Physiology

nervous system & endocrine system have control of our bodies to keep it in homeostasis .

nervous system has an immediate action & endocrine system has prolonged & delayed action .

	Nervous System	Endocrine System
Mechanism of Control	Neurotransmitters released in response to nerve impulses	Hormones delivered to tissues throughout the body by blood
Cells Affected	Muscle cells, gland cells, other neurons	Virtually all body cells
Type of action that Results	Muscular contraction or glandular secretion	Changes in metabolic activities whether it was anabolism or catabolism
Time to onset of action	Typically, within milliseconds It is usually fast	Seconds to hours or days. It is usually delayed and takes days “throughout life“. But sometimes when in need, it is immediate and takes seconds to hours.
Duration of action	Generally briefer	Generally longer

Endocrine • No ducts • Secrete hormones into blood

Autocrine produces hormone that affect the same cell

Paracrine produces hormone that affect the neighboring cells

Neuroendocrine are represented by neurons

Pheromonal : hormones are volatile, and affect nearby individuals

In skeletal muscles; Insulin: stimulates glucose uptake, glycolysis, glycogenesis, inhibits glycogenolysis, stimulates amino acids uptake, stimulates protein synthesis, and inhibits protein degradation.

Some hormones are known to have different effects on different types of tissues • Example: testosterone "the male sex steroid" promotes normal sperm formation in the testes, stimulates the growth of accessory sex glands such as prostate and seminal vesicles, and promotes the development of several secondary sex characteristics such as beard growth and deepening of the voice.

A single hormone may be secreted by more than one endocrine gland • Example: hypothalamus and pancreas, both secrete the hormone somatostatin

Several different hormones including insulin, glucagon, epinephrine, thyroid hormones, and adrenal cortisol may regulate liver glycogen metabolism.

Target cells can change the number of receptors.
• Desensitization The chronic exposure of a cell to a hormone may cause the cell to become less responsive to that hormone
• homologous desensitization exposure of a cell to a specific hormone causes a desensitizing effect on the action of the same hormone
• heterologous desensitization exposure of a cell to a specific hormone causes a desensitizing effect on the action of a different hormone
• Sensitization

Some of the glands produce only hormones while others have other functions (mixed organs)

effect of hormones

blood circulation	regulate blood pressure by altering cardiac output, vascular constriction, and blood volume via the control of water excretion by the kidneys
transport of substrates to tissues (blood composition)	regulate blood plasma concentrations of glucose, minerals (e.g. sodium, potassium, calcium), gases (oxygen, carbon dioxide), blood cells, water, and hydrogen ions (pH regulation)
defence against pathogens	regulate immune system responses, including leucocyte activation, inflammation, antibody production, and fever

structure of hormones: Proteins , Amino acid derivatives , Steroids

Feedback control

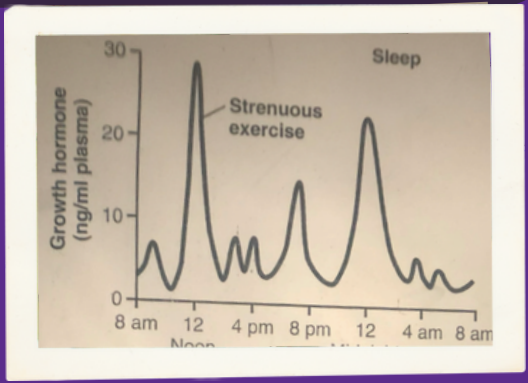
Hormone-hormone
Substrate-hormone
Mineral-hormone

Negative feedback reverse the stimulus

positive feedback more stimulus

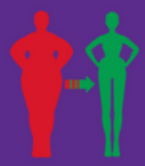
Neural Control Pain, emotion, sexual excitement, fright, injury, and stress; all can affect hormone secretion

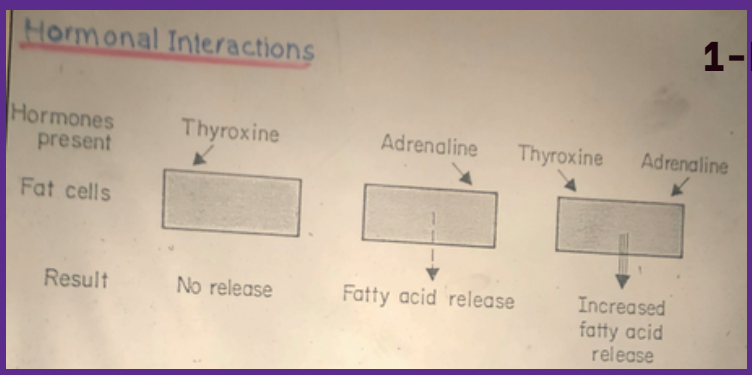
Chronotropic Control :duration and timing of secretion • Oscillating patterns • Pulsatile patterns • Diurnal rhythm "Sleep-wake rhythm" • Menstrual rhythm • Seasonal rhythm • Developmental rhythm



Receptors Regulation :
Up regulation // Sensitization : Low stimulation causes an increase in the number and affinity of the receptors .
Down regulation // Desensitization: High stimulation causes a decrease in the number and affinity of the receptors

Receptors Regulation : treatment of Diabetes Meletus (Type 2) Exercise, good diet, and weight loss





1-Permissive hormonal interaction

Thyroxine → Fat cell → No release of FA
Adrenaline → Fat cell → Little release of FA
Thyroxine + Adrenaline → High release of FA

the effect of one hormone on a target cell requires a previous or simultaneous exposure to another hormone

2-Synergism : hormones complement each other

Estrogen, Progesterone, Prolactin and Oxytocin → Proper milk production

3-Antagonism

Opposite effects

PTH → increases Calcium. Calcitonin → decreases Calcium
Insulin → decreases Glucose. Glucagon → increases Glucose

