Chapter 14 – Hormonal Communication, Endocrine Glands, and Hormones

Objectives

Given the synopsis in this chapter, competence in each objective will be demonstrated by writing short essays, drawing diagrams, and responding to multiple choices or matching questions, at the level of 85% or greater proficiency for each student.

A. To compare and contrast the general patterns of organization seen in neural, neuroendocrine, and endocrine communication; including the general actions of hormones.
B. To describe the major endocrine glands, and to name representative hormones produced by these glands and their functions.
C. To explain the characteristics, synthesis and secretion of catecholamine hormones.
D. To explain the characteristics, synthesis and secretion of thyroid hormones.
E. To explain the characteristics, synthesis and secretion of peptide hormones.
F. To explain the characteristics, synthesis and secretion of steroid hormones.
G. To summarize the synthesis and secretion of water-soluble hormones.
H. To summarize the synthesis and secretion of lipid-soluble hormones.
I. To explain the role of extracellular receptors and second messenger systems in the actions of water-soluble hormones, using as an example the control of cellular metabolism by insulin.
J. To explain the role of intracellular receptors and modulation of gene expression in the actions of lipid soluble hormones, using as an example the control of cellular metabolism by cortisol.

Neural *vs.* Hormonal Communication

As discussed previously, the various organ systems of the body must communicate and function together. The nervous system (brain, spinal cord and nerves) and endocrine system (glands and hormones) are central to communication, control, and regulation within the body. We explored in the previous section how nerves and neurotransmitters are involved in communication, control, and regulation within the body. We will now examine how glands and hormones are similarly central to communication, control, and regulation. As a matter of fact, nerves and neurotransmitters and glands and hormones frequently intercommunicate, and often are inseparable.

General Neural Communication

In neural communication, electrical and chemical signals are sent by neurons directly to other neurons or muscle cells, as shown in Figure 14.1. Neural communication is characterized by the following features.

- Neural signals are transmitted along an axon to the synaptic bulb of the neuron.
- From the synaptic bulb chemical messengers are released from the **presynaptic membrane** into the **synaptic cleft**.
- The chemical messenger travels across the synaptic cleft to act on the **postsynaptic membrane** of a muscle cell or another neuron.
- By definition the chemical messenger is called a **neurotransmitter**.
- Neurotransmitters are **water soluble**.
- The neurotransmitter exerts its influence by attaching to **extracellular receptors** in the postsynaptic membrane of the target cells.

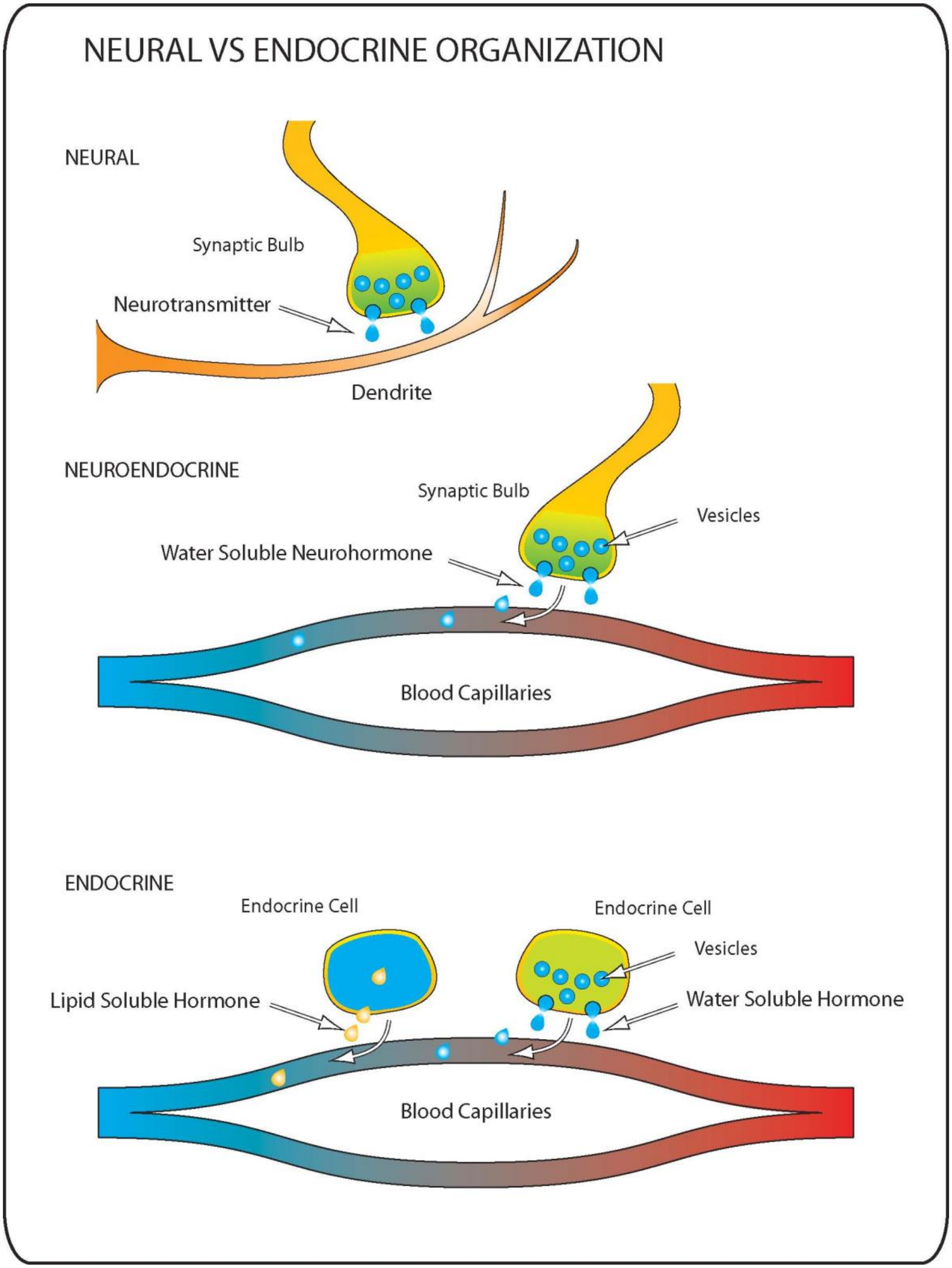

Figure 14.1 © 2007 David G. Ward, Ph.D.

General Endocrine Communication

In endocrine communication, chemical signals are sent from neurons *or* from endocrine cells through the blood to reach other cells, as shown in Figure 14.1. Chemical messengers in the blood are called hormones. Endocrine communication is characterized by the following features.

Neuroendocrine (from neurons)

- Neural signals are transmitted along an axon to the synaptic bulb of the neuron.
- From the synaptic bulb chemical messengers are released into surrounding **interstitial space**.
- The chemical messenger is transported into the blood to act on other cells.
- By definition, the chemical messenger is often called a **neurohormone**. (One can easily make a case to simply call the messenger a hormone.)
- Neurohormones are **water soluble**.
- The neurohormone exerts its influence by attaching to **extracellular receptors** in the membrane of the target cells.

Endocrine (from endocrine cells)

- Chemical signals traveling through the blood attach to receptors in the membrane of endocrine cells (glandular epithelial cells).
- The endocrine cells (glandular epithelial cells) respond to this signal and in turn release a chemical messenger into the surrounding interstitial space.
- The chemical messenger is transported into the blood to act on other cells.
- By definition the chemical messenger is called a **hormone**.
- Some hormones are water-soluble, other hormones are lipid-soluble.
- The **water-soluble** hormones exert their influence by attaching to **extracellular receptors** in the membrane of the target cells.
- The **lipid-soluble** hormones exert their influence by attaching to **intracellular receptors** in the cytosol or nucleus of the target cells.

General Actions of Neurohormones and Hormones

After a hormone (either a neurohormone or a hormone) enters the blood it will act either on a target organ to cause a response, or on another endocrine gland to cause the release of another hormone, as shown in Figure 14.2. Hormones that act on another endocrine gland to cause the release (or inhibition of release) of another hormone are called **tropic hormones**.

