Department of Veterinary Physiology

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ENDOCRINOLOGY

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ENDOCRINOLOGY

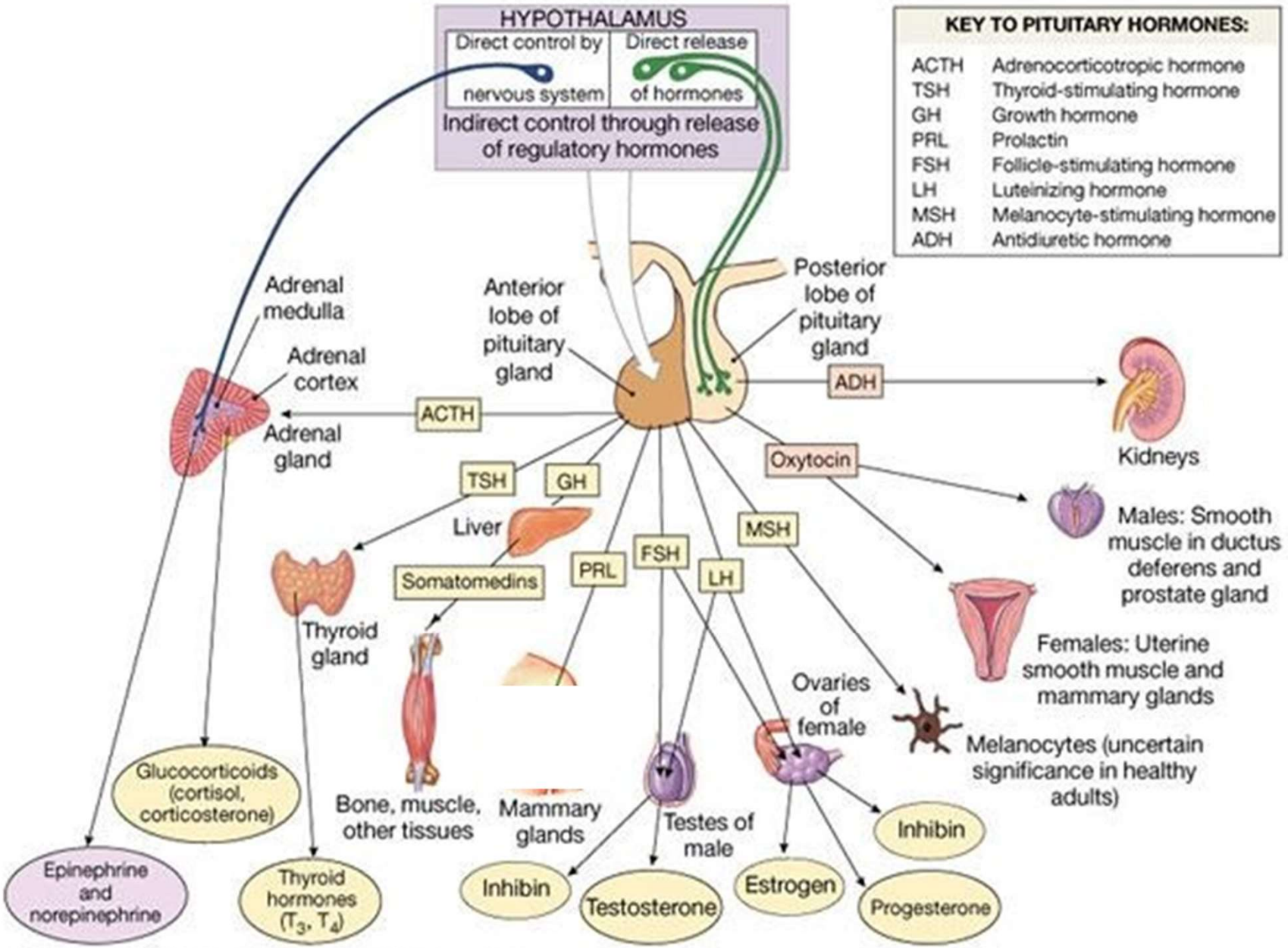
- Introduction
- Terminology
- Glands and their secretions
- feed-back regulation
- Classification
- Biosynthesis
- Receptors