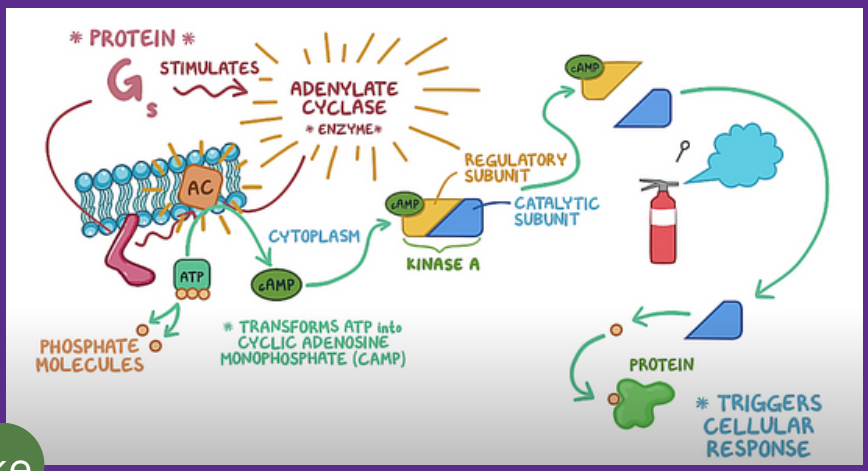
Hormone receptors

- Cell-surface receptors

for protein hormones and catecholamines
Cannot pass the plasma membrane
Needs second messenger

- Cytoplasmic (or nuclear) receptors

for steroid and amino acid derived hormones (except catecholamines)
Can pass the plasma membrane



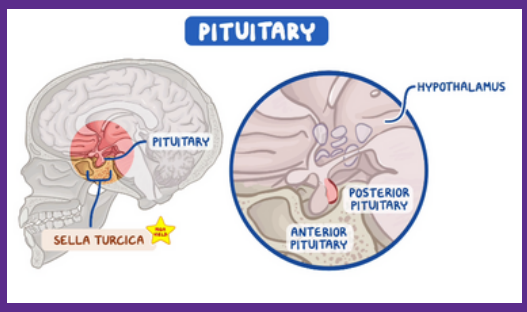
Cell Surface + Adenylyl cyclase like

Adrenocorticotropic hormone (ACTH)
Angiotensin II (epithelial cells)
Calcitonin
Catecholamines (β receptors)
Corticotropin-releasing hormone (CRH)
Follicle-stimulating hormone (FSH)
Glucagon
Human chorionic gonadotropin (HCG)
Luteinizing hormone (LH)
Parathyroid hormone (PTH)
Secretin
Somatostatin
Thyroid-stimulating hormone (TSH)
Vasopressin (V_2 receptor, epithelial cells)

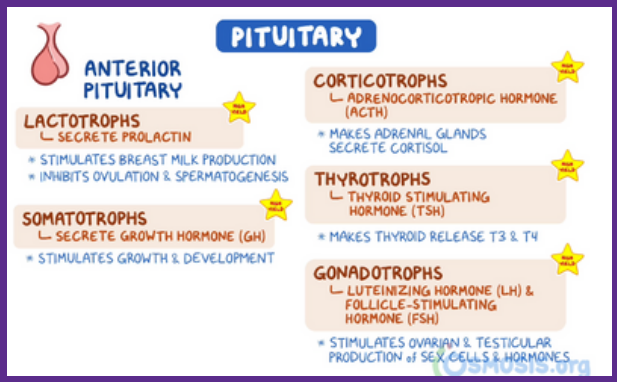
Cell Surface + Phospholipase C

- Examples:
- Angiotensin II
- Gonadotropin-releasing hormone (GnRH)
- Growth hormone-releasing hormone (GHRH)
- Thyrotropin releasing hormone
- Oxytocin
- Vasopressin (V1 receptors)
- Catecholamines (α receptors)

pituitary gland



Composed of two parts; each has different embryology, histology and physiology:
1. Anterior Pituitary [Adenohypophysis]
glandular tissue
2. Posterior Pituitary [Neurohypophysis]
nervous tissue
Posterior Pituitary Hormones
[1] Oxytocin delivery & milk ejection
[2] Antidiuretic Hormone (ADH) or Vasopressin Water reabsorption & vasoconstriction
Similar in structure (differ in just 2 amino acids)
Synthesized by Nuclei in the Hypothalamus
1. Paraventricular nucleus mainly oxytocin and a little bit of ADH
2. The Supraoptic nucleus mainly ADH and a little bit of oxytocin



Anterior Pituitary :Not directly connected with the hypothalamus
1. Growth Hormone (GH) Somatotrophs
2. Adrenocorticotropic hormone (ACTH) Corticotropes
3. Prolactin (PRL) Lactotrophs (Mammotropes)
4. Thyroid-stimulating hormone (TSH) Thyrotropes
5. Luteinizing hormone (LH) Gonadotrophs
6. follicle-stimulating hormone (FSH) Gonadotrophs

30-40% of the anterior pituitary are somatotrophs that secrete growth hormone while 20% are corticotropes

pituitary gland hormones - GH

Growth Hormone :

• Secreted by Somatotrophs in the Anterior Pituitary • Increases the growth of the cells & the number of cells (which are capable to grow) • Affects almost all body cells .

growth hormone (GH), insulin – like growth factors (IGF-I and -II), insulin, thyroid hormones, Glucocorticoids, androgens & estrogens contribute to the growth process in humans . GH & IGF-I have been implicated as the major determinants of growth in normal post-uterine life.

Combination of GH and insulin → Much growth.

