeogenesis<br>↓ Aminoacids<br>↑ Protein synthesis | ↑ Gluconeogenesis<br>↑ Protein catabolism<br>↓ Protein synthesis |
| Purines | ↑ Uric acid clearance<br>↓ Uric acid formation | Hyperuricemia |

# Insulin is a hormone associated with energy abundance

1. Insulin is secreted when there is great abundance of energy-giving foods in the diet (carbohydrates).
2. It plays an important role in storing the excess energy.
3. In the case of excess carbohydrates, it causes them to be stored as glycogen mainly in the liver and muscles.
4. Also carbohydrates are converted under the stimulus of insulin into fats and stored in the adipose tissue.
5. It has a direct effect in promoting amino acid uptake by cells and conversion of these amino acids into protein.
6. In addition, it inhibits the breakdown of the proteins that are already in the cells.

# Insulin chemistry and synthesis

- It is a polypeptide containing two amino acid chains (21 and 30 amino acids, respectively) connected by disulfide bridges.
- When split apart, the functional activity of the insulin molecule is lost.
- Insulin circulates unbound to carrier proteins and have short half-lives of 6 minutes. (as well as glucagon)
- Approximately 50% of the insulin in blood is metabolized in the liver most of the remaining hormone is metabolized by the kidneys.



## Insulin chemistry and synthesis [redacted]

- Insulin synthesis starts with translation of the insulin RNA by ribosomes attached to the endoplasmic reticulum to form an insulin preprohormone.

- This initial preprohormone is then cleaved in the endoplasmic reticulum to form a proinsulin most of this is further cleaved in the Golgi apparatus to form insulin and peptide fragments before being packaged in the secretory granules.

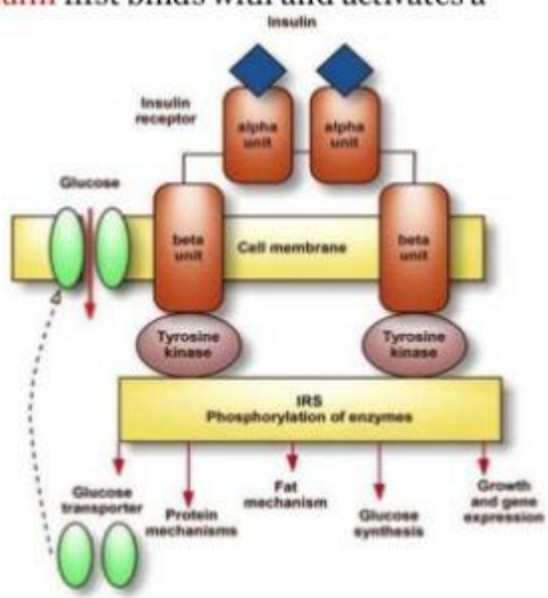
- One sixth of the final secreted product is still in the form of proinsulin.

- The proinsulin has virtually no insulin activity

## Activation of target cell receptors by insulin and the resulting cellular effects

- To initiate its effects on target cells, insulin first binds with and activates a membrane receptor protein.

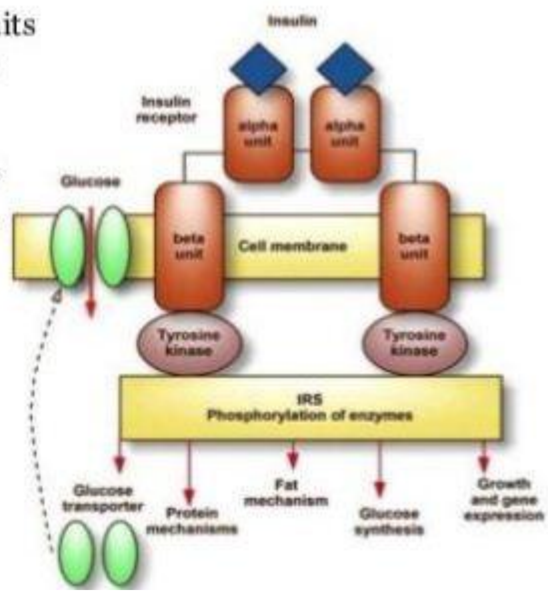
- The insulin receptor is a tetramer made up of two α-subunits that lie outside the cell membrane and two β-subunits that penetrate the cell membrane and protrude into the cytoplasm



- When insulin binds with the alpha subunits on the outside of the cell, portions of the beta subunits protruding into the cell become autophosphorylated.

- Thus, the insulin receptor is an example of an enzyme-linked receptor.

- Autophosphorylation of the beta subunits of the receptor activates a local *tyrosine kinase*, which in turn causes phosphorylation of multiple other intracellular enzymes including a group called <u>insulin-receptor substrates (IRS).</u>




- The net effect is to activate some of these enzymes while inactivating others.

- In this way, insulin directs the intracellular metabolic machinery to produce the desired effects on carbohydrate, fat, and protein metabolism.

# Effect of Insulin on Carbohydrate Metabolism

- Immediately after a high-carbohydrate meal, glucose that is absorbed into the blood causes rapid secretion of insulin.

- Insulin causes rapid uptake, storage, and use of glucose by almost all tissues of the body, but especially by the muscles, adipose tissue, and liver.

## Insulin Promotes Muscle Glucose Uptake and Metabolism

- Mostly, muscle tissue depends not on glucose for its energy but on *fatty acids*. (slightly permeable to glucose).

- Under two conditions the muscles do use large amounts of glucose:

1. During moderate or heavy exercise; because exercising muscle fibers become more permeable to glucose even in the absence of insulin.
2. During few hours after a meal: at this time the blood glucose concentration is high and the pancreas is secreting large quantities of insulin. The extra insulin causes rapid transport of glucose into the muscle cells.

Abundant glucose transported into the muscle cells is stored in the form of muscle glycogen

## Insulin Promotes Liver Uptake, Storage, and Use of Glucose

- Insulin causes most of the glucose absorbed after a meal to be stored almost immediately in the liver in the form of glycogen.

- The mechanism of glucose uptake and storage in the liver :

1. Insulin inactivates liver *phosphorylase*, which normally causes liver glycogen to split into glucose.

2. Insulin causes enhanced uptake of glucose from blood by liver by increasing the activity of the enzyme *glucokinase*, causes the initial phosphorylation of glucose after it diffuses into liver

3. Insulin also increases the activities of the enzymes that promote glycogen synthesis, *glycogen synthase*

## Glucose Is Released from the Liver Between Meals

- Between meals, blood glucose level ↓ the liver releases glucose back into the circulating blood:

1. The decreasing blood glucose causes the pancreas to decrease its insulin secretion.
2. The lack of insulin then reverses all the effects for glycogen storage.
3. The lack of insulin activates the enzyme *phosphorylase*, causes the splitting of glycogen into glucose phosphate.
4. The enzyme glucose *phosphatase*, now becomes activated by the insulin lack and causes the phosphate radical to split away from the glucose.

## Insulin Promotes Conversion of Excess Glucose into Fatty Acids and Inhibits Gluconeogenesis in Liver

- When the quantity of glucose entering the liver cells is more than can be stored as glycogen, insulin promotes the conversion of all this excess glucose into fatty acids.

- These are packaged as triglycerides in VLDL and transported by blood to the adipose tissue and deposited as fat.

- Insulin also inhibits gluconeogenesis. (↓ quantities and activity of the enzymes)

## Lack of Effect of Insulin on Glucose Uptake and Usage by the Brain

- The brain cells are permeable to glucose and can use glucose without the intermediation of insulin.
- Normally use only glucose for energy and can use other energy substrates, such as fats, only with difficulty.

It is essential that the blood glucose level always be maintained above a critical level.

When the blood glucose falls too low (20-50 mg/100ml), symptoms of hypoglycemic shock develop, characterized by progressive nervous irritability that leads to fainting, seizures and coma.

## Effect of Insulin on Carbohydrate Metabolism in Other Cells

- Insulin increases glucose transport into and glucose usage by most other cells of the body.

- The transport of glucose into adipose cells mainly provides substrate for the glycerol portion of the fat molecule. Therefore, in this indirect way, insulin promotes deposition of fat in these cells.

## Effect of Insulin on Fat Metabolism

- Insulin's effects on fat metabolism are, in the long run, as equally important as to the effects on the carbohydrates.

- The long-term effect of insulin lack in causing extreme atherosclerosis, often leading to heart attacks, cerebral strokes, and other vascular accidents.

## Insulin Promotes Fat Synthesis and Storage

- Insulin has several effects that lead to fat storage in adipose tissue:

1. Insulin increases the utilization of glucose by most of the body's tissues. (↓ utilization of fat)
2. Insulin promotes fatty acid synthesis, in liver cells. Fatty acids are then transported from the liver by way of the blood lipoproteins to the adipose cells to be stored.

## Role of Insulin in Storage of Fat in the Adipose Cells

- Insulin has two other essential effects that are required for fat storage in adipose cells:

1. Insulin inhibits the action of hormone-sensitive *lipase;* this is the enzyme that causes hydrolysis of the triglycerides already stored in the fat cells.
2. Insulin promotes glucose transport through the cell membrane into the fat cells. Some of this glucose is then used to synthesize minute amounts of fatty acids, but forms large quantities of *alpha-glycerol phosphate;* this substance supplies the glycerol that combines with fatty acids to form the triglycerides that are the storage form of fat in adipose cells.

## Insulin Deficiency Increases Use of Fat for Energy

All aspects of fat breakdown and use for providing energy are greatly enhanced in the absence of insulin.

- The resulting effects as follows:

1. Insulin deficiency causes lipolysis of storage fat and release of free fatty acids.

The most important effect is that the enzyme hormone-sensitive *lipase* in the fat cells becomes strongly activated. Consequently, the plasma concentration of free fatty acids begins to rise within minutes.

This free fatty acid then becomes the main energy substrate used by essentially all tissues of the body besides the brain.

## Insulin Deficiency Increases Use of Fat for Energy

2. Insulin deficiency increases plasma cholesterol and phospholipid concentrations

The excess of fatty acids in the plasma promotes liver conversion of some of the fatty acids into phospholipids and cholesterol. (two of the major products of fat metabolism)

These two substances, along with excess triglycerides formed at the same time in the liver, are then discharged into the blood in the lipoproteins

All this promotes the development of atherosclerosis in people with serious diabetes.

