I. Cataloging Hormone Structure and Function

A. There are six major categories of chemical signals:
1. Autocrine signals act on the cells that secrete them.
a. Cytokines are released by cells and bind to the cells that release, amplifying their response to stimuli.
b. Interleukin 2 is a cytokine that is released by and binds to T cells, helping them to fight infection.
2. Paracrine signals act locally by binding to neighboring cells.
3. Endocrine signals are hormones that travel through the blood to distant locations where they act on target cells in those tissues.
4. Neural signals are chemical messengers called neurotransmitters.
5. Neuroendocrine signals are released from neurons and act on distant cells.
6. Pheromones are signals that are released into the environment and act on cells of a different individual.

B. How Do Researchers Identify a Hormone?
1. Research on hormones began with the discovery of secretin.
a. Dilute HCl added to dog intestine caused secretion of enzymes from the pancreas, even though all nerves to the pancreas had been cut.
b. Hypothesis: A chemical messenger traveled from the small intestine to the pancreas.
c. Experiment: Inject an extract of the small intestine into the dog's neck.
d. Result: The dog's pancreas secreted enzymes.
e. The hormone secretin was isolated from the intestinal extract.
2. The first evidence that a tissue produces a hormone often comes from removing the tissue and observing the effects on the animal.
a. Removal of dog adrenal gland reduced formation of glycogen in the liver.
b. This implied that the adrenal gland produces a hormone that activates glycogen formation.
3. An extract is made from the tissue and injected into animals that lack the tissue.
a. If the symptoms are alleviated, the extract contained a hormone.
b. Injection experiments provide strong evidence of a chemical messenger.
4. The hormone is purified from the tissue extract.
a. The purified molecule is injected into animals to determine if it alleviates the symptoms.
b. These types of experiments demonstrated how corticosterone and cortisol (glucocorticoids) work.
c. The adrenal medulla produces epinephrine (adrenaline) and norepinephrine.

C. Chemical Characteristics of Hormones
1. Three general types of hormones are found in animals.
a. Polypeptides
b. Amino acid derivatives
c. Steroids
2. Despite structural differences, all three types of hormones:
a. Are secreted from the cells in which they are synthesized
b. Act on target cells remote from their point of origin
c. Are present and effective at extremely low concentrations
3. The three types of hormones differ in their interaction with target cells.
a. Steroid hormones are lipid soluble.
b. Polypeptide and amino acid hormones are not lipid soluble.

D. The Human Endocrine System—an Overview
1. The endocrine system is a collection of cells, tissues, and organs that produce and secrete hormones.
2. Organs that secrete hormones are called endocrine glands.
3. Hormones coordinate the activities of different cells in response to changes in the internal or external environment.

II. What Do Hormones Do?

A. Hormones exert a wide range of effects.
   1. One hormone can activate more than one response.
      a. Thyroxine stimulates oxygen consumption by cells, heart rate, and red blood cell production.
      b. Thyroxine is derived from the amino acid tyrosine.
      c. Thyroxine (T_4) binds 4 iodine atoms; triiodothyronine (T_3) binds 3.
      d. People deficient in T_3 and T_4 are lethargic and tolerate cold poorly.
      e. People with too much T_3 and T_4 are restless, excitable, prone to mood swings, and tend to tire easily.
      f. Graves' disease is one form of hyperthyroidism.
      g. Exposure to radioactive iodine increases susceptibility to thyroid cancer.
      h. Goiter is caused by a diet deficient in iodine.
   2. One physiological process may be modulated by multiple hormones.
   3. Hormones coordinate the activities of the cell in response to three general situations:
      a. Environmental challenges
      b. Growth, development, and reproduction
      c. Homeostasis

B. Hormones coordinate responses to environmental challenges.
   1. Feeding changes the internal environment.
      a. Digestive hormones are activated by the presence of food.
      b. The hormone cholecystokinin triggers the secretion of digestive enzymes and bile.
      c. The enzymes and bile break down molecules and emulsify fats.
   2. Short-term responses to stress
      a. The fight-or-flight response is a short-term reaction to stress.
      b. Human volunteers were injected with epinephrine.
      c. Epinephrine triggers a state of heightened alertness and rapid energy utilization by coordinating many tissues and organs throughout the body.
   3. Long-term responses to stress
      a. Individuals under prolonged stress have increased levels of the glucocorticoids cortisol and corticosterone in the blood.
      b. Hypothesis: Glucocorticoids prepare an individual for long-term stress by conserving glucose.

