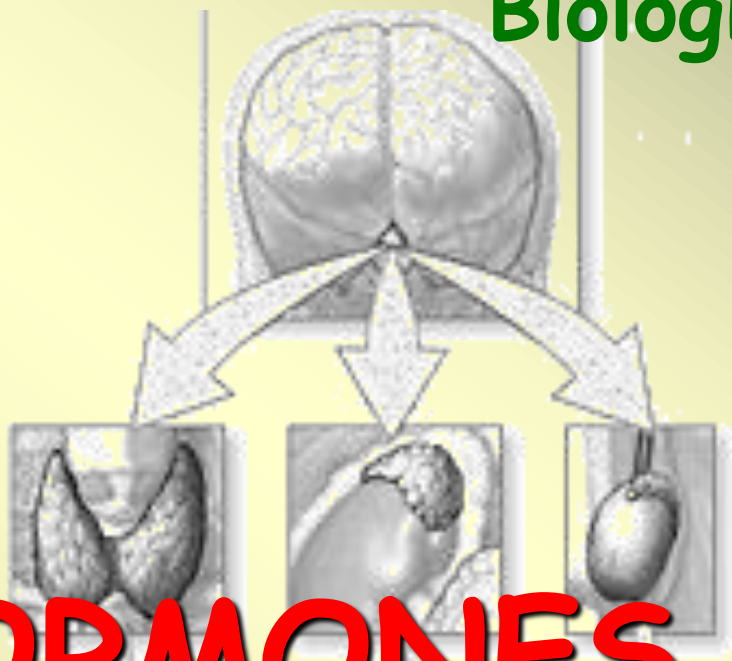




# Biological Chemistry Department Biological Chemistry



# HORMONES AND NEUROMEDIATORS

Speciality: Pharmacy for foreign students (Language of instructions - English)

Lecturer: ass. prof. Kravchenko G.B.



# Lecture Plan

1. **General Characteristics of Endocrine System.**
2. **General Mechanisms of the Hormone Action.**
3. **Hypothalamic Hormones.**
4. **Pituitary Hormones.**
5. **Pineal Gland Hormones.**
6. **Adrenal Medullary Hormones.**
7. **Adrenal Cortical Hormones.**
8. **Pancreatic Hormones.**
9. **Hormones of Thyroid and Parathyroid glands.**
10. **Hormones of the Reproductive Systems.**

## Individual work

1. **Neuromediators: Structure and Functions.**

# Information Resources

1. *Biological Chemistry: Textbook* / A.L. Zagayko, L.M. Voronina, G.B. Kravchenko, K.V. Strel`chenko. - Kharkiv: NUPh; Original, 2011. - 212-238 p.
2. *Training Journal for Licensed Exam "KROK-1": Study Material in Biological Chemistry*. - Kharkiv: NUPh, 2017. - 143-172 p.
3. *Laboratory Manual on Biochemistry*. Kharkiv: NUPh, 2017. - 69-71 p.
4. *Table of Major Human Hormones: Water and Fat Soluble: The Medical Biochemistry Page*. Available on:  
<https://themedicalbiochemistrypage.org/hormone-table.php>.
5. *Steroid Hormones and Receptors: The Medical Biochemistry Page*. Available on:  
<https://themedicalbiochemistrypage.org/steroid-hormones.php>.
6. *Peptide Hormones and Receptors: The Medical Biochemistry Page*. Available on:  
<https://themedicalbiochemistrypage.org/peptide-hormones.php>.

# HORMONES

Hormones are your body's chemical messengers. They travel in your bloodstream or lymph to tissues and organs. They work quickly or slowly, over time, and affect many different processes, including:

- ✓ Growth and development
- ✓ Metabolism - body gets energy from the foods you eat
- ✓ Sexual function
- ✓ Reproduction
- ✓ Mood

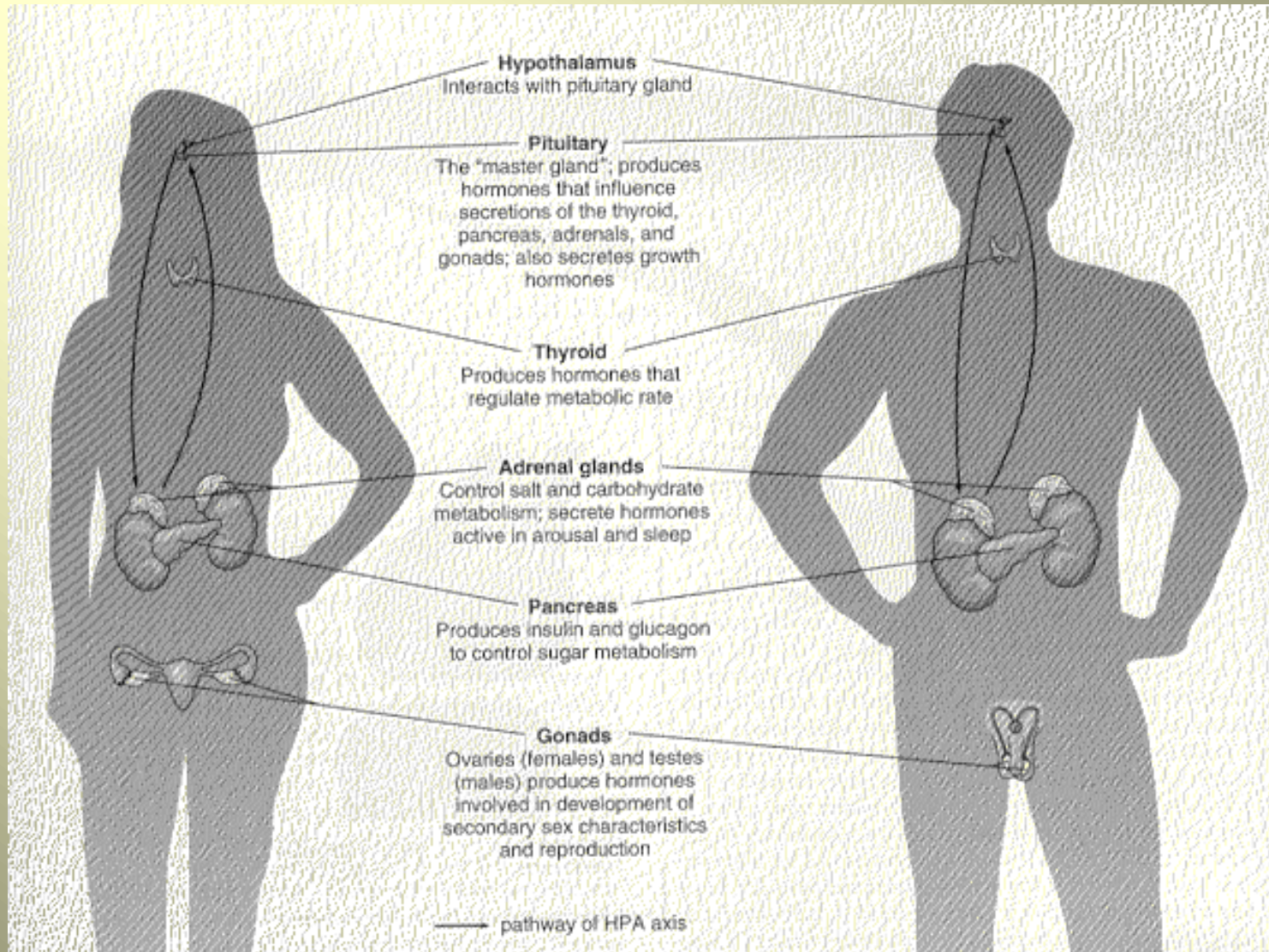


Endocrine glands, which include special groups of cells, produce hormones. The major endocrine glands are the hypothalamus, pineal, thymus, thyroid, adrenal glands and pancreas. In addition, men get sexual hormones primarily from their testes and women - from their ovaries.

Hormones are powerful. It takes only a tiny amount to cause great changes in a cell or even in the whole body. That is why too much or too little of a certain hormone can be a serious factor of influence.



# The endocrine system



*The main hormones produced in humans and the diseases and conditions associated with imbalance in their production*

<b>Endocrine Gland</b>	<b>Location/Description</b>	<b>Hormones Gland Produces</b>	<b>Examples of Disorders Associated with Improper Function</b>
<i>Hypothalamus</i>	<i>Lower middle of the brain</i>	<i>Growth hormone-releasing factor; Thyrotropin-releasing factor; Corticotropin-releasing factor; Gonadotropin-releasing factor; Prolactin Inhibitory Factor and some others</i>	<i>Precocious puberty (early GnRF production); Thyroid diseases</i>
<i>Pituitary</i>	<i>Below hypothalamus, behind sinus cavity</i>	<i>Prolactin, Growth Hormone, ACTH, TSH, LH, FSH and some others</i>	<i>Galactorrhea (milk production not during pregnancy due to high prolactin); Acromegaly or Gigantism; Cushing's disease (excess ACTH); Loss of menstrual period; Loss of sex drive</i>

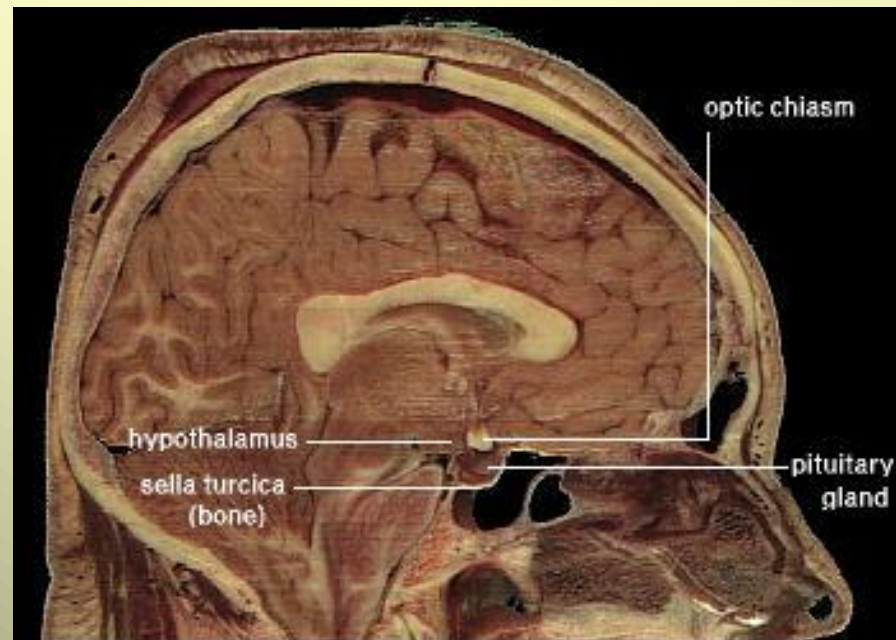
<b>Endocrine Gland</b>	<b>Location/Description</b>	<b>Gland Produces Hormones</b>	<b>Examples of Disorders Associated with Improper Function</b>
<i>Thyroid</i>	<i>Butterfly-shaped</i>	<i>T4 (thyroxine); T3 (triiodothyronine); Calcitonin</i>	<i>Thyroid diseases</i>
<i>Para thyroid</i>	<i>Behind, next to, or below the thyroid</i>	<i>Calcitonin; Parathyroid hormone</i>	<i>Hyperparathyroidism; Hypoparathyroidism</i>
<i>Adrenal</i>	<i>On top of each kidney</i>	<i>Epinephrine; Norepinephrine; Aldosterone; Cortisole</i>	<i>Pheochromocytoma; Addison's Disease</i>
<i>Ovaries</i>	<i>In the pelvis</i>	<i>Estrogen; Progesterone</i>	<i>Polycystic ovary syndrome</i>
<i>Testes</i>	<i>In the groin</i>	<i>Testosterone</i>	<i>Hypogonadism</i>
<i>Pancreas</i>	<i>Behind the stomach</i>	<i>Insulin; Glucagon; Somatostatin</i>	<i>Diabetes mellitus</i>



