Ministry of Public Health of Ukraine
Poltava State Medical University
Department of biological and bioorganic chemistry

Hormones: biochemical and molecular-biological mechanisms of hormone action; protein and peptide hormones.

Assoc. Prof. Bilets M.V.

Lecture plan

- Classification of protein-peptide hormones.
- Synthesis and secretion of hormones.
- Molecular-cellular action mechanisms of hormones.
- Hormones of hypothalamus and hypophysis

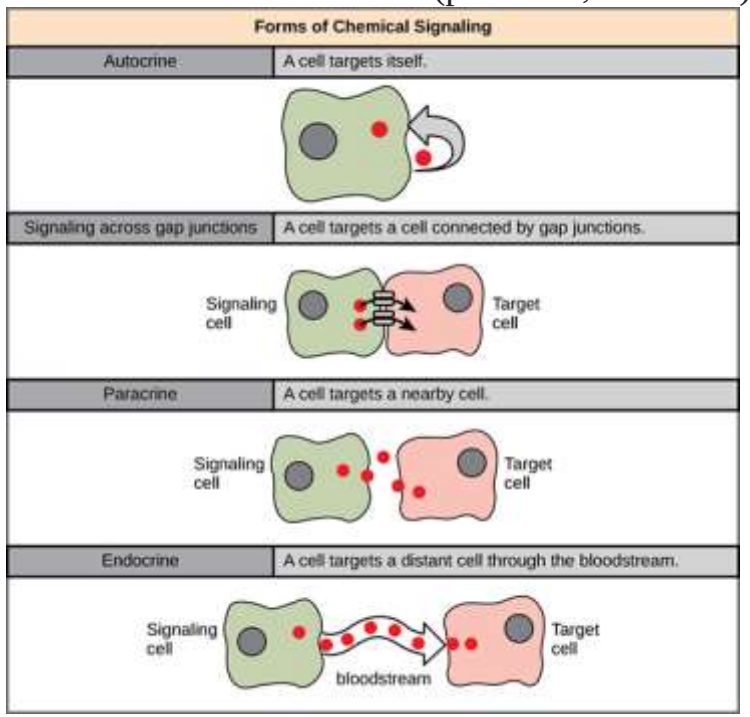
Hormones. Definition, general characteristics

Hormones are organic substances of various structures that have a regulatory effect on the metabolism and physiological functions of organs. Hormones are used to communicate between organs and tissues. Hormones are responsible for the regulation of many physiological processes and behavioral activities such as:

- stimulation or inhibition of growth
- wake-sleep cycle and other circadian rhythms
- mood swings
- induction or suppression of apoptosis (programmed cell death)
- activation or inhibition of the immune system
- regulation of metabolism
- preparation of the body for a new phase of life, such as puberty, parenting, and menopause
- control of the reproductive cycle
- hunger cravings
- A hormone may also regulate the production and release of other hormones. Hormone signals control the internal environment of the body through homeostasis.

Properties of homones

- Distant nature of action. Homones act on the functions of organs located at a considerable distance from the gland in which they were formed. Hormones are secreted by organs - endocrine glands, they do not have excretory ducts and secrete hormones directly into the blood (endocrine action). Some tissue hormones have different mechanisms of action (paracrine, autocrine)



- Hormones have **high biological activity** - act in very low concentrations.

- The specificity of the action. Certain hormones have a regulatory effect on certain processes. Usually, several hormones affect the activity of each organ, each function. The action of these hormones is either synergistic (in one direction) or antagonistic (in opposite directions).

Rapid destruction of hormones by tissues. Hormones are quickly destroyed by tissues, so the endocrine glands must produce them constantly.

Hormone secretion occurs in response to specific biochemical signals and is often subject to negative feedback regulation.

Hormonal signaling involves the following steps:

- Biosynthesis of a particular hormone in a particular tissue
- Storage and secretion of the hormone
- Transport of the hormone to the target cell (a cell that has a specific receptor for a hormone)
- Recognition of the hormone by an associated cell membrane or intracellular receptor protein
- Relay and amplification of the received hormonal signal via a signal transduction process: This then leads to a cellular response. The reaction of the target cells may then be recognized by the original hormone-producing cells, leading to a downregulation in hormone production. This is an example of a homeostatic negative feedback loop.
- Breakdown of the hormone.

https://ib.bioninja.com.au/standard-level/topic-6-human-physiology/66-hormones-homeostasis-and/types-of-hormones.html

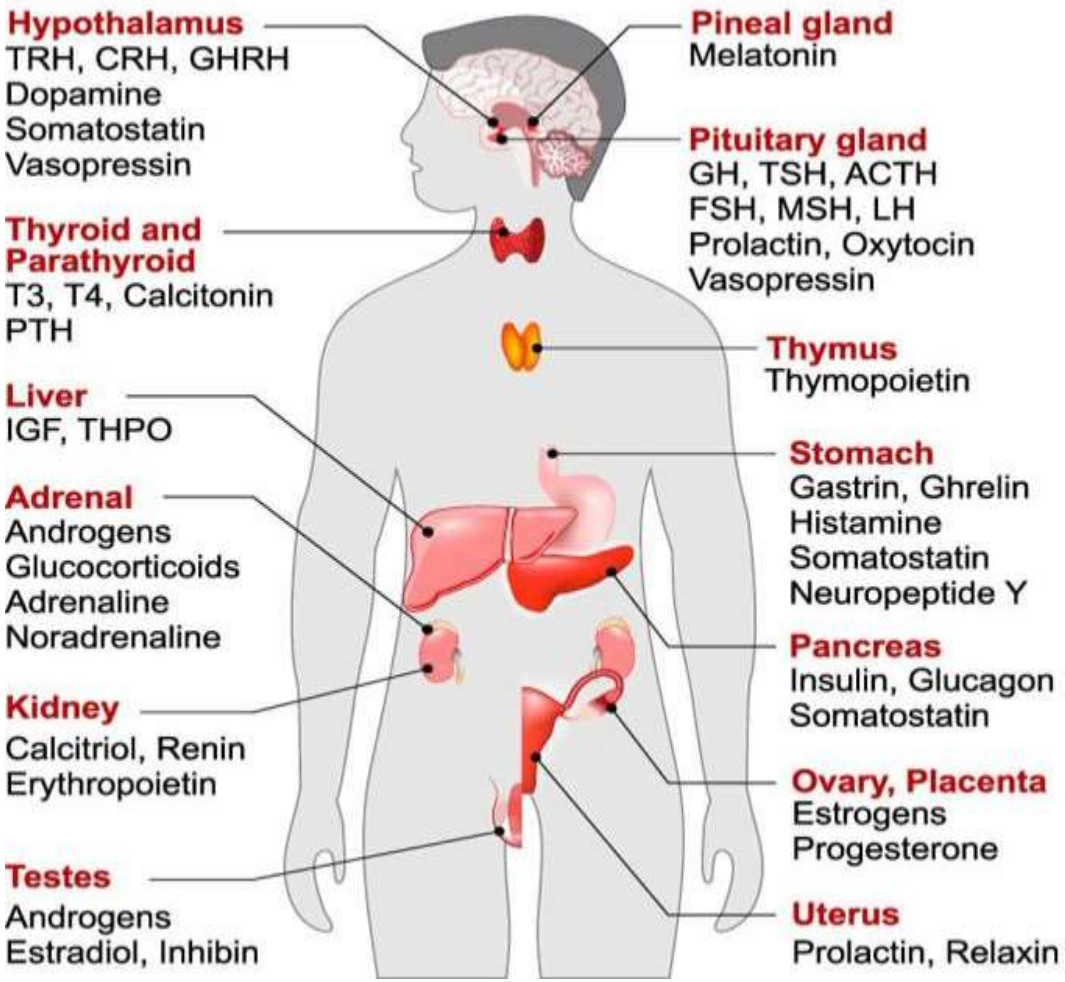
Hormones classification

According to their chemical structure, hormones are divided into three groups:

- **amino acid derivatives** (amines and iodothyronines);
- **protein-peptide hormones** (small peptides, glycoproteins, proteins),
- **lipid derivatives** (steroids, eicosanoids).

SN	Types	Description
1	Protein or peptide	Peptide or protein hormones are made of a chain of amino acids. Examples include oxytocin and insulin. They are packed in vesicles and are hydrophilic, meaning that they are soluble in water. Due to their hydrophilicity, they can only bind to receptors on the membrane, as travelling through the membrane is unlikely.
2	Amino acid	Amino acid hormones are derived from amino acid, most commonly tyrosine. They are stored in vesicles. Examples include melatonin and thyroxine.
3	Steroid	Steroid hormones are derived from cholesterol. Examples include the sex hormones estradiol and testosterone as well as the stress hormone cortisol. Steroids contain four fused rings. They are lipophilic and hence can cross membranes to bind to intracellular nuclear receptors.
4	Eicosanoid	Eicosanoids hormones are derived from lipids such as arachidonic acid, lipoxins and prostaglandins. Examples include prostaglandin and thromboxane. These hormones are produced by cyclooxygenases and lipoxygenase. They are hydrophobic and act on membrane receptors.