C. Hormones direct developmental processes.
   1. Early embryonic development
      a. Primary sex determination is not dependent on hormone action.
      b. Once testes or ovaries develop, they begin producing sex hormones.
   2. Juvenile-to-adult transition
      a. Surges of sex hormones lead to puberty in early adolescence.
      b. Puberty produces the adult phenotype and the ability to reproduce.
      c. Secondary sex characteristics develop in males and females.
      d. Insect metamorphosis from juvenile to adult is also hormonally controlled.
   3. Attaining full adult stature
      a. This process is dependent on the growth of long bones in the limbs and the vertebrae in the spinal column.
      b. This growth is mediated by growth-factor hormones.
      c. The action of growth hormones is augmented by sex hormones.
   4. Seasonal or cyclical sexual activity
      a. Most long-lived animals reproduce seasonally.
      b. Environmental cues, such as the onset of rains or increasing day length, trigger surges in sex hormones.

D. How Are Hormones Involved in Homeostasis?
   1. Homeostatic systems have three components:
      a. A sensory receptor that monitors conditions relative to a set point
      b. An integrator that processes information from the sensor

c. Effector cells that return conditions to the set point

2. Messages often travel from integrators to effectors in the form of hormones.
   a. During the thirst response, ADH is released from the pituitary and causes the kidney to retain more water, thus increasing water in the blood and quelling thirst.
   b. Alcohol disturbs homeostasis in the thirst response.
   c. Erythropoietin (EPO) is also involved in homeostasis.
   d. Calcitonin and parathyroid hormone work in tandem to maintain homeostasis of blood Ca^{2+} levels.
3. Homeostasis of the body's energy reserve
   a. Individuals must store energy in reserve for use during periods of decreased food availability.
   b. Energy reserves are usually stored as triglycerides in adipocytes.
   c. In the 1970s researchers discovered that total adipose tissue was subject to homeostatic regulation.

III. How Is the Production of Hormones Regulated?

A. The Hypothalamus and Pituitary Gland
1. Removal of the pituitary from laboratory rats causes multiple symptoms:
   a. Cessation of growth
   b. Inability to maintain normal body temperature
   c. Atrophy of genitals, thyroid, and adrenal cortex
   d. Decreased life span
2. Controlling the release of glucocorticoids
   a. The pituitary molecule that affects the adrenal gland is adrenocorticotropic hormone (ACTH).
   b. The release of ACTH from the pituitary is controlled by corticotropin-releasing factor (CRF).
3. All the hormones in the feedback inhibition loop for glucocorticoids act as regulators.
   a. All are involved in feedback inhibition.
   b. Glucocorticoids serve a regulatory role in addition to their job as active hormones.
   c. The existence of multiple regulatory elements makes possible precise control of the system.
4. The hypothalamic-pituitary axis—an overview
   a. Neurosecretory cells of the hypothalamus extend directly into the posterior pituitary.
   b. The hypothalamus communicates with the anterior pituitary through its releasing hormones.

B. Control of Epinephrine by Sympathetic Nerves
1. Epinephrine acts as both a hormone and a neurotransmitter.
   a. During the fight-or-flight response, sympathetic nerves trigger secretion of epinephrine from the adrenal medulla into the bloodstream.
   b. Some sympathetic nerves secrete epinephrine into the synapse as a neurotransmitter.
2. As a neurotransmitter, epinephrine delivers a specific message to one cell; but as a hormone, it broadcasts the message through the bloodstream.