## Excess Usage of Fats During Insulin Lack Causes Ketosis and Acidosis

- Insulin lack causes excessive amounts of *acetoacetic acid* to be formed in the liver cells.
- At the same time, the absence of insulin also depresses the utilization of *acetoacetic acid* in the peripheral tissues.
- After cessation of insulin secretion, sometimes concentrations of *acetoacetic acid* reach 10 mEq/L or more. (severe state of body fluid acidosis)

## Excess Usage of Fats During Insulin Lack Causes Ketosis and Acidosis

- Some of the *acetoacetic acid* is also converted into *beta-hydroxybutyric acid* and *acetone.*
- **Ketone bodies**: *beta-hydroxybutyric acid, acetone and acetoacetic acid.* And their presence in large quantities in the body fluids is called ketosis.
- In severe diabetes the *acetoacetic acid* and the *beta-hydroxybutiric acid* can cause severe acidosis and coma...death

# Effect of Insulin on Protein Metabolism and on Growth

## Insulin Promotes Protein Synthesis and Storage

- During the few hours after a meal proteins are also stored in the tissues by insulin.

1. Insulin stimulates transport of many of amino acids into the cells, most common: *valine*, *leucine*, *isoleucine*, *tyrosine*, and *phenylalanine*.

2. Insulin increases the translation of mRNA, thus forming new proteins.

3. Over a longer period of time, insulin also increases the rate of transcription of selected DNA, forming increased quantities of RNA and still more protein synthesis.

4. Insulin inhibits the catabolism of proteins.

5. In the liver, insulin depresses the rate of gluconeogenesis, this suppression, conserves the amino acids in the protein stores of the body.

- In summary, insulin promotes protein formation and prevents the degradation of proteins.

- Insulin Lack Causes Protein Depletion and Increased Plasma Amino Acids

- The resulting protein wasting is one of the most serious of all the effects of severe diabetes mellitus.

- It can lead to extreme weakness as well as many deranged functions of the organs.

- Insulin and Growth Hormone Interact Synergistically to Promote Growth

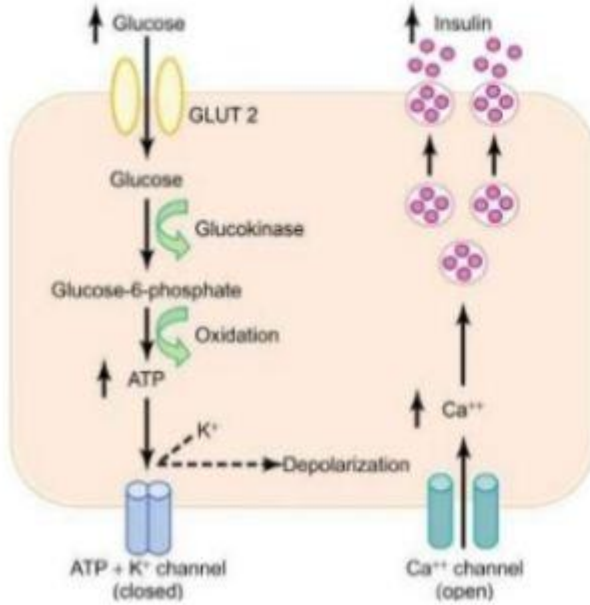
- A combination of these hormones causes dramatic growth.

- It appears that the two hormones function synergistically to promote growth each performing a specific function that is separate from that of the other. ( different selections of amino acids)

# Mechanism of Insulin Secretion

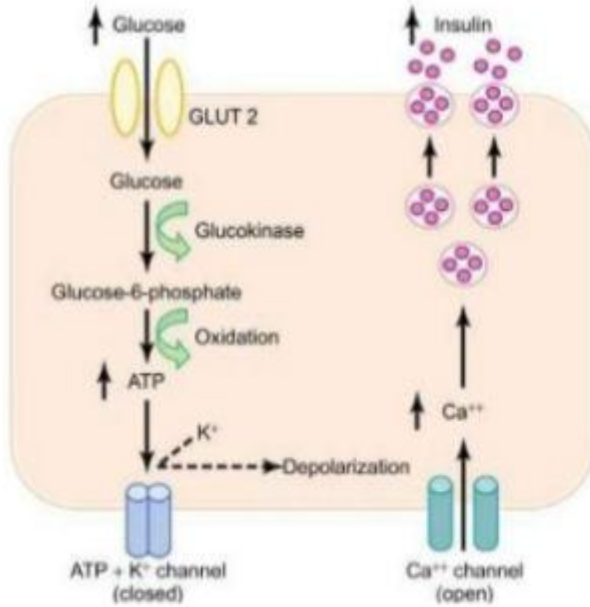
- The beta cells have a large number of glucose transporters **(GLUT- 2)**; permit a rate of glucose influx . (proportional to the blood concentration in the physiologic range)

- *glucose* is phosphorylated to glucose-6-phosphate by *glucokinase*



# Mechanism of Insulin Secretion

- Glucose-6-phosphate is subsequently oxidized to form ATP; which inhibits the ATP-sensitive potassium channels of the cell
- Depolarization of the cell membrane
- Voltage-gated calcium channels open, this produces an influx of calcium that stimulates fusion of the docked insulin-containing vesicles with the cell membrane and secretion of insulin into the extracellular fluid by **exocytosis**




# Other Factors That Stimulate Insulin Secretion

**Table 78–1**

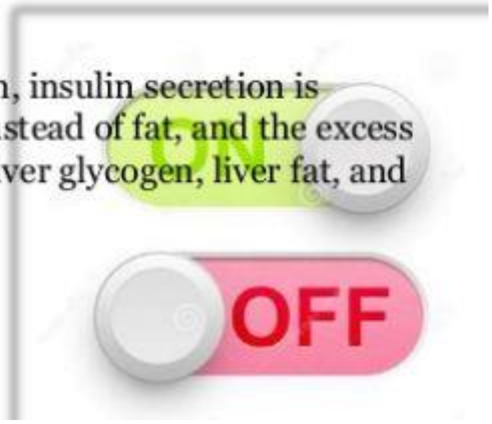
**Factors and Conditions That Increase or Decrease Insulin Secretion**

| Increase Insulin Secretion | Decrease Insulin Secretion |
|---|---|
| • Increased blood glucose | • Decreased blood glucose |
| • Increased blood free fatty acids | • Fasting |
| • Increased blood amino acids | • Somatostatin |
| • Gastrointestinal hormones (gastrin, cholecystokinin, secretin, gastric inhibitory peptide) | • α-Adrenergic activity |
| • Glucagon, growth hormone, cortisol | • Leptin |
| • Parasympathetic stimulation; acetylcholine | |
| • β-Adrenergic stimulation | |
| • Insulin resistance; obesity | |
| • Sulfonylurea drugs (glyburide, tolbutamide) | |

## Role of Insulin (and Other Hormones) in "Switching" Between Carbohydrates and Lipid Metabolism

- The signal that controls the switching mechanism is principally the blood glucose concentration. When the glucose concentration is low, insulin secretion is suppressed and fat is used almost exclusively for energy everywhere except in the brain.

- When the glucose concentration is high, insulin secretion is stimulated and carbohydrate is used instead of fat, and the excess blood glucose is stored in the form of liver glycogen, liver fat, and muscle glycogen.




## Glucagon and its Functions

- It is secreted by the alpha cells of the islets of Langerhans when the blood glucose concentration falls.

- It has several functions that are diametrically opposed to those of insulin; most important of these functions is to increase the blood glucose concentration.

- Like insulin, glucagon is a large polypeptide.

- It is composed of a chain of 29 amino acids.

- "Hyperglycemic hormone"

- Most of the Actions of Glucagon Are Achieved by Activation of Adenylyl Cyclase in hepatic cell membrane

- The binding of glucagon to hepatic receptors results in activation of adenylyl cyclase and generation of the second messenger cyclic AMP, which in turn activates protein *kinase*, leading to phosphorylation that results in the activation or deactivation of a number of enzymes.

# Glucagon and its Functions

- Effects on Glucose Metabolism

1. Breakdown of liver glycogen (glycogenolysis)
2. Increased gluconeogenesis in the liver.

Both of these effects greatly enhance the availability of glucose to the other organs of the body

## Other Effects of Glucagon

- The most important effect is that glucagon activates adipose cell *lipase*, making increased quantities of fatty acids available to the energy systems of the body.

- Glucagon also inhibits the storage of triglycerides in the liver, which prevents the liver from removing fatty acids from the blood; this also helps make additional amounts of fatty acids available for the other tissues of the body
- Glucagon in very high concentrations also

(1) Enhances the strength of the heart
(2) Increases blood flow in some tissues, especially the kidneys
(3) Enhances bile secretion; and
(4) Inhibits gastric acid secretion.

All these effects are probably of minimal importance in the normal function of the body.

"Your blood sugar is too high."

# Regulation of Glucagon Secretion

**Increased Blood Glucose Inhibits Glucagon Secretion. (most potent factor)**

- A decrease in the blood glucose concentration from its normal fasting level of about 90 mg/100 ml of blood down to hypoglycemic levels can increase the plasma concentration of glucagon several fold.

## Increased Blood Amino Acids Stimulate Glucagon Secretion

- High concentrations of amino acids, as occur in the blood after a protein meal (especially the amino acids alanine and arginine), stimulate the secretion of glucagon.

- This is the same effect that amino acids have in stimulating insulin secretion. Thus, in this instance, the glucagon and insulin responses are not opposites.

## Exercise Stimulates Glucagon Secretion

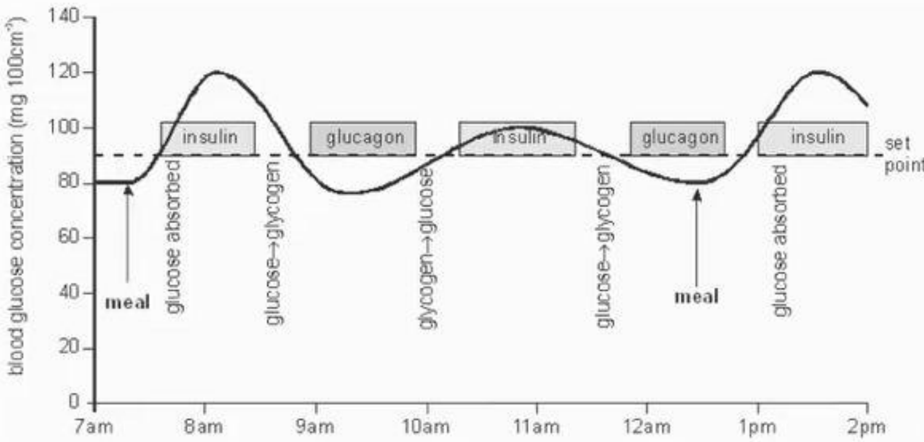
- The blood concentration of glucagon often increases fourfold to fivefold.

