Instructor's Answer Key

Chapter 11: Endocrine Glands: Secretion and Action of Hormones

Answers to Test Your Understanding of Concepts and Principles

1. Both organs are derived from the embryonic ectoderm tissue that gives rise to the nervous system. The neurohypophysis is formed as a downgrowth of the hypothalamus portion of the brain and the adrenal medulla is derived from the same nervous tissue that produces sympathetic ganglia. As a result of this embryonic derivation, both glands receive innervation by nerve fibers and the hormone secretions of both endocrine glands are consequently directly regulated by action potentials from the nervous system. [Note: This question is also answered in the Student Study Guide.]

2. Steroid hormones are derived from cholesterol. Since they are nonpolar and can dissolve in lipids, they pass easily through the phospholipid core of the plasma membrane of target cells. Because of its nonpolar chemistry, thyroxine is also considered a lipophilic hormone. Once inside the target cell, these hormones attach to cytoplasmic receptor proteins that translocate into the nucleus and bind to nuclear hormone receptors that function as genetic transcription factors in the activation of specific target genes. As a result, new enzyme proteins may be produced that change the metabolism of the target cell in ways characteristic of that hormone. These hormones activate nuclear hormone receptors with two regions, or domains: a ligand (hormone)-binding domain and a DNA-binding domain. Once activated this complex binds to a specific hormone-response element on the DNA and regulates expression of the genes. The hormone-response element consists of two half-sites that require two hormone-receptor complexes for activation (as either homodimers of heterodimers).

3. By contrast, polypeptide hormones are polar and cannot pass through the plasma membrane. Instead, they interact with receptor proteins expressed on the outer surface that indirectly activate a specific enzyme in the plasma membrane. This interaction causes the increased concentration of an intracellular mediator of the hormone's action called a second messenger. The second messenger may be cAMP, cGMP, or Ca^{2+}. As a result of the increased intracellular concentration of the second messenger, a previously inactive enzyme protein becomes activated; this in turn affects other cellular proteins in a cascade-like action. For example, certain polypeptide hormones activate adenylate cyclase, resulting in the intracellular production of cyclic AMP. As a second messenger, cyclic AMP activates a cytoplasmic enzyme called protein kinase, which phosphorylates specific enzyme proteins and thereby changes the metabolism of the target cell for those hormones that use cAMP as a second messenger.

4. Some polar (polypeptide) hormones bind to a receptor in the plasma membrane, which activates the enzyme phospholipase C, causing the release of inositol triphosphate into the cell. Inositol triphosphate (IP3) stimulates the release of Ca^{2+} from the endoplasmic reticulum and into the cytoplasm of the target cell. The transient increase in intracellular Ca^{2+} leads to its binding to regulatory proteins, such as calmodulin that in turn activate specific protein kinase enzymes (add phosphate groups to protein). This activation of enzymes influences metabolism of the target cell in ways analogous to that by cAMP-dependent mechanisms.

5. The term *trophic* refers to "feeding." This term can be used to describe anterior pituitary hormones because many of these six hormones help promote growth and nourishment of their target organs, while a deficiency of these anterior pituitary hormones causes their target organs to atrophy.

6. Since the conversion of T_4 to T_3 is required for the action of thyroid hormone in the target cell cytoplasm. This drug would interrupt normal stimulation of thyroxine target cells and metabolism would be slowed (mimic hypothyroidism). With a slowed metabolism and less circulating T_3 negative feedback effect on the hypothalamus, (a) the secretion of TSH would increase. High TSH would (b) stimulate the thyroid to secrete larger amounts of thyroxine (which, because of the action of the drug, would have little effect in the body), and (c) would stimulate enlargement of the thyroid gland to meet this demand.

7. The six trophic hormones secreted by anterior pituitary stimulate and nourish other endocrine glands: ACTH stimulates the adrenal cortex, TSH stimulates the thyroid, and FSH and LH stimulate the gonads. The anterior pituitary is thus often called the "master gland." This term is misleading because the anterior pituitary is itself controlled indirectly by another endocrine gland—the hypothalamus. The hypothalamus exerts its control by secreting releasing hormones (RHs) that travel down the hypothalamo-hypophyseal portal system to direct the release of specific anterior pituitary hormones. Secondly, the anterior pituitary is not a master gland since its own secretion of hormones is under negative feedback regulation by hormones released from its target endocrine glands.

8. If the antibodies blocked the insulin receptor proteins, insulin could not act on its target organs. Since insulin stimulates the cellular uptake of glucose and fatty acids that stimulates the synthesis of glycogen and fat, the blocking of insulin action would promote the breakdown of glycogen (glycogenolysis) and fat (lipolysis). This person's overall metabolism would be primarily dependent on fat (lipid) and protein metabolism as fuel for energy, conditions resembling that seen in type 1 diabetes mellitus.

9. Daytime or light, through the neural pathways from the retina, depresses the activity of the suprachiasmatic nucleus (SCN) in the hypothalamus and decreases the sympathetic stimulation and the secretion of melatonin from the pineal gland. By contrast, the production and secretion of melatonin is stimulated by increased activity of the SCN shortly after dark that peaks by the middle of the night. Since cycles of light and dark directly influence the levels of melatonin secretion by the pineal, the SCN becomes the primary center for circadian rhythms in the body through its control over the ebb and flow of melatonin. The regulatory effect of light on the SCN, and thus the ability of light to inhibit melatonin secretion, appears to require a pigment called *melanopsin*, found in ganglion cells of the retina.