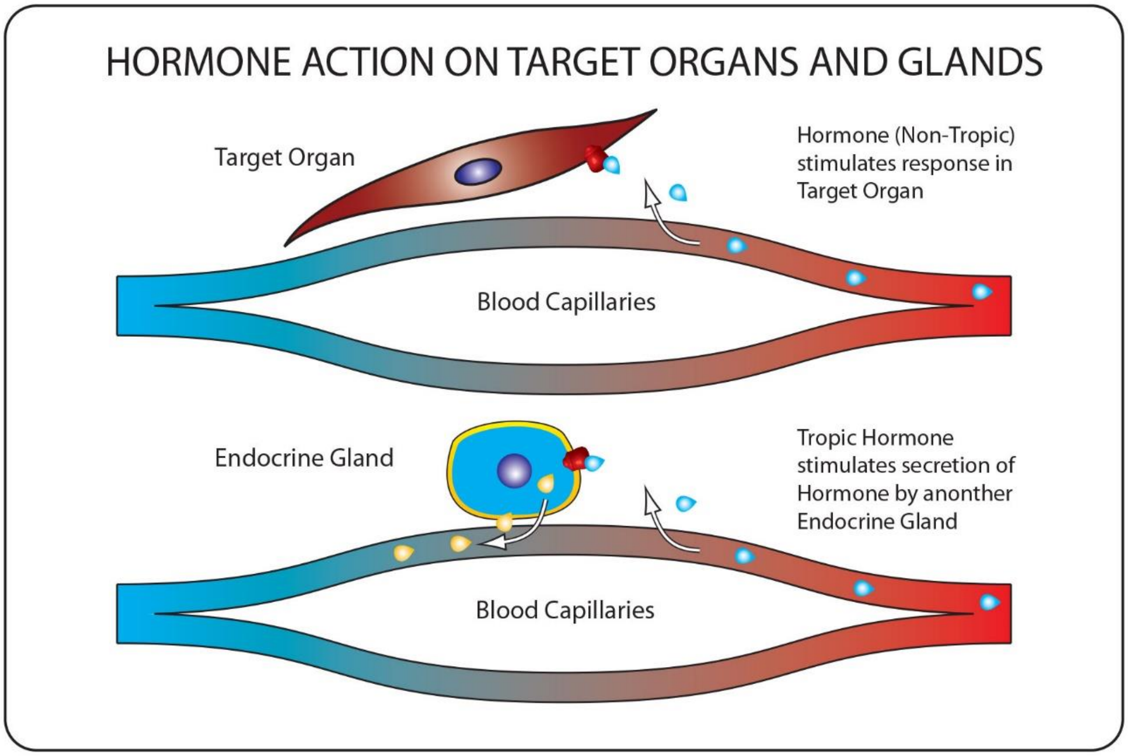

Figure 14.2 © 2014 David G. Ward, Ph.D.

Overview of Endocrine Glands and Hormones

The endocrine glands and hormones make up a large and complex component of the body as shown in Figure 14. 3. In this section we will explore the anatomical organization of key endocrine glands and relate these structures to the hormones produced. The major endocrine glands of the body and the hormones produced by these glands are summarized in Appendix A, Tables A.1 through A.12. Each table summarizes the stimulus, source and actions (including cellular mechanism of action) of each hormone produced by a specific gland. The remaining sections of this chapter will focus on hormone synthesis and secretion/release and cellular mechanisms of action. The hypothalamus, pituitary, thyroid, and adrenal are considered more extensively in chapter 15.

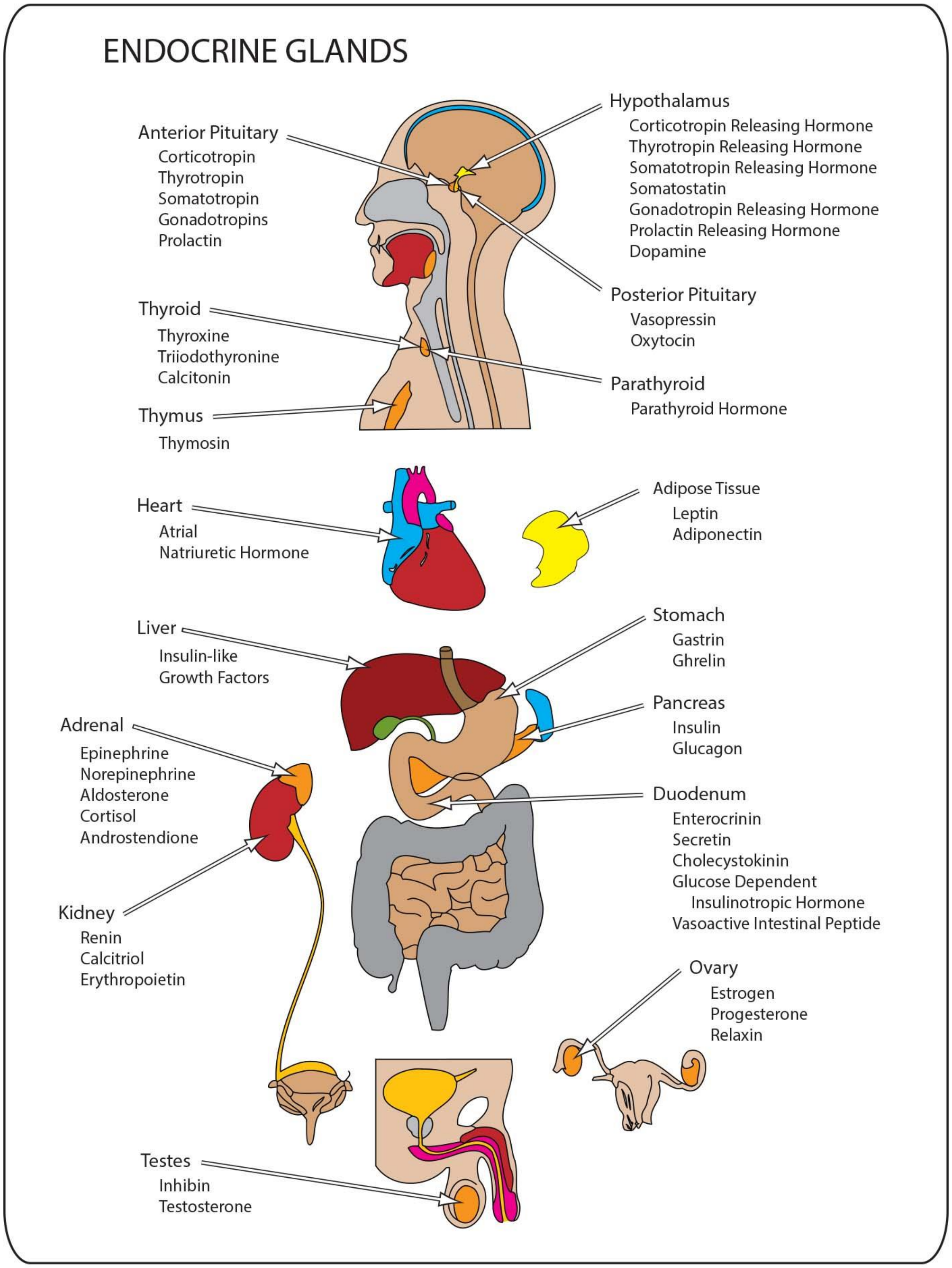

Figure 14.3 © 2020 David G. Ward, Ph.D.

The pituitary gland is located at the base of the skull and is attached to and just inferior to the hypothalamus. As shown in Figure 14.4, the pituitary is separated into a posterior division and an anterior division. The posterior pituitary is a direct continuation of the hypothalamus and contains axons of hypothalamic neurons that secrete vasopressin (antidiuretic hormone [ADH]) and oxytocin. The anterior pituitary is a separate structure that is composed of endocrine cells rather than neurons. The anterior pituitary secretes corticotropin (adrenocorticotropic hormone [ACTH]), thyrotropin (thyroid stimulating hormone [TSH]), somatotropin (growth hormone [GH]), gonadotropins (follicle stimulating hormone [FSH] and luteinizing hormone [LH]), and prolactin (PRL). The anterior pituitary cells respond to hormonal signals from the hypothalamus. A system of hypothalamic neurons sends their axons to the median eminence where chemical messengers (called hypothalamic regulatory hormones) are secreted into the pituitary portal vessels (not shown) and continue into the anterior pituitary.

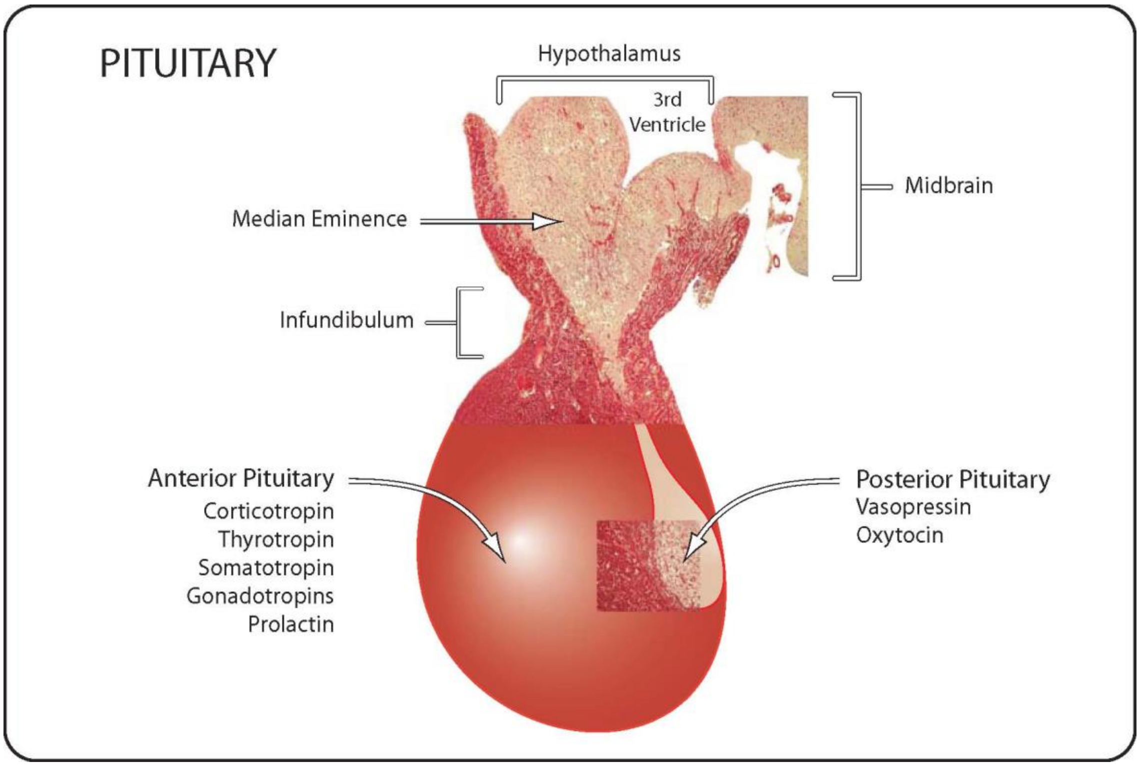

Figure 14.4 © 2007 David G. Ward, Ph.D.

