Endocrine Control Systems

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This lecture covers general principles of endocrine control systems. It covers the following pages in the textbook: 12; 121-124; 319-332[1]. The goals of this lecture are to demonstrate the basic concepts of endocrinology including what hormones do, how they are classified and generally how they function. This is the first of seven lectures, the next six of which will go into various endocrine systems in much more detail. The concepts in this lecture are essential to the understanding of the rest of the lecture.

[1] E Widmaier, H. Raff, and K. Strang. *Vander's Human Physiology: The Mechanisms of Body Function*. McGraw-Hill Science/Engineering/Math, 13th edition, 2013. ISBN 0073378305

Learning Objectives

For this lecture, the learning objectives are:

- Define endocrine, paracrine, autocrine, and exocrine systems, define neuro-secretory cells by giving a few examples.
- List major categories of hormones and give several examples that belong to each class.
- List important factors that determine hormone levels in circulation.
- Describe four general functions of hormones.
- Explain with examples neuroendocrine integration.
- Explain cellular actions of hormones via membrane receptors.
- Explain cellular action of hormones via protein synthesis.
- Discuss major categories of cellular signal pathways of hormones via membrane receptors.
- Discuss major categories of cellular signal pathways of hormones via cytosolic/nuclear receptors.
- Define basal secretion and stimulated secretion of endocrine glands.
- Describe negative and positive feedback system using an example.

General Hormonal Principles

A MAJOR ADVANTAGE OF MULTICELLULARITY, is that biological roles are divided into specialized organs and tissues. In a single cellular organism, such as *Saccharomyces cerevisiae*[2], all cells need to autonomously be able to sense the environment, cellular conditions and respond appropriately. Multicellular organisms are able to use more sophisticated mechanisms to sense the environment and make these decisions. Essential to this division of labor is the ability of these organ systems to communicate efficiently and effectively with each other. This is accomplished through hormones, which are secreted from one organ to another.

[2] also known as brewer's yeast

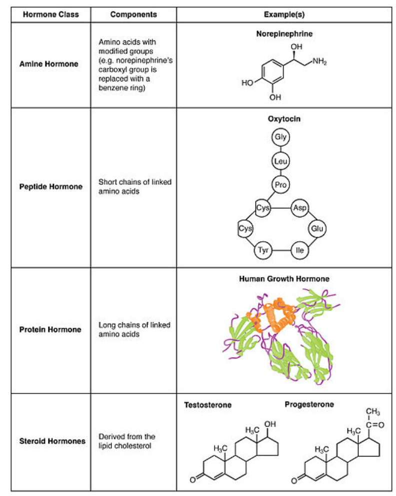

Figure 1: Chemical classification of hormones.

Hormonal Classification

There are hundreds, if not thousands hormones, if defined loosely to mean *chemicals derived from one cell that can affect another cell*. Remembering what these all do, how they are made, where they come from can be a challenge. To simplify this, these can be grouped several ways including chemically, anatomically or functionally.

CHEMICALLY, hormones can be small molecules such as amino acids or lipids, or can be small polypeptides, or even large proteins with three dimensional structures (see Figure 1). Often, an endocrine organ only releases hormones of a particular chemical class. An example of this is the adrenal gland which secretes several steroid hormones, each of which have different roles and target tissues.

ANATOMICALLY, hormones can be grouped based on where they are secreted from. Some major exocrine organs include the pancreas, the adrenal gland and the brain. Another way of considering anatomical classification of hormones is the relationship between the secreting cell and the target cell. Hormones can act on the secreting cell, or a very close cell or a cell in a (relatively) far away tissue. These are known as autocrine, paracrine and endocrine actions (see Table 1).

Type	Target	Example
Autocrine	Secreting cell	Monocyte IL-1
Paracrine	Nearby cell	Hedgehog
Endocrine	Far away cell	Insulin

Table 1: Types of hormones, based on the proximity of target and secreting cells

FUNCTIONALLY, one can group hormones together based on collective regulation of a set of organs. These are often considered *axes* and some examples include the hypothalamic-pituitary-adrenal (HPA) axis, gut-liver-brain axis or the sympathetic -adrenal-medullary (SAM) axis.