Direct Effects

1. Adipose Tissue Decreases adiposity, (by increasing lipolysis and decreasing the glucose uptake)

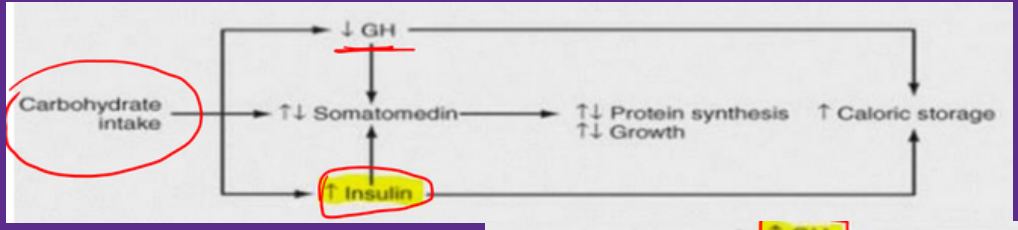
2. Liver a) Increases RNA synthesis to increase protein production b) Increases the rate of protein synthesis c) Increases Gluconeogenesis d) Stimulate production of Somatomedins "insulin-like growth hormones" (IGF)

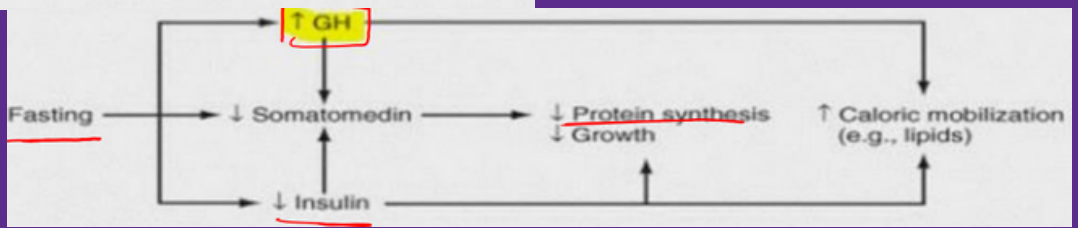
3. Muscle Tissue a) decrease glucose uptake. b) increase amino acid uptake. c) increase protein synthesis

Indirect Effects IGF → increase in organ size and function (growth)

Metabolic Effects of Growth Hormone 1. Increase the rate of protein synthesis 2. Increase mobilization of fatty acids from adipose tissue & increased its oxidation to produce energy 3. Decrease the rate of glucose utilization throughout the body Net effect: Growth hormone enhances the body protein, uses up the fatty stores and conserves carbohydrates GH ↑ Glu – Insulin ↓ Glu = (normalize the blood glucose level) It also stimulates beta cells to produce insulin Abnormally high GH → Diabetes (diabetogenic)

• Increases the free fatty acids in the blood by increase the lipolysis • Fatty acids concentration increases in body fluids • Under the excessive of GH, great amount of fat is mobilized • ketogenic effect





Factors Affecting The Secretion of GH

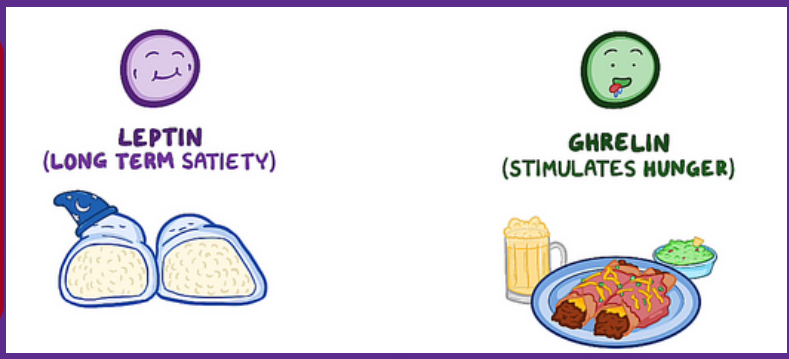
Developmental Rhythm • GH secretion levels are higher in children than adults with a peak period during puberty • GH declines with aging .

Sleep - wake cycle (diurnal Rhythm)

Stimulate Growth Hormone Secretion	Inhibit Growth Hormone Secretion
Decreased blood glucose	Increased blood glucose
Decreased blood free fatty acids	Increased blood free fatty acids
Increased blood amino acids (arginine)	Aging
Starvation or fasting, protein deficiency	Obesity
Trauma, stress, excitement	Growth hormone inhibitory hormone (somatostatin)
Exercise	Growth hormone (exogenous)
Testosterone, estrogen	Somatomedins (insulin-like growth factors)
Deep sleep (stages II and IV)	Increased blood glucose
Growth hormone–releasing hormone	Increased blood free fatty acids
Ghrelin	Aging

Control of Food Intake

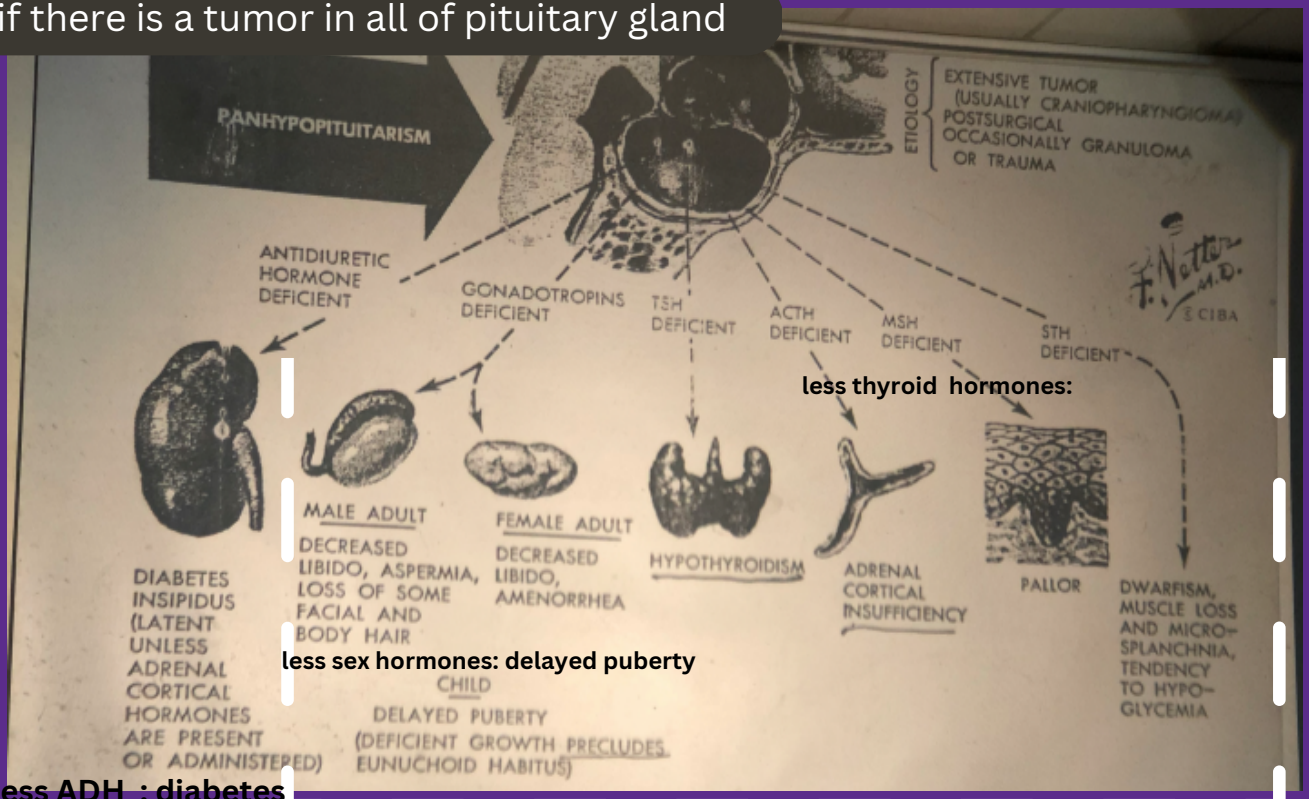
- **Stomach stretch receptors → satiety**
- **Leptin → Satiety**
- **CCK, insulin, → Satiety**
- **Ghrelin → Hunger**