10. Endocrine regulation occurs when hormones travel through the blood to reach one or more target tissues. *Paracrine* regulators are produced within one tissue and regulate a different tissue of the same organ. Some *autocrine* regulators are produced in many different organs and are active within the organ in which they are produced – acting on the same cell type that produces them. Because the same molecule can function as either an autocrine or a paracrine regulator, the term autocrine is used in this text in a generic sense to refer to both types of regulation. Autocrine regulators include: cytokines (regulate different cells of the immune system), growth factors (promote growth and cell division in any organ), neurotrophins, nerve growth factors, nitric oxide, endothelins, bradykinin, prostaglandins, leukotrienes, and others.

Answers to Test Your Ability to Analyze and Apply Your Knowledge

1. Brenda has an under active thyroid or hypothyroidism probably due to an iodine-deficiency (endemic) goiter. Her lack of thyroxine (T_4) production has lowered her basal metabolic rate, explaining her putting on weight and has made her lethargic, explaining her lack of energy and weakness. Brenda also is less able to adapt to cold stress so she always feels cold. Her heart rate is slow and blood pressure is low due to both indirect and direct effects of missing thyroid hormones. Inadequate thyroxine causes an indirect decrease in adrenergic stimulation of the heart and blood vessels (dilation) but also causes a direct decrease of thyroxine-induced stimulation of the myocardium excitability and contractility. The lack of T_4 negative feedback inhibition at the hypothalamus has raised her blood TSH levels. The treatment for Brenda should include consultation with a dietician to appropriately introduce iodine into the diet by recommending such food items as iodized salt or ocean fish.

2. Growth hormone (somatotropin) secretion from the anterior pituitary follows a circadian pattern, increasing during sleep and decreasing during periods of wakefulness. Knowing this, you (the friend) cleverly injected growth hormone at night. The problem is that Bud is too old and as an adult his epiphyseal discs of cartilage in his long bones have ossified so he will not grow taller. Furthermore, due to your nightly growth hormone injections, your friend is now suffering the effects of too much growth hormone – elongation and thickening of bones and the growth of soft tissues, particularly in the face, hands, and feet. These changes mimic a condition called *acromegaly*.

3. Joe is probably ingesting synthetic anabolic steroids that are related to natural androgen hormones secreted by the male gonad (testes) and to a lesser extent by the adrenal cortex. Although the administration of exogenous androgens will promote protein synthesis in muscles resulting in his increase in muscularity and in other organs, it can also cause a number of undesirable side effects. Since the liver and adipose tissue can change androgens into estrogens, Joe has experienced an abnormal growth of female-like mammary tissue or breasts – a condition called *gynecomastia*. Also, high levels of exogenous androgens in his blood exerted a negative feedback effect on the hypothalamus and the anterior pituitary, thereby inhibiting the secretion of FSH and LH gonadotropins and resulting in the atrophy of Joe's testes and most likely, erectile dysfunction. The exogenous steroids may also be responsible for Joe's aggressive behavior and perhaps other characteristics such as acne, male pattern baldness, and premature closure of the epiphyseal discs.

4. The receptors for the lipophilic hormones are the nuclear hormone receptors, divided into two major families: the steroid family and the thyroid hormone (or nonsteroid) family. In addition to the receptor for thyroid hormone, the latter family also includes the receptors for the active form of vitamin D and for retinoic acid (derived from vitamin A, or retinol). When the steroid hormone ligand binds to its receptor and together translocate into the nucleus, the DNA-binding domain binds to the specific hormone-response element of the DNA. This hormone-response element of the DNA consists of two half-sites, each six nucleotide bases long, separated by a three-nucleotide spacer segment. One steroid hormone-receptor unit attaches to one half-site while a second hormone-receptor unit binds to the other half-site. Since both receptor units of the pair are the same, the steroid receptor complex is said to form a *homodimer*. This dimerization stimulates transcription of particular genes and thus hormonal regulation of the target cell. By contrast, the thyroid (nonsteroid) hormone binds to inactive receptor proteins located in the nucleus. The active form of thyroxine is T_3. Once in the nucleus, T_3 binds to the ligand-binding domain of its receptor and together they attach, using the DNA-binding domain to one half-site of the DNA hormone-response element. The other half-site, however, requires a different ligand-receptor unit. The ligand required here is 9-*cis*-retinoic acid (a vitamin A derivative) that binds to its receptor called the *retinoid X receptor* (RXR). Since a different ligand-receptor unit occupies each of the half-sites, the thyroid hormone receptor complex is said to form a *heterodimer*, which leads to genetic transcription. In this way, the action of thyroxine hormone in its target cell nucleus requires vitamin A to fulfill one half-site of the heterodimer in the DNA hormone-response element. It is of interest that the receptor for the active form of vitamin D also forms heterodimers with the RXR receptor in its own target cell nuclei.

5. *Human chorionic gonadotropin* (hCG) is a hormone secreted by the early placenta and is similar to luteinizing hormone (or luteotropin, LH) released from the anterior pituitary. Incubation of rat testes with hCG should produce actions that mimic those of LH (also known as interstitial cell stimulating hormone, ICSH). In the rat testes, hCG should stimulate the secretion of male sex hormones (mainly testosterone) from the interstitial cells of Leydig. This selective action on the interstitial cells could have potential clinical or research significance in settings where the specific release and activity of testosterone is desired.