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Basic Medical Endocrinology

Fourth Edition

H. Maurice Goodman

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Background: **FIGURE 3-2** Histology of the human thyroid. Simple cuboidal cells (arrows) make up the follicles. C _ thyroid colloid (thyroglobulin), which fills the follicles. (From Borysenko, M. and Beringer, T. (1979) *Functional Histology*, 312. Little, Brown, Boston by permission of Lippincott, Williams and Wilkins, Philadelphia.)

Black/green: **FIGURE 7-11** Confocal fluorescent microscope images of cultured mouse adipocytes that were transfected with a GLUT4-enhanced green fluorescent protein fusion construct and then incubated in the absence (A) or presence (B) of insulin for 30 min. Insulin stimulation results in the translocation of GLUT4 from intracellular storage sites to the plasma membrane. (From Watson, R.T., Kanzaki, M., and Pessin, J. (2004) Regulated membrane trafficking of the insulin-responsive glucose transporter 4 in adipocytes. *Endocr. Revs.* **25**: 177–204, by permission of The Endocrine Society.)

Blue figure: **FIGURE 10-14** Low-power photomicrograph of a portion of the thyroid gland of a normal dog. Parafollicular (C) cells are indicated in the walls of the follicles. (From Ham, A.W. and Cormack, D. H. (1979) *Histology*, 8th Edition, 802, by permission of Lippincott, Williams and Wilkins, Philadelphia.)

Red, white and blue: **FIGURE 11-3** Schematic representation of the tibial epiphyseal growth plate. (Modified from Nilsson, O., Marino, R., De Luca, F., Phillip, M., and Baron, J. (2005) Endocrine regulation of the growth plate. *Hormone Research* **64**: 157–165 by permission of S. Karger AG, Basel.)

Pink, yellow, white: **FIGURE 12-1** Histological section of human testis. The transected tubules show various stages of spermatogenesis. (From di Fiore, M.S.H. (1981) *Atlas of Human Histology*, 5th Edition, 209. Lea & Febiger, by permission of Lippincott, Williams and Wilkins, Philadelphia.)

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This volume is dedicated to my children's children:
Dylan, Adam, Rebecca, and Joshua

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CHAPTER 14

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- Fig. 19. Relation of hormonal events in lactation to calcium metabolism.

- Fig. 20. Control of oxytocin secretion during lactation.**
- Fig. 21. Relation of blood oxytocin concentrations to suckling: McNeilly, A.S., Robinson, I.C.A., Houston, M.J., et al. (1983) Release of oxytocin and prolactin in response to suckling. *Br. Med. J.* 286: 257; with permission by the BMJ Publishing Group.**
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Preface to the Fourth Edition

The body of knowledge in endocrinology has expanded enormously since the first edition of this text appeared two decades ago, and the pace of discovery has been no less robust since the appearance of the third edition. Research in endocrinology continues to produce new revelations and insights, sometimes deepening our level of understanding of well-established phenomena, and sometimes leading us to reevaluate and reinterpret long-held doctrines. This edition of *Basic Medical Endocrinology* endeavors to capture these advances and integrate them into the general discourse without unduly expanding the length of the text or overloading it with unmanageable details. The text continues to focus on the integrative and regulatory roles of the endocrine system in humans, and in this context, to incorporate present understanding of underlying cellular and molecular mechanisms.

Endocrinology has evolved from the study of special functions at the whole body level, through studies of functions of organs, tissues, cells, organelles, and now individual genes and their products. The advent of molecular biology has driven major progress toward uncovering the cellular and molecular bases for hormonal actions and introduced new tools and new strategies for studying phenomena that have been known for a half century or longer. Genomic mapping, among other things, inspired the quest for ligands for “orphan receptors” and predicted functions of newly identified gene products. The technologies for knocking out, knocking in, or knocking down expression of particular genes in particular cells have revolutionized ways to explore signaling pathways within cells and to define functions of individual proteins within intact animals. Though knowledge is still incomplete, we now can describe hormone actions in exciting, and sometimes bewildering molecular detail. I have

tried to keep the excitement of these new discoveries in perspective and not let them overshadow the importance of classic findings in the overall understanding of how the body works.