Hormones abnormalities

- **Panhypopituitarism → ↓ all pituitary hormones**
- **↓ ADH → more water secretion → Diabetes insipidus**
- **↓ Oxytocin → no clear effects**
- **↓ FSH & LH → ↓ Libido + (aspermia, ↓body hair) in males (Amenorrhea) in females**
- **↓ TSH → 2^ hypothyroidism**
- **↓ ACTH → adrenal cortex insufficiency**
- **↓ MSH → pallor**

if there is a tumor in all of pituitary gland



less thyroid hormones:

less sex hormones: delayed puberty

less ADH : diabetes insipidus

when the tumor is just in the (anterior) adeno part , only these are affected.

anterior pituitary deficiency

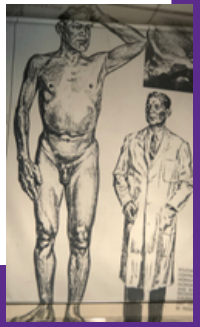
severe : all hormones are deficient

modorate : all hormones are deficient except STH normal : normal growth

mild : all hormones are normal except gonadotropins (sex hormones)

Gigantism

all bone will grow rapidly , height 8-9 feet , 10% hyperglycemia , diabetic , without treatment there will be a panhypopituitarism (all the pituitary)

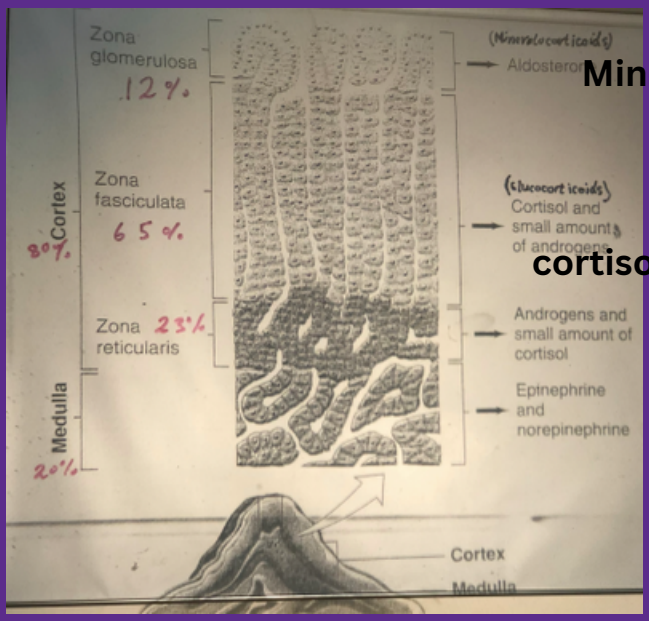


Acromegaly

not taller

ADRENAL GLAND

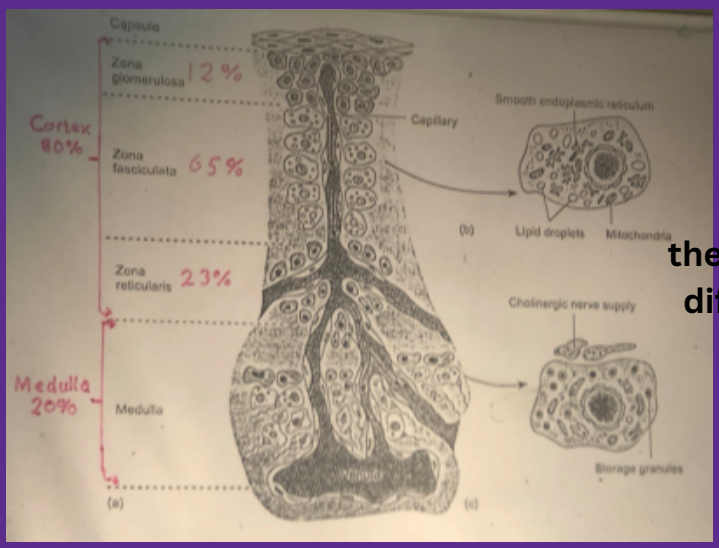
one should be sufficient , blood supply directly from aorta , consists of cortex and medalla .
cortex is more important, patient can't live without it