# HORMONES OF THE CENTRAL ENDOCRINE GLANDS

## *Hypothalamus and Pituitary Gland*

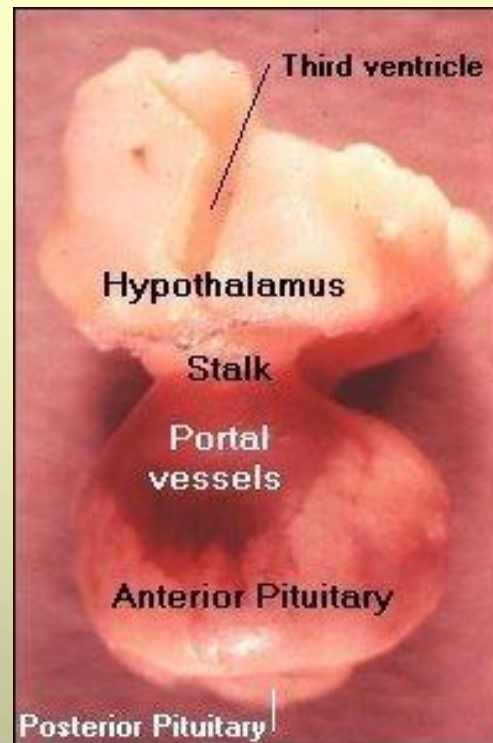
*The hypothalamus is a region of the brain that controls an immense number of body functions. It is located in the middle of the base of the brain, and encapsulates the ventral portion of the third ventricle. The pituitary gland, also known as hypophysis, is a roundish organ that lies immediately beneath the hypothalamus, resting in a depression of the base of the skull called the sella turcica ("Turkish saddle").*





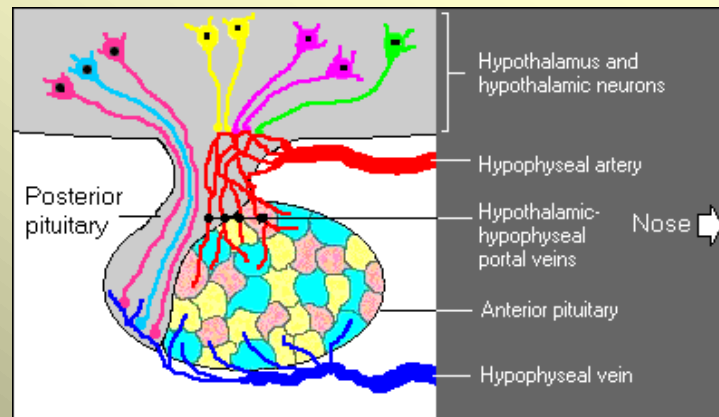
Careful examination of the pituitary gland reveals that it is composed of two distinctive parts:

- ✓ **the anterior pituitary** or adenohypophysis is a classical gland composed predominantly of cells that secrete protein hormones;
- ✓ **the posterior pituitary** or neurohypophysis is not really an organ, but an extension of the hypothalamus. It is composed largely of the axons of hypothalamic neurons which extend downward as a large bundle behind the anterior pituitary. It also forms the so-called pituitary stalk, which appears to suspend the anterior gland from the hypothalamus.



A key to understanding the endocrine relationships between hypothalamus and anterior pituitary is to appreciate the vascular connections between these organs. Secretion of hormones from the anterior pituitary is under the strict control of the hypothalamic hormones. These hypothalamic hormones reach the anterior pituitary through the following routes:

- ✓ a branch of the hypophyseal artery ramifies into a capillary bed in the lower hypothalamus, and hypothalamic hormones destined for the anterior pituitary are secreted into that capillary blood;
- ✓ blood from those capillaries drains into the hypothalamic-hypophyseal portal veins. Portal veins are defined as veins between two capillary beds; the hypothalamic-hypophyseal portal veins branch again into another series of capillaries within the anterior pituitary.
- ✓ capillaries within the anterior pituitary, which carry hormones secreted by that gland, coalesce into veins that drain into the systemic venous blood. Those veins also collect capillary blood from the posterior pituitary gland.



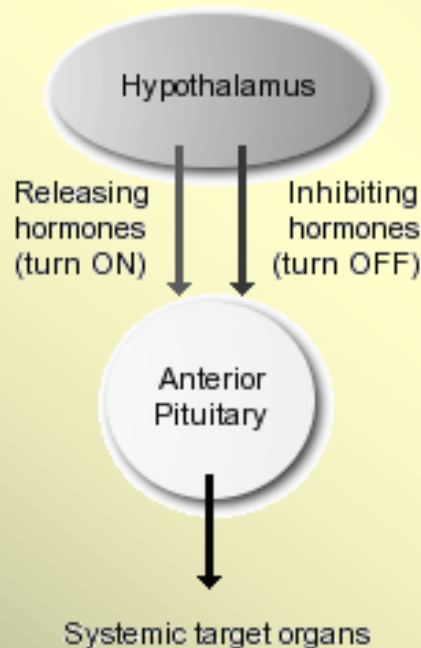
The pituitary gland is often portrayed as the "master gland" of the body. Such praise is justified in the sense that the anterior and posterior pituitary secrete a group of hormones that collectively influence all cells and affect virtually all physiologic processes.

The pituitary gland may be a king, but the power behind the throne clearly belongs to the hypothalamus. As alluded to in the last section, some of the neurons within the hypothalamus - neurosecretory neurons - secrete hormones that strictly control secretion of hormones from the anterior pituitary. The hypothalamic hormones are referred to as **releasing hormones** and **inhibiting hormones**, reflecting their influence on anterior pituitary hormones.

Hypothalamic releasing and inhibiting hormones are carried directly to the anterior pituitary gland via the hypothalamic-hypophyseal portal veins. Specific hypothalamic hormones bind to the receptors on specific anterior pituitary cells, modulating release of the hormone they produce.

**As an example**, thyroid-releasing hormone from the hypothalamus binds to the receptors on anterior pituitary cells called thyrotrophs, stimulating them to secrete thyroid-stimulating hormone or TSH. The anterior pituitary hormones enter the systemic circulation and bind to their receptors on other target organs. In the case of TSH, a target organ is the thyroid gland.

Clearly, robust control systems must be in place to prevent over or under-secretion of hypothalamic and anterior pituitary hormones. A prominent mechanism for control of the releasing and inhibiting hormones is a **negative feedback**.





<b><i>Hormone</i></b>	<b><i>Major target organ(s)</i></b>	<b><i>Major Physiologic Effects</i></b>
<b><i>Growth hormone</i></b>	<b><i>Liver, adipose tissue</i></b>	<b><i>Promotes growth (indirectly), control of protein, lipid and carbohydrate metabolism</i></b>
<b><i>Thyroid-stimulating hormone</i></b>	<b><i>Thyroid gland</i></b>	<b><i>Stimulates secretion of thyroid hormones</i></b>
<b><i>Adrenocorticotropic hormone</i></b>	<b><i>Adrenal gland (cortex)</i></b>	<b><i>Stimulates secretion of glucocorticoids</i></b>
<b><i>Prolactin</i></b>	<b><i>Mammary gland</i></b>	<b><i>Milk production</i></b>
<b><i>Luteinizing hormone</i></b>	<b><i>Ovary and testis</i></b>	<b><i>Control of reproductive function</i></b>
<b><i>Follicle-stimulating hormone</i></b>	<b><i>Ovary and testis</i></b>	<b><i>Control of reproductive function</i></b>
<b><i>Antidiuretic hormone</i></b>	<b><i>Kidney</i></b>	<b><i>Conservation of body water</i></b>
<b><i>Oxytocin</i></b>	<b><i>Ovary and testis</i></b>	<b><i>Stimulates milk ejection and uterine contractions</i></b>

# Growth Hormone (GH)

Human GH has about 200 amino acids, 2 disulfide bonds, and no glycosylation.

In humans, growth hormone promotes gluconeogenesis and is consequently hyperglycemic. It promotes amino acid uptake by cells, with the result that GH therapy puts an organism into positive nitrogen balance, similar to that seen in growing children. Finally, growth hormone is lipolytic, inducing the breakdown of tissue lipids and thus providing energy supplies that are used to support the stimulated protein synthesis induced by increased amino acid uptake.

There are a number of genetic deficiencies associated with GH. GH-deficient dwarfs lack the ability to synthesize or secrete GH. The production of excessive amounts of GH before epiphyseal closure of the long bones leads to **gigantism**, and when GH becomes excessive after epiphyseal closure, acral bone growth leads to the characteristic features of **acromegaly**.



## **Prolactin (PRL)**

PRL initiates and maintains lactation in mammals, but normally only in mammary tissue that has been primed with estrogenic.

## **The Gonadotrophins**

The molecular weight of the gonadotrophins (**follicle stimulating hormone, FSH; luteinizing hormone, LH**) is about 25,000 Daltons. All of them are highly glycosylated.

The gonadotrophins bind to cells in the ovaries and testes, stimulating the production of the steroid sex hormones estrogens, testosterone and dihydrotestosterone. In males, luteinizing hormone binds to Leydig cells of the testes to induce the secretion of T, while follicle stimulating hormone binds to Sertoli cells and induces the secretion of T and DHT. In females, LH induces thecal cells to secrete estradiol, and FSH stimulates estrogen synthesis by granulosa cells.