Every chapter has been revised, though some more than others. Progress in endocrine research is uneven, driven by novel discoveries, technological advances, or the infusion of financial support in response to human health needs. In this regard the growing epidemic of obesity, diabetes, and the metabolic syndrome coupled with the discovery of leptin and other adipocyte secretions has fueled perhaps the most significant advances in recent years. Driven in part by continuing fallout from the discovery of the calcium receptor, and in part by improvements in assays for parathyroid hormone and its metabolites, understanding of calcium homeostasis also has progressed significantly since the last edition of this text. Finally, increased understanding of postsecretory events that produce local modifications in hormone concentrations and actions, and the finding of hormone receptors in unexpected places stimulated reassessment of long-held views and fueled progress in several areas.

Although study of gastrointestinal physiology has a prominent place in the history of endocrinology, the physiology of the hormones of the gastrointestinal tract traditionally has been omitted from textbooks of endocrinology, and has been covered instead in texts of gastroenterology. However, it is increasingly apparent that, as is true for many other hormones, the actions of GI hormones are not limited to the roles that we traditionally have assigned to them. It is apparent also that the GI hormones are closely related structurally, functionally, and ancestrally to the hormones that reside in the traditional realms of endocrinology and neuroendocrinology. I therefore have reunited the

hormones of the GI tract with their brethren. Chapter 6 is devoted to their physiology and Chapter 8 integrates them in the discussion of metabolic regulation.

Finally, as must be obvious, the appearance of the fourth edition is dramatically different from its predecessors thanks to technological advances that allow affordable introduction of color. Virtually all the figures have been redrawn in color, which hopefully enhances their value in illustrating the text. In addition, following the premise that “a picture is worth a thousand words,” more than 75 new figures have been added. Once again, I have chosen to avoid burdening the text with countless references to

original literature, but instead end each chapter with a list of relevant review articles that can direct the interested student to primary literature. It remains my hope that this text will provide students with somewhat more than sufficient understanding of contemporary endocrine physiology to pass required examinations, and, more importantly perhaps, to provide them with a solid foundation for continuing study of human biology.

H. Maurice Goodman
Worcester, Massachusetts
2008

Preface to the First Edition

This volume is the product of more than 25 years of teaching endocrine physiology to first-year medical students. Its focus is human endocrinology with an emphasis on cellular and molecular mechanisms. In presenting this material, I have tried to capture some of the excitement of a dynamic, expanding discipline that is now in its golden age. It is hoped that this text provides sufficient understanding of normal endocrine physiology to prepare the student to study not only endocrine diseases but the cellular and molecular derangements that disrupt normal function and must therefore be reversed or circumvented by rational therapy. It is further hoped that this text provides the necessary background to facilitate continuing self-education in endocrinology.

Endocrinology encompasses a vast amount of information relating to at least some aspect of virtually every body function. Unfortunately, much of the information is descriptive and cannot be derived from first principles. Thorough, encyclopedic coverage is neither appropriate for a volume such as this one nor possible at the current explosive rate of expansion. On the other hand, limiting the text to the bare minimum of unadorned facts might facilitate memorization of what appear to be the essentials this year but would preclude acquisition of real understanding and offer little preparation for assimilating the essentials as they may appear a decade hence. I therefore sought the middle ground and present basic facts within enough of a physiological framework to foster understanding of both the current status of the field and those areas where new developments are likely to occur while hopefully avoiding the pitfall of burying key points in details and qualifications.

The text is organized into three sections. The first section provides basic information about

organization of the endocrine system and the role of individual endocrine glands. Subsequent sections deal with complex hormonal interactions that govern maintenance of the internal environment (Part II) and growth and reproduction (Part III). Neuroendocrinology is integrated into discussions of specific glands or regulatory systems throughout the text rather than being treated as a separate subject. Although modern endocrinology has its roots in gastrointestinal (GI) physiology, the gut hormones are usually covered in texts of GI physiology rather than endocrinology; therefore, there is no chapter on intestinal hormones. In the interests of space and the reader's endurance, a good deal of fascinating material was omitted because it seemed either irrelevant to human biology or insufficiently understood at this time. For example, the pineal gland has intrigued generations of scientists and philosophers since Descartes, but it still has no clearly established role in human physiology and is therefore ignored in this text.

Human endocrinology has its foundation in clinical practice and research, both of which rely heavily on laboratory findings. Where possible, points are illustrated in the text with original data from the rich endocrine literature to give the reader a feeling for the kind of information on which theoretical and diagnostic conclusions are based. Original literature is not cited in the text, in part because such citations are distracting in an introductory text, and in part because proper citation might well double the length of this volume. For the reader who wishes to gain entrée to the endocrine literature or desires more comprehensive coverage of specific topics, review articles are listed at the end of each chapter.