Hormones are produced by specific endocrine glands:



https://www.toppr.com/ask/content/concept/introduction-to-hormones-233552/

Regulation of hormones secretion

- The rate of hormone biosynthesis and secretion is often regulated by a homeostatic negative feedback control mechanism. Such a mechanism depends on factors that influence the metabolism and excretion of hormones. Thus, higher hormone concentration alone cannot trigger the negative feedback mechanism. Negative feedback must be triggered by overproduction of an "effect" of the hormone.

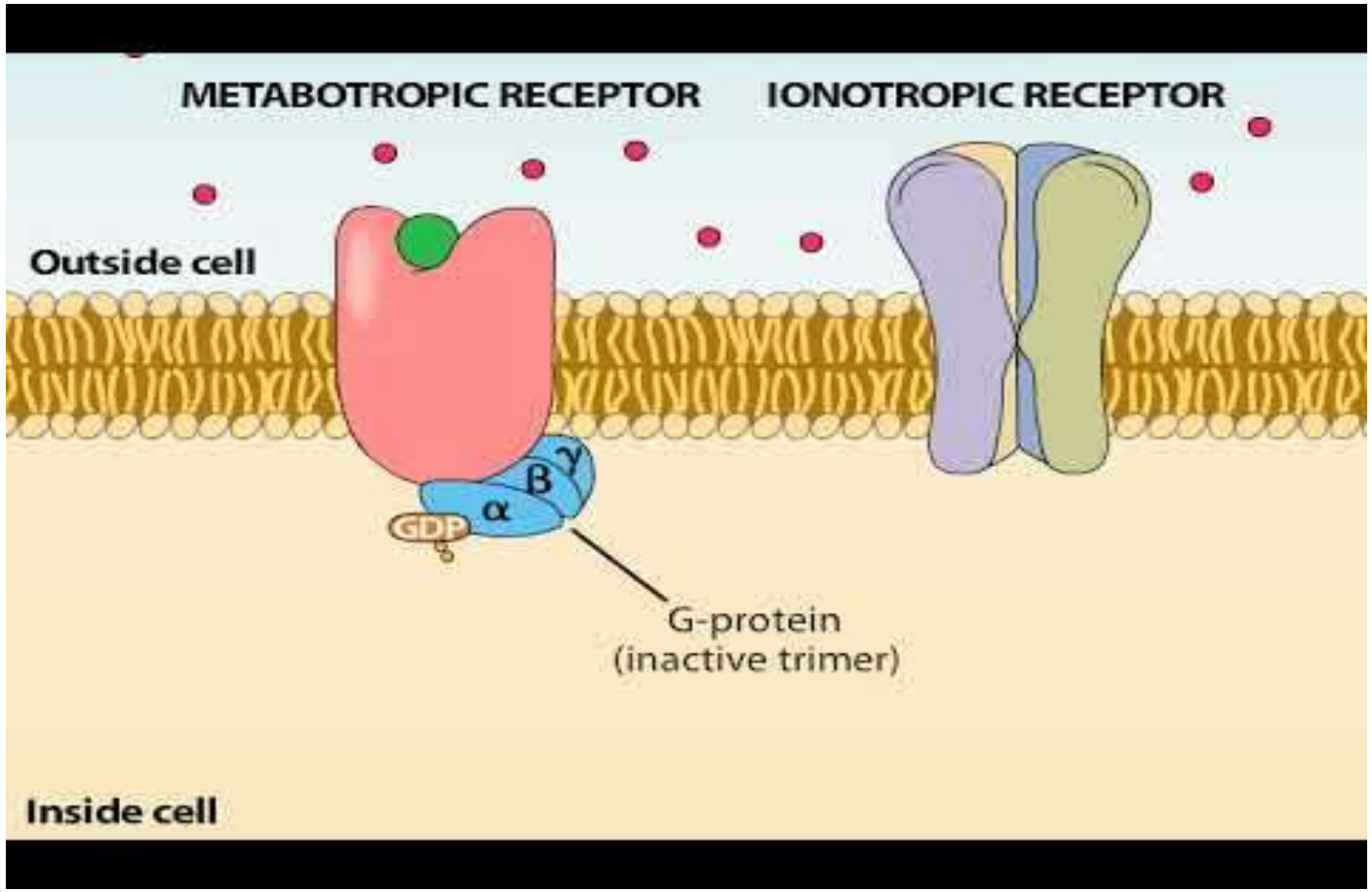
Hormone secretion can be stimulated and inhibited by:

- Other hormones (*stimulating*- or *releasing* -hormones)
- Plasma concentrations of ions or nutrients, as well as binding globulins
- Neurons and mental activity
- Environmental changes, e.g., of light or temperature
- One special group of hormones is the tropic hormones that stimulate the hormone production of other endocrine glands. For example, thyroid-stimulating hormone (TSH) causes growth and increased activity of another endocrine gland, the thyroid, which increases output of thyroid hormones.
- To release active hormones quickly into the circulation, hormone biosynthetic cells may produce and store biologically inactive hormones in the form of pre- or prohormones. These can then be quickly converted into their active hormone form in response to a particular stimulus.
- Eicosanoids are considered to act as local hormones. They are considered to be "local" because they possess specific effects on target cells close to their site of formation. They also have a rapid degradation cycle, making sure they do not reach distant sites within the body.
- Hormones are also regulated by receptor agonists. Hormones are ligands, which are any kinds of molecules that produce a signal by binding to a receptor site on a protein. Hormone effects can be inhibited, thus regulated, by competing ligands that bind to the same target receptor as the hormone in question. When a competing ligand is bound to the receptor site, the hormone is unable to bind to that site and is unable to elicit a response from the target cell. These competing ligands are called antagonists of the hormone.

Mechanisms of hormones action.

Types of receptors
(membrane associated receptors)

- **Hormones initiate a cellular response by initially binding to either cell receptors.** **Hormone+receptor = lock + key**
- A cell may have several different receptor types that recognize the same hormone but activate different signal transduction pathways, or a cell may have several different receptors that recognize different hormones and activate the same biochemical pathway.
- Receptors can be: **membrane associated (extracellular, external)** and **intracellular (internal).**
- **Membrane associated (extracellular, external)** – These are the transmembrane receptors which are embedded into the membrane. Three types of membrane bound receptors: ionotropic, metabotropic, receptors with enzymatic activity.
- **Ionotropic receptors** are a group of transmembrane ion channels that open or close in response to the binding of a chemical messenger. Hormones with this type of receptor are characterized by a **membrane mechanism of action**:
- **Hormone + receptor → hormone-receptor complex → a change in the permeability of the cell membrane for molecules or ions**
- **Metabotropic receptor** are a type of G protein-coupled receptor. When a metabotropic receptor is activated, a series of intracellular events are triggered. The interaction of hormone and receptor typically triggers a cascade of secondary effects within the cytoplasm of the cell, described as signal transduction, often involving phosphorylation or dephosphorylation of various other cytoplasmic proteins, changes in ion channel permeability, or increased concentrations of intracellular molecules that may act as secondary messengers (e.g., cyclic AMP). This type of receptors can be used for peptide , amino acid derivates hormones. Hormones with this type of receptor are characterized by a membrane-cytosolic mechanism of action:
- **Hormone (primary messenger) + receptor → hormone-receptor complex → protein-transducer (G-protein) → secondary messenger → protein kinase → cell response (for example, changes in enzyme activity)**



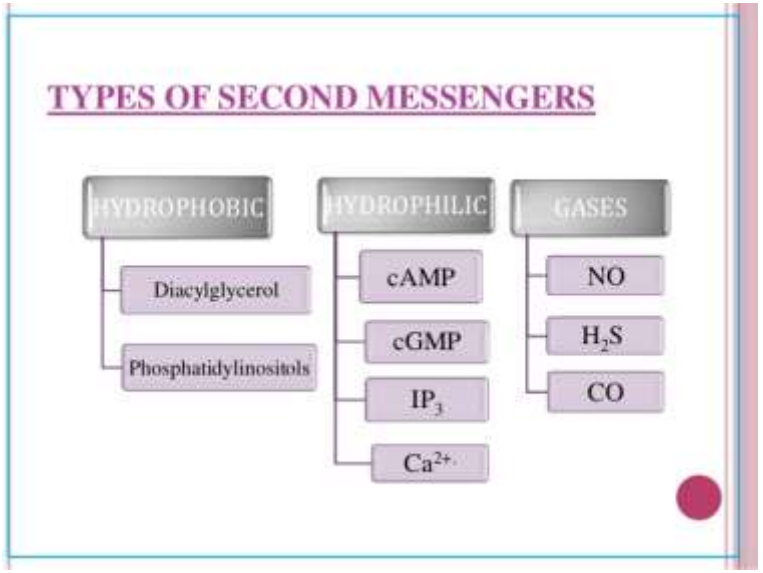
https://www.youtube.com/watch?v=P4cuTwgfjBY

G-proteins

- G proteins are a family of membrane-bound proteins that couple hormone receptors to effector enzymes (e.g., adenylyl cyclase). Thus, G proteins serve as “molecular switches” that decide whether the hormone action can proceed.
- At the molecular level, G proteins are heterotrimeric (i.e., they have three subunits) proteins. The three subunits are designated alpha (α), beta (β), and gamma (γ). The α subunit can bind either guanosine diphosphate (GDP) or GTP, and it contains GTPase activity. When GDP is bound to the α subunit, the G protein is inactive; when GTP is bound, the G protein is active and can perform its coupling function. Guanosine nucleotide releasing factors (GRFs) facilitate dissociation of GDP so that GTP binds more rapidly, whereas GTPase activating factors (GAPs) facilitate hydrolysis of GTP. Thus, the relative activity of GRFs and GAPs influences the overall rate of G protein activation.
- Types of G proteins:
  Gs – adenylyl-cyclase activator;
  Gi - adenylyl-cyclase inhibitor;
  Gq - phospholipase C activator