The thyroid glands are located in the neck on each side of the larynx. Attached to each thyroid gland are two small parathyroid glands. As shown in Figure 14.5, the parathyroid and thyroid gland are clearly separate structures. The parathyroid gland is composed of endocrine cells (called chief cells) that secrete parathyroid hormone (PTH) in response to low blood calcium. The thyroid gland is composed of thyroid follicles that synthesize and release triiodothyronin (T3) and thyroxin (T4) in response to thyrotropin (thyroid stimulating hormone [TSH]) secreted by the anterior pituitary. A magnification of the thyroid gland is shown in Figure 14.6 revealing the presence of thyroglobulin inside of the follicles and scattered interfollicular cells outside and between the follicles. Thyroglobulin is critical for the synthesis of T3 and T4. The interfollicular cells function as separate endocrine glands and secrete calcitonin in response to high blood calcium.

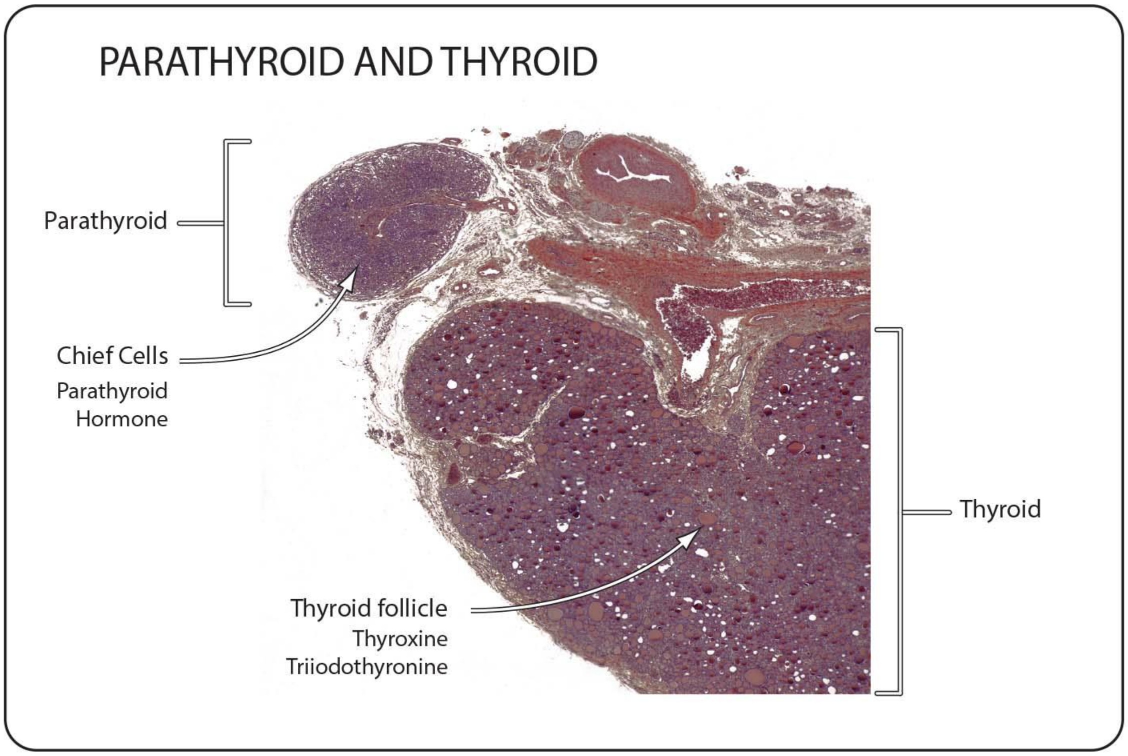

Figure 14.5 © 2020 David G. Ward, Ph.D.

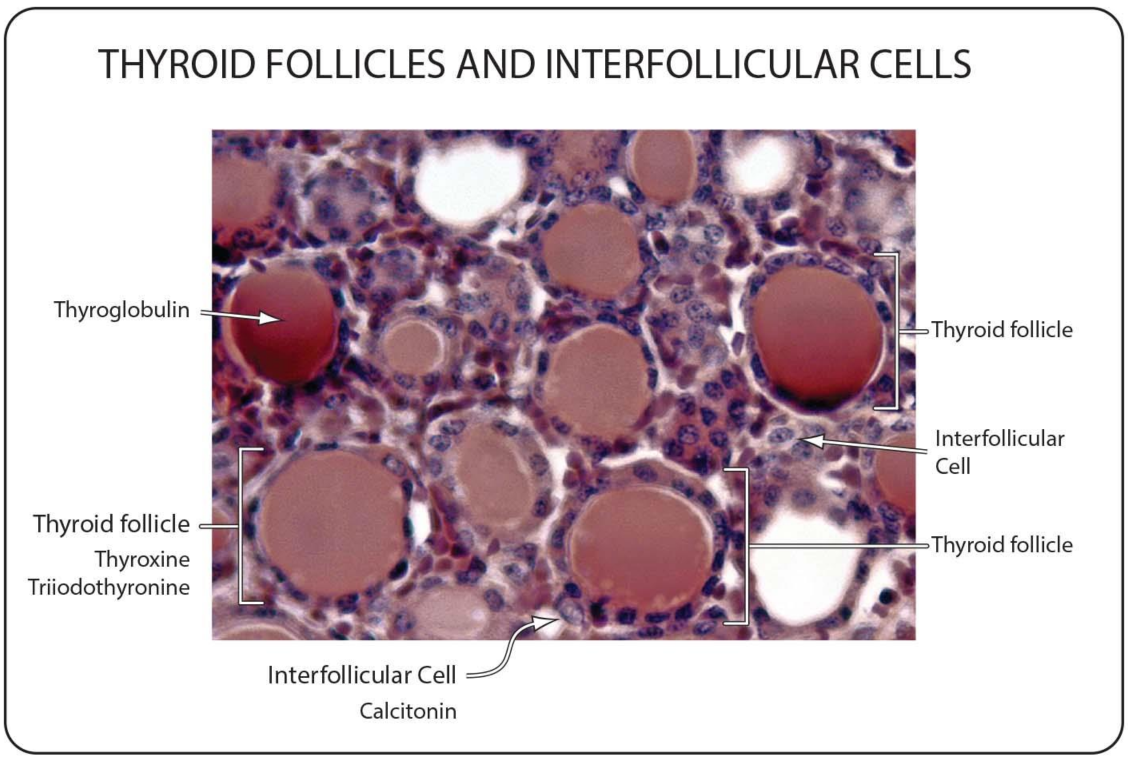

Figure 14.6 © 2020 David G. Ward, Ph.D.

The pancreas is located in the upper abdomen largely behind the stomach. Most of the pancreas is involved in producing exocrine secretions for the gastrointestinal tract. However, as shown in Figure 14.7 each pancreatic lobule contains pancreatic islets with endocrine cells. Alpha cells secrete glucagon in response to low blood glucose, and beta cells secrete insulin in response to high blood glucose.