## **Adrenocorticotrophic hormone (ACTH)**

The biological role of ACTH is to stimulate the production of adrenal cortex steroids, principally cortisol and corticosterone.

# Vasopressin and Oxytocin

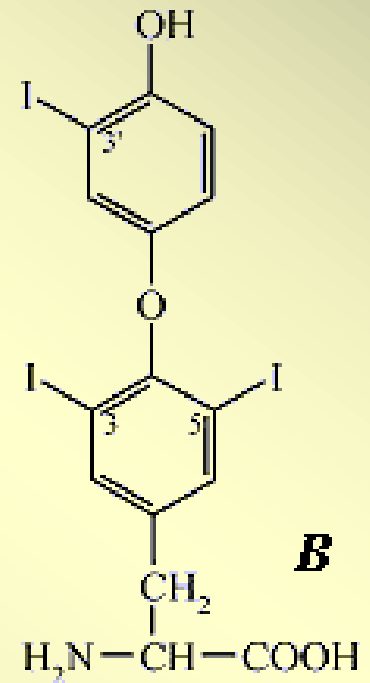
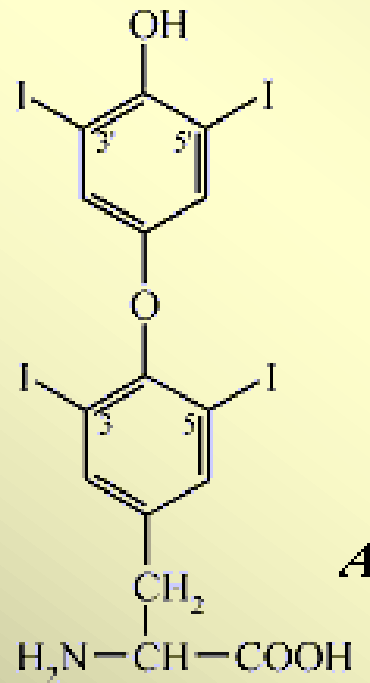
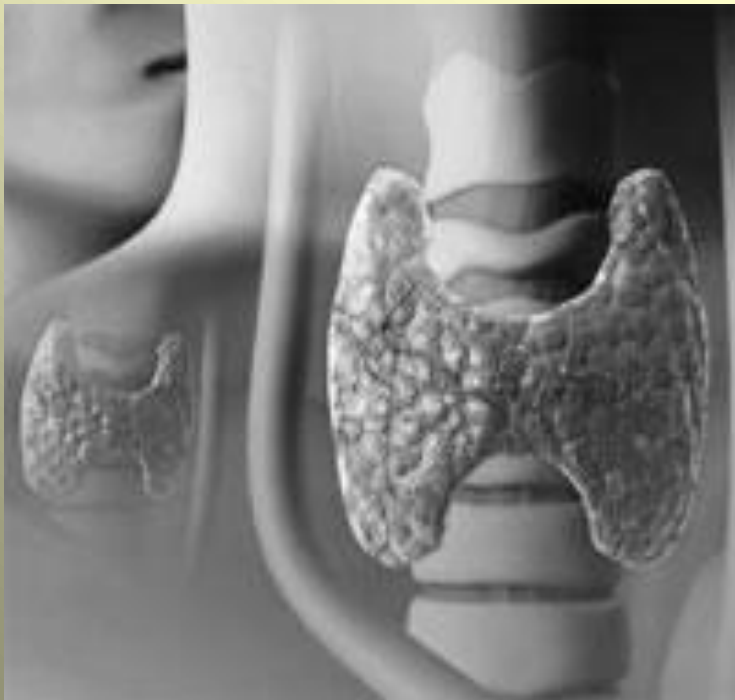
Vasopressin is also known as antidiuretic hormone (ADH), because it is the main regulator of body fluid osmolarity. The secretion of vasopressin is regulated in the hypothalamus by osmoreceptors, which sense water concentration and stimulate increased vasopressin secretion when plasma osmolarity increases. The secreted vasopressin increases the reabsorption rate of water in kidney tubule cells, causing the excretion of urine that is concentrated in  $\text{Na}^+$  and thus yielding a net drop in osmolarity of body fluids. Vasopressin deficiency leads to watery urine and polydipsia, a condition known as **diabetes insipidus**.

Oxytocin secretion in nursing women is stimulated by direct neural feedback obtained by stimulation of the nipple during suckling. Its physiological effects include the contraction of mammary gland myoepithelial cells, which induces the ejection of milk from mammary glands, and the stimulation of uterine smooth muscle contraction leading to childbirth.



# Thyroid hormones

The thyroid is a small, butterfly-shaped gland located just below the Adam's apple. This gland plays a very important role in the controlling of body metabolism, i.e. the rate at which your body uses energy fuels. It does this by producing thyroid hormones (primarily **thyroxine**, or T4 (A), and **triiodothyronine**, or T3 (B)). These thyroid hormones tell the cells in your body how fast to use energy and create proteins. The thyroid gland also produces **calcitonin**, a hormone that helps to regulate calcium levels in the blood by inhibiting the breakdown (resorption) of bones and increasing calcium excretion through the kidneys.



# Thyroid hormones' effects

Thyroid hormones have profound effects on many "big time" physiologic processes, such as **development**, **growth** and **metabolism**. They are clearly necessary for normal growth of children, as evidenced by the growth-retardation observed in thyroid deficiency. Of critical importance in mammals is the fact that normal levels of thyroid hormone are essential to the development of the fetal and neonatal brain. Thyroid hormones stimulate diverse metabolic activities in most tissues, leading to an increase in basal metabolic rate. One consequence of this activity is to increase body heat production, which seems to result from increased oxygen consumption, rates of ATP hydrolysis and influence of uncoupling proteins.

Increased thyroid hormone levels stimulate **fat mobilization**, leading to a build-up of free fatty acids in plasma. They also enhance oxidation of fatty acids in many tissues. Finally, plasma concentrations of cholesterol and triacylglycerols are inversely correlated with thyroid hormone levels - one diagnostic criterion of hypothyroidism is increased blood cholesterol concentration. Thyroid hormones stimulate almost all aspects of carbohydrate metabolism, including enhancement of insulin-dependent entry of glucose into the cells and increased **gluconeogenesis** and **glycogenolysis** to generate free glucose.

# Thyroid diseases

Thyroid diseases are primarily conditions that affect the amount of thyroid hormones being produced. Some create too few, leading to **hypothyroidism** and a slowing of body functions that causes symptoms such as weight gain, dry skin, constipation, cold intolerance, puffy skin, hair loss, fatigue, and menstrual irregularity in women. Severe untreated hypothyroidism, called **myxedema**, can lead to heart failure, seizures, and coma. In children, hypothyroidism can stunt growth and delay sexual development. In infants it can cause a mental retardation.



**Myxedema**



**Mental retardation**

If a thyroid disorder creates excessive amounts of thyroid hormones, the result is **hyperthyroidism** and the acceleration of body functions (**Graves disease**). This can lead to symptoms such as increased heart rate, anxiety, weight loss, difficulty of sleeping, tremors in the hands, weakness, and sometimes diarrhea. There may be puffiness around the eyes, dryness, irritation, and, in some cases, bulging of the eyes. The affected person may experience light sensitivity and visual disturbances. Because the eyes may not move normally, the person may appear to be staring.



**Hyperthyroidism**



# PARATHYROID HORMONES

Parathyroid hormone is the most important endocrine regulator of calcium and phosphorus concentration in extracellular fluid. This hormone is secreted from cells of the parathyroid glands and finds its major target cells in bones and kidneys.

## Parathyroid Hormone (PTH)

Parathyroid hormone (molecular weight 9,500) is synthesized and secreted by chief cells of the parathyroid in response to systemic  $\text{Ca}^{2+}$  levels. The body response to PTH is complex but is aimed in all tissues at increasing  $\text{Ca}^{2+}$  levels in extracellular fluids. PTH induces the dissolution of bones by stimulating osteoclast activity, which leads to elevated plasma  $\text{Ca}^{2+}$  and phosphate concentrations. In the kidneys, PTH reduces renal  $\text{Ca}^{2+}$  clearance by stimulating its reabsorption; at the same time, PTH reduces the reabsorption of phosphate and thereby increases its clearance. Finally, PTH acts on the liver, kidneys, and intestine to stimulate the production of calcitriol, which is responsible for  $\text{Ca}^{2+}$  absorption in the intestine.

## Calcitonin (CT)

Calcitonin has the ability to decrease blood calcium levels by effects on two well-studied target organs. Calcitonin suppresses resorption of bones by inhibiting the activity of osteoclasts, a cell type that "digests" bone matrix, releasing calcium and phosphorus into the blood.

# Disease States

Excessive PTH secretion is known as **hyperparathyroidism**, and is often the result of a benign parathyroid tumor (primary hyperparathyroidism) that loses its sensitivity to circulating calcium levels. In chronic renal failure a secondary hyperparathyroidism can be a result. Common manifestations of this disorder are chronic elevations of blood calcium concentration (hypercalcemia), kidney stones and decalcification of bones.