Second messengers

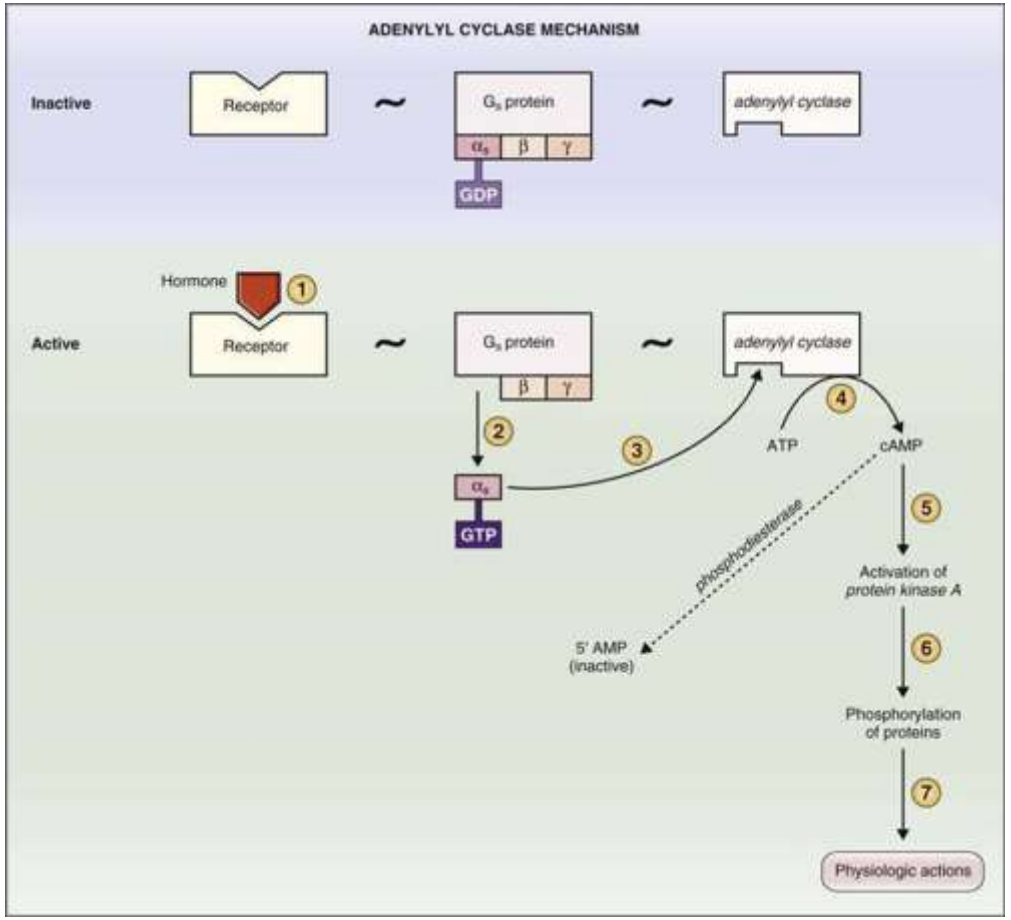
- Second messengers are molecules that relay signals received at receptors on the cell surface — such as the arrival of protein hormones, growth factors, etc. — to target molecules in the cytosol and/or nucleus.
- These intracellular messengers have some properties in common:
- They can be synthesized/released and broken down again in specific reactions by enzymes or ion channels.
- Some (such as Ca^{2+}) can be stored in special organelles and quickly released when needed.
- Their production/release and destruction can be *localized*, enabling the cell to limit space and time of signal activity.



https://www.slideshare.net/damarisb/second-messenger-system

Adenylyl Cyclase Mechanism

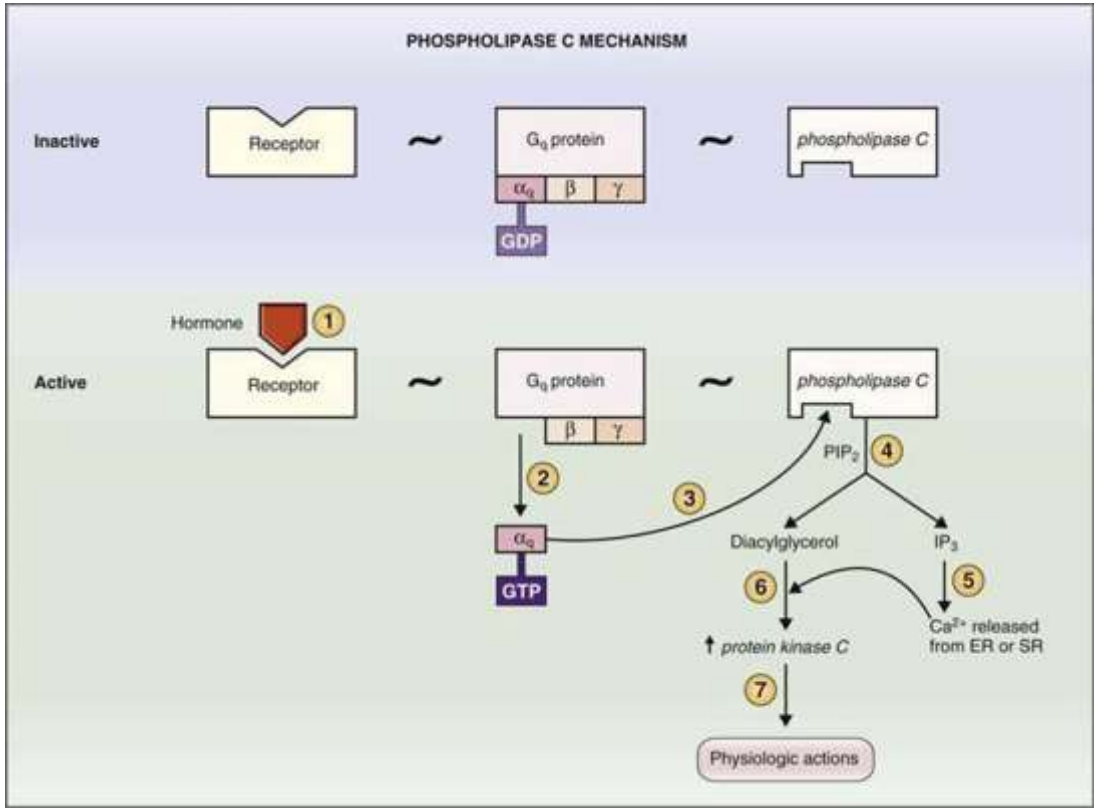
- The adenylyl cyclase/cAMP mechanism is utilized by many hormonal systems. This mechanism involves binding of a hormone to a receptor, coupling by a Gs or Gi protein, and then activation or inhibition of adenylyl cyclase, leading to increases or decreases in intracellular cAMP. cAMP, the second messenger, then amplifies the hormonal signal to produce the final physiologic actions.
- The receptor–Gs–adenylyl cyclase complex is embedded in the cell membrane. When no hormone is bound to the receptor, the αs subunit of the Gs protein binds GDP. In this configuration, the Gs protein is inactive. When hormone binds to its receptor, the **following steps occur:**
- *Hormone binds to its receptor in the cell membrane, producing a conformational change in the αs subunit, which produces two changes: GDP is released from the αs subunit and is replaced by GTP, and the αs subunit detaches from the Gs protein .*
- *The αs-GTP complex migrates within the cell membrane and binds to and activates adenylyl cyclase . Activated adenylyl cyclase catalyzes the conversion of ATP to cAMP, which serves as the second messenger . Intrinsic GTPase activity in the G protein converts GTP back to GDP, and the αs subunit returns to its inactive state.*
- *cAMP, via a series of steps involving activation of protein kinase A, phosphorylates intracellular proteins. These phosphorylated proteins then execute the final physiologic actions.*
- *Intracellular cAMP is degraded to an inactive metabolite, 5′ AMP, by the enzyme phosphodiesterase, thereby turning off the action of the second messenger.*



https://doctorlib.info/physiology/physiology-2/81.html

Phosphatidylinositol system (phospholipase C Mechanism)