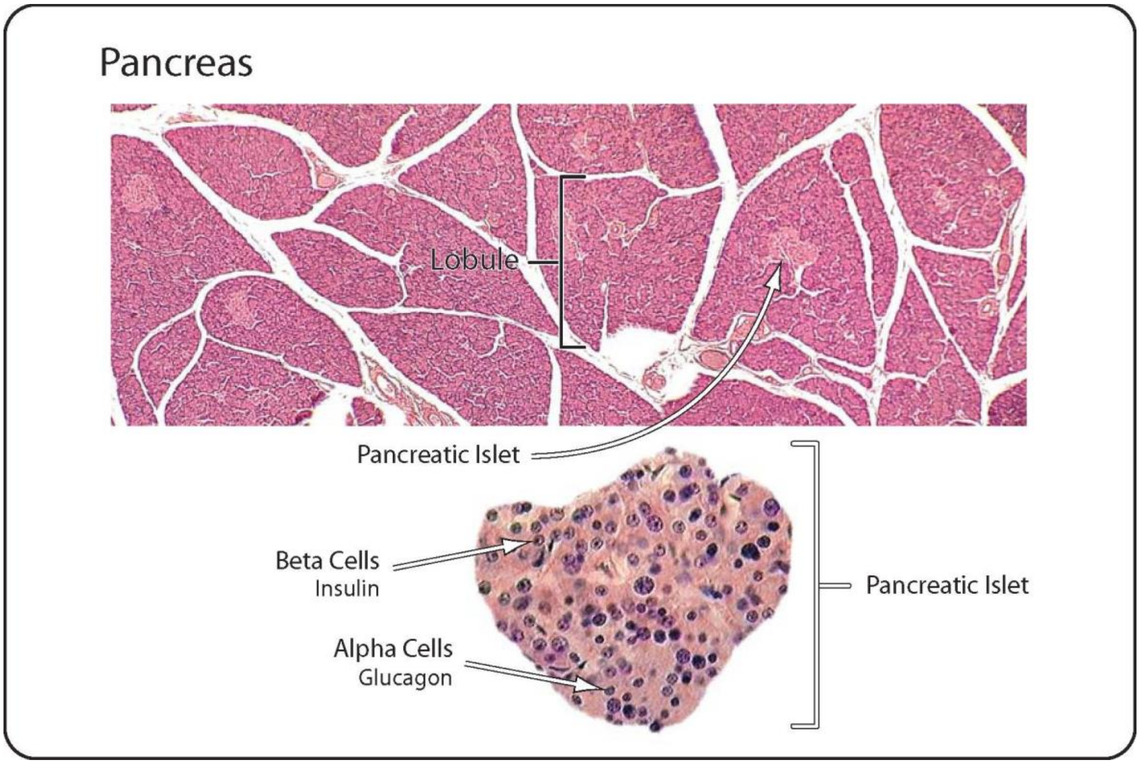

Figure 14.7 © 2007 David G. Ward, Ph.D.

The adrenal glands are located on top of the kidneys. Each adrenal gland is composed of two major parts. As shown in Figure 14.8, the central portion is the adrenal medulla and around the central portion is the adrenal cortex. The adrenal medulla is anatomically a sympathetic ganglion composed of chromaffin cells (sympathetic ganglionic neurons) that secrete epinephrine or norepinephrine. The chromaffin cells respond to acetylcholine secreted from sympathetic preganglionic neurons. In contrast, the adrenal cortex is composed of endocrine cells, and these cells are separated into three layers. The outermost layer of the cortex, the zona glomerulosa, synthesizes and releases aldosterone in response to elevated blood potassium or the hormone angiotensin II. The middle layer, the zona fasciculata, synthesizes and releases cortisol in response to corticotropin (ACTH) from the anterior pituitary. The inner layer of the cortex, the zona reticularis synthesizes and releases androstenedione, also in response to corticotropin.

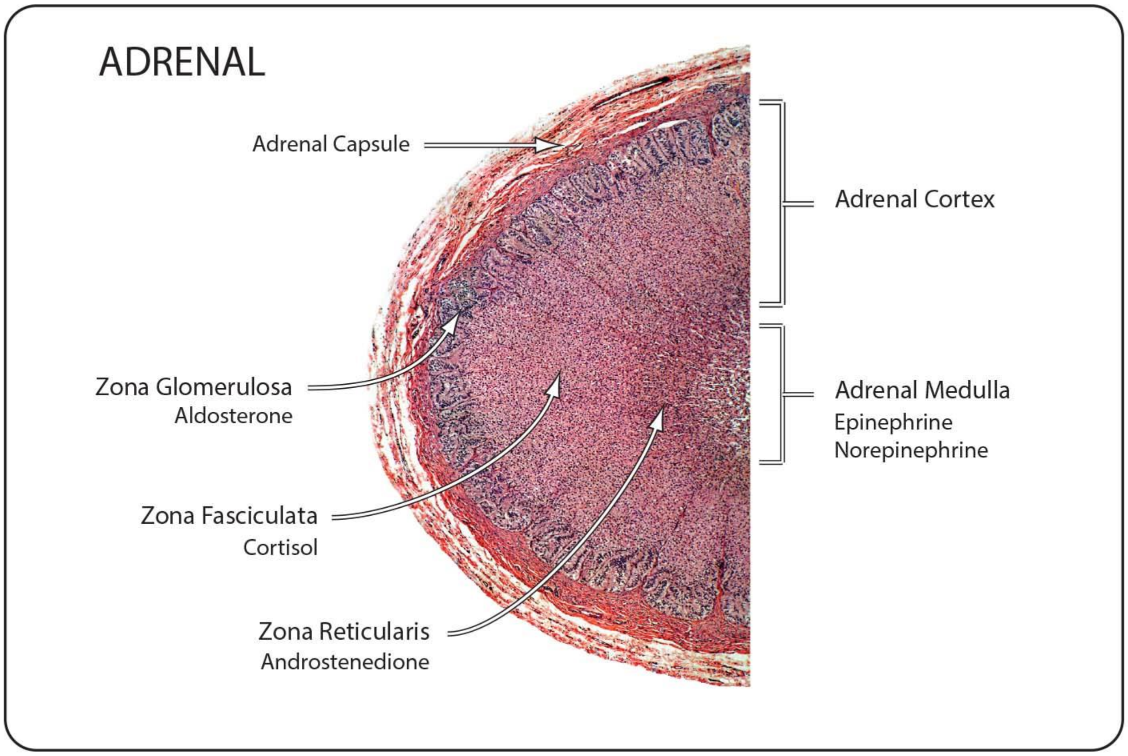

Figure 14.8 © 2020 David G. Ward, Ph.D.

Hormone Synthesis and Secretion/Release

As described in chapter 6, chemical messengers fall into a small number of chemical classes; amino acids, amines, peptides, steroids, and eicosanoids. The neurohormones and hormones include the amines, peptides, and steroids.

Amine Hormones

The amine hormones include:

1) Catecholamines (dopamine, norepinephrine, and epinephrine) secreted by the chromaffin cells (sympathetic ganglionic neurons) of the adrenal medulla
2) Major thyroid hormones (triiodothyronin (T3) and thyroxin (T4)) released from the endocrine cells of the thyroid follicles.

Catecholamines

The catecholamines include dopamine, norepinephrine, and epinephrine and are synthesized from tyrosine, as shown in Figure 14.9.

- In the cytosol, tyrosine is converted to L-dopa by tyrosine hydroxylase and L-dopa in turn is converted to dopamine by dopa decarboxylase.
- Dopamine is transported into vesicles where it is stored or converted to norepinephrine by dopamine β-hydroxylase.
- Norepinephrine is stored in the vesicles or transported into the cytosol to be converted to epinephrine by phentolamine N-methyltransferase.
- Epinephrine is transported into vesicles where it is stored.

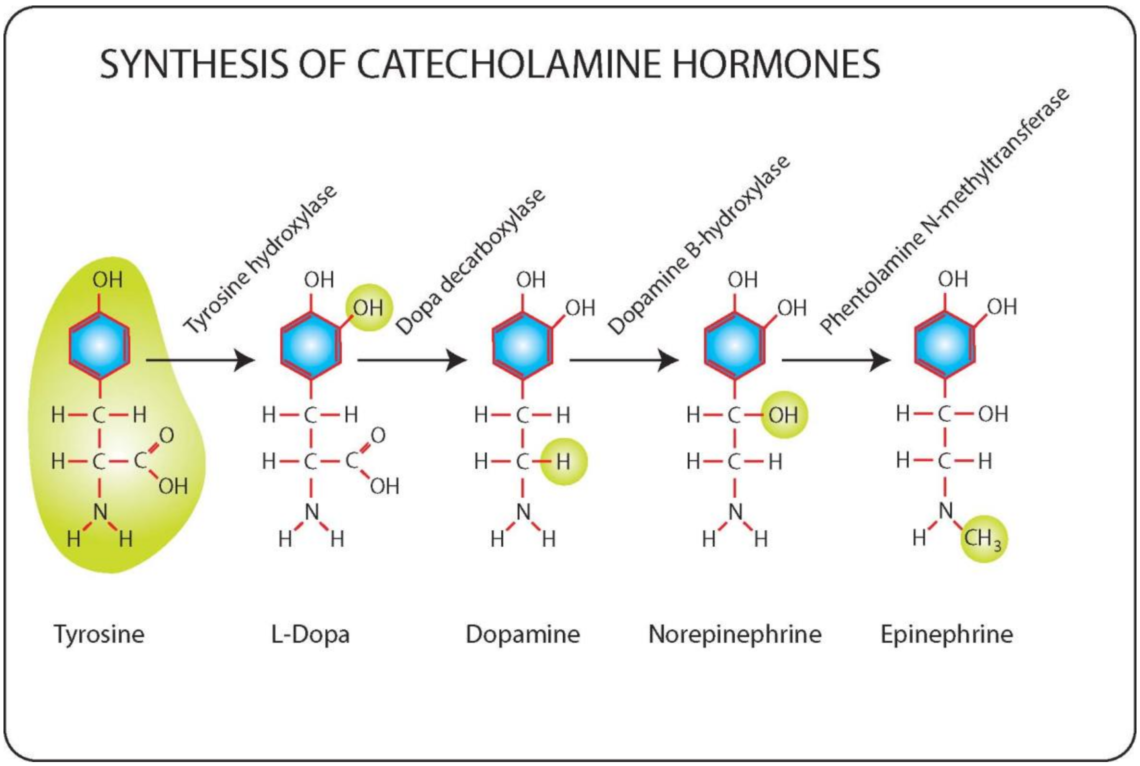

Figure 14.9 © 2007 David G. Ward, Ph.D.