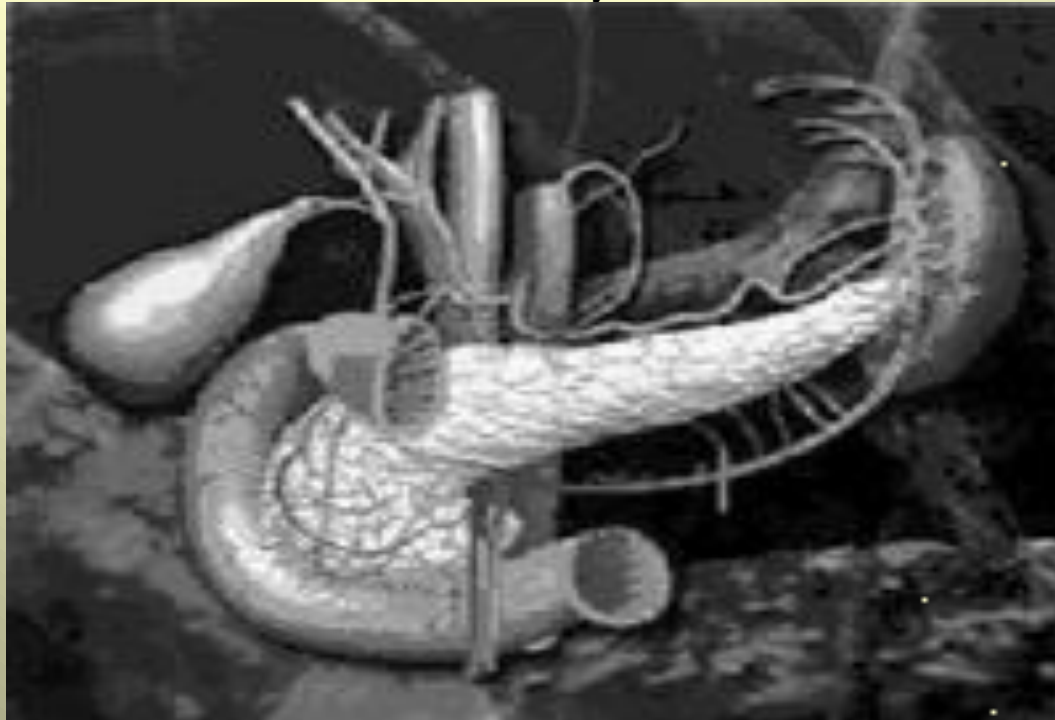
Insufficient PTH secretion is known as **hypoparathyroidism**, and is commonly caused by surgical misadventure (e.g. inadvertent removal during routine thyroid surgery), autoimmune disorder, or inborn errors of metabolism. The resulting hypocalcemia often leads to tetany and convulsions, and can be acutely life-threatening. Treatment focuses on restoring normal blood calcium concentrations by calcium infusions, oral calcium supplements and vitamin D therapy.

Increased levels of calcitonin are associated with two rare conditions, medullary thyroid cancer and benign C-cell hyperplasia. When excessive calcitonin is produced, the patient may experience chronic diarrhea.

# PANCREATIC HORMONES

Scattered throughout the exocrine tissue are several hundred thousand clusters of endocrine cells (**islets of Langerhans**), which house three major cell types, each of which produces a different endocrine product:

- ✓ $\alpha$  (A cells) secrete the hormone glucagon.
- ✓ $\beta$  (B cells) produce insulin and are the most abundant of the islet cells.
- ✓ $\delta$  (D cells) secrete the hormone somatostatin, which is also produced by a number of other endocrine cells in the body.





# Insulin action

Insulin is a quite simple protein consisting of two polypeptide chains with 51 amino acid residues. The major function of insulin is to counter the concerted action of a number of hyperglycemia-generating hormones and to maintain low blood glucose levels. In addition to its role in regulating glucose metabolism, insulin stimulates **Lipogenesis**, diminishes **Lipolysis**, and increases amino acid transport into cells. Insulin also modulates transcription, altering the cell content of numerous mRNAs. It stimulates growth, DNA synthesis, and cell replication.

In liver glucose uptake is dramatically increased by insulin because of increased activity of the enzymes **glucokinase**, **phosphofructokinase-1**, and **pyruvate kinase**, the key regulatory enzymes of **Glycolysis**. In most nonhepatic tissues, insulin increases glucose uptake by increasing the number of plasma membrane glucose transporters: **GLUTs**.

Insulin promotes synthesis of fatty acids in the liver and inhibits breakdown of fat in adipose tissue by inhibiting the intracellular lipase that hydrolyzes triglycerides to release fatty acids. Insulin facilitates entry of glucose into adipocytes, and within those cells, glucose can be used to synthesize glycerol. This glycerol and the fatty acids delivered from the liver, are used to synthesize triglyceride within the adipocyte. By these mechanisms, insulin is involved in further accumulation of triglyceride in fat cells. In addition to insulin's effect on entry of glucose into cells, it also stimulates the uptake of amino acids, again contributing to its **overall anabolic effect**.



# Glucagon action

Glucagon is a polypeptide which consists of 29 amino acid residues. The major effect of glucagon is to stimulate an increase in blood concentration of glucose. Glucagon exerts control over two pivotal metabolic pathways within the liver, leading that organ to dispense glucose to the rest of the body. Glucagon stimulates breakdown of glycogen stored in the liver. When blood glucose levels begin to fall, glucagon is secreted and acts on hepatocytes to activate the enzymes that depolymerize glycogen and release glucose. At the same time glucagon activates hepatic **Gluconeogenesis**. As such, it provides another source of glucose for blood.

Glucagon also appears to have a minor effect of enhancing **Lipolysis** of triglyceride in adipose tissue, which could be viewed as an additional means of conserving blood glucose by providing fatty acid fuel to most cells.

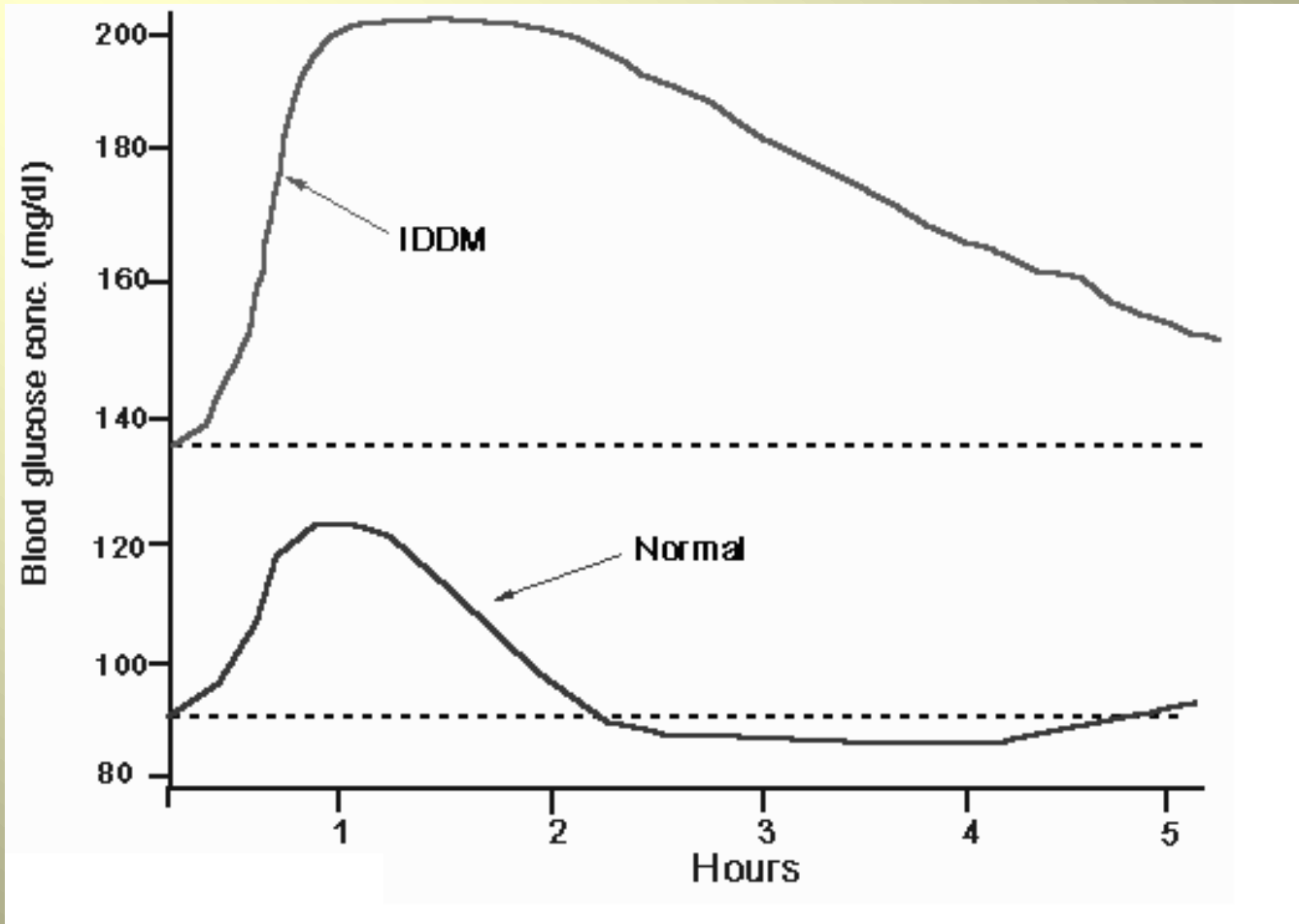
# Definition of Diabetes

Diabetes is any disorder characterized by excessive urine excretion. The most common form of diabetes is **Diabetes mellitus**, a metabolic disorder in which there is an inability to oxidize carbohydrate due to disturbances in insulin function. **Diabetes mellitus** is characterized by elevated glucose in the plasma and episodic ketoacidosis. Additional symptoms of **Diabetes mellitus** include excessive thirst, glucosuria, polyuria, lipemia and hunger. Another form is **Diabetes insipidus**. It is the result of a deficiency of antidiuretic hormone. The major symptom of **Diabetes insipidus** (excessive urine output) results from an inability of the kidneys to resorb water.

Criteria, which clinically establish an individual as suffering from **Diabetes mellitus**, include:

- ✓having a fasting plasma glucose level in excess of 126 mg/dL (7 mmol/L). Normal levels should be less than 100 mg/dL (5.6 mmol/L) or
- ✓having plasma glucose levels in excess of 200 mg/dL (11 mmol/L) at two times points during an oral glucose tolerance test, OGTT, one of which must be within 2 hrs of ingestion of glucose.

# Oral glucose tolerance test



# Insulin-Dependent Diabetes Mellitus (IDDM)

Type I **Diabetes** has been shown to be the result of an autoimmune reaction to antigens of the islet cells of the pancreas.

## Metabolism abnormalities

Uncontrolled **IDDM** leads to increased hepatic glucose output. First, liver glycogen stores are mobilized, then hepatic **Gluconeogenesis** is activated to produce glucose. Insulin deficiency also impairs non-hepatic tissue utilization of glucose. Reduced glucose uptake by peripheral tissues in turn leads to a reduced rate of glucose metabolism. The combination of increased hepatic glucose production and reduced peripheral tissue metabolism leads to elevated plasma glucose levels. When the capacity of the kidneys to reabsorb glucose is surpassed, **glucosuria** ensues. Glucose is an osmotic diuretic and an increase in renal loss of glucose is accompanied by loss of water and electrolytes, termed **polyuria**.

In uncontrolled **IDDM** there is a rapid mobilization of triglycerides leading to increased levels of plasma free fatty acids. The free fatty acids are taken up by numerous tissues and metabolized to provide energy. In hepatocytes the majority of acetyl-CoA is metabolized into the ketone bodies: **acetoacetate**,  **$\beta$ -hydroxybutyrate** and **acetone**. Production of the ketone bodies, in excess of the organism ability to utilize them leads to **ketoacidosis**. Insulin deficiency leads to increased catabolism of proteins. The increased rate of proteolysis leads to elevated concentrations of amino acids in plasma.