- The mechanism involves binding of hormone to a receptor and coupling via a Gq protein to phospholipase C. Intracellular levels of IP3 and Ca2+ are increased, producing the final physiologic actions. The steps in the phospholipase C (IP3/Ca2+) mechanism:
- The receptor–Gq–phospholipase C complex is embedded in the cell membrane. With no hormone bound to the receptor, the αq subunit binds GDP. In this configuration, the Gq protein is inactive. When the hormone binds to the receptor, Gq is activated, which activates phospholipase C, in the **following steps:**
- *Hormone binds to its receptor in the cell membrane, producing a conformational change in the αq subunit.*
- *GDP is released from the αq subunit, is replaced by GTP, and the αq subunit detaches from the Gq protein.*
- *The αq-GTP complex migrates within the cell membrane and binds to and activates phospholipase C. Activated phospholipase C catalyzes the liberation of diacylglycerol and IP3 from phosphatidylinositol 4,5-diphosphate (PIP2), a membrane phospholipid. The IP3 generated causes the release of Ca2+ from intracellular stores in the endoplasmic or sarcoplasmic reticulum, resulting in an increase in intracellular Ca2+concentration.*
- *Together, Ca2+ and diacylglycerol activate protein kinase C, which phosphorylates proteins and produces the final physiologic actions .*



https://doctorlib.info/physiology/physiology-2/81.html

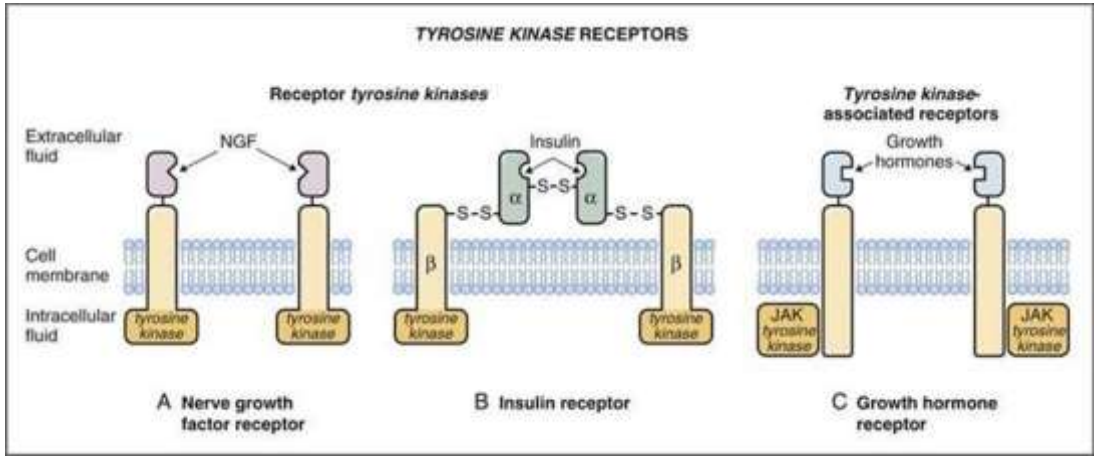
Mechanisms of hormones action.

Catalytic Receptor Mechanisms

- **Receptors with enzymatic activity** An enzyme-linked receptor, also known as a catalytic receptor, is a transmembrane receptor, where the binding of an extracellular ligand causes enzymatic activity on the intracellular side. Catalytic receptor is an integral membrane protein possessing both enzymatic catalytic and receptor functions. They have two important domains, an extra-cellular ligand binding domain and an intracellular domain, which has a catalytic function; and a single transmembrane helix. The signaling molecule binds to the receptor on the outside of the cell and causes a conformational change on the catalytic function located on the receptor inside the cell.
- Examples of the enzymatic activity include:
- receptor tyrosine kinase, as in fibroblast growth factor receptor;
- serine/threonine-specific protein kinase, as in bone morphogenetic protein;
- guanylate cyclase, as in atrial natriuretic factor receptor.
- Receptor tyrosine kinases have intrinsic tyrosine kinase activity within the receptor molecule. Tyrosine kinase-associated receptors do not have intrinsic tyrosine kinase activity but associate noncovalently with proteins.
- Receptor tyrosine kinases have an extracellular binding domain that binds the hormone or ligand, a hydrophobic transmembrane domain, and an intracellular domain that contains tyrosine kinase activity. When activated by hormone or ligand, the intrinsic tyrosine kinase phosphorylates itself and other proteins.

One type of receptor tyrosine kinase is a monomer (e.g., nerve growth factor [NGF] and epidermal growth factor receptors).
Another type of receptor tyrosine kinase is already a dimer (e.g., insulin and insulin-like growth factor [IGF]. In this dimeric type, binding of the ligand (e.g., insulin) activates intrinsic tyrosine kinase and leads to phosphorylation of itself and other proteins and ultimately the hormone's physiologic actions.

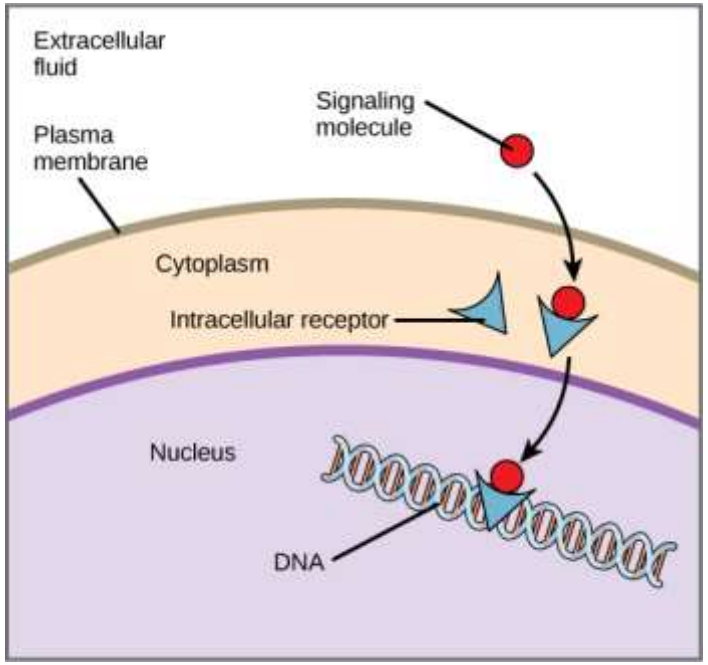
Tyrosine kinase-associated receptors (e.g., growth hormone receptors also have an extracellular domain, a hydrophobic transmembrane domain, and an intracellular domain. However, unlike the receptor tyrosine kinases, the intracellular domain does not have tyrosine kinase activity but is noncovalently "associated" with tyrosine kinase such as those in the Janus kinase family (JAK, Janus family of receptor-associated tyrosine kinase, or "just another kinase"). Hormone binds to the extracellular domain, leading to receptor dimerization and activation of tyrosine kinase in the associated protein (e.g., JAK). The associated tyrosine kinase phosphorylates tyrosine moieties on itself, the hormone receptor, and other proteins. Downstream targets of JAK include members of the STAT (signal transducers and activators of transcription) family, which cause transcription of mRNAs and ultimately new proteins involved in the hormone's physiologic actions.



https://doctorlib.info/physiology/physiology-2/81.html

Mechanisms of hormones action.
(intracellular receptors).

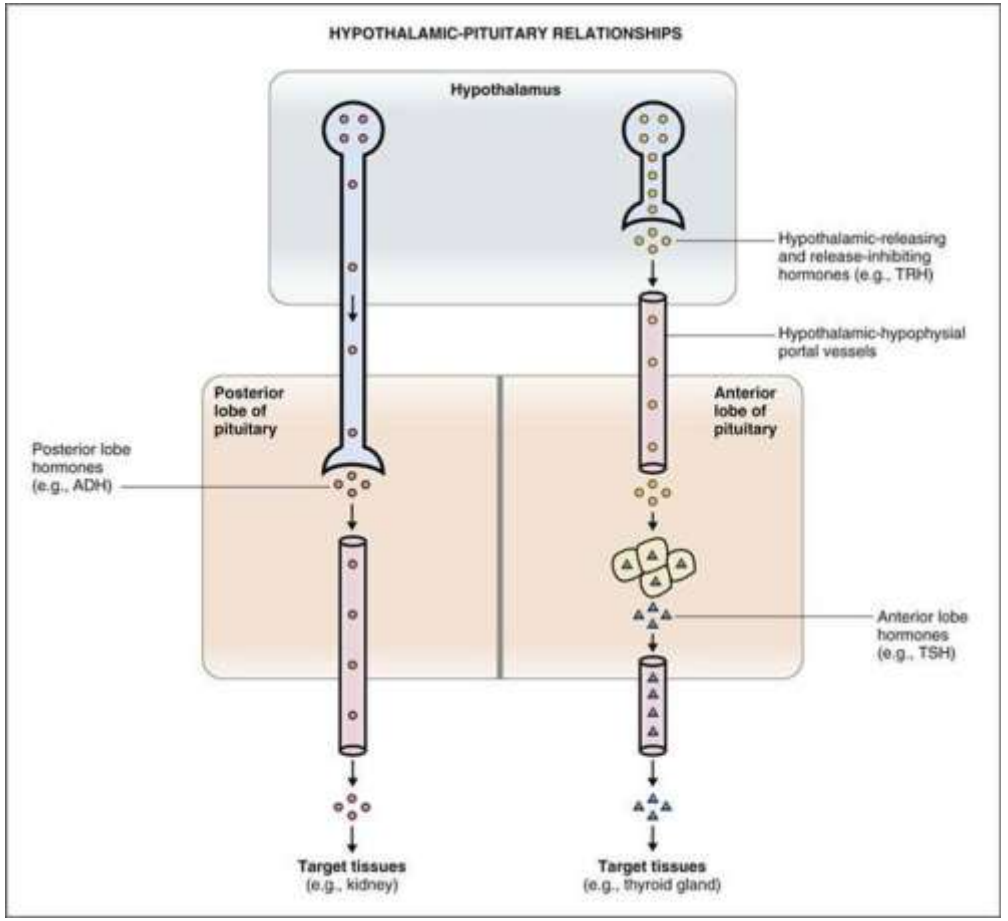
- **Intracellular (internal)** receptors – they can be either nuclear or cytoplasmic. Nuclear receptors are found on the nuclear membrane while the cytoplasmic receptors are found in the cytoplasm of the cell. These receptors are for the steroid and thyroid hormones. These receptors belong to the nuclear receptor family of ligand-activated transcription factors. To bind their receptors, these hormones must first cross the cell membrane. They can do so because they are lipid-soluble. The combined hormone-receptor complex then moves across the nuclear membrane into the nucleus of the cell, where it binds to specific DNA sequences, regulating the expression of certain genes, and thereby increasing the levels of the proteins encoded by these genes. Hormones with this type of receptor are characterized by a cytosolic щог nuclear mechanism of action:
- **Hormone + receptor → hormone-receptor complex → DNA → RNA → protein**