The catecholamines are water soluble, stored in vesicles, and secreted out of the cell by exocytosis, as shown in Figure 14.10.

- In the adrenal medulla sympathetic preganglionic neurons release acetylcholine which binds to nicotinic-n receptors on chromaffin cells (sympathetic ganglionic neurons).
- Ligand gated sodium channels open, sodium enters and depolarizes the chromaffin cells and voltage gated calcium channels open.
- Calcium then enters the chromaffin cells and causes the secretory vesicles to fuse with the plasma membrane.
- The hormone (most commonly epinephrine in the adrenal medulla) diffuses out of the vesicles and into the interstitial space and then into the blood of the adrenal medulla.

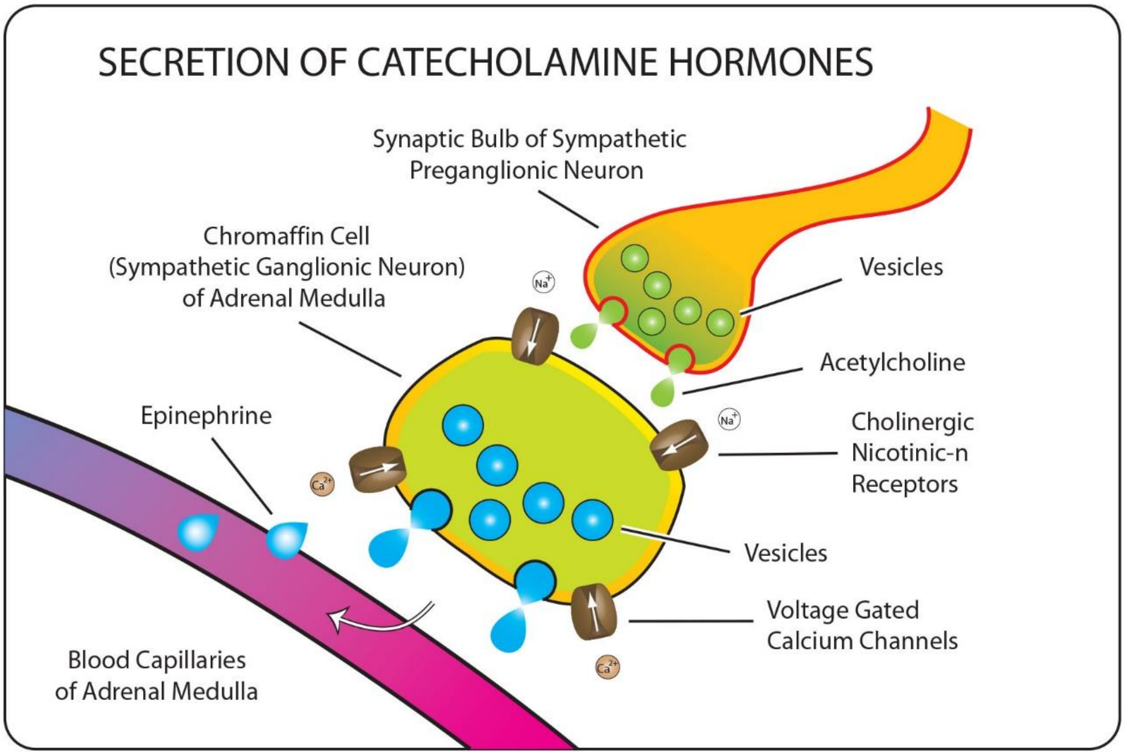

Figure 14.10 © 2014 David G. Ward, Ph.D.

In summary,

- Catecholamines are water soluble hormones.
- Catecholamines are synthesized in chromaffin cells (sympathetic ganglionic neurons) and other neurons and stored in vesicles.
- Catecholamines are secreted out of the cell by exocytosis in response to stimulation of the cell.

Thyroid Hormones

The major thyroid hormones include triiodothyronin (T3) and thyroxin (T4), are lipid soluble, and are synthesized from tyrosine, as shown in Figure 14.11.

- Thyroglobulin is synthesized in the cytoplasm of the thyroid follicular cells and transported to the lumen of the thyroid follicles by exocytosis.
- Iodine is co-transported with sodium into the cytosol of the follicular cells where it diffuses into the lumen of the thyroid follicles.
- In the lumen iodine is attached to tyrosine of the thyroglobulin to make monoiodotyrosine (MIT) or diiodotyrosine (DIT).
- The phenolic ring of a molecule of MIT or DIT is removed from the remainder of its tyrosine and coupled to another DIT on the thyroglobulin molecule to produce either T3 or T4.

- Thyroid follicles are stimulated by thyroid stimulating hormone (TSH) binding to G-protein coupled receptors (not shown), that in turn control the Na/I co-transporters.
- By way of adenylyl cyclase, cAMP, and protein kinase-A, an endocytosis process is activated that transports sections of the thyroglobulin containing T3 and T4 into the follicular cells.
- In addition, lysosomal enzymes are activated that release T3 and T4 from the thyroglobulin.
- T3 and T4 diffuse out of the follicular cell and into interstitial fluid and blood.

In summary,

- T3 and T4 are lipid soluble hormones.
- T3 and T4 are synthesized in the thyroid follicles on demand.
- T3 and T4 are released from the thyroid follicular cells by diffusion.

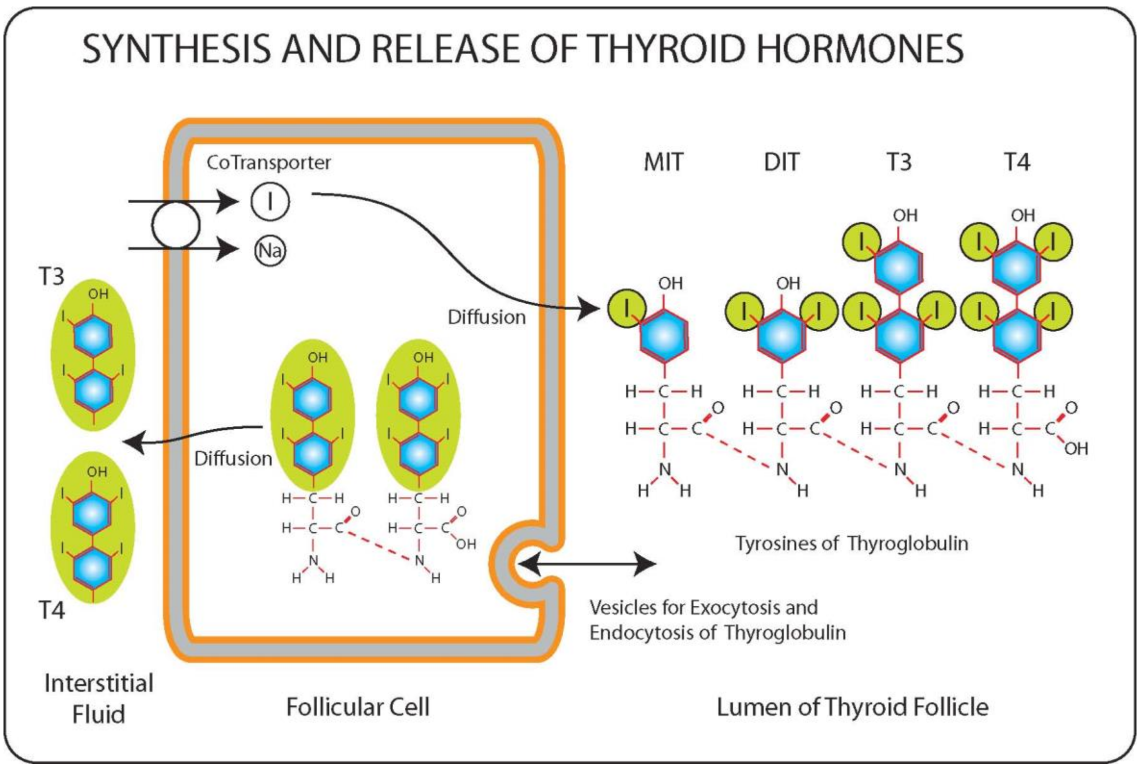

Figure 14.11 © 2007 David G. Ward, Ph.D.