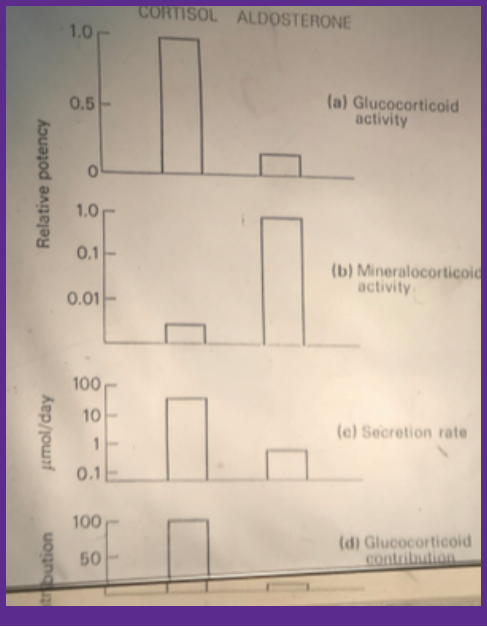
Minerales

cortisol & androgen

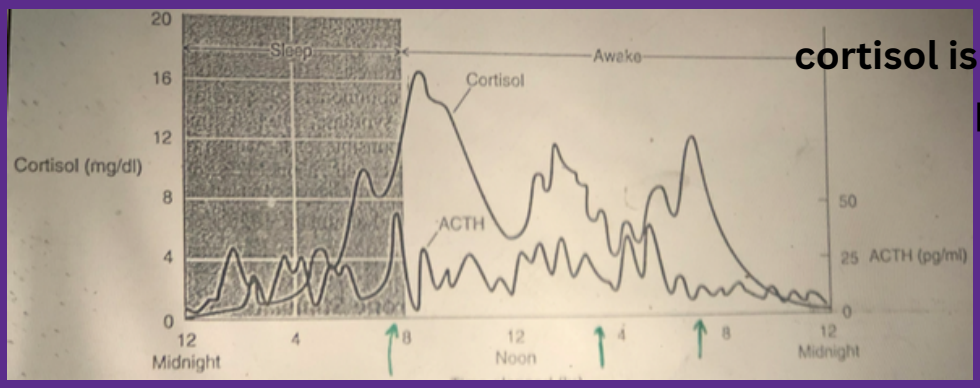
adrenal gland gets stimulated by ACTH from pituitary gland



the zona of reticularis does not fully differentiated until 6-8 years old .



A comparison of cortisol and of aldosterone. Glucocorticoid activity was measured as ability to increase glycogen in the liver: cortisol is very potent in this assay Mineralocorticoid effects were measured in terms of the ability to reduce the ratio of the excretion of sodium to the excretion of potassium in urine; aldosterone is much more potent However, since the rate of secretion of cortisol is much higher, it can have significant mineralocorticoid effects



cortisol is more than ACTH when the person is awake .

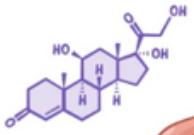
Table 5.4.2 Plasma protein binding of corticosteroids

	Cortisol (%)
Corticosteroid-binding protein (CBG)	90
Albumin	6

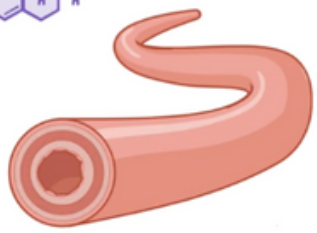
cortisol work freely , so depending on the image there is 4% are free and making effect

magic drug

CORTISOL



* STRESS HORMONE
  - ↳↑ GLUCONEOGENESIS
  - ↳PROTEOLYSIS
  - ↳LIPOLYSIS
  - –MAINTAIN BLOOD PRESSURE
    - CATECHOLAMINES - EPINEPHRINE & NOREPINEPHRINE
    - NARROWS BLOOD VESSEL LUMEN
  - –DAMPENS INFLAMMATORY & IMMUNE RESPONSE
    - REDUCE PRODUCTION and RELEASE of PROSTAGLANDINS and INTERLEUKINS
    - INHIBITS PROLIFERATION of T-LYMPHOCYTES
  - –RECEPTORS PRESENT IN BRAIN



Glucocorticoids

- Cortisol (very potent, accounts for about 95 per cent of all glucocorticoid activity)
- Corticosterone (provides about 4 per cent of total glucocorticoid activity, but much less potent than cortisol)
- Cortisone (synthetic, almost as potent as cortisol)
- Prednisone (synthetic, four times as potent as cortisol)
- Methylprednisone (synthetic, five times as potent as cortisol)
- Dexamethasone (synthetic, 30 times as potent as cortisol)

is 30times more potent one

The adrenal cortex produces stomids that regulate Na and K balance (mineralocorticoids), steroids that regulate glucose balance (glucocorticoide), and small amounts of sex steroid hormones

Table 5.4.2 Plasma protein binding of corticosteroids

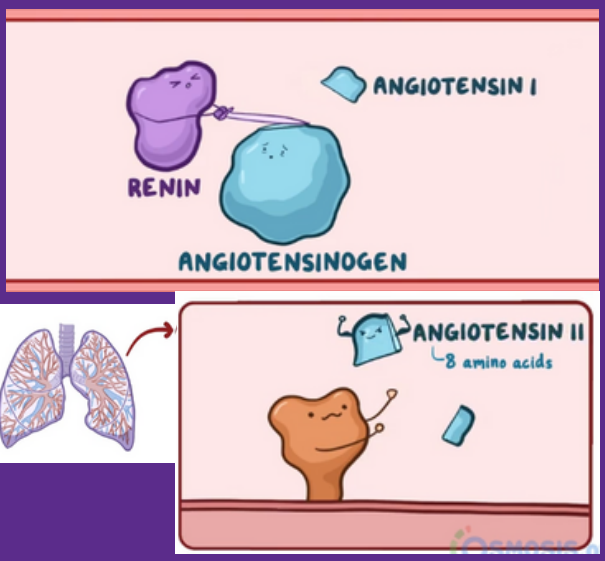
	Aldosterone (%)
Corticosteroid-binding protein (CBG)(Transcortin)	20
Albumin	40