ENDOCRINE
SYSTEM

ENDOCRINOLOGY

- *Endocrinology* is the branch of science that deals with chemical integration of the body. Endocrinology is concerned with the study of **biosynthesis, storage, chemistry, and physiological functions** of chemical signaling molecules and with the cells of the endocrine glands that secrete them.

- Signals sent to target organs are modified based on information received from the target cells. This type of regulation is called ***feed-back regulation***.
- In some reflex activities the nervous system serves as an afferent pathway in sending impulse to the hypothalamus, which in turn stimulates the endocrine system (hypophysis) to release humoral substances, which act peripherally to complete the reflex. These humoral substances travel rather slowly, since they are dependent upon the circulatory system for their transportation to the effector organs.
- E.g., **Milk ejection** – suckling stimulate sensory receptors in the teat which sends neural impulses to the hypothalamus which in turn causes release of oxytocin from the posterior pituitary glands. The oxytocin is carried by blood to reach the udder where it causes contraction of myoepithelial cells ejecting milk. This type of reflex is called as *neuroendocrine reflex.*


HYPOTHALAMUS
Direct control by nervous system
Direct release of hormones
Indirect control through release of regulatory hormones
KEY TO PITUITARY HORMONES:
ACTH Adrenocorticotropic hormone
TSH Thyroid-stimulating hormone
GH Growth hormone
PRL Prolactin
FSH Follicle-stimulating hormone
LH Luteinizing hormone
MSH Melanocyte-stimulating hormone
ADH Antidiuretic hormone
Adrenal medulla
Adrenal cortex
Adrenal gland
Anterior lobe of pituitary gland
Posterior lobe of pituitary gland
ACTH
ADH
Kidneys
Oxytocin
TSH
GH
Liver
Somatomedins
Thyroid gland
PRL
FSH
LH
MSH
Males: Smooth muscle in ductus deferens and prostate gland
Females: Uterine smooth muscle and mammary glands
Ovaries of female
Melanocytes (uncertain significance in healthy adults)
Glucocorticoids (cortisol, corticosterone)
Bone, muscle, other tissues
Mammary glands
Testes of male
Inhibin
Epinephrine and norepinephrine
Thyroid hormones (T_3, T_4)
Inhibin
Testosterone
Estrogen
Progesterone

HORMONE TERMINOLOGY

- **Hormone**: Hormones are substance produced by endocrine cells which are added directly to blood/lymph and distributed throughout the body through circulatory system. They regulate the activity of target cells / organs; also called as ***"chemical messenger"***
- **Neurohormone**: A hormone produced by nerve cells called neuroendocrine cells which enter blood and carried to different parts of the body (e.g.) **oxytocin, vasopressin**
- **Neuropeptide**: A peptide hormone produced by neuroendocrine cells (e.g. **Substance P**).
- **Nonpeptidergic neurohormone**: Neurohormone that is not peptide; **acetylcholine, histamine, norepinephrine**
- **Local hormone** Hormones that act on target cells located nearby the secretory cells – local hormones may produce ***paracrine* effect** when they influence the functions of neighbouring cells or *autocrine* effect when the hormone acts on the cell that has secreted it (gut hormones have paracrine and / or autocrine effects).