Peptide Hormones

The peptide hormones make up a huge proportion of hormones, are water soluble, and include:

1) Hypothalamic regulatory hormones (Corticotropin Releasing Hormone, Thyrotropin Releasing Hormone, Somatotropin Releasing Hormone, Somatostatin, Gonadotropin Releasing Hormone, Prolactin Releasing Hormone) secreted from hypothalamic neurons;
2) Anterior pituitary hormones (Corticotropin, Thyrotropin, Somatotropin, Gonadotropins, Prolactin) secreted from endocrine cells of the anterior pituitary
3) Posterior pituitary hormones (Vasopressin, Oxytocin) secreted from hypothalamic neurons ending in the posterior pituitary
4) Minor thyroid hormones (Calcitonin) secreted by interfollicular cells of the thyroid
5) Parathyroid hormones (Parathyroid Hormone) secreted by chief cells of the parathyroid
6) Thymus hormones (Thymosin) secreted by endocrine cells of the thymus
7) Cardiac hormones (Atrial Natriuretic Peptide) secreted by atrial myocytes of the heart
8) Adipose hormones (Leptin, Adiponectin) secreted by adipocytes of adipose tissue
9) Hepatic hormones (Insulin-like Growth Factors) secreted by hepatocytes of the liver
10) Gastric hormones (Gastrin) secreted by endocrine cells of the stomach
11) Pancreatic hormones (Glucagon, Insulin) secreted by alpha and beta cells of the islets of the pancreas
12) Renal Hormones (Erythropoietin, Renin) secreted by renal and juxtaglomerular cells of the kidney
13) Intestinal hormones (Secretin, Gastrin, Enterocrinin, Cholecystokinin, Glucose Dependent Insulinotropic Hormone, Vasoactive Intestinal Peptide) secreted by endocrine cells of the small intestine
14) Female reproductive hormones (Relaxin) secreted by luteal cells of the corpus luteum of the ovary
15) Male reproductive hormones (Inhibin) secreted by the Sertoli cells of the seminiferous tubules of the testes

The major steps in the synthesis and secretion of peptide hormones are shown in Figure 14.12. Please refer to Figure 4.7 for a review of critical cellular organelles involved in peptide synthesis.

- Peptides are water soluble hormones.
- A preprohormone (prepolypeptide) is synthesized at the ribosomes.
- The preprohormone is, cleaved in the rough endoplasmic reticulum to yield a prohormone (propeptide).
- The prohormone is transported in vesicles to the Golgi complex where it is cleaved to yield the final hormone (peptide).
- The hormone is packaged and stored in secretory vesicles.

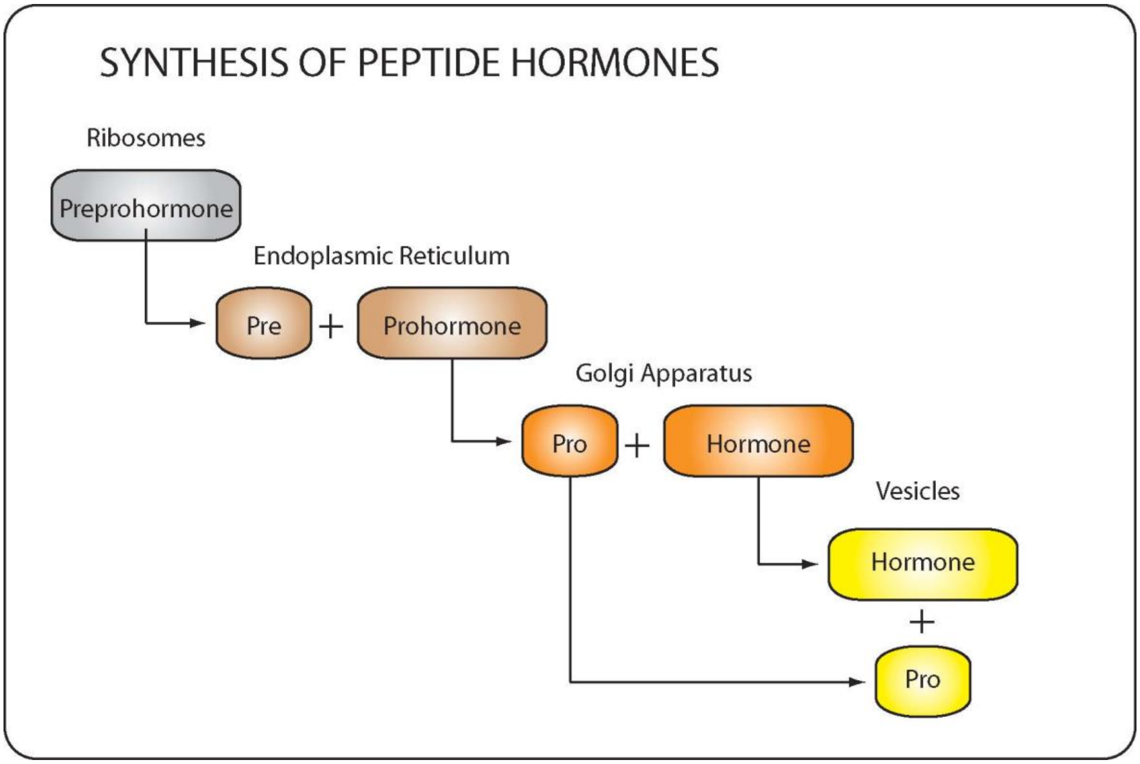

Figure 14.12 © 2007 David G. Ward, Ph.D.

The peptide hormones that are stored in vesicles are secreted out of the cell by exocytosis. Figure 14.13 uses the hypothalamus and anterior pituitary as an example and shows the exocytosis of corticotropin releasing hormone (CRH) from hypothalamic neurons and of corticotropin (ACTH) from the anterior pituitary.

- Action potentials reach the synaptic bulbs of hypothalamic neurons that synthesize CRH.
- The opening of sodium channels depolarizes of the synaptic bulb and voltage gated calcium channels open.
- Calcium enters the synaptic bulb and causes the secretory vesicles to fuse with the synaptic membrane.
- CRH diffuses out of the vesicles and into the interstitial space and then into the blood of the pituitary portal vessels.
- CRH reaches the anterior pituitary and binds to G-protein coupled receptors on corticotrophs that synthesize corticotropin in the anterior pituitary.
- By way of adenylyl cyclase, cAMP, and protein kinase-A, potassium channels close depolarizing the corticotrophs and voltage gated calcium channels open.
- Calcium then enters the corticotrophs and causes the secretory vesicles to fuse with the plasma membrane.
- Corticotropin (ACTH) diffuses out of the vesicles of the corticotrophs and into the interstitial space and then into the blood of the anterior pituitary.

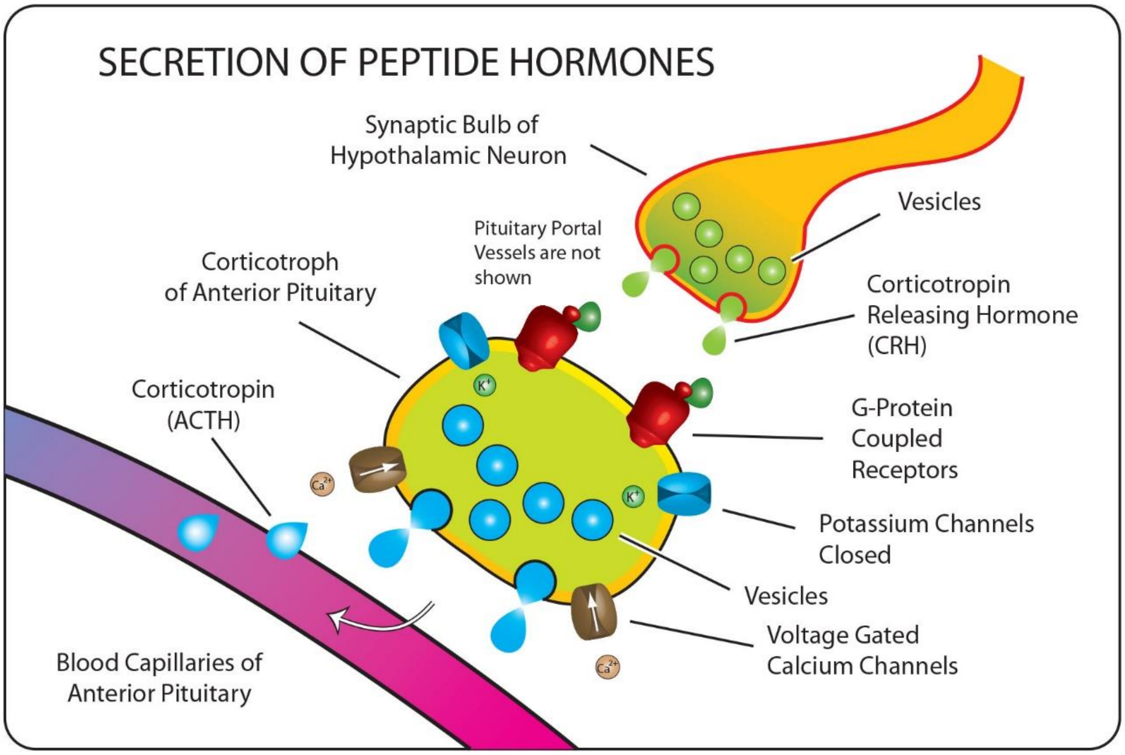

Figure 14.13 © 2014 David G. Ward, Ph.D.

In summary,

- Peptide hormones are water soluble.
- Peptide hormones are synthesized in neurons or endocrine cells and stored in secretory vesicles.
- Peptide hormones are secreted out of the cell by exocytosis in response to stimulation of the cell.

Steroid Hormones

Steroid hormones are a well-known class of hormones, are lipid soluble, and include

1) Adrenal cortical hormones (Aldosterone, Hydrocortisone (Cortisol), Androstenedione) synthesized and released by endocrine cells in the zona glomerulosa, fasciculata, and reticularis of the adrenal cortex
2) Ovarian steroid hormones (Estradiol, Progesterone, Androstenedione, Testosterone) synthesized and released by granulosa, luteal, and theca cells in the ovary
3) Testicular steroid hormones (Testosterone) synthesized and released by interstitial cells in the testes
4) Other steroid hormones (Calcitriol) synthesized from Vitamin D_3 in two steps that involve first the liver and second the kidney

The major steps in the synthesis of most steroid hormones are shown in Figure 14.14. Cholesterol is the foundation for all of the steroid hormones.