- What causes this is not understood, because the blood glucose concentration does not necessarily fall.

- A beneficial effect of the glucagon is that it prevents a decrease in blood glucose.

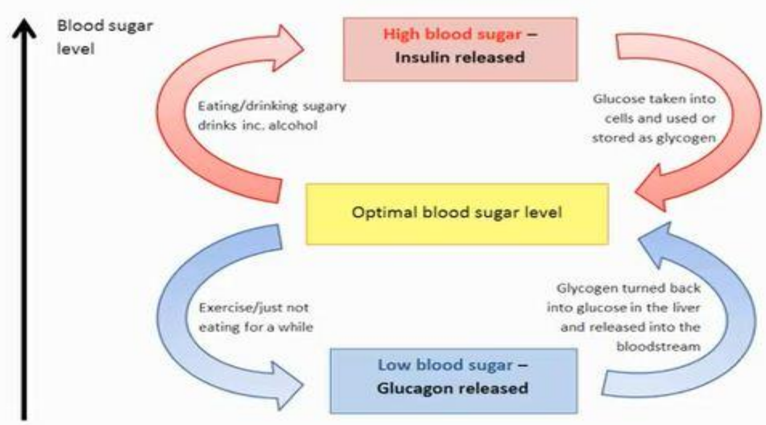
CAN'T SOMEONE ELSE JUST DO IT?

# How Glucagon Works

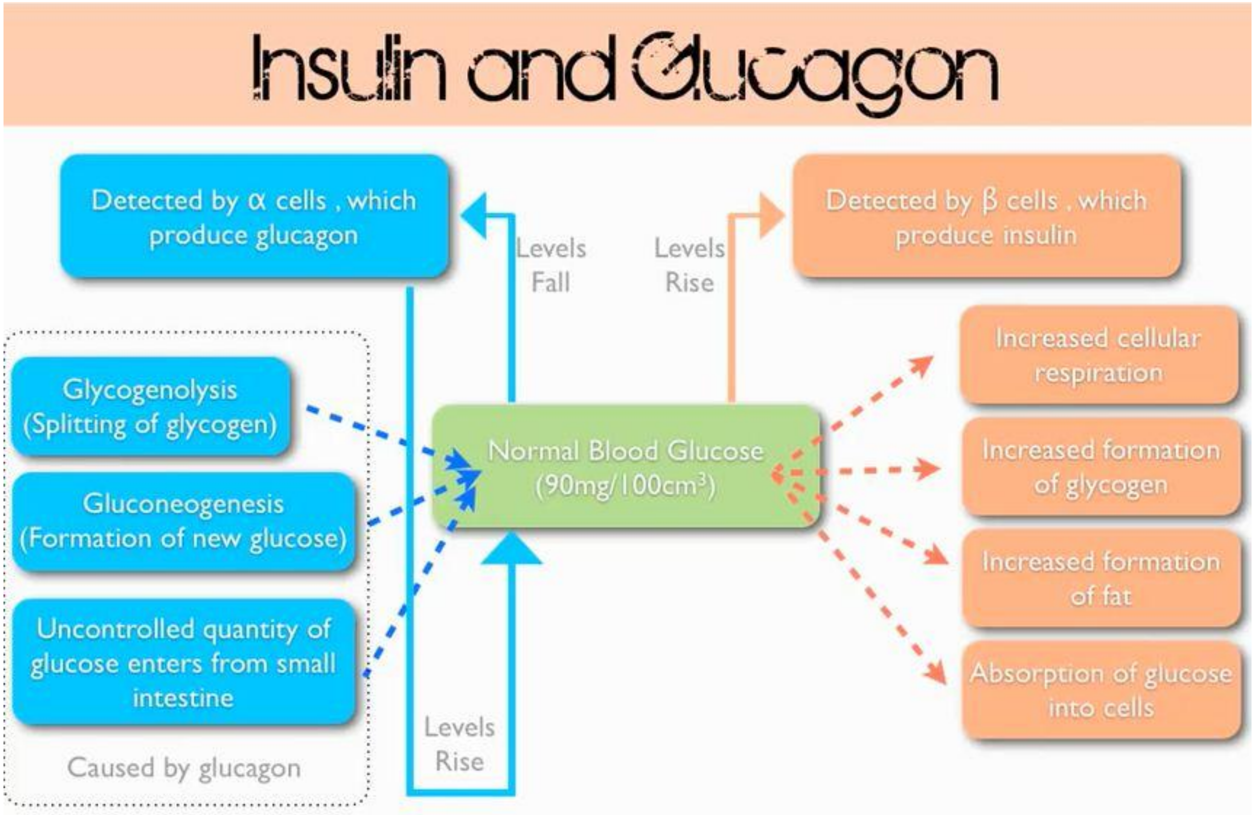



- Activates an enzymes that converts glucose to glycogen

# Negative Feedback

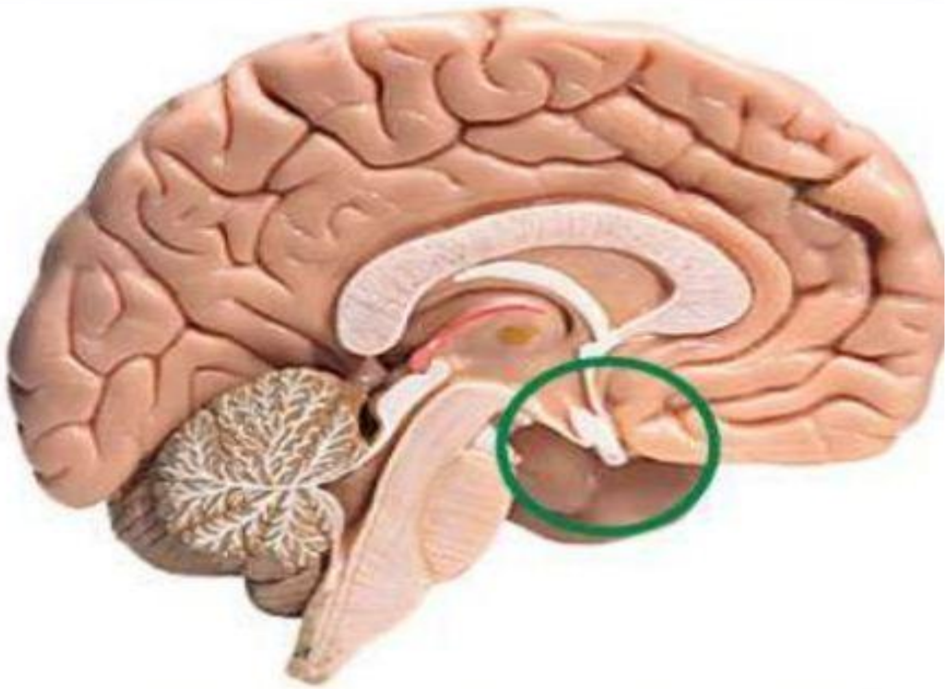



- There is a negative feedback loop in place for both Insulin and Glucagon
- Therefore the system self regulates



Insulin and Glucagon
Detected by α cells , which produce glucagon
Levels Fall
Levels Rise
Detected by β cells , which produce insulin
Glycogenolysis (Splitting of glycogen)
Gluconeogenesis (Formation of new glucose)
Uncontrolled quantity of glucose enters from small intestine
Caused by glucagon
Normal Blood Glucose (90mg/100cm³)
Levels Rise
Increased cellular respiration
Increased formation of glycogen
Increased formation of fat
Absorption of glucose into cells

## Pituitary Gland



## Pituitary Gland

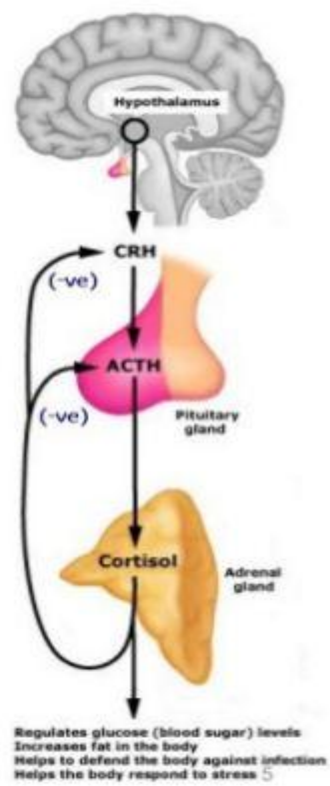
- The pituitary gland, or hypophysis, is an endocrine gland about the size of a pea and weighing 0.5 grams in humans.
- It is composed of three lobes: anterior, intermediate, and posterior.

