

## *The Endocrine System 2*

### *Hormone Activity*

#### *The Role of Hormone Receptors*

Although a given hormone travels throughout the body in the blood, it affects only specific target cells. Hormones, like neurotransmitters, influence their target cells by chemically binding to specific protein **receptors**. Only the target cells for a given hormone have receptors that bind and recognize that hormone.

For example, thyroid-stimulating hormone (TSH) binds to receptors on cells of the thyroid gland, but it does not bind to cells of the ovaries because ovarian cells do not have TSH receptors.

Receptors, like other cellular proteins, are constantly being synthesized and broken down. Generally, a target cell has 2000 to 100,000 receptors for a particular hormone.

If a hormone is present in excess, the number of target-cell receptors may decrease—an effect called **down-regulation**. For example, when certain cells of the testes are exposed to a high concentration of luteinizing hormone (LH), the number of LH receptors decreases.

Down-regulation makes a target cell *less sensitive* to a hormone. In contrast, when a hormone is deficient, the number of receptors may increase. This phenomenon, known as **upregulation**, makes a target cell *more sensitive* to a hormone.

#### *Clinical Connection : Blocking Hormone Receptors*

*Synthetic hormones that block the receptors for some naturally occurring hormones are available as drugs.*

*For example, RU486 (mifepristone), which is used to induce abortion, binds to the receptors for progesterone (a female sex hormone) and prevents progesterone from exerting its normal effect, in this case preparing the lining of the uterus for implantation.*

*When RU486 is given to a pregnant woman, the uterine conditions needed for nurturing an embryo are not maintained, embryonic development stops, and the embryo is sloughed off along with the uterine lining.*

*This example illustrates an important endocrine principle: If a hormone is prevented from interacting with its receptors, the hormone cannot perform its normal functions.*

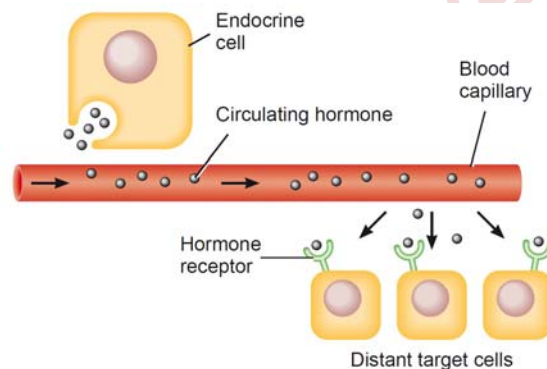
#### *Circulating and Local Hormones*

Most endocrine hormones are **circulating hormones**—they pass from the secretory cells that make them into interstitial fluid and then into the blood (Figure 3 a).

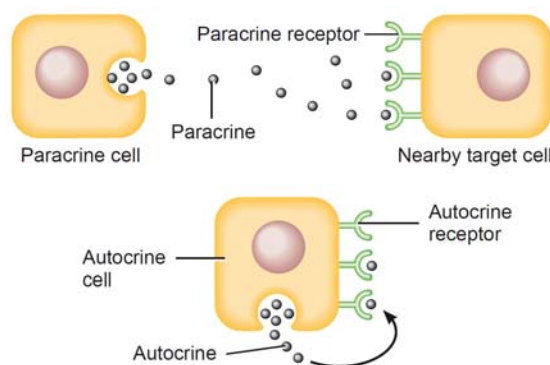
Other hormones, termed **local hormones**, act locally on neighboring cells or on the same cell that secreted them without first entering the bloodstream (Figure 3 b). Local hormones that act on neighboring cells are called **paracrines** (*para-* = beside or near), and those that act on the same cell that secreted them are called

**autocrines** (*auto-* = self ). One example of a local hormone is interleukin 2 (IL-2), which is released by helper T cells (a type of white blood cell) during immune responses . IL-2 helps activate other nearby immune cells, a paracrine effect. But it also acts as an autocrine by stimulating the same cell that released it to proliferate. This action generates more helper T cells that can secrete even more IL-2 and thus strengthen the immune response. Another example of a local hormone is the gas nitric oxide (NO), which is released by endothelial cells lining blood vessels. NO causes relaxation of nearby smooth muscle fibers in blood vessels, which in turn causes vasodilation (increase in blood vessel diameter). The effects of such vasodilation range from a lowering of blood pressure to erection of the penis in males. The drug *Viagra*® (sildenafil) enhances the effects stimulated by nitric oxide in the penis.

Local hormones usually are inactivated quickly; circulating hormones may linger in the blood and exert their effects for a few minutes or occasionally for a few hours. In time, circulating hormones are inactivated by the liver and excreted by the kidneys. In cases of kidney or liver failure, excessive levels of hormones may build up in the blood.



(a) Circulating hormones



(b) Local hormones (paracrines and autocrines)

**Figure 3: Comparison between circulating hormones and local hormones (autocrines and paracrines).**

Circulating hormones are carried through the bloodstream to act on distant target cells. Paracrines act on neighboring cells and autocrines act on the same cell that produced them.

### **Chemical Classes of Hormones**

Chemically, hormones can be divided into two broad classes:

Those that are soluble in lipids, and those that are soluble in water. This chemical classification is also useful functionally because the two classes exert their effects differently.

#### **Lipid-soluble Hormones**

The lipid-soluble hormones include steroid hormones, thyroid hormones, and nitric oxide.