- In the cytosol, low density lipids are converted into cholesterol by cholesterol esterase.
- Largely in the mitochondria and smooth endoplasmic reticulum, cholesterol is converted into steroids in a process using cytochrome p450
- Cholesterol is converted into progesterone.
- Progesterone in turn can be converted into cortisol, aldosterone, or testosterone.
- Testosterone can be converted into estradiol.

The steroid hormones are synthesized on demand and released. Figure 14.15 uses the adrenal cortex as an example and shows the short term regulation and long term regulation of the synthesis and release of cortisol by corticotropin (ACTH) from the anterior pituitary.

- Corticotropin (ACTH) reaches the zona fasciculata of the adrenal cortex and binds to G-protein coupled receptors on cells that synthesize cortisol.
- By way of adenylyl cyclase, cAMP, and protein kinase-A, cholesterol esterase (CE) is activated which provides for a <u>short term regulation</u> of steroid synthesis.
- Cholesterol esterase (CE) catalyzes the conversion of low density lipids to cholesterol.
- The synthesis of cortisol from cholesterol requires cytochrome p450 (CYP).
- In addition, cAMP acts as a transcription factor and provides for a <u>long term regulation</u> of steroid synthesis.
- cAMP binds to the cAMP response element of the p450 gene and stimulates the expression of the gene for the synthesis of the cytochrome p450 peptide.
- As long as there is a sufficient supply of cholesterol, and a sufficient quantity of the p450 peptide, cortisol will be synthesized.
- Cortisol once synthesized diffuses out of the cells, into the interstitial space and then into the blood of the adrenal gland.

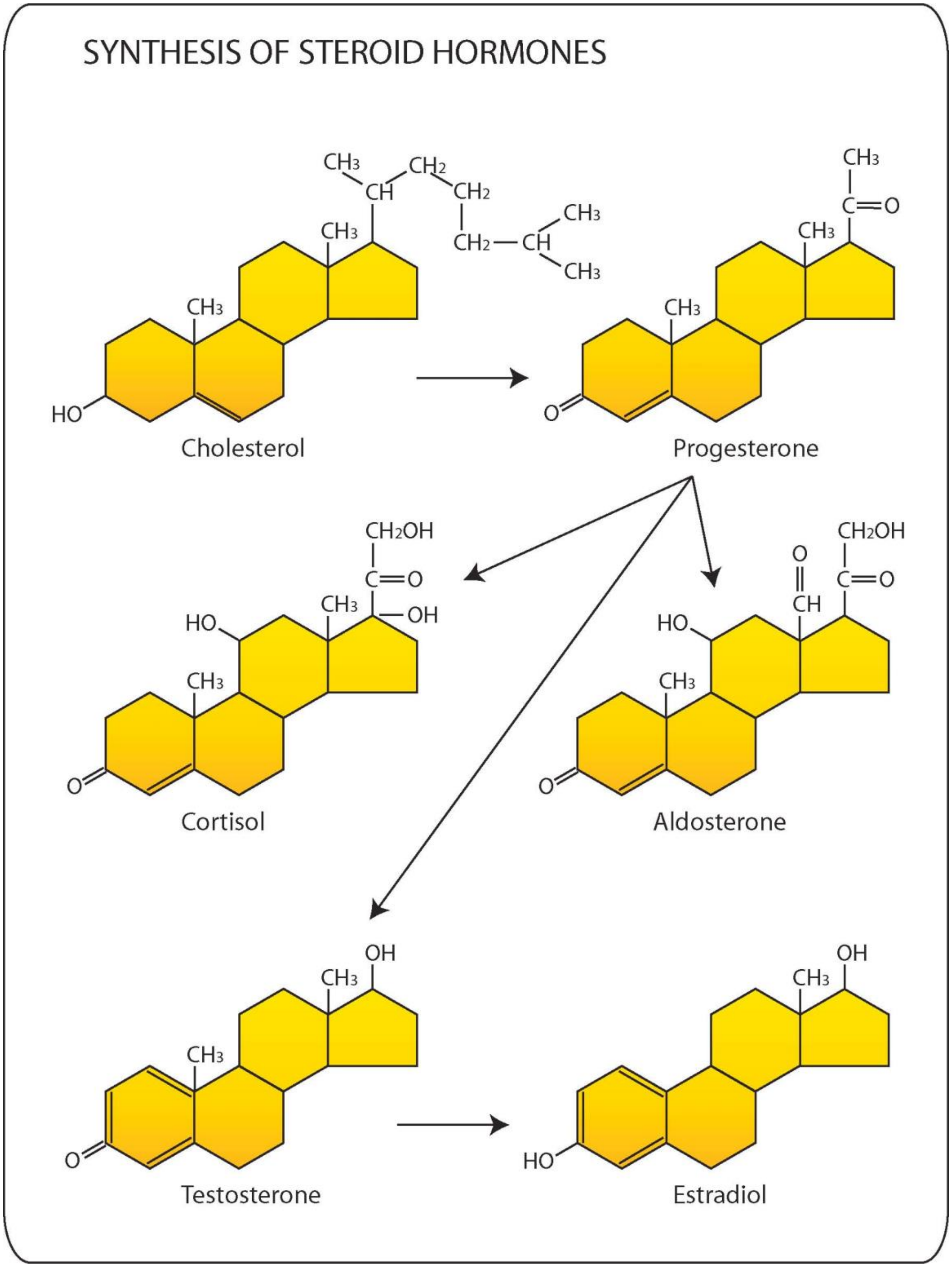

Figure 14.14 © 2007 David G. Ward, Ph.D.

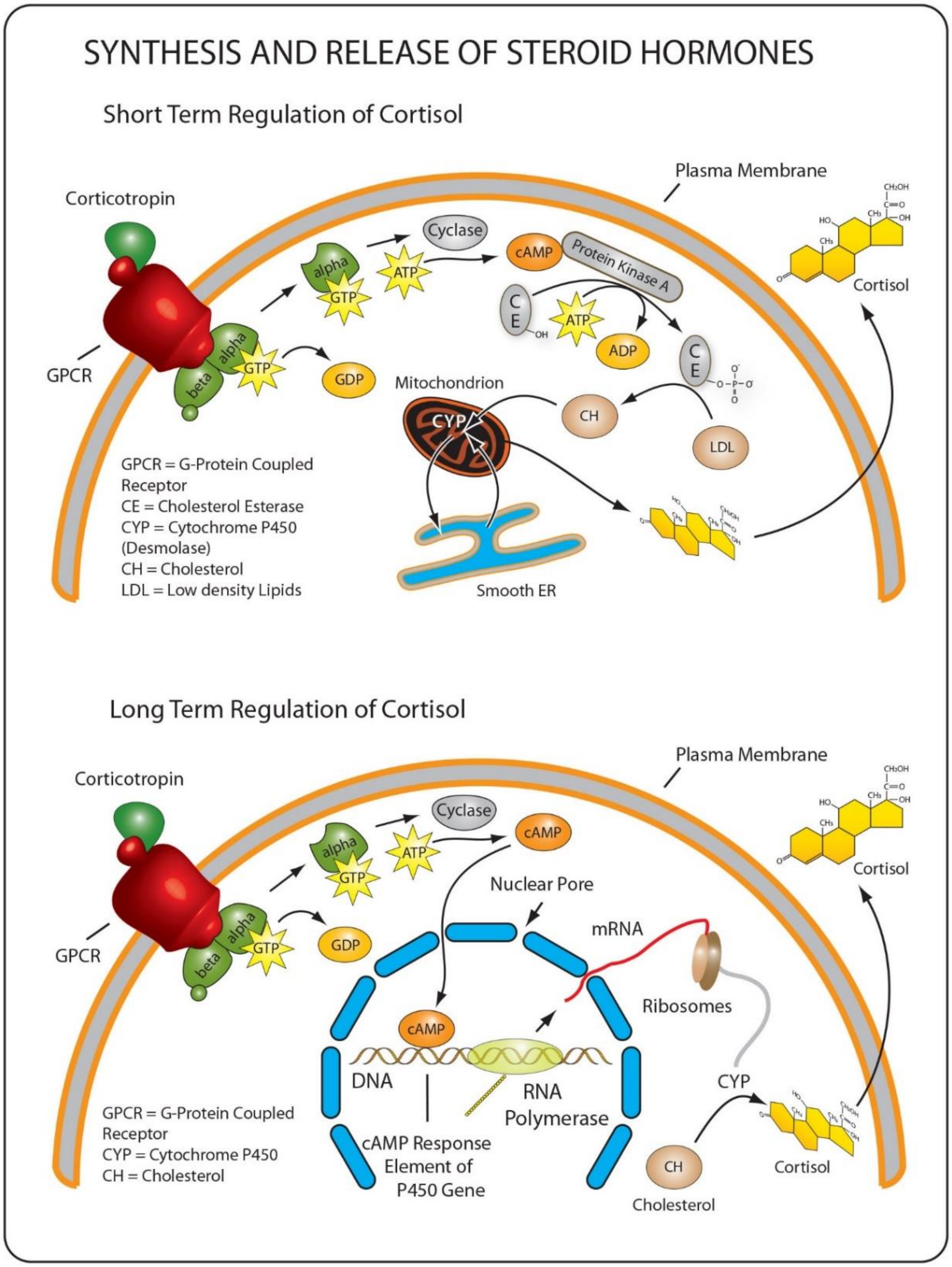

Figure 14.15 © 2014 David G. Ward, Ph.D.