https://courses.lumenlearning.com/wm-biology1/chapter/reading-signal-receptors/

Hormones of hypothalamus and hypophysis

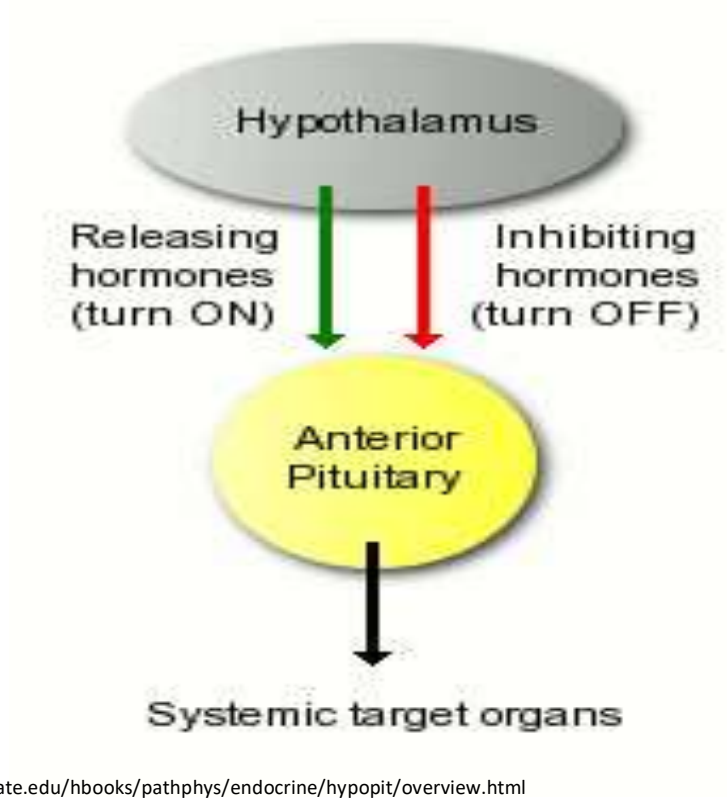
- The hypothalamus and pituitary gland function in a coordinated fashion to orchestrate many of the endocrine systems. The hypothalamic-pituitary unit regulates the functions of the thyroid, adrenal, and reproductive glands and also controls growth, milk production and ejection, and osmoregulation. It is important to visualize the anatomic relationships between the hypothalamus and the pituitary because these relationships underlie the functional connections between the glands.
- The pituitary gland, which also is called the hypophysis, consists of a posterior lobe and an anterior lobe. The **posterior lobe** (or posterior pituitary) is also called the neurohypophysis. The **anterior lobe** (or anterior pituitary) is also called the adenohypophysis. The hypothalamus is connected to the pituitary gland by a thin stalk called the **infundibulum.** Functionally, the hypothalamus controls the pituitary gland by both neural and hormonal mechanisms.



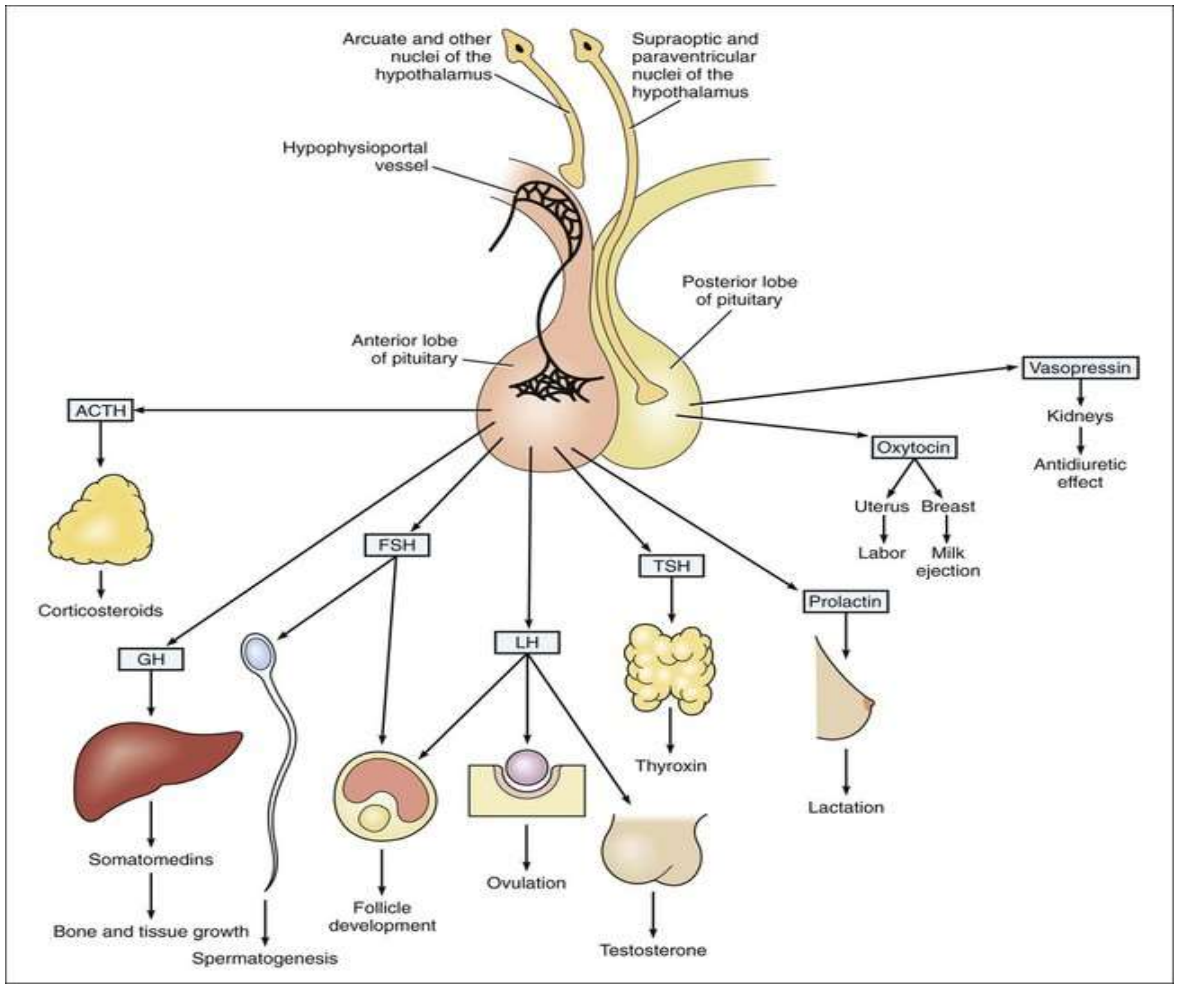
https://doctorlib.info/physiology/physiology-2/82.html

Hormones of hypothalamus

- The system hypothalamus – hypophysis can be divided into two particular systems with different relation between the hypothalamus and respective part of the hypophysis:
- 1) Hypothalamus – adenohypophysis (= anterior pituitary gland) The hypothalamus produces **liberins and statins** that get with blood through the vascular portal system (two capillary systems) and hypothalamus-pituitary stalk in the adenohypophysis, where they control production of anterior pituitary hormones. The adenohypophysis produces hormones acting on peripheral tissues (growth hormone, prolactin) and glandotropic hormones (adrenocorticotropin, thyrotropin, gonadotropins) control activity of peripheral glands (i.e. the adrenal cortex, thyroid gland, gonads).
- The main hypothalamic liberins and statins are:
- **Liberins** (activate secretion of adenohypophysis hormones): corticoliberin (corticotropin-releasing hormone, CRH; corticotropin releasing factor, CRF), thyroliberin (thyrotropin-releasing hormone, TRH), somatoliberin (growth hormone-releasing hormone, GRH), gonadoliberin (gonadotropin-releasing hormone, GnRH).
- **Statins** (inhibit secretion of adenohypophysis hormones): somatostatin (growth hormone-inhibiting hormone), prolactostatin (prolactin-inhibiting hormone, PIH).
- 2) Hypothalamus – neurohypophysis (= posterior pituitary gland) Hypothalamus (nc. supraopticus, nc. paraventricularis) synthetizes vasopressin (= antidiuretic hormone, ADH) and oxytocin that are transported by axons of the hypothalamic neurones producing these hormones passing through the hypothalamicpituitary stalk (axonal transport) into the neurohypophysis that is only a place of their release into the blood.