- **Neurotransmitter**: Neurohormones that act at synapse for transmission of nerve impulse
- **Neuromodulator**: A hormone that modulates the response of a neuron to a neurotransmitter or to other hormone **eg. NPY modulates the release of norepinephrine.**
- **Pheromones**: Chemical messengers released to the exterior of one animal to stimulate a response in another member of the same species
- **Lumones**: Chemical messengers released into the lumen of GI tract
- **Chalones**: Putative (*believed to be*) cellular mitotic inhibitors
- **Growth factors**: Mitogenic peptides – stimulate growth of various tissues in the body

Glands and their hormones

Endocrine glands	Hormones produced
Hypothalamus	TRH, GnRH, CRH, GHRH and GH-RIH, PRF and PIF
Anterior pituitary (adenohypophysis)	GH, PRL, TSH, FSH, LH, ACTH, MSH, β-endorphin
Posterior pituitary (neurohypophysis)	Oxytocin , Vasopressin
Pineal	Melatonin
Parathyroid	PTH
Thyroid	T4, T3, calcitonin
Adrenal cortex	Cortisol, corticosterone, aldosterone
Adrenal medulla	Epinephrine, norepinephrine, dopamine
Gonads	Androgens, oestrogens, progestins, inhibin, relaxin
Pancreas	Insulin, glucagon
Gastrointestinal tract	Gastrin, GIP, secretin, CCK, Motilin, neurotensin, VIP
Kidney	Erythropoietin
Various tissues	Eicosanoids, Growth factors

Chemical Classification

1) Amines		
Epinephrine	Adrenaline Catecholamine	Adrenal Medulla, CNS, Sympathetic nerves
Norepinephrine	Nor-adrenaline Catecholamine	Adrenal medulla, CNS, sympathetic nerves
Dopamine	Catecholamine	CNS, Sympathetic
2) Glycoproteins		
Thyroid stimulating hormone	TSH	Adenohypophysis
Luteinizing hormone	LH, ICSH	Adenohypophysis
Follicle stimulating hormone	FSH	Adenohypophysis
3) Iodinated Amino Acids		
Thyroxine	T4	Thyroid gland
Triiodothyronine	T3	Thyroid gland

4) Steroids			
	Cortisol	**Hydrocortisone**	**Adrenal cortex**
	Oestradiol	**E4**	**Ovary, testis, placenta**
	Testosterone		**Testis, Ovary, Adrenal cortex**
	Progesterone	**P4**	**Ovary, placenta, adrenal cortex**
	Aldosterone	**Electrocortin**	**Adrenal cortex**
	Dihydroxycholecalciferol	**Calcitriol, Dihydroxy-vit D**	**Kidney**
5) Fatty Acid Derivatives			
	Eicosanoids	**Prostaglandins (PG), prostacyclins (PGI), thromboxanes, leukotrienes**	**All tissues**

Based on chemical structure

- Hormones can be grouped into 6 families.
  1. **ACTH family**: ACTH, MSH
  2. **Somatomammotropic family**: GH, prolactin, chorionic somatomammotropin
  3. **Glycoprotein family**: FSH, LH, TSH, hCG, eCG
  4. **Insulin family**: Insulin, IGF I, IGF II, relaxin
  5. **Oxytocin family**: Oxytocin, vasopressin
  6. **Steroid family**: Gonadal steroid and adrenal steroid hormones

Physiological Classification

- **Hormones Regulating Energy Metabolism**
  - Insulin, glucagon, glucocorticoids, epinephrine, ACTH, thyroid hormone
- **Hormones Regulating Mineral Metabolism**
  - Aldosterone, renin-angiotensin II & natriuretic hormone, PTH, CT
- **Hormones Regulating Growth**
  - GH, insulin, oestrogen, androgen & somatostatin
- **Hormones Regulating Reproduction**
  - GnRH, FSH, LH /ICSH, oestrogen, inhibin progestrone, testosterone, oxytocin, prostaglandins and relaxin
- **Hormones Regulating Milk Secretion**
  - Oestrogen, prolactin, TSH, ACTH, GH, glucocorticoid, placental lactogen,

