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基础与临床内分泌学

Basic & Clinical Endocrinology

Francis S. Greenspan
David G. Gardner

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Preface

The 21st century has witnessed a tremendous resurgence of interest in and understanding of the physiology and genetics of endocrinology. This is due largely to the application of modern molecular methods to the study of hormones, their synthesis, and their mechanisms of action. These advances have in turn engendered a host of newly created hormone agonists and antagonists as well as diagnostic tests for clinical endocrine problems. The current sixth edition of *Basic & Clinical Endocrinology* has incorporated many of these new concepts and therapies into a succinct, comprehensive, and up-to-date endocrinology textbook. Each chapter has been revised to incorporate important changes since the last edition.

Following the overview in Chapter 1, "Introduction to Endocrinology," new concepts of hormone synthesis, release, and actions are carefully reviewed. There is a new chapter on endocrine autoimmunity. Recent advances in diagnosis and management of major endocrine syndromes are reviewed, including new chapters on metabolic bone disease, obesity, multiple endocrine neoplasia, and the hormonal aspects of malignancy. There is a new review of the endocrinopathies associated with AIDS and how to diagnose and manage them. In addition, there is a chapter dealing with endocrine emergencies that includes specific recommendations on the management of endocrine crises.

The reader will find that these chapters, each written by specialists in their fields, provide an authoritative review of the subject matter. The many tables, figures, and charts will help to facilitate understanding of the concepts presented.

This overview of the field of endocrinology should provide a solid foundation from which to view the exiting future developments in this rapidly moving discipline.

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San Francisco
October 2000

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Introduction to Endocrinology

1

John D. Baxter, MD, & Ralff C. J. Ribeiro, MD, PhD

THE ENDOCRINE SYSTEM

The endocrine and nervous systems are the major controllers of the flow of information between different cells and tissues, thereby regulating most functions of the body (Figure 1–1). The term "endocrine" denotes internal secretion of biologically active substances—in contrast to "exocrine," which denotes secretion outside the body, eg, through sweat glands or ducts that lead into the gastrointestinal tract. The endocrine system uses hormones to convey its information. Hormones are typically defined as substances released by endocrine glands and transported through the bloodstream to tissues where they act to regulate specific functions. These actions are mediated by binding of the hormone to receptor molecules (Chapter 3). Hormones are allosteric effectors that alter the conformation of the receptors to which they bind. Re-

ACRONYMS USED IN THIS CHAPTER

ACTH	Adrenocorticotropic hormone; corticotropin
ADH	Antidiuretic hormone; vasopressin
ADP	Adenosine diphosphate
ANP	Atrial natriuretic peptide
AP1	Activating protein 1
ATP	Adenosine triphosphate
cAMP	Cyclic adenosine monophosphate
CBG	Corticosteroid-binding globulin; transcortin
CCK	Cholecystokinin
CG	Chorionic gonadotropin
cGMP	Guanosine 3′,5′-cyclic monophosphate
CGRH	Calcitonin gene-related hormone
COMT	Catechol-*O*-methyltransferase
CRH	Corticotropin-releasing hormone
CS	Chorionic somatomammotropin, placental lactogen
EGF	Epidermal growth factor
ELISA	Enzyme-linked immunosorbent assay
ERE	Estrogen response element
FGF	Fibroblast growth factor
FSH	Follicle-stimulating hormone
GABA	γ-Aminobutyric acid
GH	Growth hormone
GHRH	Growth hormone-releasing hormone
GnRH	Gonadotropin-releasing hormone
HRE	Hormone response element
IGF-1	Insulin-like growth factor-1
IGF-2	Insulin-like growth factor-2
LDL	Low-density lipoprotein
LH	Luteinizing hormone
MAO	Monamine oxidase
MEN	Multiple endocrine neoplasia
MRI	Magnetic resonance imaging
mRNA	Messenger RNA
PAS	**P**eriod gene, **A**ryl hydrocarbon receptor nuclear translocator, and **S**ingle-minded gene
PCR	Polymerase chain reaction
PGDF	Platelet-derived growth factor
PRL	Prolactin
PTH	Parathyroid hormone
RFLP	Restriction fragment length polymorphism
SHBG	Sex hormone-binding globulin
TBG	Thyroid hormone-binding globulin
TBPA	Thyroid hormone-binding prealbumin; transthyretin
TGF	Transforming growth factor
TNF	Tumor necrosis factor
TRH	Thyrotropin-releasing hormone
TSH	Thyroid-stimulating hormone, thyrotropin
VIP	Vasoactive intestinal peptide
VMA	Vanillylmandelic acid