# Non-Insulin-Dependent Diabetes Mellitus (NIDDM)

**NIDDM** is characterized by a lack of the needed sensitivity to insulin of corresponding tissue receptors to prevent **ketoacidosis**. Type II of **Diabetes** refers to as the common form of idiopathic **NIDDM**. **NIDDM** is not an autoimmune disorder, however, there is a strong genetic correlation with the susceptibility to **NIDDM**. Obesity is a major risk factor that predisposes a man to **NIDDM**.

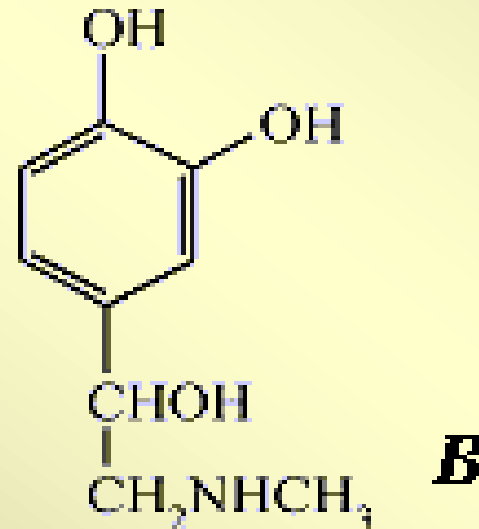
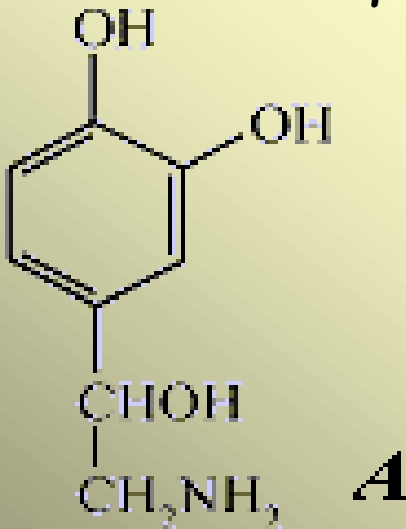


*Oral hypoglycemic drugs*



## ADRENAL MEDULLARY HORMONES

Cells in the adrenal medulla synthesize and secrete Norepinephrine (noradrenaline, **A**) and Epinephrine (adrenaline, **B**). In humans roughly 80% of the catecholamine output is epinephrine.

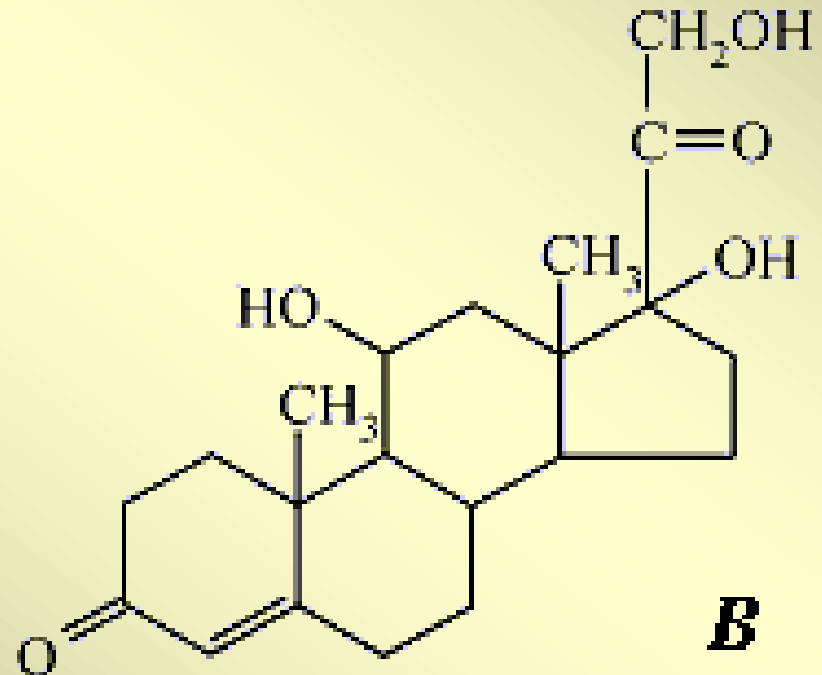
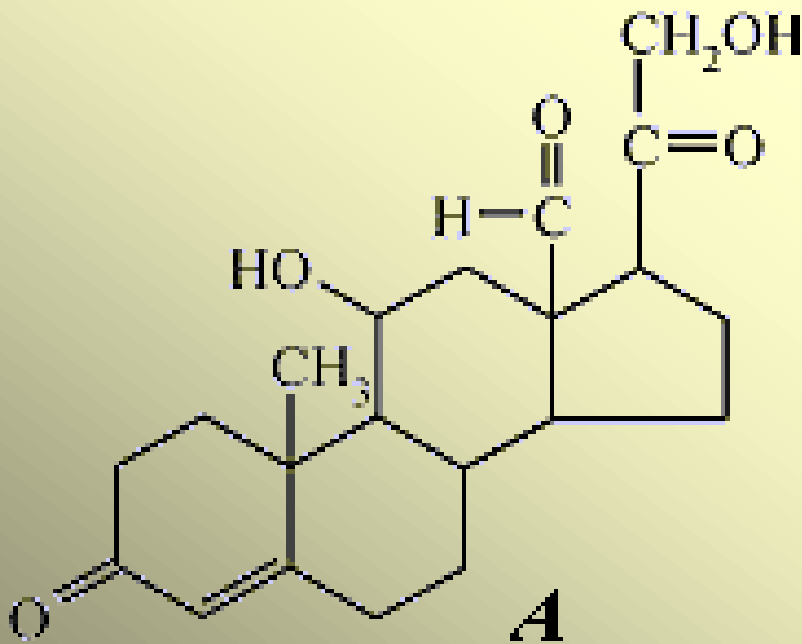


## ***Major effects mediated by epinephrine and norepinephrine :***

- ✓ **Increased rate and force of contraction of the heart muscle:** this is predominantly an effect of epinephrine acting through  $\beta$ -receptors.
- ✓ **Constriction of blood vessels:** norepinephrine, in particular, causes widespread vasoconstriction, resulting in increased resistance and hence high arterial blood pressure.
- ✓ **Dilation of bronchioles:** assists in pulmonary ventilation.
- ✓ **Stimulation of *Lipolysis* in fat cells:** this provides fatty acids for energy production in many tissues and aids in conservation of dwindling reserves of blood glucose.
- ✓ **Increased metabolic rate:** oxygen consumption and heat production increase throughout the body in response to epinephrine. Medullary hormones also promote breakdown of glycogen in skeletal muscle to provide glucose for energy production.
- ✓ **Dilation of the pupils.**
- ✓ **Inhibition of certain "non-essential" processes:** an example is inhibition of gastrointestinal secretion and motor activity.
- ✓ **It elevates blood sugar level by increasing hydrolysis of glycogen to glucose in the liver.**
- ✓ **Suppressive effect on the adaptive immune system.**

# ADRENAL CORTICAL HORMONES

The adrenal cortex produces steroid hormones. In total, at least two to three dozen different steroids are synthesized and secreted from this tissue, include some sex steroids. But two classes are of particular importance: **mineralocorticoids** (aldosterone, A), and **glucocorticoids** (cortisole, B).

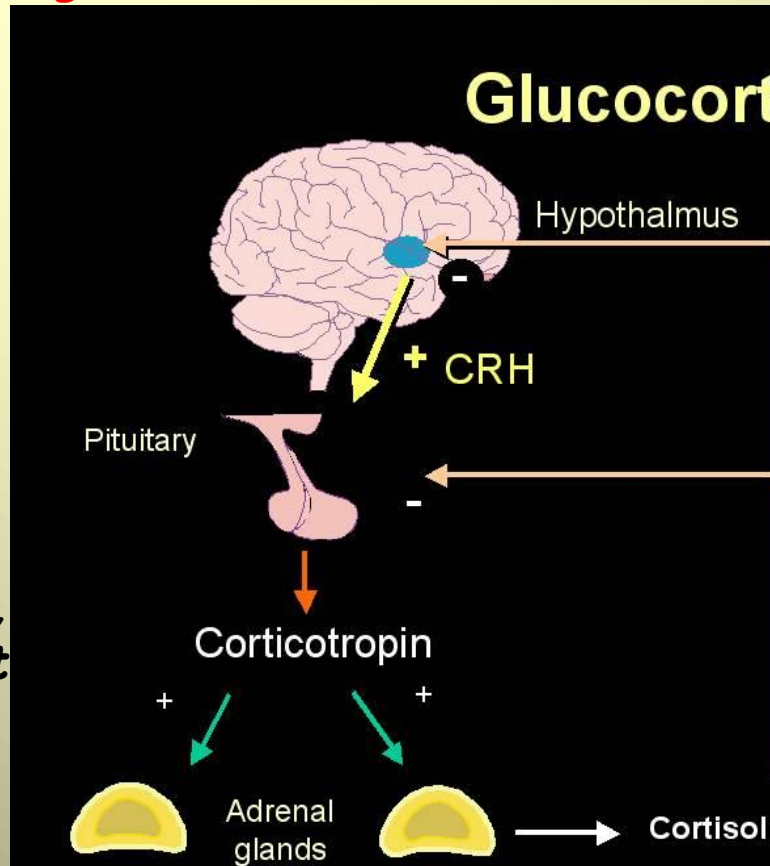




# GLUCOCORTICOIDS

Glucocorticoids stimulate **Gluconeogenesis**, particularly in the liver. Enhancing the expression of the enzymes involved in **Gluconeogenesis** is probably the best-known metabolic function of glucocorticoids. It inhibits the glucose uptake in muscle and adipose tissue and stimulates the fat breakdown in adipose tissue - the fatty acids released by **Lipolysis** are used for production of energy in tissues like muscle, and the released glycerol provides another substrate for **Gluconeogenesis**.

Glucocorticoids have potent **anti-inflammatory** and **immunosuppressive** properties. This is particularly evident when they administered at pharmacologic doses, but also is important in normal immune responses.