- **Hormones Regulating Blood Pressure**
  - Renin-angiotensin, epinephrine, norepinephrine, vasopressin, ACTH
- **Hormones Regulating Water Balance**
  - Vasopressin (ADH), renin-angiotensin, glucocorticoids & insulin
- **Local Hormones**
  - PGs, histamine, serotonin
- **Gut Hormones**
  - Gastrin, secretin, CCK, motilin, bombesin somatostatin, gastric inhibitory peptide (GIP), vasoactive intestinal polypeptide & substance P

Based on solubility

	Water soluble (Hydrophilic)	Lipid soluble (Lipophilic / hydrophobic)
Chemistry	Polypeptides, amino acid derivatives	Steroids, thyronines
Receptors	Plasma membrane	Intracellular
Transduction	Second messengers, phosphorylation,	DNA binding, transcription
Kinetics	Fast	Prolonged
Example	Insulin, epinephrine	Cortisol, thyroxine

SYNTHESIS OF PROTEIN HORMONES

- Amino acid polymers consisting of less than 100 amino acids are generally termed as *polypeptides* and those with more than 100 amino acids are termed as *proteins*. When proteins are conjugated with carbohydrates it is termed as *glycoproteins*.
- The protein and peptide hormones are initially synthesized on ribosomes attached on rough endoplasmic reticulum (RER) as directed by mRNA as large precursor proteins called *pre-pro-hormone* which immediately moves to the interior of RER and the pre portion of the hormone is cleaved to form *prohormone*.
- The presence of peptidase within the wall of the RER allows the rapid removal of the pre portion and the *prohormone* leave the RER in vesicles. These vesicles move to the Golgi apparatus and attach with Golgi membrane to form secretory granules (**hormone may be sulphated or glycosylated**) and the hormone is in its final form within the Golgi apparatus.
- Protein hormones are stored in granules within the gland until needed for release. Although some of the hormones are secreted continuously, most are excreted by a process of ***exocytosis*** of granules in response to specific signal. Exocytosis requires **ATP and Ca^{2+}.**
- When the hormone is secreted from the secretory vesicle, it automatically leads to synthesis of new hormones and the hormone stores are replenished.

SYNTHESIS OF STEROID HORMONES

- Steroid hormones are produced in the gonads and the adrenal gland. The steroids produced in the gonads include progestins, estrogens and androgens
- Although the steroids can be synthesized *de novo* within the cell from the two-carbon molecule, the *acetate*, majority of steroids are formed from ***cholesterol,*** which is synthesized by the liver. Cholesterol is present in the plasma as low-density lipoproteins (LDL)
- The LDL enters the steroid-producing cells through interaction with the membrane receptor. Cholesterol is released through the degradation of LDL by lysosomal enzymes. Cholesterol is either utilized immediately for steroid synthesis or stored in granules in ester form within the cells.
- Steroid hormones are synthesized within the smooth endoplasmic reticulum.

SYNTHESIS OF STEROID HORMONES

- The first step in the synthesis of all steroid hormones from cholesterol involves cleavage of side chain of cholesterol to form pregnenolone, which occurs within the mitochondrion. Subsequently modification of the steroid molecules may occur within the mitochondrion (or) may involve the endoplasmic reticulum of the cell.
- The type of steroid hormone that is eventually synthesized depends upon the specific enzymes within the particular cell type. For e.g., only the cells of the adrenal cortex contain the enzyme *hydroxylase* for **hydroxylation of 11 and 21 carbon molecules** essential for the production of glucocorticoids and mineralocorticoids.
- There is no provision for storage of steroid hormones within the cells. They are secreted immediately after formation by simple diffusion across the cell membrane because of their lipophilic nature.
- Most steroid hormones have a plasma half life of **1 to 3 h** after which they are inactivated mainly in the liver and to a less extent in kidney.

SYNTHESIS OF THYROID HORMONES

- They are synthesized extracellularly (within the lumen) by iodination of amino acid tyrosine present on thyroglobulin molecule located in the follicles of thyroid gland and taken up by the follicular cells by endocytosis; within the follicular cells they are enzymatically cleaved from the thyroglobulin before secretion.

