

McCance: Pathophysiology, 6th Edition

Chapter 20: Mechanisms of Hormonal Regulation

Key Points – Print

SUMMARY REVIEW

Mechanisms of Hormonal Regulation

1. The endocrine system has diverse functions, including sexual differentiation, growth and development, and continuous maintenance of the body's internal environment.
2. Hormones are chemical messengers synthesized by endocrine glands and released into the circulation.
3. Hormones have specific negative- and positive-feedback mechanisms. Most hormone levels are regulated by negative feedback, in which tropic hormone secretion raises the level of a specific hormone, which feeds back causing secretion of the tropic hormone to subside.
4. Endocrine feedback is described in terms of short, long, and ultrashort feedback loops.
5. Water-soluble hormones circulate throughout the body in unbound form, whereas lipid-soluble hormones (i.e., steroid and thyroid hormones) circulate throughout the body bound to carrier proteins.
6. Hormones serve as first messengers and affect only target cells with appropriate receptors and then act on those cells to initiate specific cell functions or activities.
7. Hormones have two general types of effects on cells: direct effects, or obvious changes in cell function, and permissive effects, or less obvious changes that facilitate cell function.
8. Receptors for hormones are proteins and may be located on or in the plasma membrane or in the cytosol or nucleus of the target cell. Receptors may be G protein-linked, ion channels, or enzyme linked.
9. Water-soluble hormones act as first messengers, binding to receptors on the cell's plasma membrane. The signals initiated by hormone-receptor binding are then transmitted into the cell by the action of second messengers.
10. Second messengers that have been identified include cAMP, cGMP, and calcium, which associates with IP₃, and DAG to produce physiologic effects.
11. For cells that have cAMP as their second messenger, a series of interactions within the plasma membrane must activate adenylyl cyclase.
12. For cells that have calcium as their second messenger, a rise in intracellular calcium causes calcium to bind with calmodulin, a regulatory protein. This step then initiates other intracellular processes.
13. Cells that have cGMP as their second messenger are activated by the enzyme guanylyl cyclase.
14. Lipid-soluble hormones (including steroid and thyroid hormones) may have rapid effects by binding to a plasma membrane or receptor or crossing the plasma membrane through

diffusion. These hormones then either bind to cytoplasmic proteins or diffuse directly into the cell nucleus and bind to nuclear receptors.

Structure and Function of the Endocrine Glands

1. The pituitary gland, consisting of anterior and posterior portions, is connected to the central nervous system through the hypothalamus.
2. The hypothalamus regulates anterior pituitary function by secreting releasing hormones into the portal circulation.
3. Hypothalamic hormones include dopamine, which inhibits prolactin secretion; TRH, which affects release of thyroid hormones; GnRH, which facilitates release of ACTH and endorphins; and substance P, which inhibits ACTH release and stimulates release of a variety of other hormones.
4. The pineal gland produces melatonin, which affects sleep, immune function, and aging.
5. The posterior pituitary secretes ADH, also called *arginine vasopressin*, and oxytocin.
6. ADH controls serum osmolality, increases permeability of the renal tubules to water, and causes vasoconstriction when administered pharmacologically in high doses. ADH also may regulate some central nervous system functions.
7. Oxytocin causes uterine contraction and lactation in women and may have a role in sperm motility in men. In men and women, oxytocin has an antidiuretic effect similar to that of ADH.
8. Hormones of the anterior pituitary are regulated by (a) secretion of hypothalamic-releasing hormones or factors, (b) negative feedback from hormones secreted by target organs, and (c) mediating effects of neurotransmitters.
9. Hormones of the anterior pituitary include ACTH, MSH, somatotrophic hormones (GH and prolactin), and glycoprotein hormones (FSH, LH, and TSH).
10. Growth hormone stimulates growth of bone, increased protein metabolism in muscles, and lipolysis. Its effects are mediated in part by IGFs.
11. Prolactin functions to produce milk during pregnancy and lactation.
12. The two-lobed thyroid gland contains follicles, which secrete some of the thyroid hormones, and C cells, which secrete calcitonin and somatostatin.
13. Regulation of TH levels is complex and involves the hypothalamus, anterior pituitary, thyroid gland, and numerous biochemical variables.
14. TH secretion is regulated by thyroid-releasing hormone through a negative-feedback loop that involves the anterior pituitary and hypothalamus.
15. TSH, which is synthesized and stored in the anterior pituitary, stimulates secretion of TH by activating intracellular processes, including uptake of iodine necessary for the synthesis of TH.