- ↓  $\text{Ca}^{2+}$  absorption from intestine
- ↑ Renal  $\text{Ca}^{2+}$  excretion
- ↑ Osteoclastic bone resorption and ↓ bone formation
- ↑ PTH and ↓ gonadal steroids

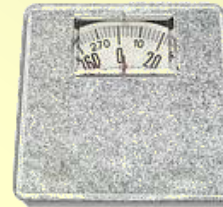
# MINERALOCORTICOIDS

Mineralocorticoids play a critical role in regulating concentrations of minerals - particularly **sodium** and **potassium** in extracellular fluids. The major targets of **aldosterone** are the distal tubules of the kidney, where it stimulates exchange of **sodium** and **potassium**. This results in increased reabsorption of **sodium** and **water**, with consequent expansion of extracellular fluid volume. This is an osmotic effect directly related to increased reabsorption of **sodium**. But **aldosterone** increases renal excretion of **potassium**.

## Conn's syndrome

Conn's syndrome is another name for primary **hyperaldosteronism**, which is the most common cause of secondary hypertension and may also be referred to as **aldosteronism**. It is a condition characterized by the excess secretion of **aldosterone** from the cortex - the outer layer - of the adrenal glands. Increased **aldosterone** leads to **polyuria** (frequent urination), increased **thirst**, **weakness**, **temporary paralysis**, **headaches**, **muscle cramps**, and **tingling**.

Sudden weight gain



Edema



High blood pressure



ADAM.

# Addison's disease

Adrenal insufficiency is a disorder characterized by underactive adrenal glands and an insufficient production of the hormones **cortisol** and, sometimes, **aldosterone**. Addison's disease is accompanied by numerous clinical abnormalities, including **cardiovascular disease, lethargy, diarrhea, and weakness.**



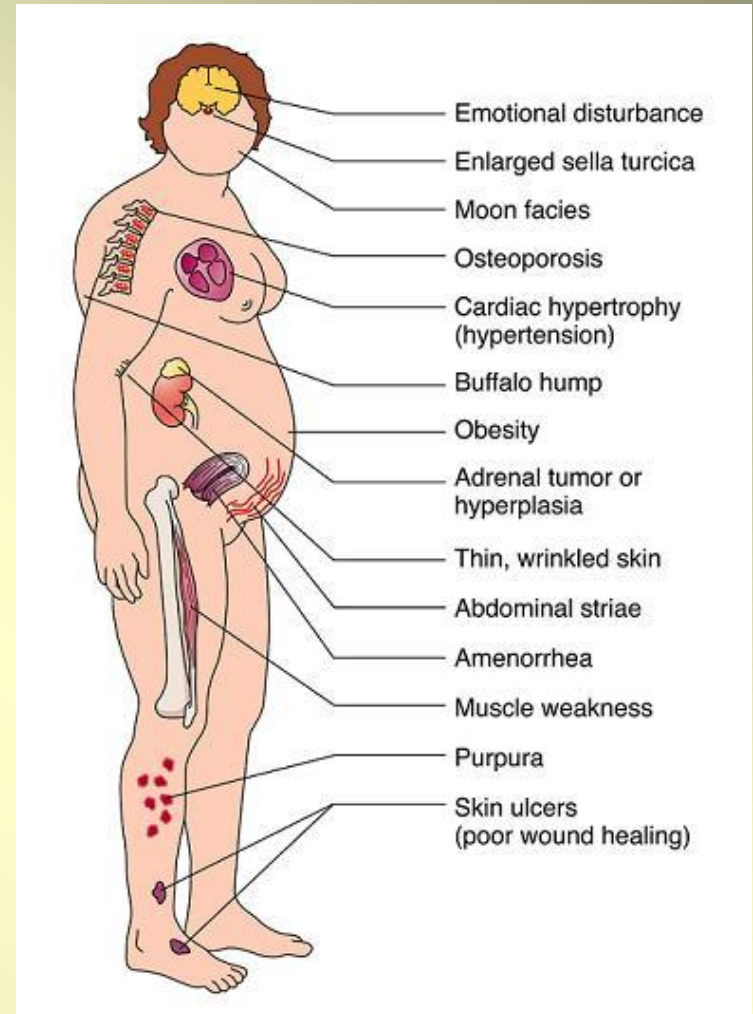
## Addison's disease:

- Note the generalised skin pigmentation (in a Caucasian patient) but especially the deposition in the palmer skin creases, nails and gums.

- She was treated many years ago for pulmonary TB. What are the other causes of this condition?



# Itsenko-Cushing's Disease manifestations



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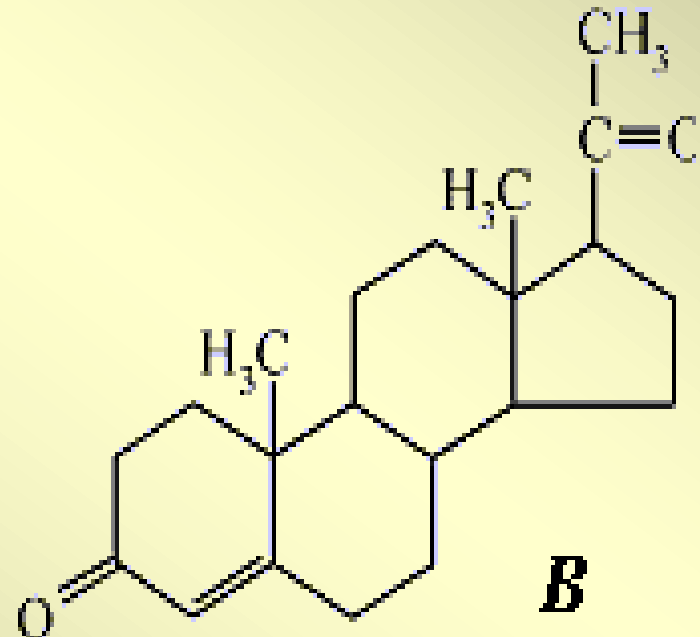
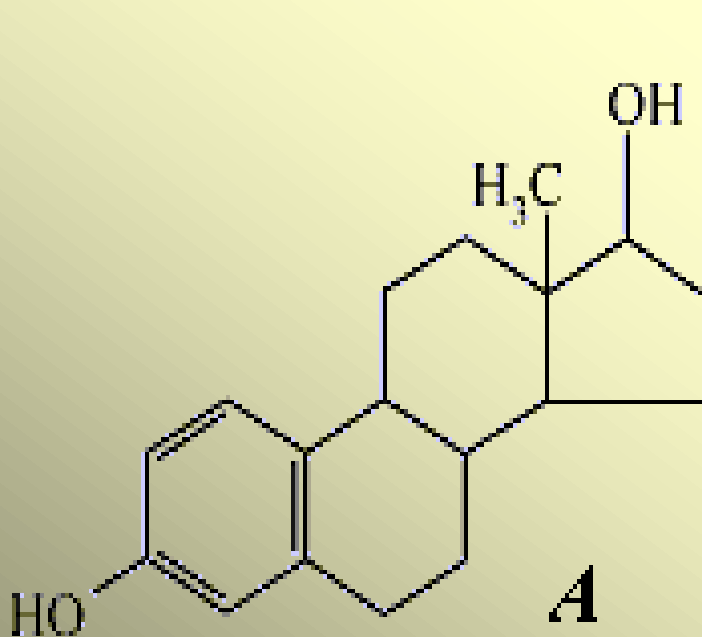
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# HORMONES OF THE REPRODUCTIVE SYSTEM

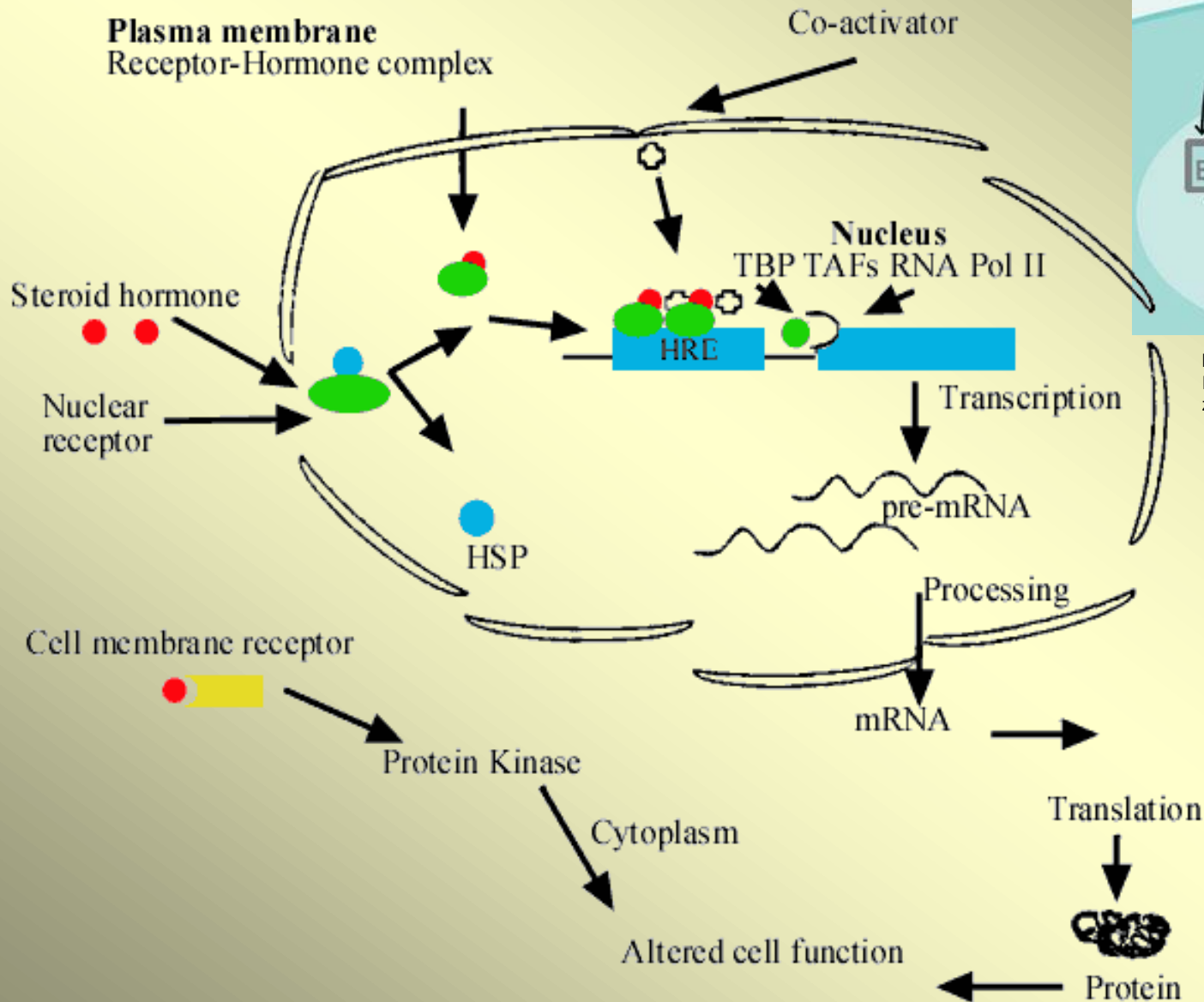
## FEMALE SEX HORMONES

The ovaries of sexually-mature females secrete a mixture of three estrogens (*estradiol*, *estriol* and *estrone*) of which *17 $\beta$ -estradiol* (A) is the most abundant (and most potent) and *progesterone* (B). Smaller amounts of estrogens are also produced by the adrenal cortex. In men, the testes produce some estradiol.