H. Maurice Goodman
1988

Preface to the Second Edition

In the five years that have passed since the first edition of this text, the information explosion in endocrinology has continued unabated and may have even accelerated. Application of the powerful tools of molecular biology has made it possible to ask questions about hormone production and action that were only dreamed about a decade earlier. The receptor molecules that initiate responses to virtually all of the hormones have been characterized and significant progress has been made in unraveling the events that lead to the final cellular expression of hormonal stimulation. As more details of intracellular signaling emerge, the complexities of parallel and intersecting pathways of transduction have become more evident. We are beginning to understand how cells regulate the expression of genes and how hormones intervene in regulatory processes to adjust the expression of individual genes. Great strides have been made in understanding how individual cells talk to each other through locally released factors to coordinate growth, differentiation, secretion, and other responses within a tissue. In these regards, endocrinology

and immunology share common themes and have contributed to each other's advancement.

In revising the text for this second edition of Basic Medical Endocrinology, I have tried to incorporate many of the exciting advances in our understanding of cellular and molecular processes into the discourse on integrated whole body function. I have tried to be selective, however, and include only those bits of information that deepen understanding of well-established principles or processes or that relate to emerging themes. Every chapter has been updated, but not surprisingly, progress has been uneven, and some have been revised more extensively than others. After reviewing the past five years of literature in as broad an area as encompassed by endocrinology, one cannot help but be humbled by the seemingly limitless capacity of the human mind to develop new knowledge, to assimilate new information into an already vast knowledge base, and to apply that knowledge to advancement of human welfare.

H. Maurice Goodman
1993

Preface to the Third Edition

Nearly a decade elapsed between publication of the second and third editions of *Basic Medical Endocrinology* due in large part to the turmoil in the publishing industry brought on by massive consolidation. Although this edition is new and the publisher is new, the aims of earlier editions of this work are unchanged. Its focus remains human endocrinology with an emphasis on cellular and molecular mechanisms presented in the context of integration of body functions. The intent is to provide a sufficient level of understanding of normal endocrine physiology to prepare students to study not only endocrine diseases, but also the cellular and molecular alterations that disrupt normal function. Such understanding is a prerequisite for institution of rational diagnostic procedures, therapeutic interventions, and research strategies. It is further hoped that this text provides the necessary background to facilitate continuing self-education in endocrinology.

A decade is a long time in this remarkable era of modern biology. Whole new vistas of inquiry have been opened since the previous edition of this text appeared, and new discoveries have mandated reinterpretation of many areas that were once thought to be solidly understood. Much of the progress of the past decade must be credited to ingenious application of rapidly evolving technology in molecular biology. Studies of gene expression and the charting of the genomes of several species, including our own, has provided a deluge of new information and new insights. The exquisite sensitivity and versatility of this technology has uncovered both hormone production and hormone receptors in unexpected places and revealed hitherto unappreciated roles for classical hormones. Classical techniques of organ ablation and extract injection

have been reapplied using the once unthinkable technology of gene ablation or overexpression to explore the functions of individual proteins instead of individual glands. The decade has also witnessed the discovery of new hormones and expanded our appreciation of the physiological importance of extraglandular metabolism of hormones. The understanding of hormone actions has grown enormously and spawned the quest for “designer drugs” that target particular, critical, biochemical reactions in combating disease.

In light of these and many other developments, every chapter of this text has been extensively revised to present the well-established factual basis of endocrinology enriched by exciting, rapidly unfolding new information and insights. The challenge has been to digest and reduce the massive literature to illuminate the regulatory and integrative roles of the endocrine system without overloading the text with arcane detail. However, the text is designed to provide somewhat more than the minimum acceptable level of understanding and attempts to anticipate and answer some of the next level of questions that might occur to the thoughtful student.

Looking back over 40 years of teaching endocrine physiology, one cannot fail but to marvel at how far we have come and how resourceful is the human mind in probing the mysteries of life. As has always been true of scientific inquiry, obtaining answers to long-standing questions inevitably raises a host of new questions to challenge a new generation of endocrinologists. It is my hope that this text will provide a foundation for students to meet that challenge both in the clinic and in the laboratory.

H. Maurice Goodman
2002