PATTERN OF HORMONE SECRETION

- Fluctuations of frequency and amplitude of hormone secretion is described as *hormone peaks, pulses, spikes or bursts*.
- The rhythm of hormone secretion may be one the following:
- ***Ultradian –*** Many short pulses occurring every few minutes to few hours each day
- **Circadian** – peaks occur approximately once in 24 h (cortisol peaks in early morning)
- **Infradian** – pulses take more than a day but less than a year to occur (preovulatory surge of LH in dogs once in 6 mon)
- GH concentrations are highest during night (10 to 11 P.M.) when cortisol level is the lowest and cortisol reaches its peak during morning (6 to 8 A.M.) with GH at its lowest level.

TRANSPORT OF HORMONES IN THE BLOOD

- Protein, peptide hormones and catecholamines are *hydrophilic* and carried in plasma in dissolved (free) form. Some peptide hormones like GH and IGF-I are transported bound with a transport protein
- The steroid and thyroid hormones are *lipophilic* and has limited solubility in aqueous solutions. Hence they are carried in plasma mainly in association with both specific and nonspecific binding proteins.
- Thyroid hormones are transported by *thyroxine binding globulin* (TBG);
- *Transcortin* is the corticosteriod-binding globulin (CBG), which has high affinity for cortisol and corticosterone,
- *Sex hormone-binding globulin* (SHBG) aids transport of oestradiol, progesterone and testosterone
- TBG, CBG and SHBG are specific binding proteins that transport lipophilic hormones
- **Albumin and prealbumin are nonspecific binding proteins that also transports steroids and thyroid hormones in circulation**
- These plasma binding proteins prolong the hormonal action by providing protection against degradation and elimination. However the bound form of hormone cannot enter into cells. Only the free form diffuses into the cell to exert physiological functions. In the circulation, free hormones have much shorter half-life than the protein bound hormones.

MECHANISM OF HORMONE ACTION

- Many of the hormones that act on distant target cells also affect neighboring cells or even have effects on the same cells that secreted the hormone.
- The hormones can act on the target cells in one of the following ways:
- **Endocrine action**: the hormone is distributed in blood and binds to distant target cells.
- **Paracrine action**: the hormone acts locally by diffusing from its source to target cells in the neighbourhood.
- **Autocrine action**: the hormone acts on the same cell that produced it.
- **Neurocrine**: Hormones diffuse through synaptic clefts between neurons as neurotransmitters
- **Neuroendocrine action**: Hormones synthesized in the neuron's cell body, stored in axons and secreted into blood

Receptor properties

- **All receptors are proteins**
- ***Specificity*:** The binding site of the receptor is highly specific for each signaling molecule (hormone, neurotransmitter); molecules that bind specifically to receptor are called ***ligands*.**
- However, some molecules having structural similarity to ligands can also bind with receptors and produce a physiological response and such molecules are called as ***agonists*.** Some molecules having structural similarity with hormone may bind with receptors without producing a response and inhibit the hormone effect are called as ***antagonists*.**
- ***High affinity*:** Usually the concentration of the hormone in the blood is very low (in pmol/l to µmol/l). Because the receptors have *high affinity* to hormones, binding occurs rapidly
- ***Binding capacity*:** Number of receptors available on the target cells at any given time is the limiting factor that determines number of hormone molecules bound to target organs; i.e. the binding capacity of target cells is decided by the receptor numbers.
- When a target cell is exposed to high level of hormone for a period of time, the number of active receptors will be reduced (by receptor degradation) known as ***down regulation*.**
- During deficiency of a hormone, there is an increase in the number of active receptors known as ***up regulation***.
- *When a receptor becomes bound to a hormone, the receptor undergoes a conformational change (known as **receptor activation**), which allows it to interact productively with other components of the cells*, leading ultimately to an alteration in the physiologic state of the cell.

Thank
You!!!