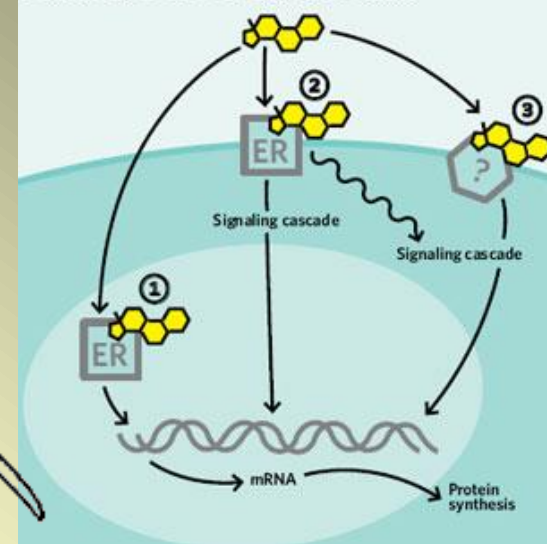




# ESTROGEN ACTION



## Pathways of estrogen action



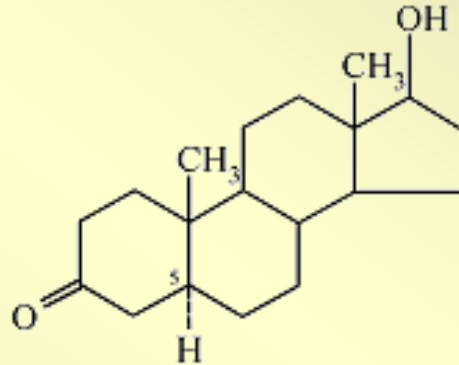
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# ***Estrogen effects***

- ✓ ***Sexual differentiation***
- ✓ ***Breast development and maintenance***
- ✓ ***Adding fat to breasts, hips, thighs during puberty***
- ✓ ***Improving bone strength and density***
- ✓ ***Accelerating bone maturation and bringing epiphyses to closure, completing growth***
- ✓ ***Growth of the uterus***
- ✓ ***Development of the endometrial lining to a thickness necessary to support pregnancy and menstruation***
- ✓ ***Thinning of cervical mucus at ovulation***
- ✓ ***Promoting and maintaining vaginal mucosal thickness and secretions***
- ✓ ***Serving as the primary feedback to the brain of sex hormone levels in both males and females.***
- ✓ ***Participating in triggering ovulation.***
- ✓ ***Preservation of egg cells.***
- ✓ ***Enabling spermatogenesis.***
- ✓ ***Effect on lipids.***
- ✓ ***Vascular effects.***
- ✓ ***Cerebral effects.***

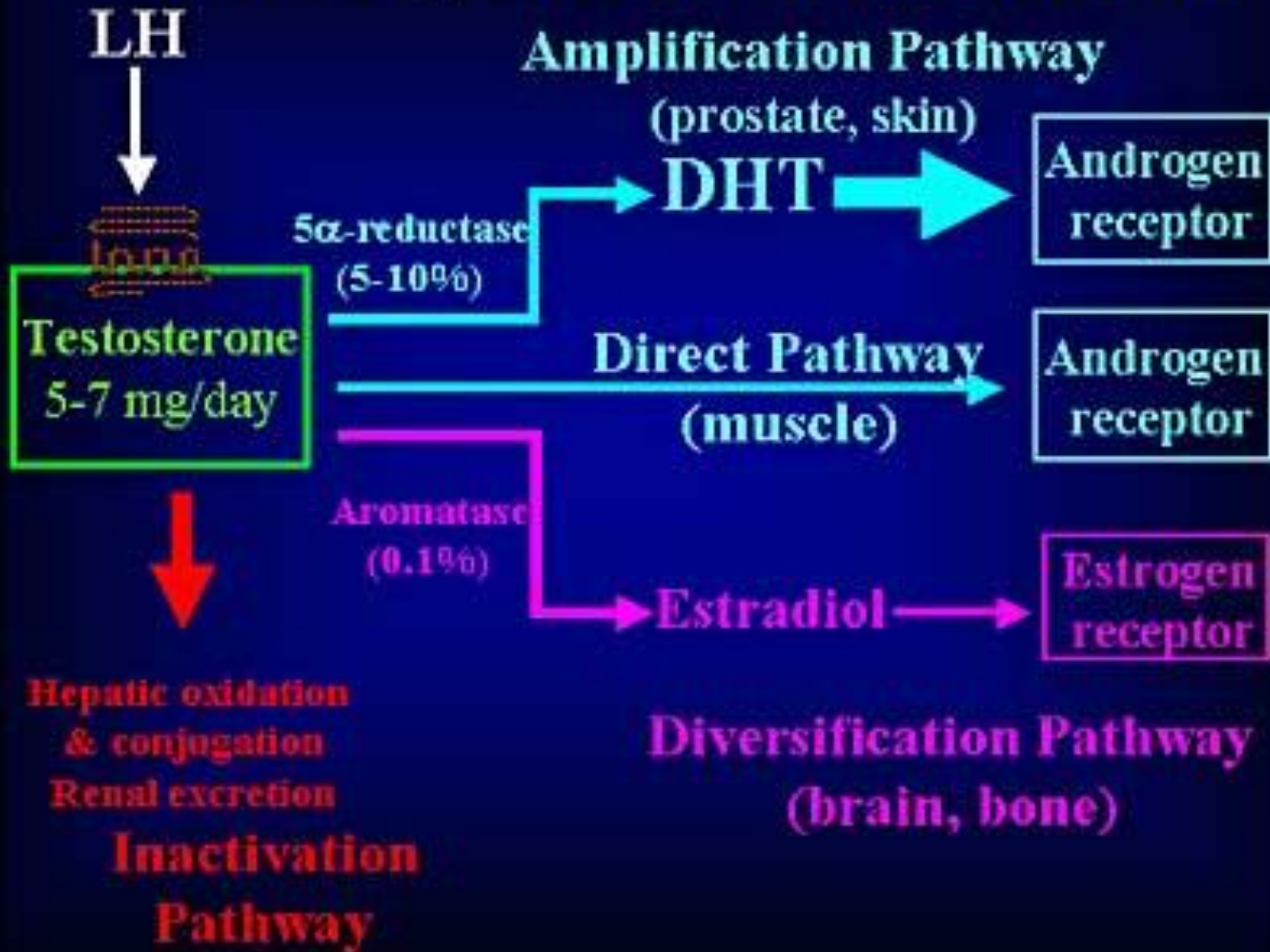
# MALE SEX HORMONES

The principal androgen (male sex hormone) is **testosterone**. This steroid is manufactured by the interstitial (Leydig) cells of the testes. Secretion of **testosterone** increases sharply at puberty and is responsible for the development of the so-called secondary sexual characteristics (e.g., beard) of men.



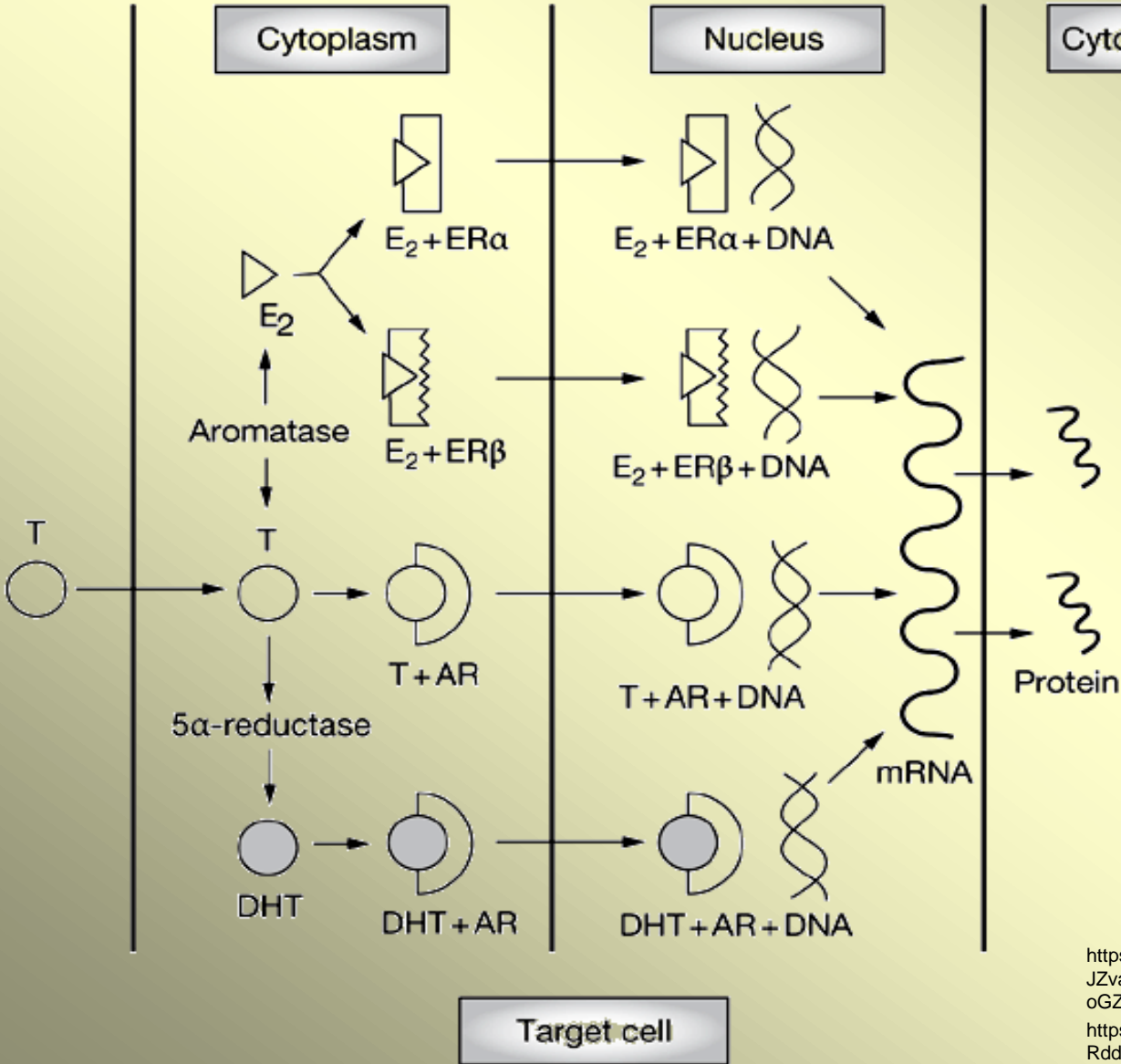
**Testosterone** effects can be classified as **virilizing** and **anabolic** effects, although the distinction is somewhat artificial, as many of the effects can be considered both. Anabolic effects include **growth of muscle mass and strength, increased bone density and strength, and stimulation of height growth and bone maturation**. Virilizing effects include **maturation of the sex organs**, particularly the penis and the formation of the scrotum in fetuses, and after birth (usually at puberty) a **deepening of the voice, growth of the beard and torso hair**. Many of these fall into the category of male secondary sex characteristics.