- 1. Steroid hormones** are derived from cholesterol. Each steroid hormone is unique due to the presence of different chemical groups attached at various sites on the four rings at the core of its structure. These small differences allow for a large diversity of functions.
- 2. Two thyroid hormones** (T3 and T4) are synthesized by attaching iodine to the amino acid tyrosine. The benzene ring of tyrosine plus the attached iodines make T3 and T4 very lipid soluble.
- 3. The gas nitric oxide (NO)** is both a hormone and a neurotransmitter. Its synthesis is catalyzed by the enzyme nitric oxide synthase.

#### **Water-soluble Hormones**

The water-soluble hormones include amine hormones, peptide and protein hormones, and eicosanoid hormones.

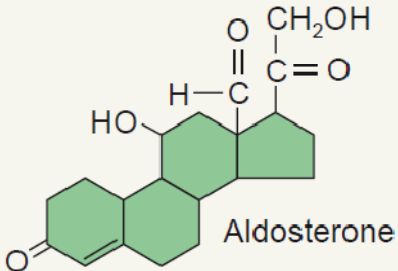
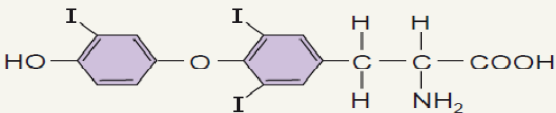
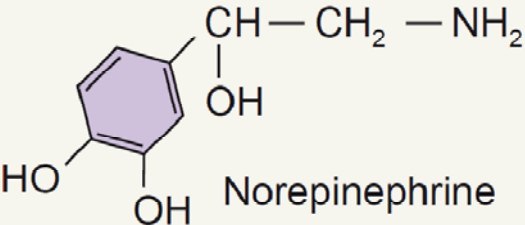
- 1. Amine hormones** are synthesized by decarboxylating (removing a molecule of CO<sub>2</sub>) and otherwise modifying certain amino acids. They are called amines because they retain an amino group (NH<sub>3</sub><sup>+</sup>). The catecholamines—epinephrine, norepinephrine, and dopamine—are synthesized by modifying the amino acid tyrosine. Histamine is synthesized from the amino acid histidine by mast cells and platelets. Serotonin and melatonin are derived from tryptophan.
- 2. Peptide hormones** and **protein hormones** are amino acid polymers. The smaller peptide hormones consist of chains of 3 to 49 amino acids; the larger protein hormones include 50 to 200 amino acids. Examples of peptide hormones are antidiuretic hormone and oxytocin; protein hormones include human growth hormone and insulin. Several of the protein hormones, such as thyroid-stimulating hormone, have attached carbohydrate groups and thus are **glycoprotein hormones**.
- 3. The eicosanoid hormones** (1<sup>-</sup>-KO<sup>-</sup>-sa-noid; *eicos-* = twenty forms; *-oid* = resembling) are derived from arachidonic acid, a 20-carbon fatty acid. The two major types of eicosanoids are **prostaglandins** and **leukotrienes**. The

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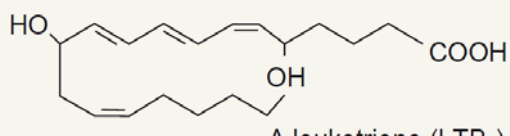
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eicosanoids are important local hormones, and they may act as circulating hormones as well.

**Table 2** summarizes the classes of lipid-soluble and watersoluble hormones and provides an overview of the major hormones and their sites of secretion.

<b>Table 2: Summary of Hormones by Chemical Class</b>		
<b>Chemical Class</b>	<b>Hormones</b>	<b>Site Of Secretion</b>
<b>Lipid-Soluble</b>		
<p style="text-align: center;"><b>Steroid hormones</b></p>  <p style="text-align: center;">Aldosterone</p>	Aldosterone, cortisol, and androgens	Adrenal cortex.
	Calcitriol.	Kidneys.
	Testosterone.	Testes.
	Estrogens and progesterone.	Ovaries.
<p style="text-align: center;"><b>Thyroid hormones</b></p> 	T3 (triiodothyronine) and T4 (thyroxine).	Thyroid gland (follicular cells).
<b>Gas</b>		
	Nitric oxide (NO).	Endothelial cells lining blood vessels.
<b>Water-Soluble</b>		
<p style="text-align: center;"><b>Amines</b></p>  <p style="text-align: center;">Norepinephrine</p>	Epinephrine and norepinephrine (catecholamines).	Adrenal medulla.
	Melatonin	Pineal gland
	Histamine.	Mast cells in connective tissues
	Serotonin.	Platelets in blood
<p style="text-align: center;"><b>Peptides and proteins</b></p> <pre>           Glutamine ——— Isoleucine                                       Asparagine     Tyrosine                                       Cysteine —S—S— Cysteine                                       Proline                         Leucine                         Glycine                           NH<sub>2</sub>           </pre> <p style="text-align: right;">Oxytocin</p>	All hypothalamic releasing and inhibiting hormones	Hypothalamus.
	Oxytocin, antidiuretic hormone	Posterior pituitary
	Human growth hormone, thyroid-stimulating hormone, adrenocorticotrophic hormone, follicle-stimulating hormone,	Anterior pituitary

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	luteinizing hormone, prolactin, melanocyte-stimulating hormone.	
	Insulin, glucagon, somatostatin, pancreatic polypeptide.	Pancreas.
	Parathyroid hormone	Parathyroid glands
	Calcitonin.	Thyroid gland (parafollicular cells).
	Gastrin, secretin, cholecystokinin, GIP (glucose-dependent insulinotropic peptide).	Stomach and small intestine (enteroendocrine cells)
	Erythropoietin	Kidneys.
	Leptin.	Adipose tissue
<p>Eicosanoids</p>  <p>A leukotriene (LTB<sub>4</sub>)</p>	Prostaglandins, leukotrienes	All cells except red blood cells

**THANK YOU**