# Functions of Pituitary Gland

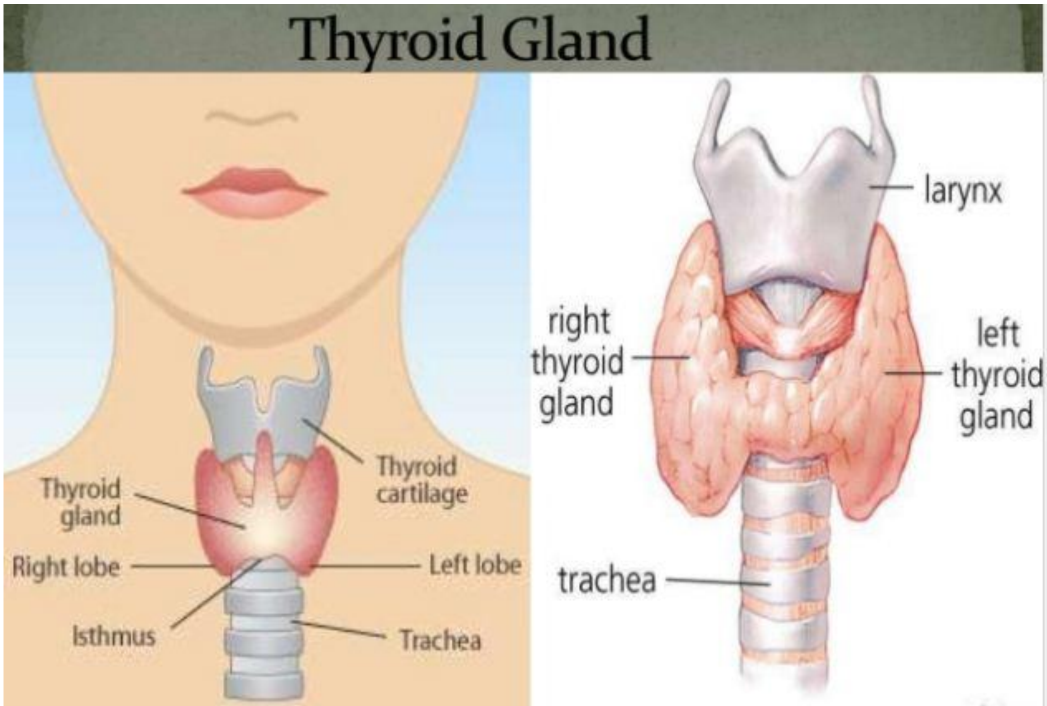
- Growth
- Blood pressure
- Some aspects of pregnancy and childbirth including stimulation of uterine contractions during childbirth
- Breast milk production
- Sex organ functions in both males and females
- Thyroid gland function
- The conversion of food into energy (metabolism)
- Water and osmolarity regulation in the body
- Water balance via the control of reabsorption of water by the kidneys
- Temperature regulation
- Pain relief

## Hypothalamus - Pituitary – Adrenal cortex- feedback loop

- Hypothalamus synthesize and secrete corticotropin-releasing hormone (CRH) and vasopressin
- CRH and vasopressin stimulate the secretion of adrenocorticotropic hormone (ACTH) from anterior pituitary
- In response to stimulation by ACTH the adrenal cortices produce cortisol
- Cortisol in turn act back on the hypothalamus and pituitary (to suppress CRH and ACTH production) in a negative feedback cycle.



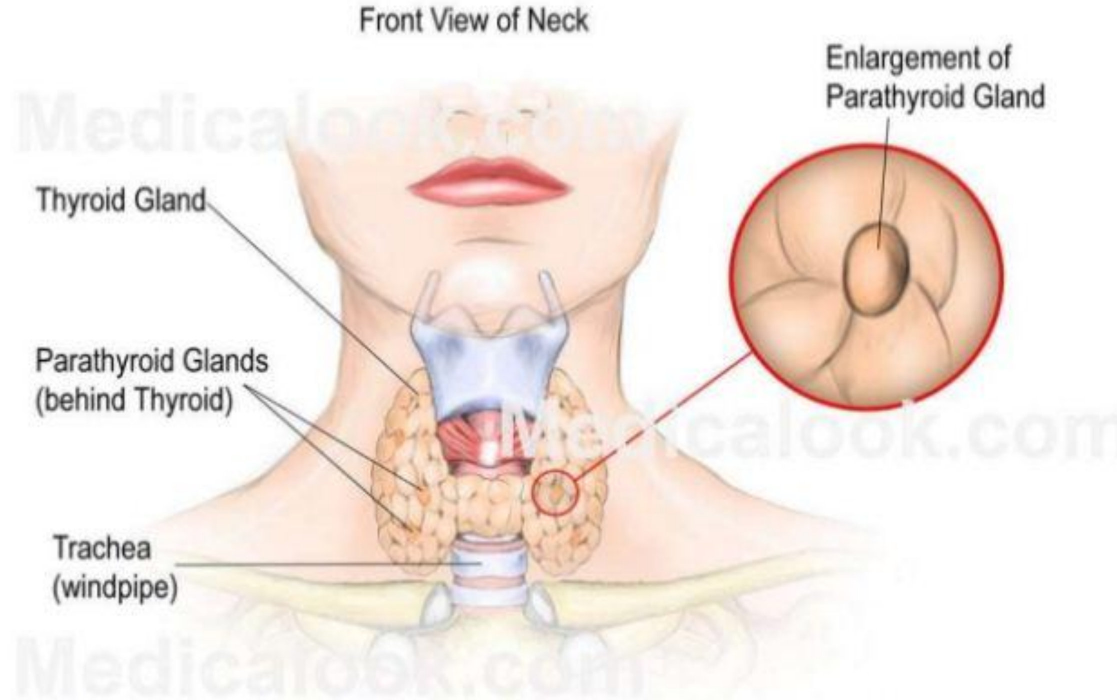

UAB 5




# Thyroid Gland

- The thyroid gland or just thyroid is one of the largest endocrine glands and consists of two connected lobes.
- Each lobe is about 5 cm long, 3 cm wide and 2 cm thick.
- The thyroid gland is a butterfly-shaped organ.
- The thyroid gland is found in the neck, below the thyroid cartilage (which forms "Adam's apple").
- It secretes throxine hormone also called T4
- The thyroid also produces calcitonin, which plays a role in calcium homeostasis.

# Parathyroid




# Parathyroid

- There are four parathyroid glands, and they are each about the size of a grain of rice.
- Though they're located near each other, the parathyroid glands are not related to the thyroid gland.
- Parathyroid hormone (PTH) has a very powerful influence on the cells of your bones by causing them to release their calcium into the bloodstream.

## Functions and Diseases of Parathyroid

- Parathyroid hormone regulates the body's calcium levels.
- The parathyroid essentially helps the nervous and muscular systems function properly.
- Calcium is the primary element that causes muscles to contract, and calcium levels are very important to the normal conduction of electrical currents along nerves.
- The most common disease of parathyroid glands is hyperparathyroidism, which is characterized by excess PTH hormone.

## Thyroid Gland/ Parathyroid Glands

- Thyroid: found at the base of the throat
- Produces two hormones:
  1. Thyroid hormone- metabolic hormone
  2. Calcitonin- responds to high calcium levels

- Parathyroids: tiny masses on the posterior of the thyroid
- Secrete parathyroid hormone (PTH)
  - Responds to low calcium levels

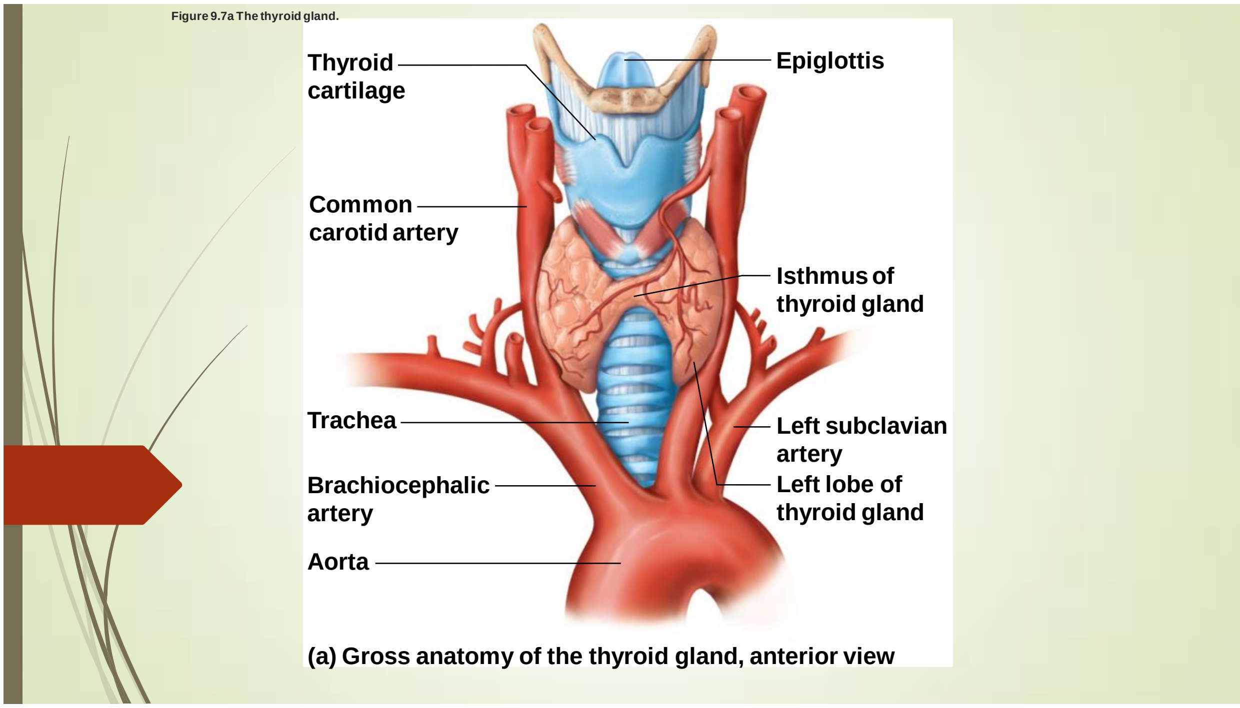
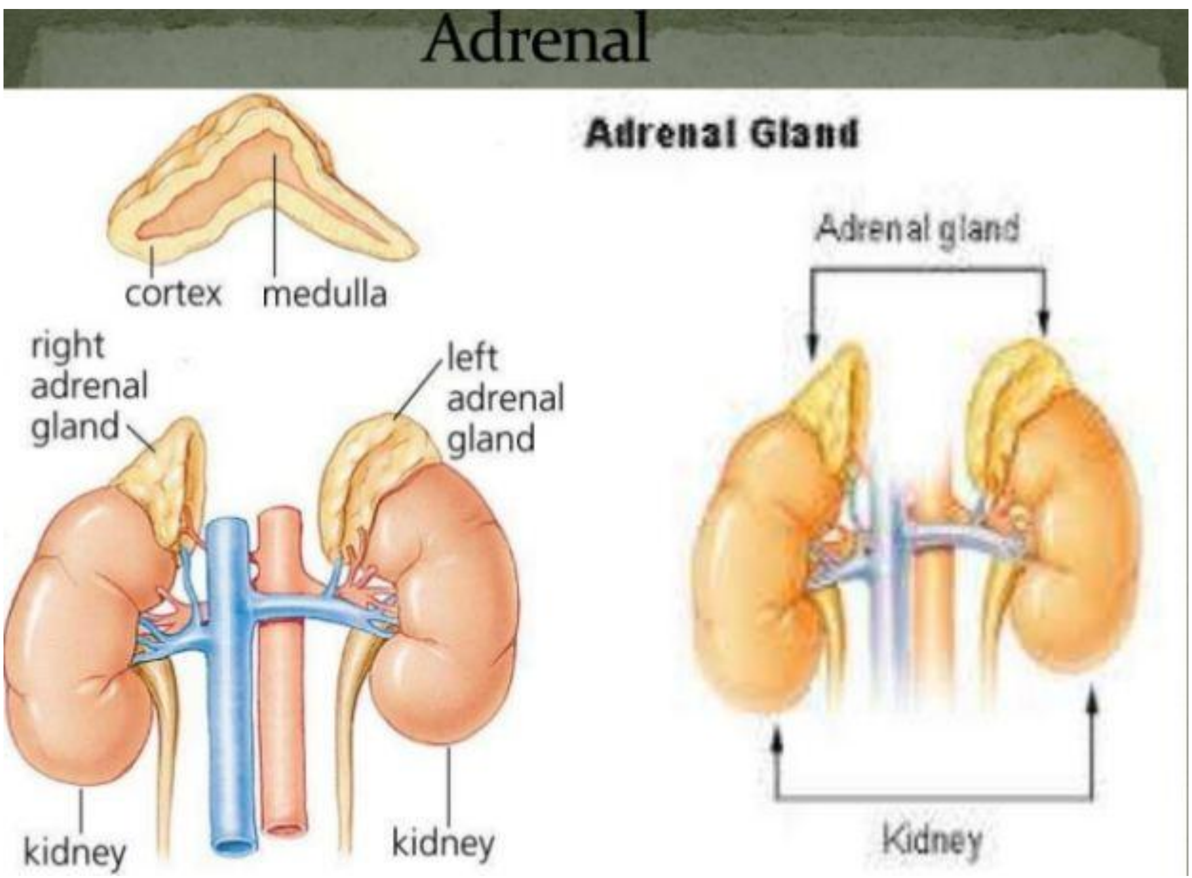