16. Synthesis of TH depends on the glycoprotein thyroglobulin, which contains a precursor of TH, tyrosine. Tyrosine then combines with iodide to form precursor molecules of the thyroid hormones T_4 and T_3 .
17. When released into the circulation, T_3 and T_4 are bound by carrier proteins in the plasma that store these hormones and provide a buffer for rapid changes in hormone levels.
18. Thyroid hormones alter protein synthesis and have a wide range of metabolic effects on proteins, carbohydrates, lipids, and vitamins. TH also affects heat production and cardiac function.
19. The paired parathyroid glands normally are located behind the upper and lower poles of the thyroid. These glands secrete PTH, an important regulator of serum calcium levels.
20. PTH secretion is regulated by levels of ionized calcium in the plasma and by cAMP within the cell. Some other substances—hormones, neurotransmitters, and ions—affect PTH secretion by inhibiting cAMP or by changing calcium levels.
21. In bone, PTH causes bone breakdown and resorption. In the kidney PTH increases reabsorption of calcium, decreases reabsorption of phosphorus and bicarbonate, and stimulates synthesis of vitamin D.
22. The endocrine pancreas contains the islets of Langerhans, which secrete hormones responsible for much of the carbohydrate metabolism in the body.
23. The islets of Langerhans consist of alpha cells, beta cells, and delta cells. Delta cells secrete somatostatin, which inhibits glucagon and insulin secretion. Beta cells secrete preproinsulin, which is ultimately converted to insulin.
24. Insulin is a hormone that regulates blood glucose concentrations and overall body metabolism of fat, protein, and carbohydrates.
25. Alpha cells produce glucagon, which is secreted inversely to blood glucose concentrations.
26. The paired adrenal glands are situated on the kidneys. Each gland consists of an adrenal medulla, which secretes catecholamines, and an adrenal cortex, which secretes steroid hormones.
27. The steroid hormones secreted by the adrenal cortex are all synthesized from cholesterol. These hormones include glucocorticoids, mineralocorticoids, and adrenal androgens and estrogens.
28. Glucocorticoids directly affect carbohydrate metabolism by increasing blood glucose concentration through gluconeogenesis in the liver and by decreasing use of glucose. Glucocorticoids also inhibit immune and inflammatory responses.
29. Cortisol secretion is related to secretion of ACTH) which is stimulated by CRH. ACTH binds with receptors of the adrenal cortex, which activates intracellular mechanisms (specifically cAMP) and leads to cortisol release.
30. Mineralocorticoids, especially aldosterone, are steroid hormones that directly affect ion transport by epithelial cells, causing sodium retention and potassium and hydrogen loss.
31. Aldosterone secretion is controlled by the rennin-angiotensin-aldosterone system and acts by binding to a site on the cell nucleus and altering protein production within the cell. Its

principal site of action is the kidney, where it causes sodium reabsorption and potassium and hydrogen excretion.

32. Androgens and estrogens secreted by the adrenal cortex act in the same way as those secreted by the gonads.
33. The adrenal medulla secretes the catecholamines epinephrine and norepinephrine. Catecholamines are synthesized from the amino acid phenylalanine. Their release is stimulated by sympathetic nervous system stimulation, ACTH, and glucocorticoids.
34. Catecholamines bind with various target cells and are taken up by neurons or excreted in the urine. They cause a range of metabolic effects that generally are characterized as the “flight or fight” response.
35. The endocrine system acts together with the nervous and immune systems to respond to stressors, providing an integrated and protective response.
36. Several assay methods are used to measure levels of hormones in the plasma. RIA compares the proportion of radiolabeled and non-radiolabeled hormone against standard reference curves.
37. ELISA is a method similar to RIA, but uses a radiolabeled enzyme rather than a radiolabeled hormone.
38. Bioassays use graded doses of hormone in a reference preparation and then compare the results with an unknown sample to determine hormone level.

Aging and the Endocrine System

1. Endocrine changes that may be associated with aging include altered biologic activity of hormones, altered circulating levels of hormones, altered secretory responses of endocrine glands, altered metabolism of hormones, and loss of circadian control of hormone release.
2. Cellular damage associated with aging, genetically programmed cell change, and chronic wear and tear may contribute to endocrine gland dysfunction or alterations in responsiveness of target organs.
3. Aging apparently causes atrophy of the thyroid gland and is associated with infiltrative glandular changes. Secretion of thyroid hormones may diminish with age.
4. Aging causes pancreatic fat deposition and is associated with a decrease in insulin secretion and insulin sensitivity.
5. Growth hormone levels decrease with aging leading to decreased bone and muscle mass.
6. Aging is associated with alterations in calcium steady states, which may be related to alterations in PTH secretion from the parathyroid glands.
7. Age-related changes in adrenal function include decreased clearance of glucocorticoids and a decrease in levels of adrenal androgens. The effects of these changes, however, are offset by feedback mechanisms that maintain glucocorticoid levels and by gonadal secretion of androgens.