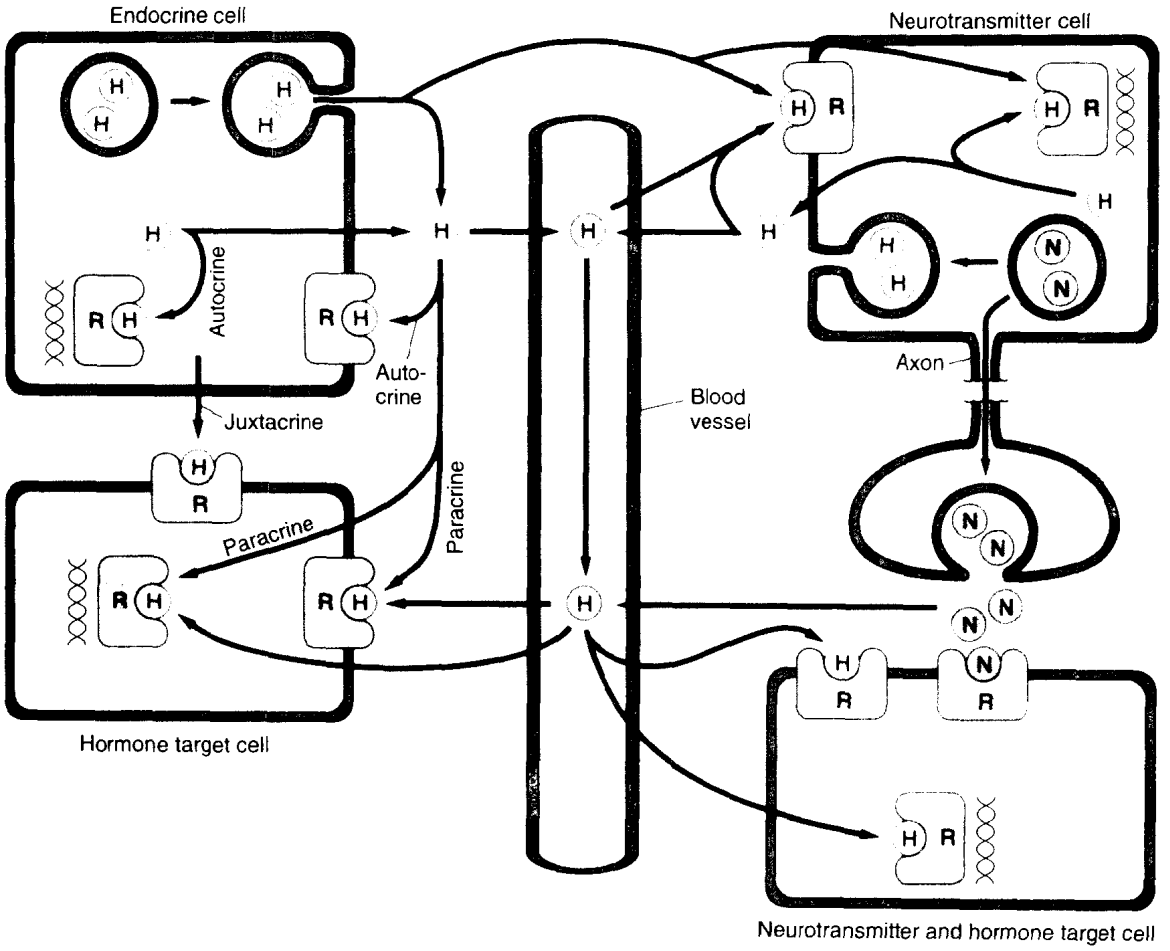

Figure 1–1. Actions of hormones and neurotransmitters and their interrelationships. Both endocrine and neurotransmitter cells synthesize and release hormones either from secretory vesicles or by diffusion. These hormones may act on the same cell in which they are produced (autocrine) without leaving the cell or after their release and subsequent binding to receptors in or on the cell. They may act on other target cells in their vicinity, including neurotransmitter cells, without entering the circulation (juxtacrine and paracrine). They may go to the target cell through the circulation (hormonal). Neurotransmitter cells produce neurotransmitters that are released at nerve terminals. These same neurotransmitters can be released to act as hormones through the synaptic junctions or directly by the cell. (H, hormone; R, receptor; N, neurotransmitter.)

ceptors are cellular proteins that have bifunctional properties of both recognition (ie, ability to distinguish the hormone from all of the other molecules to which they are exposed) and signal activation (ie, the ability to translate the binding information into postreceptor events).

The endocrine system is diverse and complex. There are varied and sophisticated mechanisms that control hormone synthesis, release, transport in the circulation, metabolism, and delivery to the surface or interior of target cells. In addition to this more traditional view of the system, many actions of hormones also occur in autocrine, paracrine, or juxtacrine fashions in which the hormones do not enter the circulation (Figure 1–1; and see below). In addition, molecules that are usually not considered hormones, such as lymphokines and Ca^{2+} ions, may act as hormones, and tissues such as the kidney, liver, and heart, ordinarily not considered being endocrine glands, produce and release hormones.