Figure 9.7a The thyroid gland.
Thyroid cartilage
Epiglottis
Common carotid artery
Isthmus of thyroid gland
Trachea
Left subclavian artery
Brachiocephalic artery
Left lobe of thyroid gland
Aorta
(a) Gross anatomy of the thyroid gland, anterior view

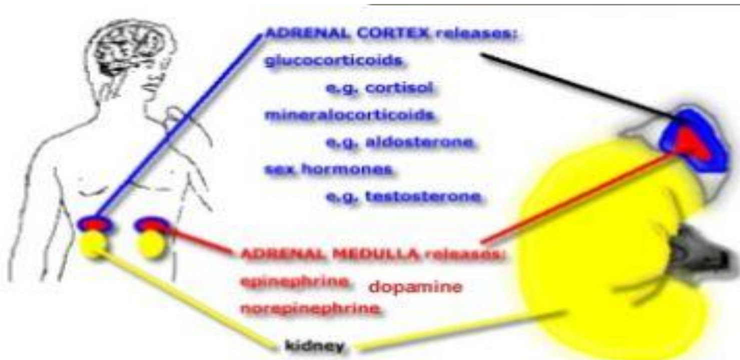

Adrenal
Adrenal Gland
cortex
medulla
right adrenal gland
left adrenal gland
kidney
kidney
Adrenal gland
Kidney

# Adrenal

- The adrenal glands are two glands that sit on top of your kidneys that are made up of two distinct parts- The adrenal cortex and The adrenal medulla.
- They are also known as suprarenal glands.
- The adrenal glands are two, triangular-shaped organs that measure about 1.5 inches in height and 3 inches in length.

# Functions of Adrenal

- The adrenal cortex and the adrenal medulla have very different functions. One of the main distinctions between them is that the hormones released by the adrenal cortex are necessary for life; those secreted by the adrenal medulla are not.





Cortex (outer layer) produces steroid hormones:
Aldosterone
Cortisol
Androgens

Medulla (inner layer) produces catecholamines:
Epinephrine (adrenaline)
Norepinephrine
Dopamine

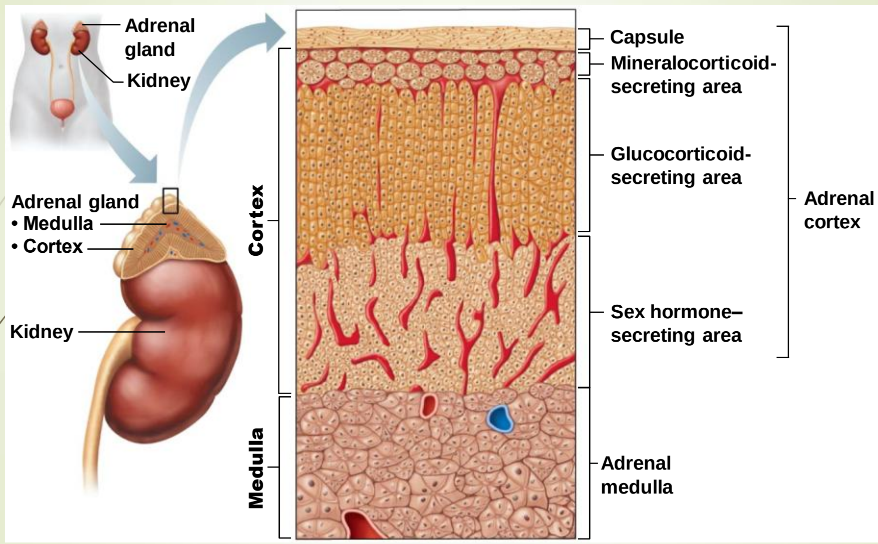
4

# Adrenal Glands

- Sit on top of the kidneys
- Two regions:
  1. Adrenal cortex—outer region; produces cortico**steroids**
     - Regulate mineral metabolism, glucose regulation, inflammation, sex horomones
  2. Adrenal medulla—inner neural tissue region
     - Managed by the ANS; releases epinephrine/norepinephrine



Figure 9.11 Microscopic structure of the adrenal gland.



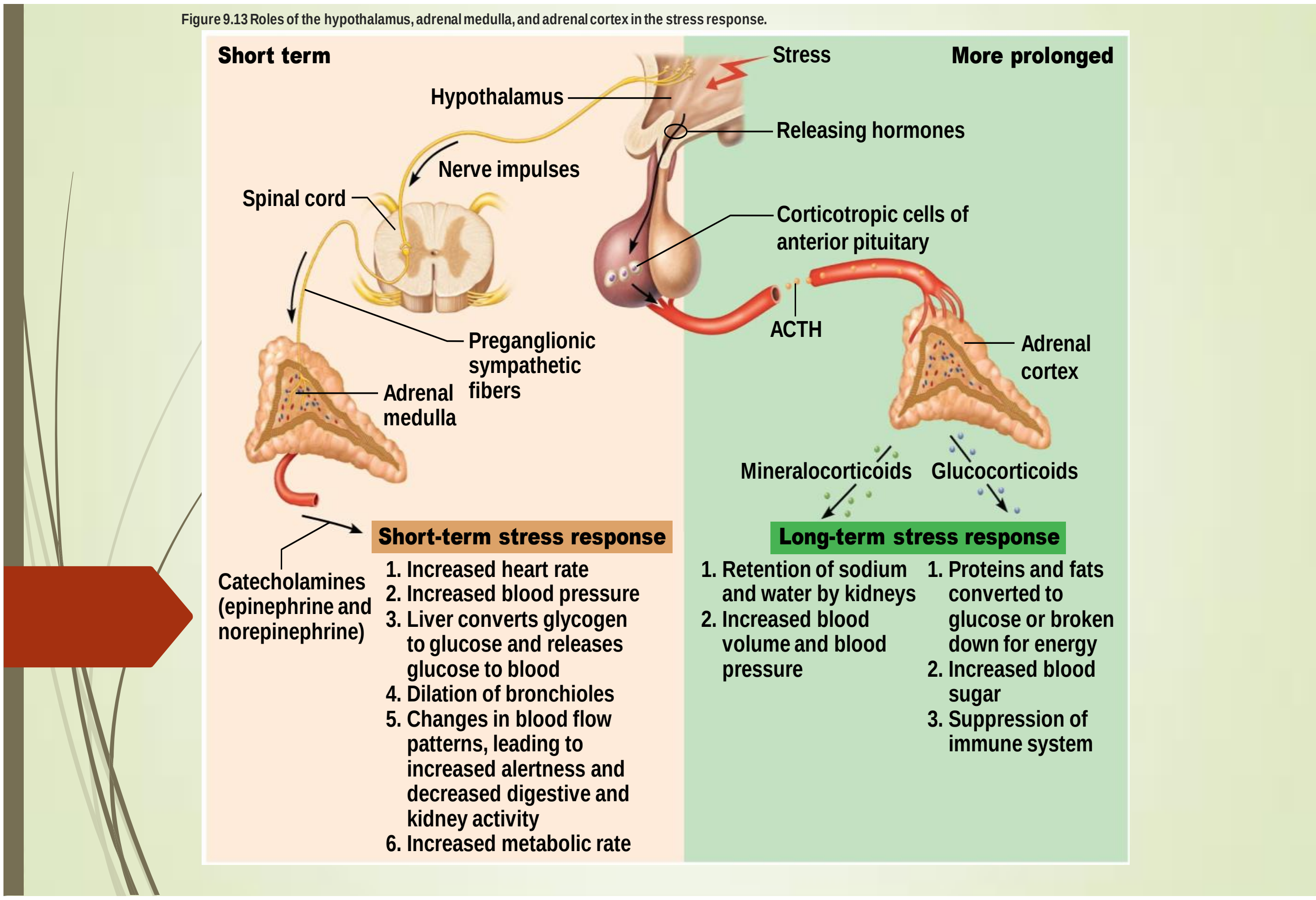


Figure 9.13 Roles of the hypothalamus, adrenal medulla, and adrenal cortex in the stress response.
Short term
More prolonged
Stress
Hypothalamus
Releasing hormones
Nerve impulses
Spinal cord
Corticotropic cells of anterior pituitary
ACTH
Preganglionic sympathetic fibers
Adrenal medulla
Adrenal cortex
Mineralocorticoids
Glucocorticoids
Catecholamines (epinephrine and norepinephrine)
Short-term stress response
1. Increased heart rate
2. Increased blood pressure
3. Liver converts glycogen to glucose and releases glucose to blood
4. Dilation of bronchioles
5. Changes in blood flow patterns, leading to increased alertness and decreased digestive and kidney activity
6. Increased metabolic rate
Long-term stress response
1. Retention of sodium and water by kidneys
2. Increased blood volume and blood pressure
1. Proteins and fats converted to glucose or broken down for energy
2. Increased blood sugar
3. Suppression of immune system