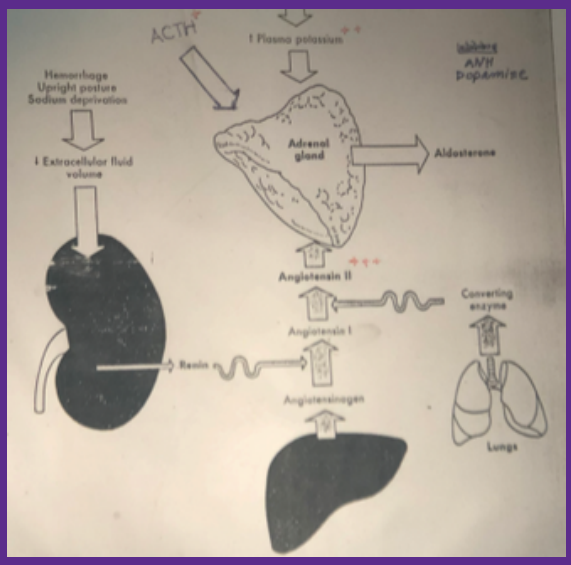
40% free in blood

Mineralocorticoids

- Aldosterone (very potent, accounts for about 90 per cent of all mineralocorticoid activity)
- Desoxycorticosterone (1/30 as potent as aldosterone, but very small quantities secreted)
- Corticosterone (slight mineralocorticoid activity)
- 9α-Fluorocortisol (synthetic, slightly more potent than aldosterone)
- Cortisol (very slight mineralocorticoid activity, but large quantity secreted)
- Cortisone (synthetic, slight mineralocorticoid activity)

Renin-angiotensin-aldosterone system



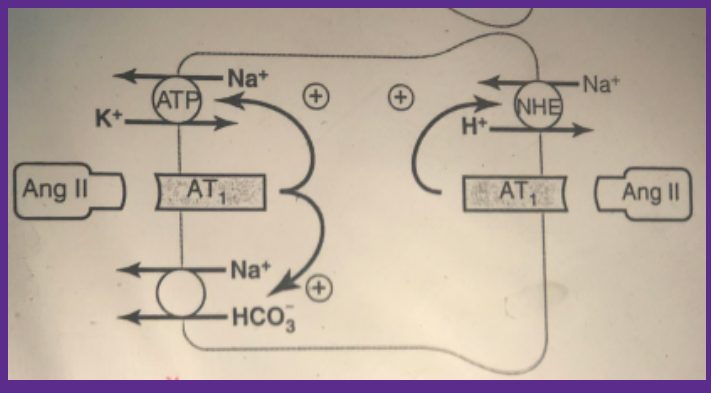


angiotensin II formation increases associated with low blood pressure and/or low extracellular fluid volume, such as during hemorrhage or Joss of salt and water from the body fluide by excessive sweating or severe diarrhea , he increased formation of angiotensin II helps to return blood pressure and extra cellular volume toward normal by increasing sodium and water reabsorption from the renal tubules through three main effects

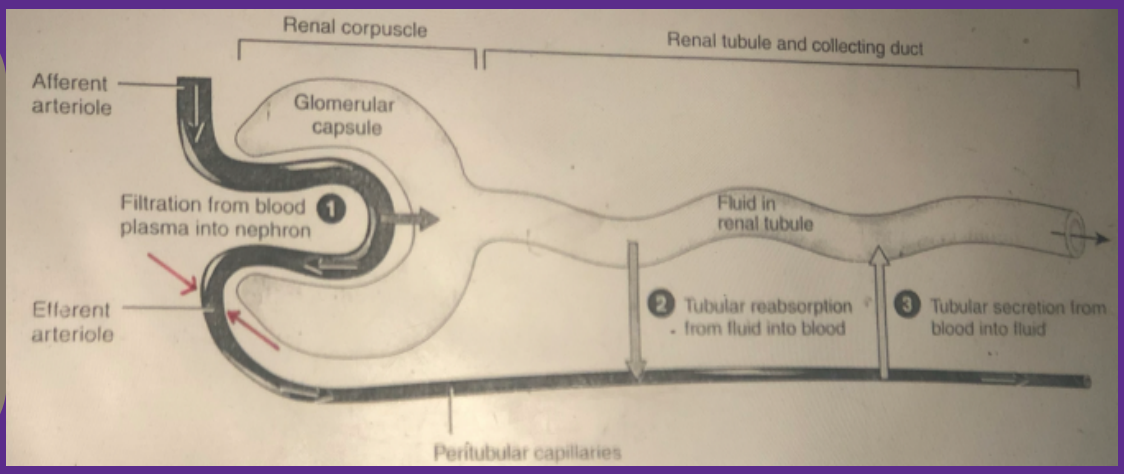
1. Angiotensin II stimulates aldosterone secretion, which in turn increases sodium reabsorption
2. Angiotensin constructs the offerent arterioles, which has two effects on peritubular capillary dynamies that increase sodium and water reabsorption

direct :

effect angiotensin II (AngII) to increase proximal tubular sodium reabsorption. Ang II stimulates sodium sodium-hydrogen exchange (NHE) on the luminal membrane and the sodium-potassium ATPase transporter as well as sodium-bicarbonate co-transport on the basolateral membrane



indirect :
Sodium excretion rises, there is a fall in blood-pressure, and plasma concentrations of angiotensin II (AII) and aldosterone are reduced.



aldosterone affects : slaivary glands , sweat glands , intestants and renal tubules

Androgens & Estrogens

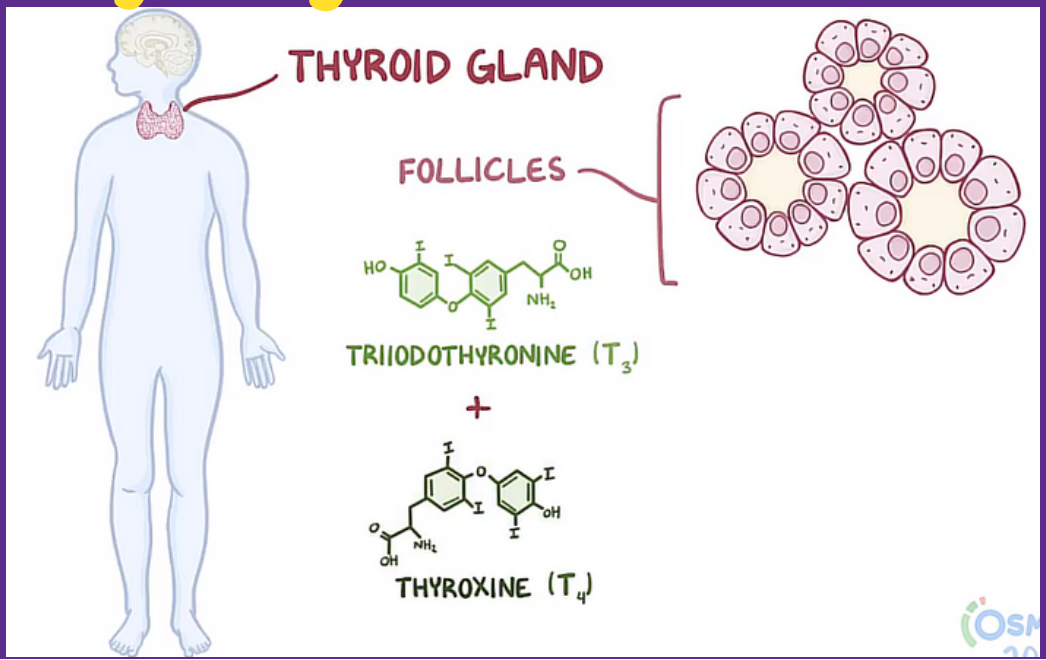
- Weak androgens:
- dehydroepiandrosterone
- androstenedione
- Strong androgens:
- Testosterone
- Dihydrotestosterone (the strongest)
- Estrogens:
- Estradiol
- Estrone
- Estriol

