

WILLIAMS
TEXTBOOK
OF
ENDOCRINOLOGY

8th Edition

8th Edition

WILLIAMS TEXTBOOK OF ENDOCRINOLOGY

Edited by

Jean D. Wilson, M.D.

Professor and Chief of the Division of Endocrinology and Metabolism
Department of Internal Medicine
The University of Texas Southwestern Medical Center at Dallas

Daniel W. Foster, M.D.

Professor and Chairman
Department of Internal Medicine
The University of Texas Southwestern Medical Center at Dallas

W. B. SAUNDERS COMPANY

Harcourt Brace Jovanovich, Inc.

Philadelphia London Toronto Montreal Sydney Tokyo

W. B. SAUNDERS COMPANY
Harcourt Brace Jovanovich, Inc.
The Curtis Center
Independence Square West
Philadelphia, Pennsylvania 19106

Library of Congress Cataloging-in-Publication Data

Williams textbook of endocrinology / [edited by] Jean D. Wilson
and Daniel W. Foster.—8th ed.

p. cm.

Includes bibliographical references.
Includes index.

ISBN 0-7216-9514-0

1. Endocrine glands—Diseases. 2. Endocrinology.
I. Williams, Robert Hardin. II. Wilson, Jean D.
III. Foster, Daniel W. IV. Title: Textbook of
endocrinology. [DNLM: 1. Endocrine Diseases.
2. Endocrine Glands. WK 100 W721]

RC648.T46 1992

616.4—dc20

DNLM/DLC

90-8913

Listed here is the latest translated edition of this book together with the language of the translation and the publisher.

Polish (*3rd Edition*)—Lekarskich, Warsaw, Poland
Spanish (*5th Edition*)—Salvat Editores, Barcelona, Spain
French (*4th Edition*)—Flammarion, Paris, France
Italian (*5th Edition*)—Piccin Editore, Padova, Italy
Japanese (*5th Edition*)—Hirokawa Publishing Company, Tokyo, Japan
Serbo-Croatian (*4th Edition*)—Medicinska Knjiga, Belgrade, Yugoslavia

Editor: W. B. Saunders Staff

Designer: Maureen Sweeney

Cover Designer: Michelle Maloney

Production Manager: Ken Neimeister

Manuscript Editors: Judith Gandy and Mary Prescott

Illustration Specialist: Lisa Lambert

Indexer: Alexandra Nickerson

WILLIAMS TEXTBOOK OF ENDOCRINOLOGY

ISBN 0-7216-9514-0

Copyright © 1992, 1985, 1981, 1974, 1968, 1962, 1955 by W. B. Saunders Company
Copyright 1950 by W. B. Saunders Company
Copyright renewed 1990 by A. B. Williams, R. L. Williams
Copyright renewed 1983 by William H. Daughadey
Copyright renewed 1978 by Robert H. Williams

All rights reserved. No part of this publication may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopy, recording, or any information storage and retrieval system, without permission in writing from the publisher.

Printed in the United States of America.

Last digit is the print number: 9 8 7 6 5 4 3 2 1

WILLIAMS
TEXTBOOK
OF
ENDOCRINOLOGY



一九四四年五月廿二日



重医附一院

00161639

CONTRIBUTORS



Thomas E. Andreoli

Professor and Chairman, Department of Internal Medicine,
University of Arkansas College of Medicine, Little Rock

The Posterior Pituitary and Water Metabolism



W. Scott Appleton

Post Doctoral Research Fellow, Department of Internal Medicine,
University of Utah School of Medicine, Salt Lake City

Humoral Manifestations of Cancer



Gerald D. Aurbach

Chief, Metabolic Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda

*Parathyroid Hormone, Calcitonin, and the Calciferols
Metabolic Bone Disease*



Edwin L. Bierman

Professor of Medicine and Head, Division of Metabolism and Endocrinology, University of Washington, Seattle

Disorders of Lipid Metabolism

vi CONTRIBUTORS



Bruce R. Carr

Paul C. MacDonald Professor of Obstetrics and Gynecology and Director, Division of Reproductive Endocrinology, The University of Texas Southwestern Medical Center at Dallas

*Disorders of the Ovary and Female Reproductive Tract
Fertility Control and Its Complications*



M. Linette Casey

Associate Professor, Cecil H. and Ida Green Center for Reproductive Biology Sciences, Departments of Biochemistry and Obstetrics-Gynecology, The University of Texas Southwestern Medical Center at Dallas

Endocrinological Changes of Pregnancy



William W. Chin

Associate Professor of Medicine and Investigator, Howard Hughes Medical Institute, Harvard Medical School, Boston