http://www.vivo.colostate.edu/hbooks/pathphys/endocrine/hypopit/overview.html



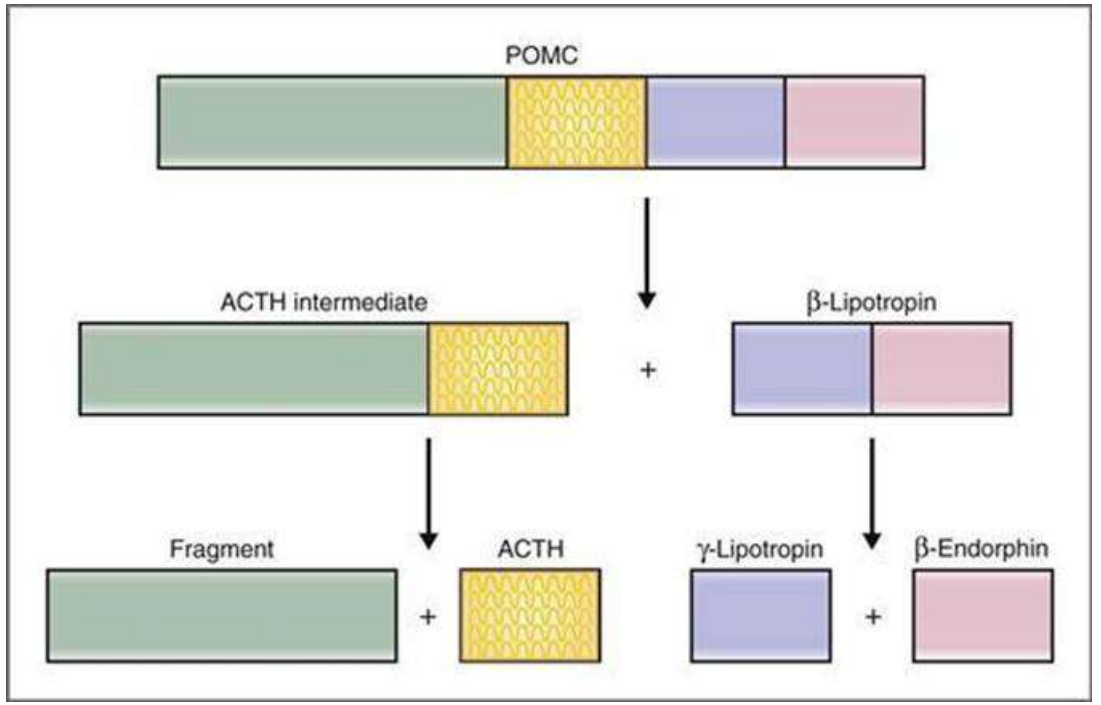
https://basicmedicalkey.com/hypothalamic-and-pituitary-drugs/

Adenohypophysis hormones

- The major hormones are secreted by the anterior lobe of the pituitary:
- ThyrotropinSH, follicle stimulating hormone, luteinizing hormone, adrenocorticotpopic hormones (ACTH), Somatotropin (growth hormone), and prolactin. Each hormone is secreted by a different cell type (except FSH and LH, which are secreted by the same cell type).
- Each of the anterior pituitary hormones is a peptide or polypeptide. As described , the synthesis of peptide hormones includes the following steps: transcription of DNA to mRNA in the nucleus; translation of mRNA to a preprohormone on the ribosomes; and posttranslational modification of the preprohormone on the endoplasmic reticulum and the Golgi apparatus to produce the final hormone. The hormone is stored in membrane-bound secretory granules for subsequent release. When the anterior pituitary is stimulated by a hypothalamic-releasing hormone or a release-inhibiting hormone (e.g., thyrotrophs are stimulated by TRH to secrete TSH), there is exocytosis of the secretory granules; the anterior pituitary hormone (e.g., TSH) enters capillary blood and is delivered by the systemic circulation to the target tissue (e.g. , thyroid gland).
- The hormones of the anterior lobe are organized in “families,” according to structural and functional homology. TSH, FSH, and LH are structurally related and constitute one family, ACTH is part of a second family, and growth hormone and prolactin constitute a third family.

ACTH Family

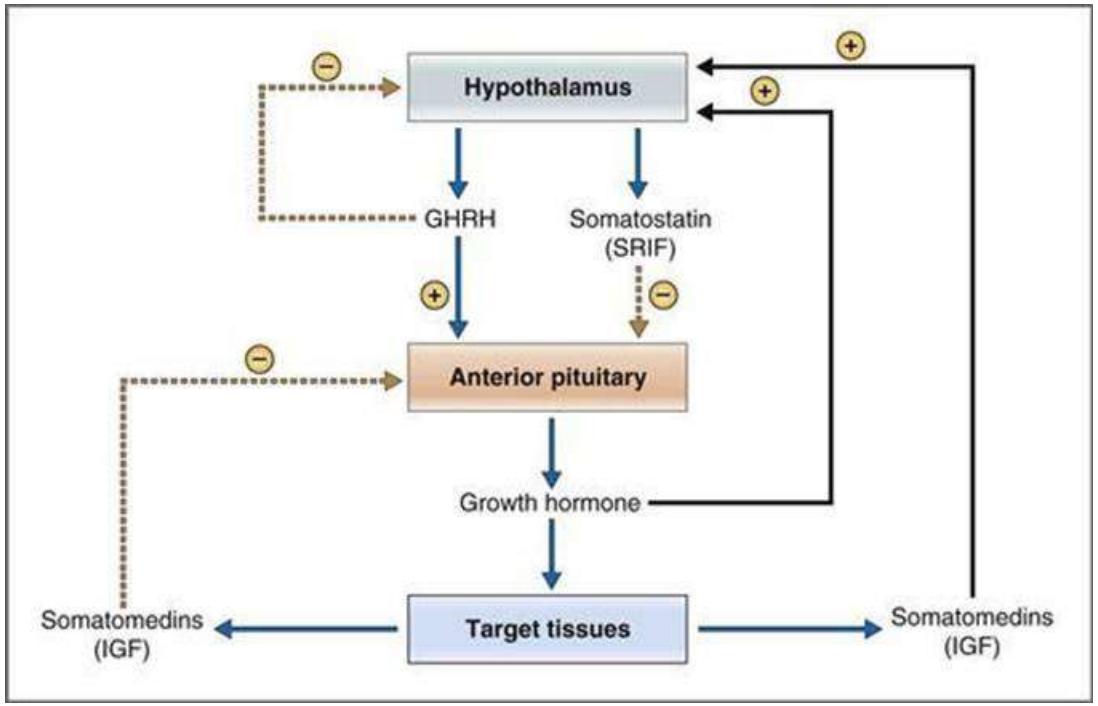
- The ACTH family is derived from a single precursor, **pro-opiomelanocortin (POMC).** The ACTH family includes ACTH, γ- and β-lipotropin, β-endorphin, and melanocyte-stimulating hormone (MSH). ACTH is the only hormone in this family with well-established physiologic actions in humans. MSH is involved in pigmentation in lower vertebrates but has little activity in humans. β-Endorphin is an endogenous opiate.
- The preprohormone for this group, **prepro-opiomelanocortin,** is transcribed from a single gene. The signal peptide is cleaved in the endoplasmic reticulum, yielding POMC, the precursor to the ACTH family. Endopeptidases then hydrolyze peptide bonds in POMC and intermediates to produce the members of the ACTH family (Fig. 9-10). The anterior pituitary in humans produces mainly ACTH, γ-lipotropin, and β-endorphin.
- The fragment contains γ-MSH; ACTH contains α-MSH; and γ-lipotropin contains β-MSH. ACTH, Adrenocorticotropic hormone; MSH, melanocyte-stimulating hormone.
- It is noteworthy that MSH activity is found in POMC and in several of its products: The "fragment," which is left over from hydrolysis of the ACTH intermediate, contains γ-MSH; ACTH contains α-MSH; and γ-lipotropin contains β-MSH. These MSH-containing fragments can cause skin pigmentation in humans if their blood levels are increased. For example, in **Addison disease** (primary adrenal insufficiency), POMC and ACTH levels are increased by negative feedback. Because POMC and ACTH contain MSH activity, skin pigmentation is a symptom of this disorder.



https://doctorlib.info/physiology/physiology-2/83.html

Growth Hormone

- Growth hormone is secreted throughout life. It is the single most important hormone for normal growth to adult stature.
- Growth hormone is synthesized in the somatotrophs of the anterior lobe of the pituitary and also is called somatotropin or somatotropic hormone. Human growth hormone contains 191 amino acids in a straight-chain polypeptide with 2 internal disulfide bridges. Secretion
- Growth hormone is secreted in a pulsatile pattern, with bursts of secretion occurring approximately every 2 hours. The largest secretory burst occurs within 1 hour of falling asleep (during sleep stages III and IV).



https://doctorlib.info/physiology/physiology-2/83.html

Growth Hormone

Actions of Growth Hormone

Growth hormone has multiple metabolic actions on liver, muscle, adipose tissue, and bone, as well as growth-promoting actions in virtually every other organ. The actions of growth hormone include effects on linear growth, protein synthesis and organ growth, carbohydrate metabolism, and lipid metabolism.