There are numerous interrelationships between the endocrine, nervous, and immune systems. Some of these are briefly described below and to some extent in Chapters 5 (hypothalamus and pituitary gland) and 11 (the adrenal medulla). Also described are the class of molecules termed "eicosanoids," including the prostaglandins and prostacyclins, which have numerous relationships with the endocrine system.

This chapter provides a broad overview of the field of endocrinology, including basic science and princi-

ples that are important for diagnosis and management of patients with endocrine disease.

PARACRINE & AUTOCRINE ACTIONS

As mentioned above, hormones not only reach target tissues through the circulation but also act locally where they are released (Figure 1–1). When they act locally on cells other than those that produce them, the action is called "paracrine," as illustrated by the actions of sex steroids in the ovary, angiotensin II in the kidney, and platelet-derived growth factor in the vascular wall. As a variant of this action, the hormone in the membrane of one cell can interact directly with a receptor on a juxtaposed cell. This is seen, for example, with some hematopoietic growth factors and is termed "juxtacrine" regulation. The hormone can also act on the cell in which it is produced, a phenomenon referred to as "autocrine"; in this case, the hormone released by the cell acts on receptors located on the same cell. Autocrine actions appear to be especially important with cancer cells that synthesize various oncogene products, which act in the same cell to stimulate cell division and promote the growth of the cancer. Hormones may also act inside the cell without ever being released, ie, an intracrine effect. For example, insulin released by the pancreatic islet B cells can inhibit insulin release by the same cells, and somatostatin can inhibit its own release from pancreatic D cells (Chapter 18).

CHEMICAL COMPOSITION OF HORMONES

Hormones derive from the major classes of compounds used by the body for general purposes (Figures 1–2 and 1–3; see also Chapter 2). In fact, derivatives of all types of small molecules provide examples of regulatory ligands that mediate autocrine, paracrine, juxtacrine, and endocrine functions. Thus, hormones can be proteins (including glycoproteins), smaller peptides or peptide derivatives, amino acid analogs, or lipids. Polypeptide hormones are direct translation products of specific mRNAs, cleavage products of larger precursor proteins, or modified peptides. Catecholamines and thyroid hormones are derivatives of amino acids. Steroid hormones and vitamin D are derived from cholesterol. Retinoids are derived from carotenoids in the diet that are modified by the body. Eicosanoids such as prostaglandins, prostacyclins, and leukotrienes are related to hormones (see below) and are derived from fatty acids. Whereas hormones are referred to as such

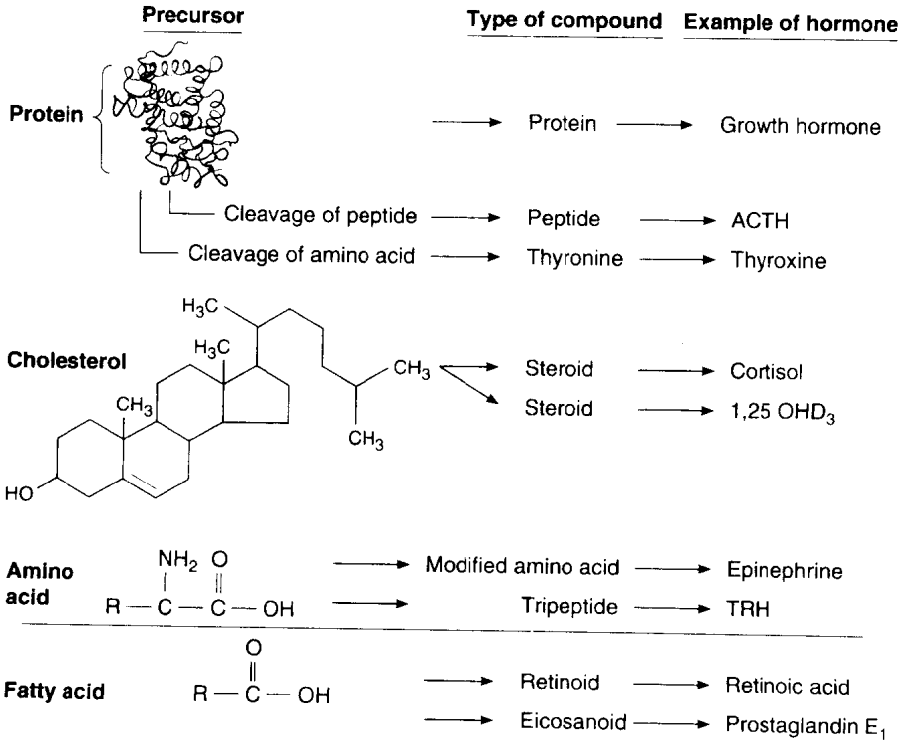

Figure 1–2. Precursors of hormones. Shown are representations of the sources of the major hormones, with examples of the molecular types of derivatives and hormones that reflect each chemical type.