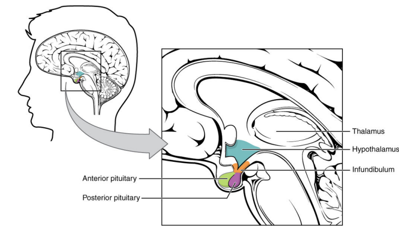

Figure 2: Location of the pituitary and hypothalamus in the human brain.

Hormonal Signaling Concepts

Principles of Hormone Receptors

Regulation of Hormone Levels

Negative and Positive Feedback of Hormones

Neuroendocrinology

Many hormonal signaling events involve the brain, which could be considered the most complex and central endocrine organ. The primary role of the brain is to integrate external sensory cues with internal signals and to decide, often subconsciously the most appropriate response. The key parts of the brain that are involved in endocrine responses are the hypothalamus and the pituitary (Figure 2).

THE HYPOTHALAMUS[3] often responds to hormones sent from either the periphery or the rest of the brain. This makes it the link between the nervous and the endocrine systems. The hypothalamus is a central node for the regulation of appetite, circadian rhythyms, body temperature and behaviors. The hypothalamus can signal to other parts of the brain, including the pituitary gland. Several endocrine circuits exploit the proximity of these two brain regions (see Table 2):

3 Under the thalamus

Table 2: Pituitary-hypothalamic axes.

Axis	Hypothalamic	Pituitary	Function
HPA	CRH	ACTH	Glucocorticoids
HPG	GnRH	FHS/LH	Reproductive hormones
HPT	TRH	TSH	Thyroid hormones

THE PITUITARY[4] is a small pea-sized gland that is divided into three lobes, a posterior, intermediate and anterior pituitary. The anterior pituitary produces and releases several hormones including growth hormone (GH), thyroid-stimulating hormone, adrenocorticotropic hormone (ACTH), prolactin, lutenizing hormone and folicle stimulating hormone. These are released in response to signals from they hypothalamus, which pass through a specialized capillary system called the hypothalamic-hypophysial portal system.

4 Named by Aelius Galenus in 200 BC as the "gland that drops slime", due to a (incorrect) role in regulating nasal mucous

Endocrine pathophysiology

Many diseases are the result of either too little or too much hormones in circulation. For example, tumors in the pituitary which cause excessive release in growth hormone or ACTH cause acromegaly[5] and Cushing's disease[6] respectively while the destruction of the cells

5 Pierre Marie. Presentation de malades atteints dâĂŹanarthrie par lesion de lâĂŹhemisphere gauche du cerveau. *Bulletins et Memoires Societe Medicale des Hopitaux de Paris*, 1:158–60, 1907

6 Harvey Cushing. The basophil adenomas of the pituitary body and their clinical manifestations. *Bulletin of the Johns Hopkins Hospital*, 50:157–8, April 1932. ISSN 0035-8843

that produce insulin or cortisol result in type I diabetes[7] and Addison's disease[8]. Hormonal deficiencies can often be corrected by providing patients with hormones produced and purified externally, while hormonal over-production requires more complicated therapies. Understanding the normal roles of these hormones is central to connecting the phenotypes associated with hormonal deficiencies or hyper-secretion to the mechanisms of disease progression.

[7] F G Banting, C H Best, J B Collip, W R Campbell, and a a Fletcher. Pancreatic Extracts in the Treatment of Diabetes Mellitus. *Canadian Medical Association journal*, 12(3):141–6, March 1922. ISSN 0008-4409. URL `http://pubmed.org/20314060`

[8] Thomas Addison. *On The Constitutional And Local Effects Of Disease Of The Supra-Renal Capsules*. Samuel Highley, London, 1855

References

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