**UNIT: II_ Chapter:4_FLUIDS AND ELECTROLYTE BALANCE**

## An Introduction to Fluid, Electrolyte, and Acid–Base Balance

- Water
  - Is 99% of fluid outside cells (extracellular fluid)
  - Is an essential ingredient of cytosol (intracellular fluid)
  - All cellular operations rely on water
    - As a diffusion medium for gases, nutrients, and waste products

- The Body
  - Must maintain normal volume and composition of:
    - **Extracellular fluid (ECF)**
    - **Intracellular fluid (ICF)**

## Body fluids

- Intra cellular – fluid occupied inside the cells. Intracellular fluid is found inside the bi-layered plasma membrane in which cellular organs are suspended and chemical reaction takes place

- Extracellular- fluid in the spaces outside the cells including interstitial fluid, plasma and trans cellular fluid of the body

## Composition and function of ICF

Composition

- Electrolyte, protein, cholesterol, phospholipids, neutral fat

Function

- Provides fluid media within the cells for chemical reaction
- Buffering action

# Composition and functions of ECF

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Composition

- Electrolyte, Glucose, Fatty acid, amino acid, chemical messenger, oxygen and other nutrients, urea

Functions

- Establishes the milieu interior
- Provides nutrients to the cells
- Removes metabolic waste materials from immediate cellular environment
- It brings to the cells hormones that co-ordinate the functions of widely separated cells
- Buffering action

- **Fluid Balance**
  - Is a daily balance between:
    - Amount of water gained
    - Amount of water lost to environment
  - Involves regulating content and distribution of body water in ECF and ICF
    - The Digestive System
      - Is the primary source of water gains
        - Plus a small amount from metabolic activity
    - The Urinary System
      - Is the primary route of water loss

- **Electrolyte Balance**
  - **Electrolytes** are ions released through dissociation of inorganic compounds
    - Can conduct electrical current in solution
  - Electrolyte balance
    - When the gains and losses of all electrolytes are equal
    - Primarily involves balancing rates of absorption across digestive tract with rates of loss at kidneys and sweat glands
- **Acid–Base Balance**
  - Precisely balances production and loss of hydrogen ions (pH)
  - The body generates acids during normal metabolism
    - Tends to reduce pH

- The Kidneys
  - Secrete hydrogen ions into urine
  - Generate buffers that enter bloodstream
    - In distal segments of distal convoluted tubule (DCT) and collecting system
- The Lungs
  - Affect pH balance through elimination of carbon dioxide

- Fluid in the Body
  - Water accounts for roughly:
    - 60% of male body weight
    - 50% of female body weight
    - Mostly in intracellular fluid

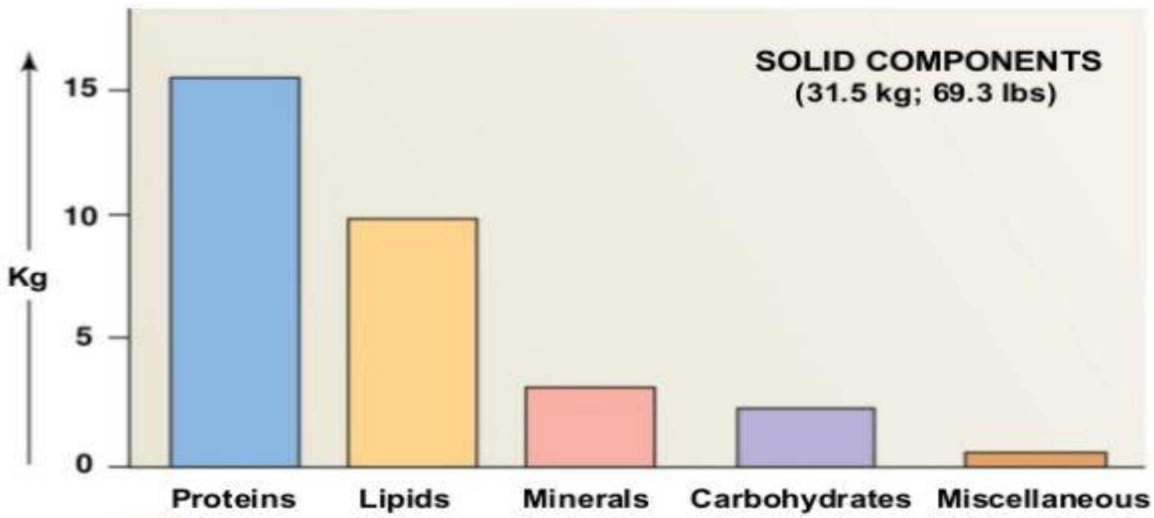
- Water Exchange
  - Water exchange between ICF and ECF occurs across plasma membranes by:
    - Osmosis
    - Diffusion
    - Carrier-mediated transport

- Major Subdivisions of ECF
  - Interstitial fluid of peripheral tissues
  - Plasma of circulating blood

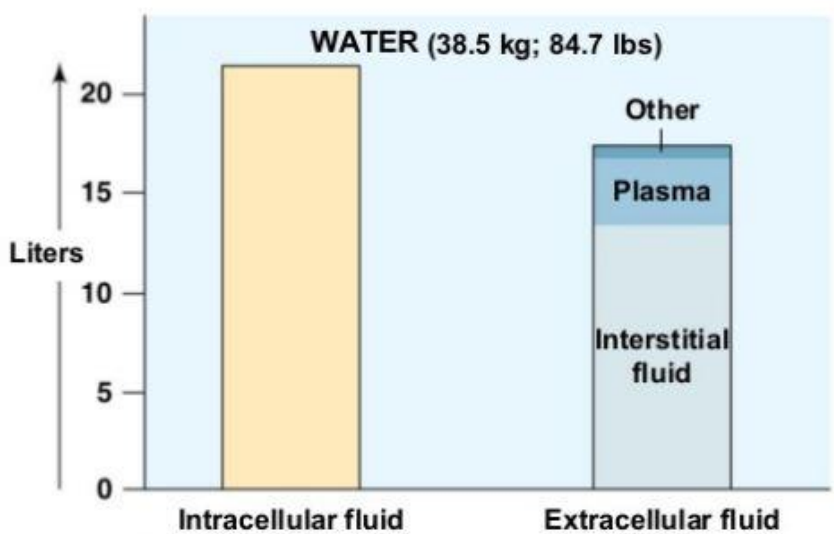
- Minor Subdivisions of ECF
  - Lymph, perilymph, and endolymph
  - Cerebrospinal fluid (CSF)
  - Synovial fluid
  - Serous fluids (pleural, pericardial, and peritoneal)
  - Aqueous humor

- Exchange among Subdivisions of ECF
  - Occurs primarily across endothelial lining of capillaries
  - From interstitial spaces to plasma
    - Through lymphatic vessels that drain into the venous system

Figure 27-1a The Composition of the Human Body

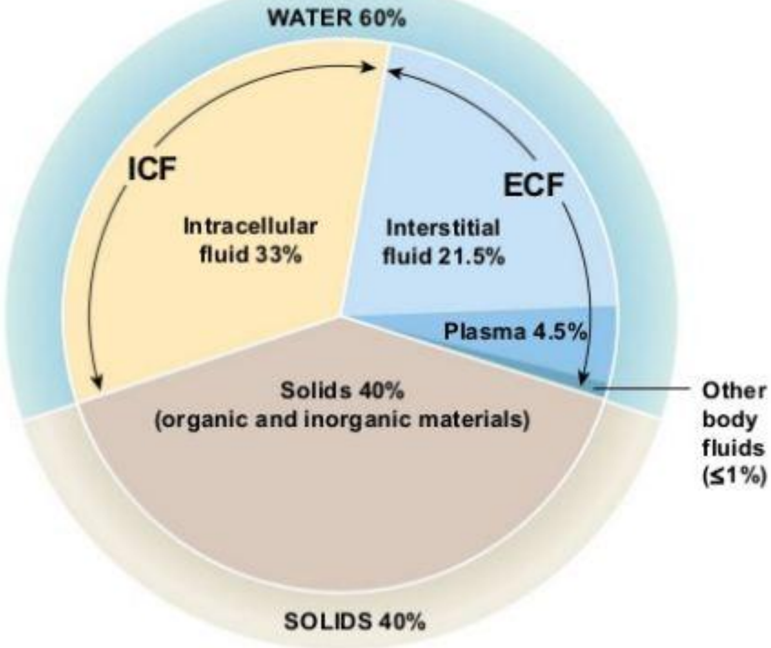



a The body composition (by weight, averaged for both sexes) and major body fluid compartments of a 70-kg individual.




a The body composition (by weight, averaged for both sexes) and major body fluid compartments of a 70-kg individual.