Some of the actions of growth hormone result from the hormone's *direct* effect on target tissues such as skeletal muscle, the liver, or adipose tissue. Other actions of growth hormone are mediated *indirectly* through the production of **somatomedins** (or insulin-like growth factors [IGFs]) in the liver. The most important of the somatomedins is somatomedin C or **IGF-1.** Somatomedins act on target tissues through autophosphorylation. The growth-promoting IGF receptors that are similar to the insulin receptor, having **intrinsic tyrosine kinase activity** and exhibiting effects of growth hormone are mediated largely through production of somatomedins.

Diabetogenic effect. Growth hormone causes **insulin resistance** and decreases glucose uptake and utilization by target tissues such as muscle and adipose tissue. These effects are called "diabetogenic" because they produce an increase in blood glucose concentration, as occurs when insulin is lacking or when tissues are resistant to insulin (e.g., diabetes mellitus). Growth hormone also increases lipolysis in adipose tissue. As a consequence of these metabolic effects, growth hormone causes an increase in blood insulin levels.

Increased protein synthesis and organ growth. In virtually all organs, growth hormone increases the uptake of amino acids and stimulates the synthesis of DNA, RNA, and protein. These effects account for the hormone's growth-promoting actions: increased lean body mass and increased organ size. As noted, many of the growth effects of growth hormone are mediated by somatomedins.

Increased linear growth. The most striking effect of growth hormone is its ability to increase linear growth. Mediated by the somatomedins, growth hormone alters every aspect of cartilage metabolism: stimulation of DNA synthesis, RNA synthesis, and protein synthesis. In growing bones, the epiphyseal plates widen and more bone is laid down at the ends of long bones. There also is increased metabolism in cartilage-forming cells and proliferation of chondrocytes.

Growth hormone deficiency

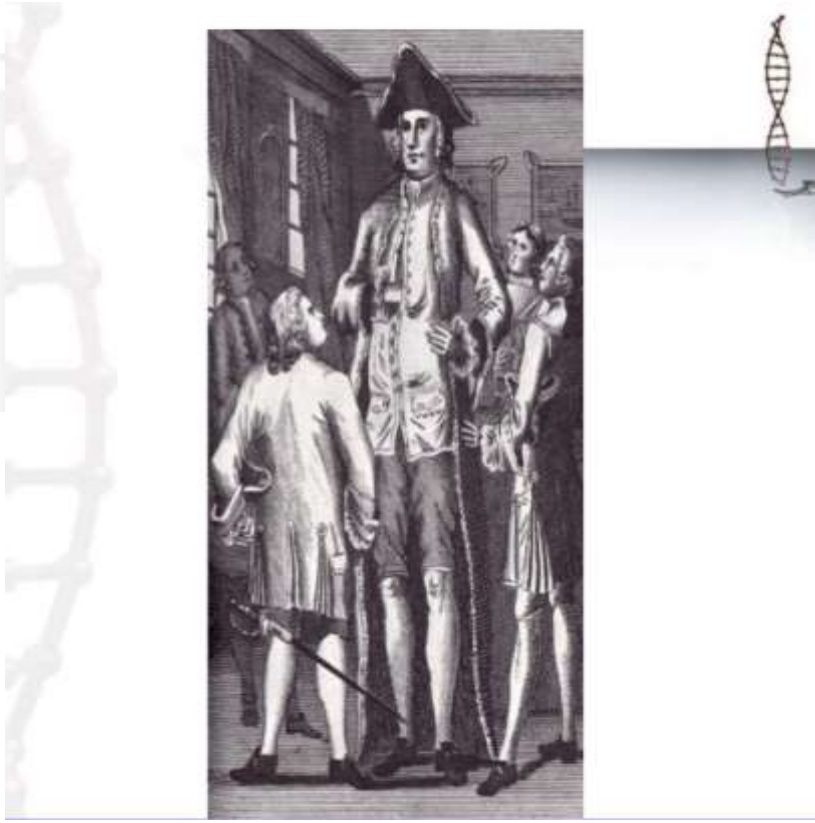
- **Growth hormone deficiency** in children results in failure to grow, short stature, mild obesity, and delayed puberty. The causes of growth hormone deficiency include defects at every step in the hypothalamic–anterior pituitary–target tissue axis: decreased secretion of GHRH due to hypothalamic dysfunction; primary deficiencies of growth hormone secretion from the anterior pituitary; failure to generate somatomedins in the liver; and deficiency of growth hormone or somatomedin receptors in target tissues (growth hormone resistance). Growth hormone deficiency in children is treated with human growth hormone replacement.

Dwarfism occurs when an organism is extremely small In humans, it is sometimes defined as an adult height of less than 147 centimetres, regardless of sex

https://www.slideshare.net/KemUnited/pituitary-disorders-1-growth-hormone

Growth hormone excess

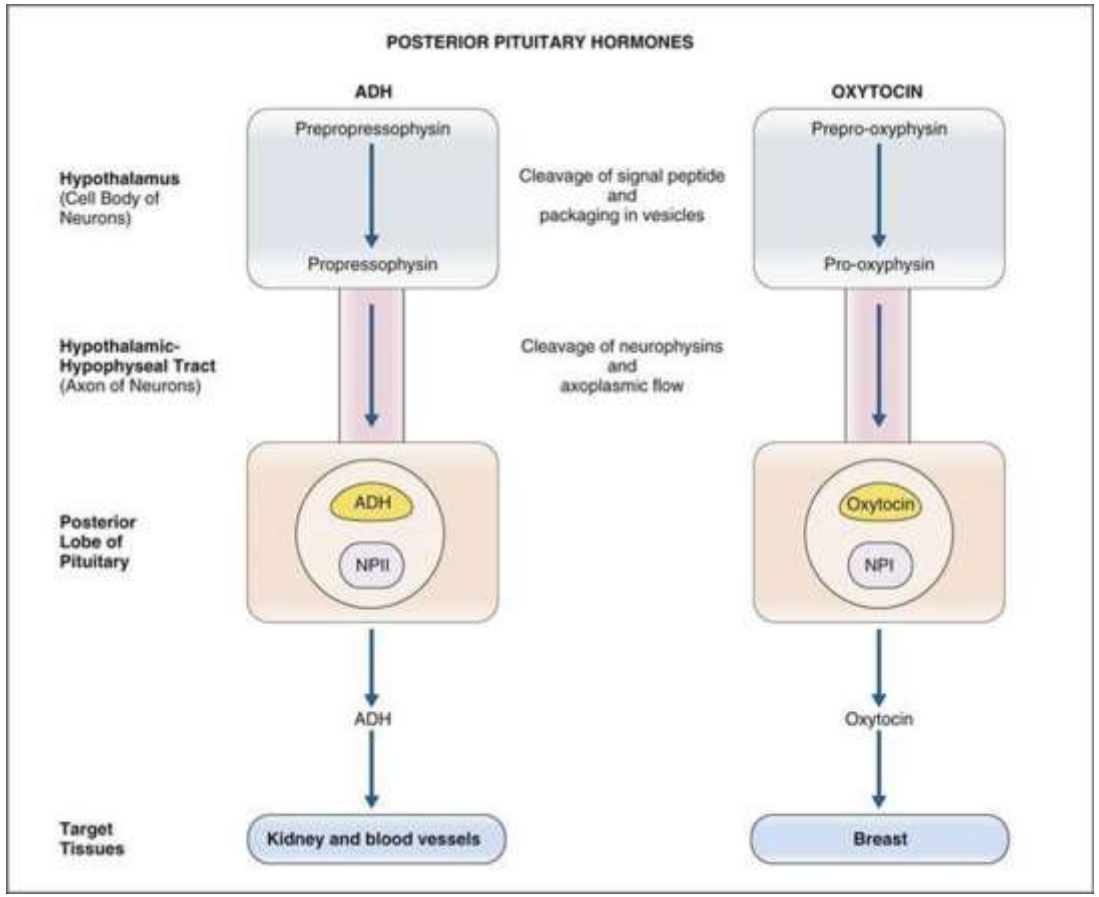
- **Growth hormone excess** causes **acromegaly** and is most often due to a growth hormone–secreting pituitary adenoma. The consequences of excess growth hormone differ, depending on whether the excess occurs before or after puberty. Before puberty, excessive levels of growth hormone cause **gigantism** (increased linear growth) because of intense hormonal stimulation at the epiphyseal plates. After puberty, when linear growth is complete and can no longer be influenced, excess levels of growth hormone cause increased periosteal bone growth, increased organ size, increased hand and foot size, enlargement of the tongue, coarsening of facial features, insulin resistance, and glucose intolerance. Conditions with excess secretion of growth hormone are treated with **somatostatin analogues** (e.g., **octreotide**), which, like endogenous somatostatin, inhibit growth hormone secretion by the anterior pituitary.