In summary,

- Steroid hormones are lipid soluble.
- Steroid hormones are synthesized on demand.
- Steroid hormones are released from the cell by diffusion.

Cellular Mechanisms of Hormone Action

Water soluble hormones do not pass through the phospholipid bilayer and must exert their influence by attaching to **extracellular receptors** in the membrane of the target cells. Most water-soluble hormones act by binding to G-protein coupled receptors. (Please refer to Chapter 6, especially Figures 6.6 and 6.7 as well as this chapter) However, some water soluble hormones, notably insulin, growth hormone, and prolactin act by binding to tyrosine kinase linked receptors. (Please refer to Chapter 6, Figure 6.5.)

- Most water-soluble hormones act by binding to <u>G-protein coupled receptors</u>.

- Some water-soluble hormones, notably insulin, growth hormone, and prolactin, act by binding to <u>tyrosine kinase linked receptors</u>.

Lipid soluble hormones pass through the phospholipid bilayer and exert their influence by attaching to **intracellular receptors** in the cytosol or nucleus of the target cells. Most lipid soluble hormones commonly bind to a response element binding protein in the cytosol to form a transcription factor that binds to a response element in the distal promoter region of the DNA. (Please refer to Chapter 6, Figure 6.1.)

- Most lipid-soluble hormones act by binding to <u>response element binding proteins</u> in the cytosol.

Figure 14.16 shows examples of actions of a water-soluble hormone and a lipid soluble hormone. First, we see how glucagon, a water soluble hormone, acts on a G-protein coupled receptor (GPCR) to cause the conversion of glycogen to glucose.

- Glucagon reaches the liver or muscle and binds to G-protein coupled receptors on hepatocytes that store glycogen.
- By way of adenylyl cyclase, cAMP, and protein kinase-A, phosphorylase kinase (PK) is activated (phosphorylated)
- Active PK activates (phosphorylates) glycogen phosphorylase (GP) which is central to the breakdown of glycogen to glucose.

Second, we see how cortisol, a lipid-soluble hormone, combines with a response element binding protein to act on a response element of a gene to cause the conversion of amino acids to glucose.

- Cortisol reaches the liver or muscle and diffuses through the plasma membrane into the cytosol.
- Cortisol binds to a glucocorticoid response element binding protein (GREB) and forms a cortisol-GREB complex.
- The cortisol-GREB complex passes through the pores of the nucleus and binds to the glucocorticoid response element of the phosphoenolpyruvate carboxy kinase (PEPCK) gene and stimulates the expression of PEPCK.
- PEPCK is central to the conversion of amino acids to glucose.

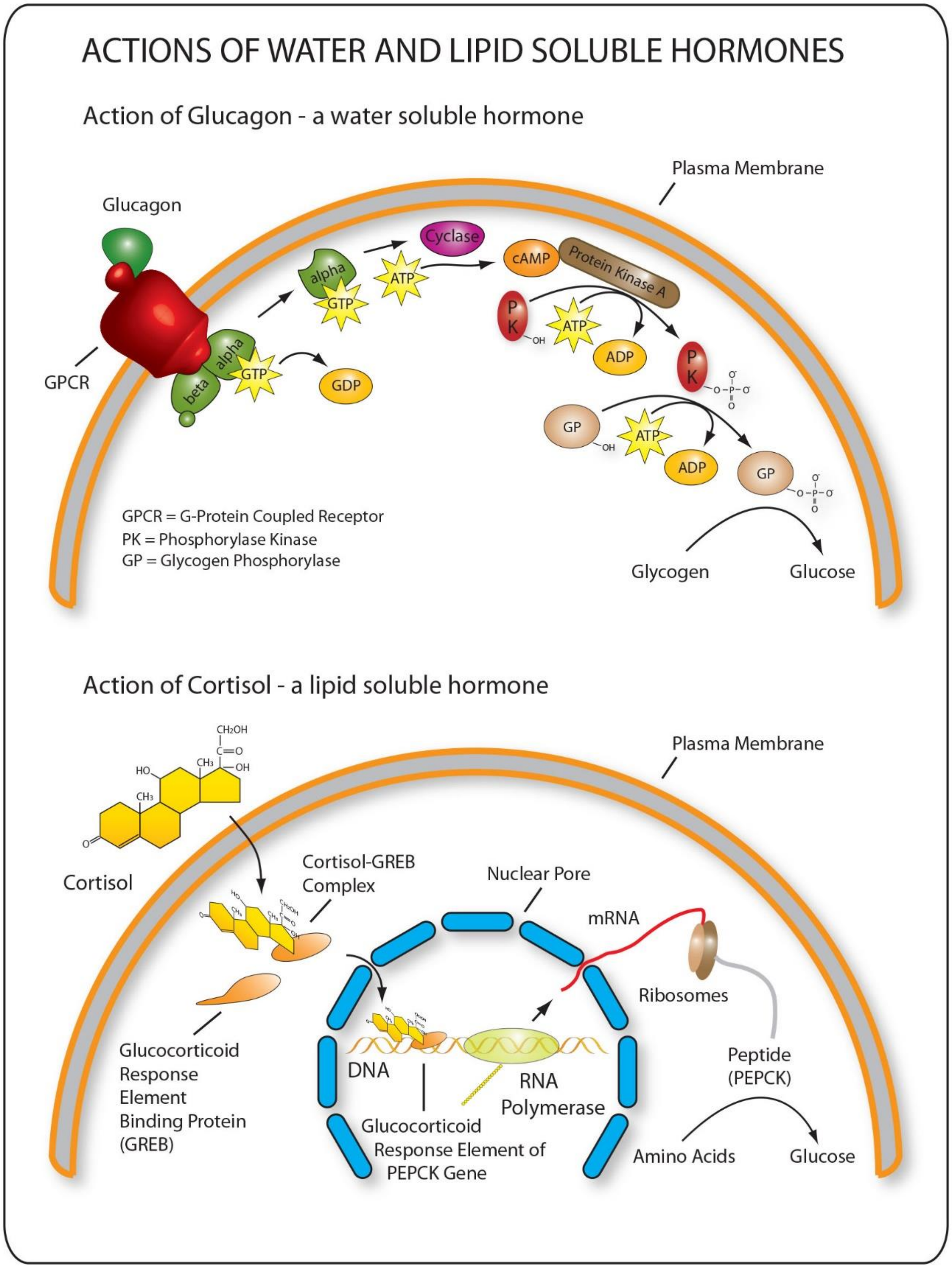

Figure 14.16 © 2014 David G. Ward, Ph.D.

Quiz Yourself

1-5. Matching (Gland : produces hormone)

A)	Thyroid	Cholecystokinin (CCK)	1) _____
B)	GI Tract	Corticotropin (ACTH)	2) _____
C)	Adrenal Cortex	Thyroxin (T4)	3) _____
D)	Anterior Pituitary	Oxytocin	4) _____
E)	Posterior Pituitary	Cortisol	5) _____

6-10. Matching

A)	water soluble	Vasopressin	6) _____
B)	lipid soluble	Testosterone	7) _____
		Thyroxin (T4)	8) _____
		Norepinephrine (NE)	9) _____
		Gonadotropin Releasing Hormone (GnRH)	10) _____

11-15. Matching

A)	a tropic hormone	Thyrotropin Releasing Hormone (TRH)	11) _____
B)	a non-tropic hormone	Epinephrine (E, Epi)	12) _____
		Triiodothyronin (T3)	13) _____
		Thyrotropin (TSH)	14) _____
		Oxytocin	15) _____

16-20. Matching (REB = response element binding; GPRC = G protein coupled receptors)

A)	acts by way of tyrosine kinase linked receptors	Insulin	16) _____
B)	acts by way of REB protein receptors	Cortisol	17) _____
C)	acts by way of GPCRs	Vasopressin	18) _____
		Norepinephrine (NE)	19) _____
		Corticotropin Releasing Hormone (CRH)	20) _____

Fill in

21. Neurotransmitters are ___________ soluble.

22. Hormones may be ___________ soluble or ___________ soluble.

23. ____________ (a hormone) will stimulate β_2 receptors in the lungs and cause bronchial dilation.

24. Catecholamine and peptide hormones are stored and secreted from _____________.

25. Steroid hormones are synthesized from _______________ and not stored.

Study Questions

1. Describe the characteristics of amine, peptide, and steroid hormones, and list some examples of hormones in each group and the glands that produce them.
2. Compare and contrast nervous communication and endocrine communication.
3. Compare and contrast how water soluble hormones and lipid soluble hormones act on target cells. Use examples, and include a description of the receptors involved.
4. Compare and contrast the synthesis and secretion/release of water soluble hormones and lipid soluble hormones.