IV. How Do Hormones Act on Target Cells?

A. Steroid Hormones and Intracellular Receptors
1. Steroid hormones are small lipids that pass directly through membranes.
   a. Steroid hormones bind to receptors inside the cell.
   b. Estrogens are steroids that direct the development of secondary sex characteristics in females.
   c. Estradiol is the most important form of estrogen in humans.
2. Identifying the estradiol receptor
   a. Researchers isolate the estradiol receptor.
   b. Later work showed the estradiol receptor is in nucleus but not membrane.
   c. The receptor is found only in target tissues of estradiol—uterus, mammary glands, hypothalamus.
   d. The structure of the estradiol receptor is similar to the receptors for testosterone, glucocorticoids, and other steroids.
3. Documenting changes in gene expression
   a. Injection of estradiol into laboratory animals causes changes in mRNAs and proteins produced.
   b. The steroid hormone receptor has a DNA-binding domain called a zinc finger.

c. The zinc-finger domain binds to the hormone-response element in an enhancer element of the target gene.

4. Steroid hormones tend to act by causing changes in gene expression through activation of transcription factors.

B. Hormones That Bind to Cell-Surface Receptors

1. Hormones that are not lipid soluble bind to receptors on the surface of cells.
2. The hormone never enters the target cell; so the message is transduced, or changed, into a form that is active in the cell.
3. Identifying the epinephrine receptor
   a. Four distinct epinephrine receptors are known.
   b. Each is found in a distinct tissue type.
   c. Each induces a different response from the cell.
   d. Tissue specificity for hormones is determined by the presence or absence of receptors for the hormone.
4. Signal transduction and the role of second messengers
   a. Signal transduction occurs when a chemical message at the cell surface elicits a response inside the cell.
   b. Epinephrine triggers release of glucose into the blood from storage cells.
   c. Cori and Cori (1940s) discovered the enzyme phosphorylase.
   d. Sutherland explored whether epinephrine causes activation of phosphorylase in liver cells during the fight-or-flight response.
      e. Model of epinephrine action in stimulating glucose release from glycogen:
5. Signal transduction amplifies the hormone signal.
   a. One hormone molecule can result in 100 molecules of cAMP being formed.
   b. Each cAMP activates many kinase molecules, which activate other enzymes.
   c. Millions or billions of glucose molecules may be released.
6. Different epinephrine receptors are present on different cells.
   a. The hormone receptor in other target cells can be linked to a completely different set of reactions.
   b. Some cells use Ca^{2+} and IP3 as second messengers.
   c. The same hormone can cause different responses in different cells.
7. Nonsteroid hormones tend to activate existing proteins, rather than inducing changes in gene expression.

Chapter Vocabulary

hormone
endocrine system
autocrine
cytokine
paracrine
glands
neural
neurotransmitter
neuroendocrine
pheromone

secretin
pancreas
Islets of Langerhans
small intestine
extract
glycogen
cholecystokinin

polypeptide
amino acid derivative
steroid
cholesterol

hypothalamus
hypothalamic-pituitary axis
neurosecretory cells
releasing hormone
follicle-stimulating hormone
luteinizing hormone
lipotrophic diabetes
inhibitory hormones
growth-hormone inhibiting hormone
prolactin-inhibiting hormone
pituitary gland
anterior pituitary
posterior pituitary
growth hormone
oxytocin

thyroid
endemic goiter
calcitonin

parathyroid gland
parafollicular cells
parathyroid hormone (PTH)

kidney
erythropoietin (EPO)

adrenal gland
adrenal cortex
adrenal medulla
aldosterone
corticosterone
cortisol
glucocorticoids
adipocytes
catecholamines
epinephrine
norepinephrine
adrenaline
fight-or-flight response

pancreas
insulin
glucagons
somatostatin

testes
testosterone
ovaries
estrogen
estradiol

primary sex determination
puberty
ecdysone
juvenile hormone
molting
metamorphosis

homeostasis
erythropoietin
triglycerides
parabiosis
leptin

sensory receptor
integrator
effector cells
set point
feedback inhibition
hormone-response element
zinc-finger DNA-binding domain

signal transduction
agonists
alpha epinephrine receptors
beta epinephrine receptors
phosphorylase
G protein
adenylyl cyclase
cyclic adenosine monophosphate (cAMP)
second messenger
cAMP-dependent protein kinase A
diacylglycerol (DAG)
inositol triphosphate (IP3)
3′, 5′ cGMP