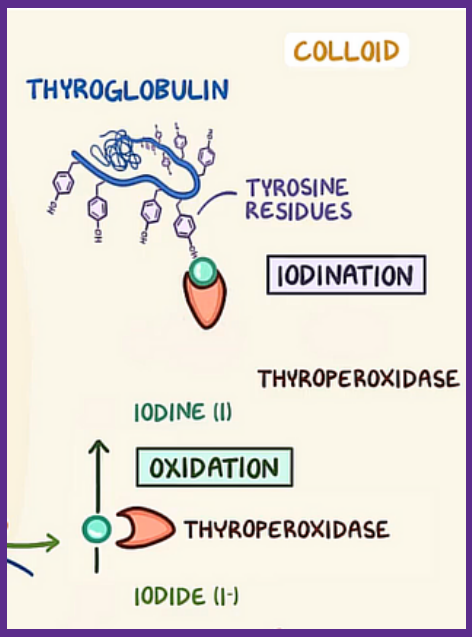
Androgens Function

- In males → Secondary sexual characteristics & Spermatogenesis
- *In females → pubic & axillary hair, libido*

Adrenal androgens are more important in females because in males, they are secreted also by the testes

thyroid gland



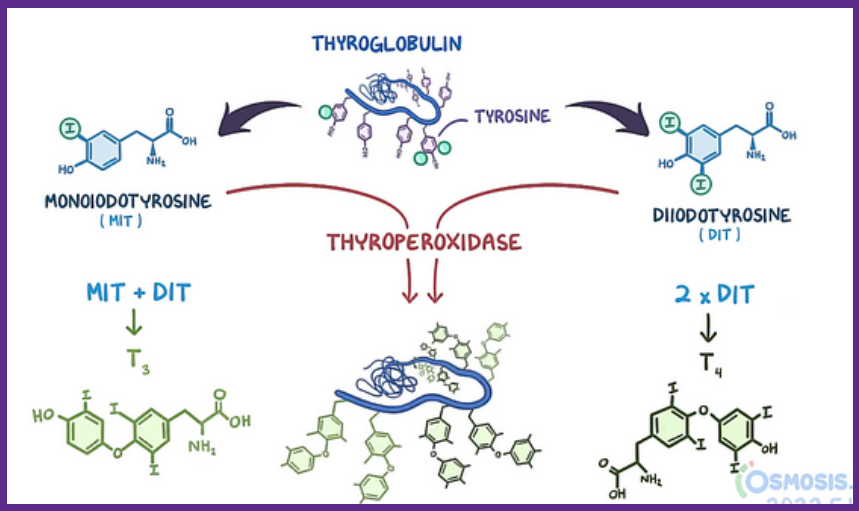


Once iodide is in the colloid, it undergoes oxidation with the enzyme thyroperoxidase, which changes it into an iodine atom.

It's then attached to tyrosine amino acid residues which are found throughout thyroglobulin.

This process is called iodination.

Some tyrosine residues are bound by only one iodine, whereas others are bound by two iodine atoms, yielding monoiodotyrosine or MIT, and diiodotyrosine or DIT, respectively.
These molecules are then linked together by thyroperoxidase.



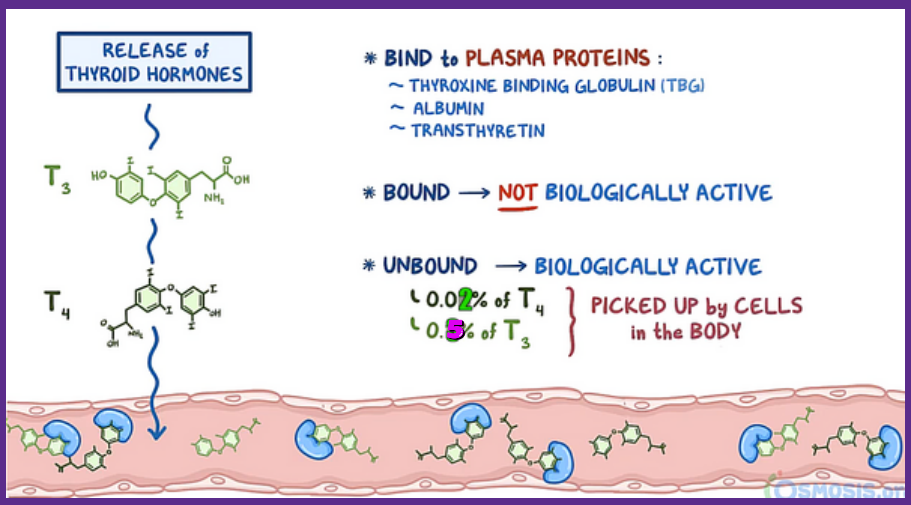
Linking one MIT with one DIT creates T3, while linking two DIT molecules creates T4 - and both T3 and T4 remain bound to thyroglobulin.