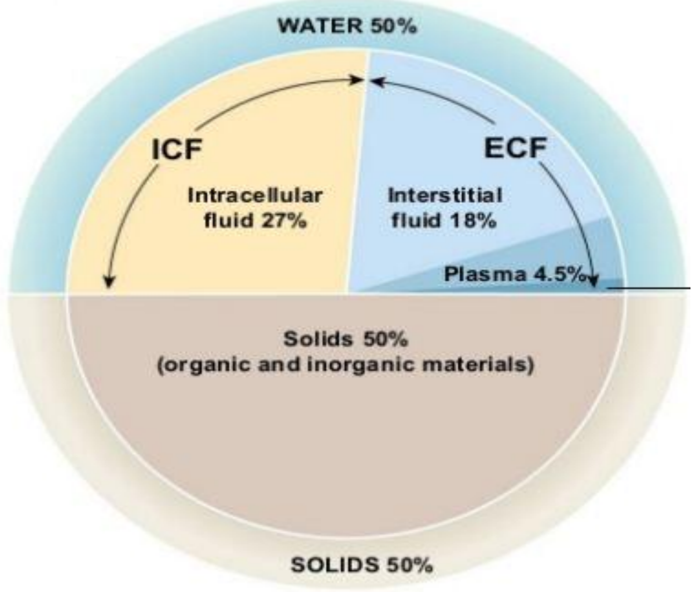
Figure 27-1b The Composition of the Human Body




Adult males

**b** A comparison of the body compositions of adult males and females, ages 18–40 years.

Figure 27-1b The Composition of the Human Body




Adult females

**b** A comparison of the body compositions of adul males and females, ages 18–40 years.

- The ECF and the ICF
  - ECF Solute Content
    - Types and amounts vary regionally
      - Electrolytes
      - Proteins
      - Nutrients
      - Waste products

- The ECF and the ICF
  - Are called **fluid compartments** because they behave as distinct entities
  - Are separated by plasma membranes and active transport

- Cations and Anions
  - In ECF
    - Sodium, chloride, and bicarbonate
  - In ICF
    - Potassium, magnesium, and phosphate ions
    - Negatively charged proteins

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Figure 27-2 Cations and Anions in Body Fluids

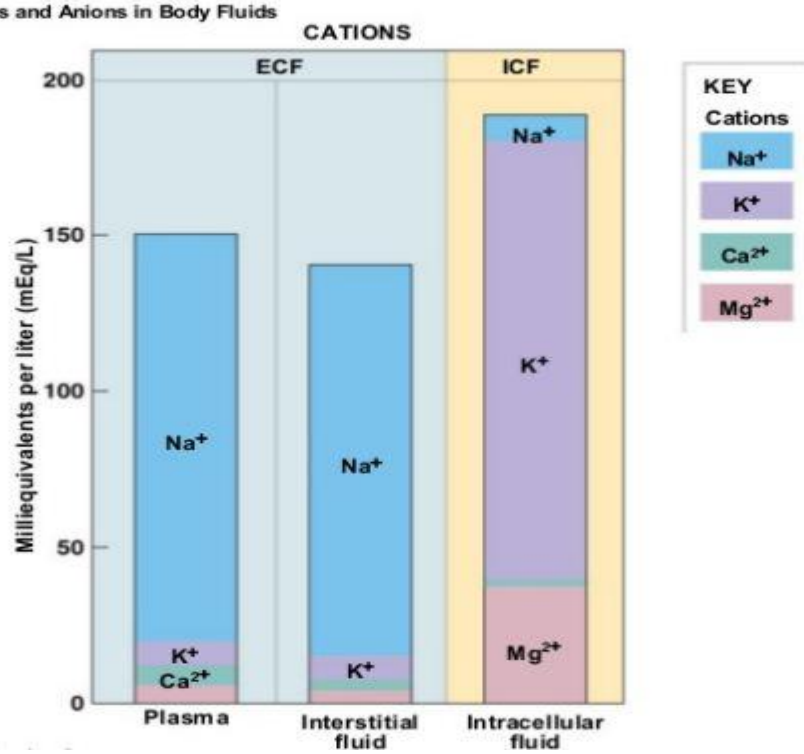
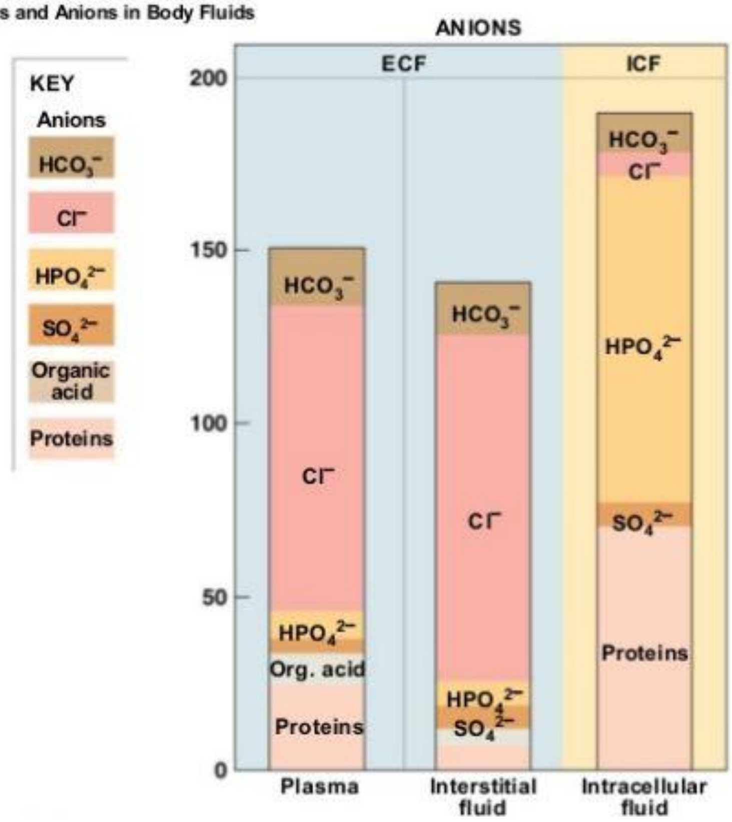



Figure 27-2 Cations and Anions in Body Fluids



- Membrane Functions
  - Plasma membranes are selectively permeable
  - Ions enter or leave via specific membrane channels
  - Carrier mechanisms move specific ions in or out of cell

- The Osmotic Concentration of ICF and ECF
  - Is identical
  - Osmosis eliminates minor differences in concentration
    - Because plasma membranes are permeable to water

- Basic Concepts in the Regulation of Fluids and Electrolytes
  1. *All homeostatic mechanisms that monitor and adjust body fluid composition respond to changes in the ECF, not in the ICF*
  2. *No receptors directly monitor fluid or electrolyte balance*
  3. *Cells cannot move water molecules by active transport*
  4. *The body's water or electrolyte content will rise if dietary gains exceed environmental losses, and will fall if losses exceed gains*

- An Overview of the Primary Regulatory Hormones
  - Affecting fluid and electrolyte balance
    1. *Antidiuretic hormone*
    2. *Aldosterone*
    3. *Natriuretic peptides*

- Antidiuretic Hormone (ADH)
  - Stimulates water conservation at kidneys
    - Reducing urinary water loss
    - Concentrating urine
  - Stimulates thirst center
    - Promoting fluid intake

- ADH Production
  - **Osmoreceptors** in hypothalamus
    - Monitor osmotic concentration of ECF
  - Change in osmotic concentration
    - Alters osmoreceptor activity
  - Osmoreceptor neurons secrete ADH

- Aldosterone
  - Is secreted by adrenal cortex in response to:
    - Rising $K^+$ or falling $Na^+$ levels in blood
    - Activation of renin–angiotensin system
  - Determines rate of $Na^+$ absorption and $K^+$ loss along DCT and collecting system

- Movement of Water and Electrolytes
  - When the body loses water:
    - Plasma volume decreases
    - Electrolyte concentrations rise
  - When the body loses electrolytes:
    - Water is lost by osmosis
  - Regulatory mechanisms are different

- Fluid Balance
  - Water circulates freely in ECF compartment
  - At capillary beds, hydrostatic pressure forces water out of plasma and into interstitial spaces
  - Water is reabsorbed along distal portion of capillary bed when it enters lymphatic vessels
  - ECF and ICF are normally in osmotic equilibrium
    - No large-scale circulation between compartments

- Fluid Movement within the ECF
  - Net hydrostatic pressure
    - Pushes water out of plasma
    - Into interstitial fluid
  - Net colloid osmotic pressure
    - Draws water out of interstitial fluid
    - Into plasma

- Fluid Movement within the ECF
  - ECF fluid volume is redistributed
    - From lymphatic system to venous system (plasma)
  - Interaction between opposing forces
    - Results in continuous filtration of fluid
  - ECF volume
    - Is 80% in interstitial fluid and minor fluid compartment
    - Is 20% in plasma

- Electrolyte Balance
  - Requires rates of gain and loss of each electrolyte in the body to be equal
    - *Electrolyte concentration directly affects water balance*
    - *Concentrations of individual electrolytes affect cell functions*

- Sodium
  - Is the dominant cation in ECF
  - Sodium salts provide 90% of ECF osmotic concentration
    - Sodium chloride ($NaCl$)
    - Sodium bicarbonate ($NaHCO_3$)

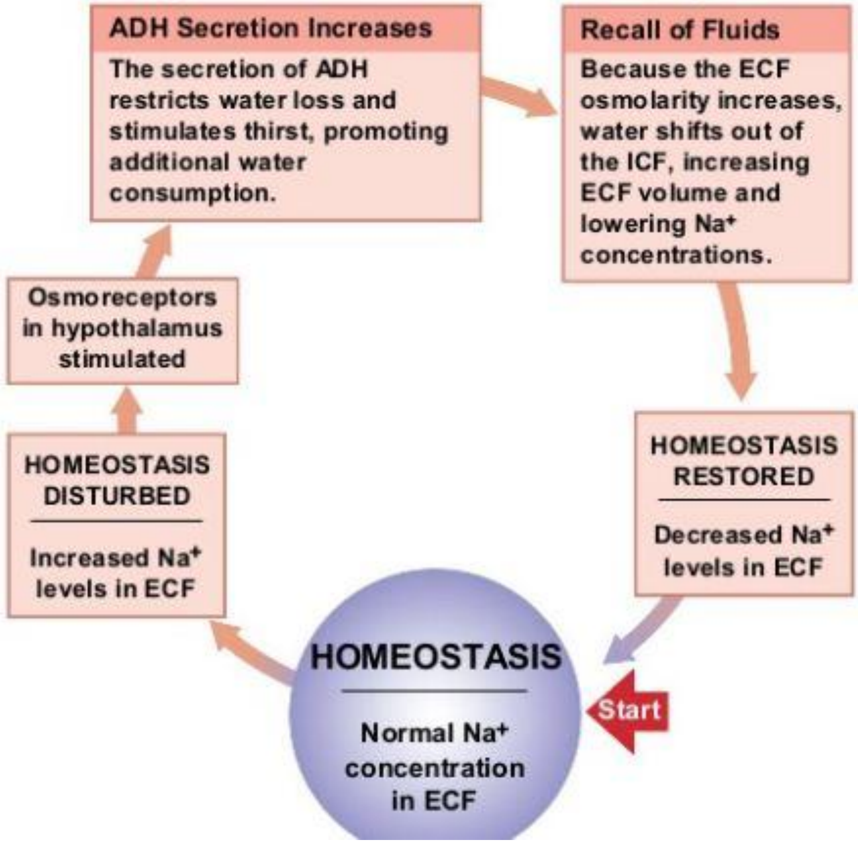
- Normal Sodium Concentrations
  - In ECF
    - About 140 mEq/L
  - In ICF
    - Is 10 mEq/L or less