http://www.pietromortini.com/acromegaly/

Neurohypophysis hormones

- The posterior lobe of the pituitary secretes **antidiuretic hormone (ADH) and oxytocin.** Both ADH and oxytocin are neuropeptides, synthesized in cell bodies of hypothalamic neurons and secreted from nerve terminals in the posterior pituitary.
- Actions of Antidiuretic Hormone ADH (vasopressin) has two actions, one on the kidney and the other on vascular smooth muscle. These actions are mediated by different receptors, different intracellular mechanisms, and different second messengers.
- Increase in water permeability. The major action of ADH is to increase the water permeability of principal cells in the late distal tubule and collecting duct. The receptor for ADH on the principal cells is aV2 receptor, which is coupled to adenylyl cyclase via a Gs protein. The second messenger is cAMP, which, via phosphorylation steps, directs the insertion of water channels, aquaporin 2 (AQP2), in the luminal membranes. The increased water permeability of the principal cells allows water to be reabsorbed by the collecting ducts and makes the urine concentrated, or hyperosmotic.
- Contraction of vascular smooth muscle. The second action of ADH is to cause contraction of vascular smooth muscle (as implied by its other name, vasopressin). The receptor for ADH on vascular smooth muscle is a V1receptor, which is coupled to phospholipase C via a Gq protein. The second messenger for this action is IP3/Ca2+, which produces contraction of vascular smooth muscle, constriction of arterioles, and increased total peripheral resistance.



https://doctorlib.info/physiology/physiology-2/84.html

Antidiuretic hormone disorders

- **Central diabetes insipidus** is caused by failure of the posterior pituitary to secrete ADH. In this disorder, circulating levels of ADH are low, the collecting ducts are impermeable to water, and the urine cannot be concentrated. Thus, persons with central diabetes insipidus produce large volumes of dilute urine, and their body fluids become concentrated (e.g., increased serum osmolarity, increased serum Na+concentration). Central diabetes insipidus is treated with an ADH analogue, dDAVP.
- In nephrogenic diabetes insipidus, the posterior pituitary is normal but the principal cells of the collecting duct are unresponsive to ADH due to a defect in the V2 receptor, Gs protein, or adenylyl cyclase. As in central diabetes insipidus, water is not reabsorbed in the collecting ducts and the urine cannot be concentrated, resulting in excretion of large volumes of dilute urine. As a result, the body fluids become concentrated and the serum osmolarity increases. In contrast to central diabetes insipidus, however, ADH levels are elevated in nephrogenic diabetes insipidus due to stimulation of secretion by the increased serum osmolarity. Nephrogenic diabetes insipidus is treated with thiazide diuretics.
- In **syndrome of inappropriate ADH (SIADH),** excess ADH is secreted from an autonomous site. High levels of ADH cause excess water reabsorption by the collecting ducts, which dilutes the body fluids (e.g., decreases plasma osmolarity and Na+ concentration). The urine is inappropriately concentrated (i.e., too concentrated for the serum osmolarity). SIADH is treated with an ADH antagonist such as demeclocycline or water restriction.

Gland of Origin	Hormones*	Chemical Classification†	Major Actions
Hypothalamus	Thyrotropin-releasing hormone (TRH)	Peptide	Stimulates secretion of TSH and prolactin
	Corticotropin-releasing hormone (CRH)	Peptide	Stimulates secretion of ACTH
	Gonadotropin-releasing hormone (GnRH)	Peptide	Stimulates secretion of LH and FSH
	Somatostatin or somatotropin release–inhibiting hormone (SRIF)	Peptide	Inhibits secretion of growth hormone
	Dopamine or prolactin-inhibiting factor (PIF)	Amine	Inhibits secretion of prolactin
	Growth hormone–releasing hormone (GHRH)	Peptide	Stimulates secretion of growth hormone
Anterior Pituitary	Thyroid-stimulating hormone (TSH)	Peptide	Stimulates synthesis and secretion of thyroid hormones
	Follicle-stimulating hormone (FSH)	Peptide	Stimulates sperm maturation in Sertoli cells of testes
			Stimulates follicular development and estrogen synthesis in ovaries
	Luteinizing hormone (LH)	Peptide	Stimulates testosterone synthesis in Leydig cells of testes
			Stimulates ovulation, formation of corpus luteum, estrogen and progesterone synthesis in ovaries
	Growth hormone	Peptide	Stimulates protein synthesis and overall growth
	Prolactin	Peptide	Stimulates milk production and secretion in breast
	Adrenocorticotropic hormone (ACTH)	Peptide	Stimulates synthesis and secretion of adrenal cortical hormones (cortisol, androgens, and aldosterone)
	Melanocyte-stimulating hormone (MSH)	Peptide	Stimulates melanin synthesis (? humans)

https://doctorlib.info/physiology/physiology-2/77.html

Gland of Origin	Hormones*	Chemical Classification†	Major Actions
Posterior Pituitary	Oxytocin	Peptide	Stimulates milk ejection from breasts and uterine contractions
	Vasopressin or antidiuretic hormone (ADH)	Peptide	Stimulates water reabsorption in principal cells of collecting ducts and constriction of arterioles
Thyroid	Triiodothyronine (T_3) and L-thyroxine (T_4)	Amine	Stimulates skeletal growth; oxygen consumption; heat production; protein, fat, and carbohydrate utilization; perinatal maturation of the central nervous system
	Calcitonin	Peptide	Decreases serum $[Ca^{2+}]$
Parathyroid	Parathyroid hormone (PTH)	Peptide	Increases serum $[Ca^{2+}]$
Adrenal Cortex	Cortisol (glucocorticoid)	Steroid	Stimulates gluconeogenesis; inhibits inflammatory response; suppresses immune response; enhances vascular responsiveness to catecholamines
	Aldosterone (mineralocorticoid)	Steroid	Increases renal Na^+ reabsorption, K^+ secretion, and H^+ secretion
	Dehydroepiandrosterone (DHEA) and androstenedione (adrenal androgens)	Steroid	See actions of testosterone from testes (see below)
Testes	Testosterone	Steroid	Stimulates spermatogenesis; stimulates male secondary sex characteristics
Ovaries	Estradiol	Steroid	Stimulates growth and development of female reproductive system, follicular phase of menstrual cycle, development of breasts, prolactin secretion; maintains pregnancy
	Progesterone	Steroid	Stimulates luteal phase of menstrual cycle; maintains pregnancy
Corpus Luteum	Estradiol and progesterone	Steroid	See actions of estradiol and progesterone from ovaries (see above)
Placenta	Human chorionic gonadotropin (HCG)	Peptide	Stimulates estrogen and progesterone synthesis in corpus luteum of early pregnancy
	Human placental lactogen (HPL), or human chorionic somatomammotropin	Peptide	Has growth hormone–like and prolactin-like actions during pregnancy
	Estriol	Steroid	See actions of estradiol from ovaries (see above)
	Progesterone	Steroid	See actions of progesterone from ovaries (see above)
Pancreas	Insulin (β cells)	Peptide	Decreases blood [glucose]
	Glucagon (α cells)	Peptide	Increases blood [glucose]
Kidney	Renin	Peptide	Catalyzes conversion of angiotensinogen to angiotensin I
	1,25-Dihydroxycholecalciferol	Steroid	Increases intestinal absorption of Ca^{2+}; bone mineralization
Adrenal Medulla	Norepinephrine, epinephrine	Amine	See actions of sympathetic nervous system (see Chapter 2)

Sources of information

- https://ib.bioninja.com.au/standard-level/topic-6-human-physiology/66-hormones-homeostasis-and/types-of-hormones.html
- https://www.youtube.com/watch?v=P4cuTwgfjBY
- https://www.slideshare.net/damarisb/second-messenger-system
- https://doctorlib.info/physiology/physiology-2/81.html
- https://courses.lumenlearning.com/wm-biology1/chapter/reading-signal-receptors/
- https://doctorlib.info/physiology/physiology-2/82.html
- https://basicmedicalkey.com/hypothalamic-and-pituitary-drugs/
- http://www.vivo.colostate.edu/hbooks/pathphys/endocrine/hypopit/overview.html
- http://www.pietromortini.com/acromegaly/
- https://www.slideshare.net/KemUnited/pituitary-disorders-1-growth-hormone
- https://doctorlib.info/physiology/physiology-2/84.html
- https://doctorlib.info/physiology/physiology-2/77.html

- Biological and Bioorganic Chemistry: in 2 books. Book 2. Biological Chemistry /Yu.Gubsky, I.V. Nizhenkovska, M.M. Korda et al. ; edited by Yu.Gubsky, I.V.Nizhenkovska. – Kyiv:AUS Medicine Publishing, 2020.- 544 p.ISBN 978-617-505-785-8
- Halkerston I.D.K. Biochemistry: 2nd edition. The National medical series for independent study / Halkerston I.D.K. - 1988. - 522 p.
- Harper`s Biochemistry. R.K.Murray, D.K.Granner, P.A.Mayes, V.W.Rodwell. Prentice-Hall International Inc., 2010. – 1134 p.
- Gubsky Yu. Biological chemistry: textbook. – Vinnytsia: Nova Knyha, 2017. – 488 p.
- Koolman J. Color Atlas of Biochemistry / J.Koolman, K.-H. Rom. – Stuttgart. New York. – Thieme Verlag. — 1996. – 435 p.
- Lehninger A. Principles of Biochemistry / Lehninger A. – New York. – W.H.Freeman and Company. – 2005. – 1010 p.
- Pamela C.Champe Lippincott’s Illustrated Reviews: Biochemistry, 3rd Edition / Pamela C.Champe and Richard A.Harvey. – Baltimore, Lippincott Williams & Wilkins, MD ©, 2005. – 534p.