# Pathways of Testosterone Action

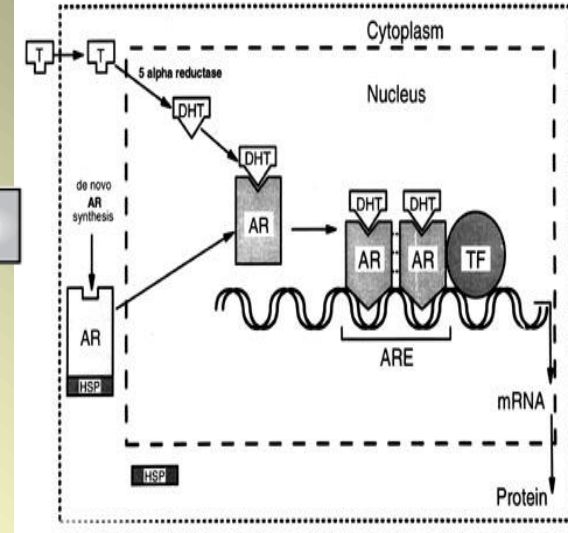




# ANDROGEN ACTION



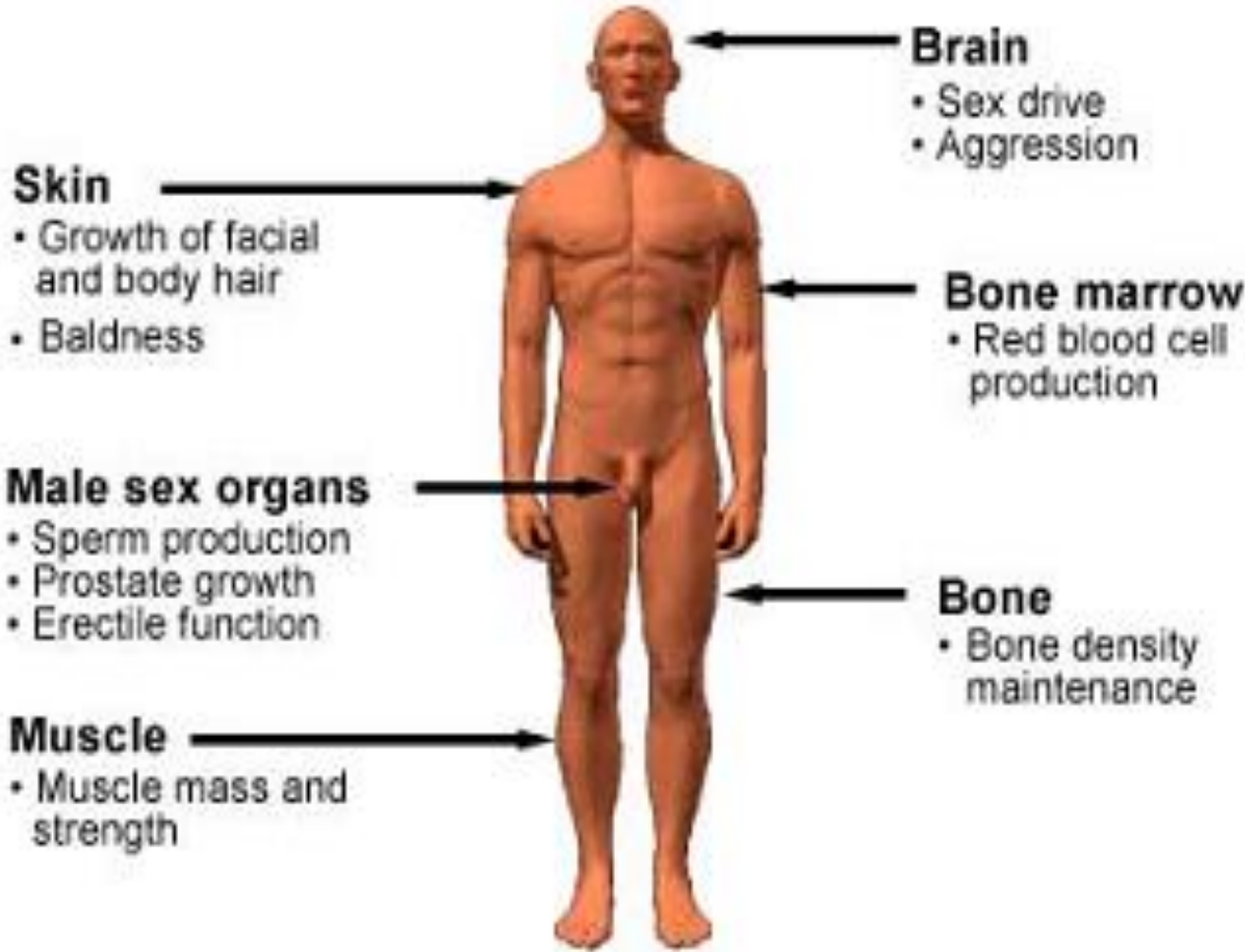
## Mechanism of Androgen Action



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# Testosterone preparation influence



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[https://lh3.googleusercontent.com/OAYkb2uciHtZ1zAp49pT3-m1jv4ZbNKIOdGmp5hHayCP9g\\_7ynzvGj9DAAG6ba\\_6lx2OgQ](https://lh3.googleusercontent.com/OAYkb2uciHtZ1zAp49pT3-m1jv4ZbNKIOdGmp5hHayCP9g_7ynzvGj9DAAG6ba_6lx2OgQ)

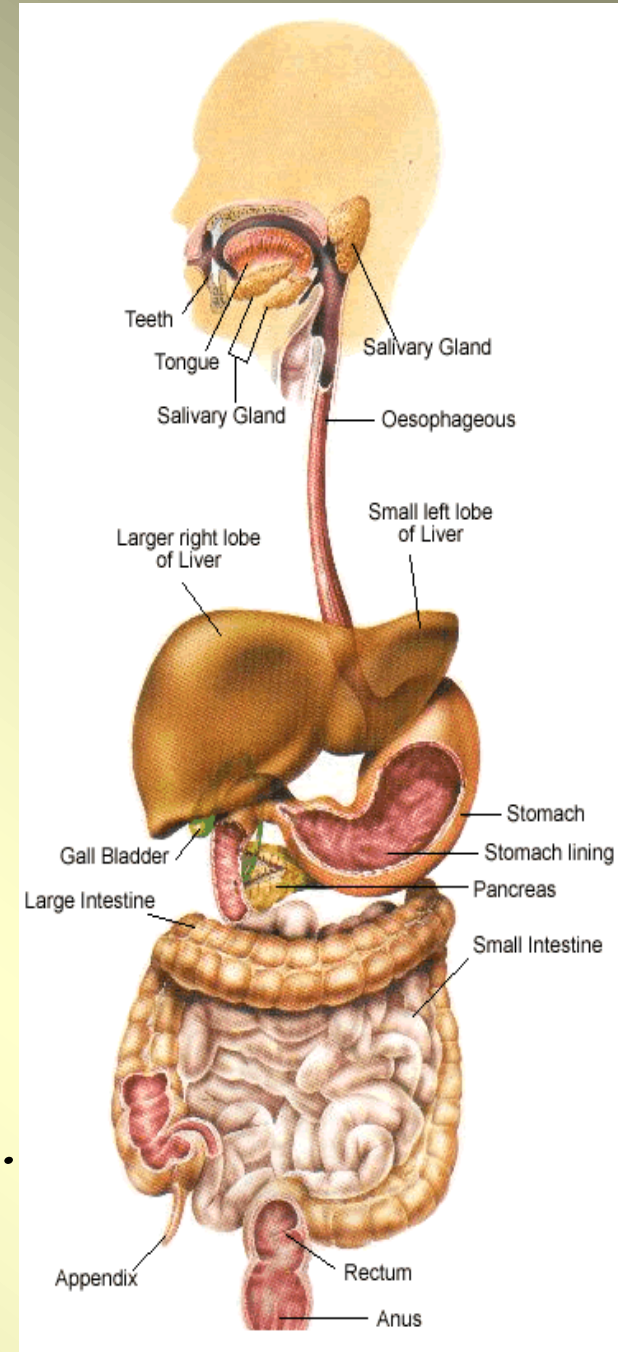
# Digestive Hormones

*Several hormones regulate the functions of the digestive process.*

**Gastrin**-stimulates gastric juice secretions. Gastrin is necessary for the normal growth of the lining of the stomach, small intestine, and colon.

**Secretin**-triggers pancreas to release bicarbonate which neutralizes stomach acids. Also stimulates stomach to produce pepsin and the liver to produce bile.

**Cholecystikinin (CCK)**- signals the stomach to shut down, therefore reducing gastric secretions. Also causes pancreas to release digestive enzymes into the small intestine and the gall bladder to excrete bile.



# Conclusions

1. Hormones are molecules that organisms use to convey information to the cells.
2. Hormones can be categorized into three chemical groups: polypeptides, amino acid derivatives and steroid.
3. Hormones interact with receptors that are located either inside the cell or within the cell membrane.
4. Endocrine system resembles a set of relays, carrying messengers through several steps from the central nervous system to a specific effector molecule in the target cells.



Do you have any questions?

Thank you for your attention!