- Potassium
  - Is the dominant cation in ICF
  - Normal potassium concentrations
    - In ICF
      - About 160 mEq/L
    - In ECF
      - 3.5–5.5 mEq/L

- Rules of Electrolyte Balance
  1. *Most common problems with electrolyte balance are caused by imbalance between gains and losses of sodium ions*
  2. *Problems with potassium balance are less common, but more dangerous than sodium imbalance*

- Sodium Balance
  - Total amount of sodium in ECF represents a balance between two factors
    1. Sodium ion uptake across digestive epithelium
    2. Sodium ion excretion in urine and perspiration

Figure 27-5 The Homeostatic Regulation of Normal Sodium Ion Concentrations in Body Fluids




- Potassium Balance
  - 98% of potassium in the human body is in ICF
  - Cells expend energy to recover potassium ions diffused from cytoplasm into ECF

- Processes of Potassium Balance
  1. Rate of gain across digestive epithelium
  2. Rate of loss into urine

- Potassium Loss in Urine
  - Is regulated by activities of ion pumps
    - Along distal portions of nephron and collecting system
    - $Na^+$ from tubular fluid is exchanged for $K^+$ in peritubular fluid
  - Are limited to amount gained by absorption across digestive epithelium (about 50–150 mEq or 1.9–5.8 g/day)

**Table 27-3 A Review of Important Terms Relating to Acid–Base Balance**

| Table 27–3 | A Review of Important Terms Relating to Acid–Base Balance |
|---|---|
| **pH** | The negative exponent (negative logarithm) of the hydrogen ion concentration ($H^+$) |
| **Neutral** | A solution with a pH of 7; the solution contains equal numbers of hydrogen ions and hydroxide ions |
| **Acidic** | A solution with a pH below 7; in this solution, hydrogen ions ($H^+$) predominate |
| **Basic, or alkaline** | A solution with a pH above 7; in this solution, hydroxide ions ($OH^-$) predominate |
| **Acid** | A substance that dissociates to release hydrogen ions, decreasing pH |
| **Base** | A substance that dissociates to release hydroxide ions or to tie up hydrogen ions, increasing pH |
| **Salt** | An ionic compound consisting of a cation other than hydrogen and an anion other than a hydroxide ion |
| **Buffer** | A substance that tends to oppose changes in the pH of a solution by removing or replacing hydrogen ions; in body fluids, buffers maintain blood pH within normal limits (7.35–7.45) |

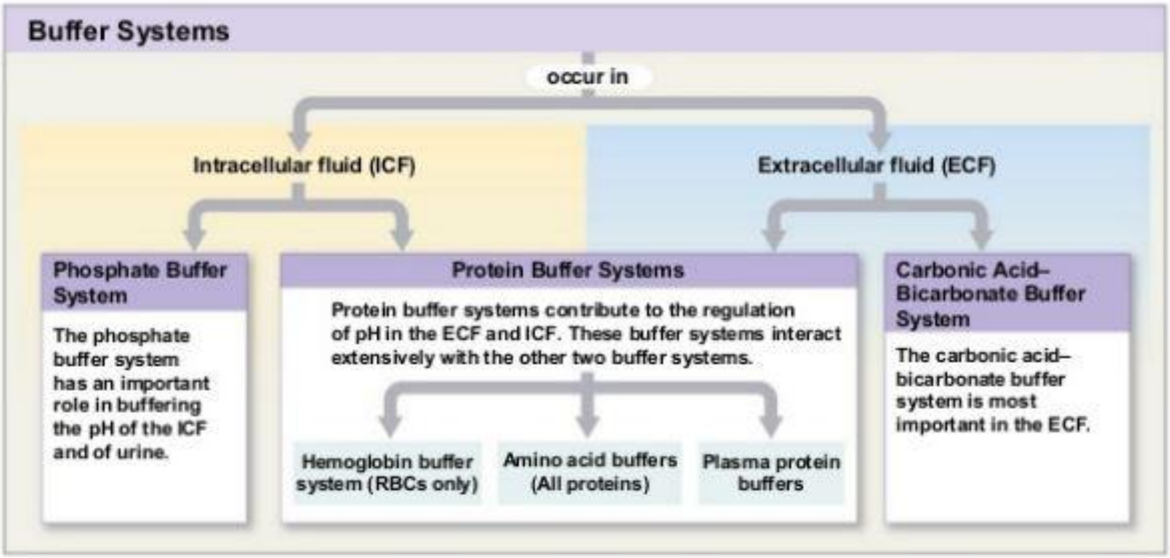
## 27-5 Acid–Base Balance

- Carbonic Acid
  - Is a weak acid
  - In ECF at normal pH:
    - Equilibrium state exists

$$H_2CO_3 \leftrightarrow H^+ + HCO_3^-$$

- The Importance of pH Control
  - pH of body fluids depends on dissolved:
    - Acids
    - Bases
    - Salts
  - pH of ECF
    - Is narrowly limited, usually 7.35–7.45

Figure 27-10 Buffer Systems in Body Fluids




# Fluid movement

- Fluid and solute constantly move within the body, which allows the body to maintain homeostasis
- Fluids along with nutrients and waste products constantly shift within the body's compartment from the cell to the interstitial spaces, to the blood vessels and back again

- Types of transport

A. Active transport

B. Passive transport

- Diffusion
- Osmosis
- filtration

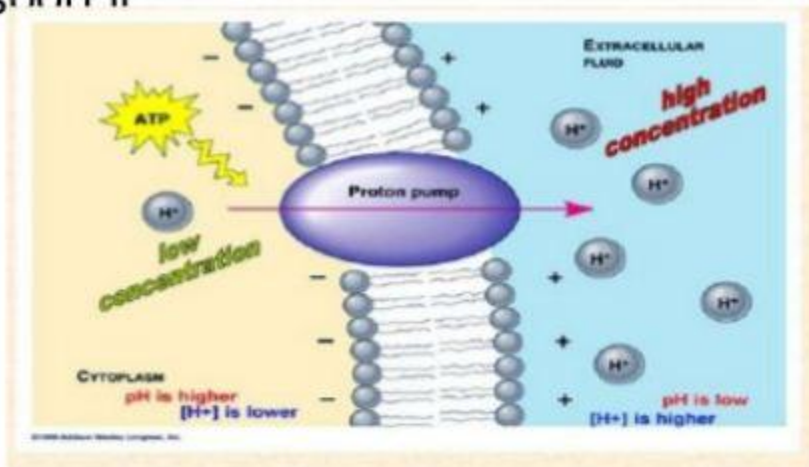
## Active Transport

- Particles to travel in the reverse direction across the membrane and have particles travel from an area of LOW concentration to an area of HIGH concentration, but in order to counteract the force of diffusion the cell must expand energy, this process is called Active Transport

- Active transport is the movement of material through a membrane Against a concentration gradient. Active transport require energy

- The energy for active transport comes from ATP(Adenosine Triphosphate) , generated inside mitochondria

- This process requires specialized protein, which are carrier protein to bind with particles and transport it




## Passive Transport

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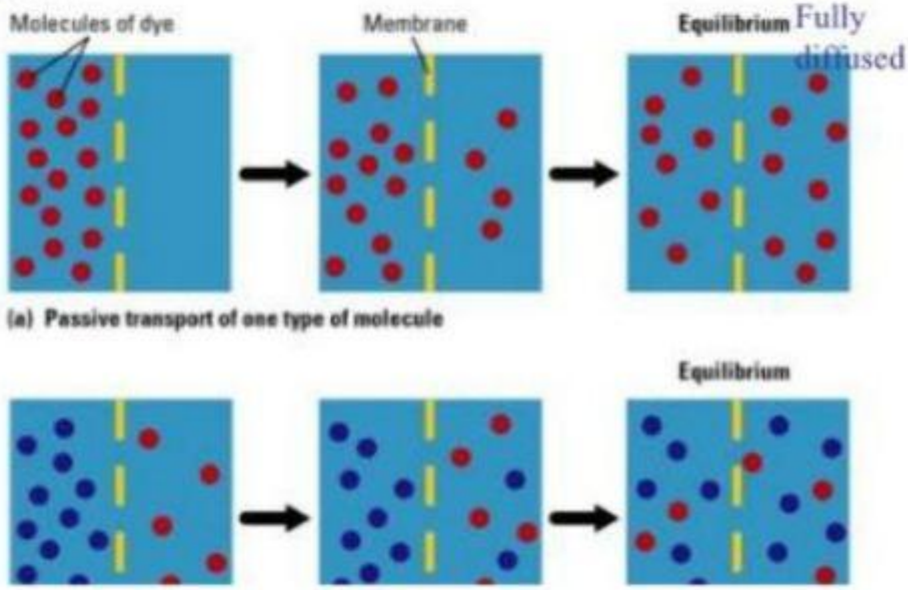
- Diffusion

The movement of molecules from a area in which they are highly concentrated to a area in which they are less concentrated.

# Diffusion process

the left



# osmosis

- Osmosis is the spontaneous net movement of solvent molecules through a partially permeable membrane into a region of higher solute concentration, in the direction that tends to equalize the solute concentrations on the two sides
- Osmosis provides the primary means by which water is transported into and out of cells
- Difference in concentration between solutions on either side of semi permeable membrane called Osmotic gradient

- For osmosis potential water molecule have to move is called osmotic potential. Distilled water has the highest potential ( Zero)
- When water has another substance dissolved in it , the water molecules have have less potential to move. Then the osmotic potential is called negative.
- The osmotic potential of a cell is known as its water potential. For a animal cell the water potential is the osmotic potential of the cytoplasm.