You see - thyroglobulin basically serves as a peptide that stores these hormones on it in the colloid, until it's ready to be used. T4 is created in greater amounts than T3.

Once released from the thyroid gland, T3 and T4 enter the blood and bind to circulating plasma proteins - the most important one being thyroxine binding globulin or TBG, but they also bind to albumin and transthyretin.

Bound T3 and T4 acts like a reservoir of hormone that's not biologically active.

In fact, only a small amount of T3 and T4 will travel unbound in the blood - about 0.02% of T4 and 0.5% of T3 - and this fraction is biologically active, which means that this is what gets picked up by virtually every cell in the body.



from slide num 18

https://quizlet.com/_cek8qv?x=1jqt&i=4golfd

good luck

Thyroid Gland

99.9% of hormone is protein.

T4 or T3 bind to plasma protein to maintain blood pressure and avoid filtration.

T4 is a prohormone for T3 and rT3, the only active form is T3, affects metabolism, growth and development of fetus.

T3 consists of thyroglobulin and iodide so any deficiency of iodide will inhibit its secretion.

hormones affect growth: GH, insulin, thyroid hormones, estrogen, cortisol and androgen.

excess hormones don't affect growth but increase catabolism.

reduced thyroid hormone activity in children produce dwarfs with mental retard.

	cretin	myxoedema
age	children	adults
symptoms	failure of skeletal, congenital (sexual) and mental	slowing of all bodily processes

symptoms of hyperthyroidism : exophthalmos and goiter which could be large malignant= high T4&T3 or small benign = low T4&T3 .

Parathyroids Gland

BLOOD CALCIUM LEVEL 11/100 mL plasma (less or more the patient dies).

all most all PTH are produced by chief cells (not the only source, there is more).

PTH stimulate cAMP production.

pthrP stimulate cAMP production AS WELL AS intracellular calcium mobilization.

hypocalcemia cause tetany by letting sodium channels opened.

all muscles can be tetanized except cardiac muscle because it can't get another stimulus without finishing the mechanical effect of the first one.

the effect of PTH is on synovial fluid not the real bone, but if there is an overactivity of PTH = calcium blood level raised = osteitis fibrosa cystica. (لين العظام)

Vitamin D

is hormone D3 (from skin) and vitamin D2 (from diet).

two of them are not enough for body, so we need two of them in blood together.

1-25 D3 = is the strongest one.

most of vitamin D is stored in fat (men with central fat have difficulty in release the vitamin from tissue) . which lead to symptoms in spring .

the vitamin is required for blood clotting .

calcium has the highest percentage of bone Contant , distributed as ionized and increased in acidosis and abundant in intestine .

Calcitonin

it is **Synergism with PTH .**

RICKETS

IN INDOOR CHILDREN , OCCUR IN SPRING BECAUSE OF STORED VITAMIN D .

Poliovirus CAN AFFECT ADULTS .

Pancreas

- The secretion of hormones from the pancreas is stimulated by: 1. Food intake
- 2. Gastrointestinal hormones.
- Beta cells: 75%, secrete Insulin, Proinsulin , C peptide, Amylin.
- Amylin which is produced along with Insulin as a neuroendocrine hormone that complements the action of insulin in postprandial glucose homeostasis via several mechanisms.
- Insulin composed of two chains: A chain which is 21 amino acids. B chain which is 30 amino acids and it's the active chain. connected through disulfide bridges.
- Insulin and C peptide are secreted equally, which help us clinically to calculate excreted insulin and exogenous Insulin.
- the liver doesn't extract C peptide.
- Insulin is the only HYPOGLYCIMIC (sends glucose to cells) , Glucagon is the most important HYPERGLYCEMIC (from cells to blood) .
- there is No disulfide linkage lying directly between the two beta subunits.
- glucose, obesity stimulate insulin.
- ca+ is needed to excrete insulin .
- normal glucose level 80-100 .
- glucose around 50 mg/dL there is almost no secretion of Insulin.
- Sensing a rapid rise in plasma glucose concentration, the beta cells first secrete their stores of presynthesized insulin. Following this acute phase, the cells begin to secrete newly synthesized insulin in the chronic phase, which lasts as long as the glucose challenge .
- Brain (except probably part of hypothalamus) , Kidney tubules, Intestinal red blood cells don't need insulin to facilitate glucose uptake (a protection for patient who can't excrete or response to insulin , so they can live 😁) .
- when plasma glucose is 70, it goes to all cells normally but less to kidney.
- when plasma glucose is 300 , it isn't going to be stored in fat or muscle and increase its secretion from liver and kidney. (Liver gives glucose more than what it takes)
- diabetes mellites = hyperglycemia = genetic and environmental = Symptoms usually include frequent urination, increased thirst, increased food consumption, and weight loss.
- diabetes mellites =when there is no glucose = body depends totally on fats (Triglycerides) , then ketone bodies , then protein catabolism which leads to acidosis then coma or death .
- doctor said if the patient in coma and you can't measure his glucose level , what would you do ? (give him candy (glucose) even though he could be having hyperglycemia) **yes** you do that , hypoglycemia is more dangerous than hyperglycemia .
- lactic acidosis may itself cause coma .
- in mild cases, diet, weight loss, and exercise can be extremely effective in diabetes therapy .
- The available oral antidiabetic agents can be divided by mechanism of action into:

- 1. Insulin sensitizers with primary action in the liver (e.g. biguanides).

Insulin sensitizers: Facilitate the action of insulin in the liver.

- 2. Insulin sensitizers with primary action in peripheral tissues (e.g. glitazones).
- 3. Insulin secretagogues which stimulate beta cells to secrete more insulin

(e.g. sulfonylureas).

- 4. Agents that slow the absorption of carbohydrates (e.g. alpha- glucosidase

inhibitors).

BMI

One approach for gauging the extent to which human body mass is appropriate for body height is to compute the body mass index (BMI):

$$BMI = \frac{\text{Weight (kg)}}{\text{Height (m)}^2}$$

BMIs fall into four major categories:

1. Underweight: less than 18.5
2. 2. Normal weight: 18.5 – 24.9
3. Overweight: 25 – 29.9
4. Obesity: 30 or more