Mechanism of Action of Hormones That Act at the Cell Surface



James H. Clark

Professor of Cell Biology, Baylor College of Medicine, Houston

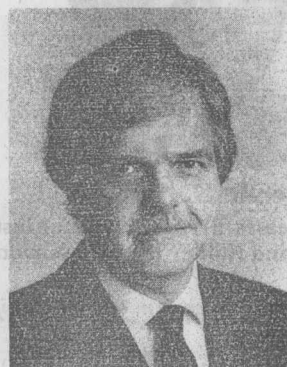
Mechanisms of Action of Steroid Hormones



Felix A. Conte

Professor of Pediatrics, University of California, San Francisco

Disorders of Sex Differentiation



Philip E. Cryer

Professor of Medicine and Director, Division of Endocrinology, Diabetes and Metabolism, Washington University School of Medicine, St. Louis

Glucose Homeostasis and Hypoglycemia



C. Rowan DeBold

Adult Endocrinologist, Park Nicollet Medical Center, Minneapolis

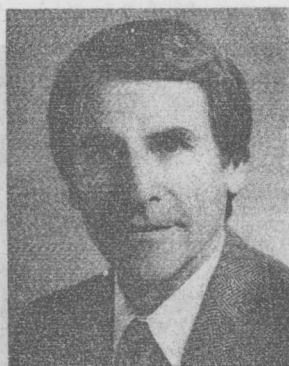
The Adrenal Cortex



George S. Eisenbarth

Associate Professor of Medicine, Harvard Medical School; Chief, Section of Immunology and Immunogenetics, Joslin Diabetes Center, Boston

The Immunoendocrinopathy Syndromes



Delbert A. Fisher

Professor of Pediatrics and Medicine, University of California, Los Angeles, School of Medicine; Director, Walter Martin Research Center, Harbor-UCLA Medical Center, Torrance

Endocrinology of Fetal Development



Daniel W. Foster

Donald W. Seldin Distinguished Chair in Internal Medicine and Chairman, Department of Internal Medicine, The University of Texas Southwestern Medical Center at Dallas

Diabetes Mellitus

Eating Disorders: Obesity, Anorexia Nervosa, and Bulimia Nervosa



Andrew G. Frantz

Professor of Medicine, Columbia University College of Physicians and Surgeons, New York

Endocrine Disorders of the Breast



Norbert Freinkel

Late Kettering Professor of Medicine; Professor of Molecular Biology; Director, Center for Endocrinology, Metabolism and Nutrition; Chief, Section of Endocrinology, Metabolism and Nutrition, Northwestern University-McGaw Medical Center, Chicago

Metabolic Changes in Pregnancy

viii CONTRIBUTORS



Robert F. Gagel

Associate Professor of Medicine and Cell Biology, Baylor College of Medicine; Clinical Investigator, Department of Veterans Affairs Medical Center, Houston

Multiple Endocrine Neoplasia



John A. Glomset

Professor of Medicine and Biochemistry, University of Washington, Seattle

Disorders of Lipid Metabolism



Phillip Gorden

Director, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda

Radioreceptor and Other Functional Hormone Assays



James E. Griffin

Professor of Internal Medicine, The University of Texas Southwestern Medical Center at Dallas

*Disorders of the Testes and the Male Reproductive Tract
Fertility Control and Its Complications
Dynamic Tests of Endocrine Function*



Melvin M. Grumbach

Edward B. Shaw Professor of Pediatrics, University of California, San Francisco

*Disorders of Sex Differentiation
Puberty: Ontogeny, Neuroendocrinology, Physiology, and Disorders*



Joel F. Habener

Professor of Medicine, Harvard Medical School; Chief, Laboratory of Molecular Endocrinology, Massachusetts General Hospital, Boston

Genetic Control of Hormone Formation



Eva Horvath

Associate Professor of Pathology, Department of Pathology,
University of Toronto
The Anterior Pituitary



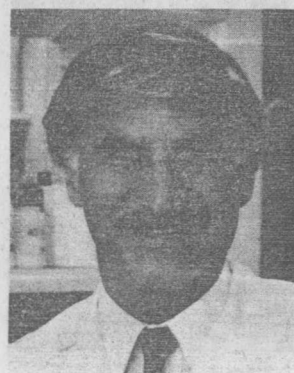
Sidney H. Ingbar

Late William Bosworth Castle Professor of Medicine, Har-
vard Medical School, Boston
The Thyroid Gland



Richard A. Jackson

Assistant Professor of Medicine, Harvard Medical School,
Boston
The Immunoendocrinopathy Syndromes



C. Ronald Kahn

Mary K. Iacocca Professor of Medicine, Harvard Medical
School; Research Director, Joslin Diabetes Center, Boston
*Mechanism of Action of Hormones That Act at the Cell
Surface*



Norman M. Kaplan

Professor of Internal Medicine, The University of Texas
Southwestern Medical Center at Dallas
Endocrine Hypertension



Stanley G. Korenman

Professor of Medicine-Endocrinology, School of Medicine,
University of California, Los Angeles
Sexual Dysfunction

x CONTRIBUTORS



Kalman Kovacs

Professor of Pathology, Department of Pathology, University of Toronto

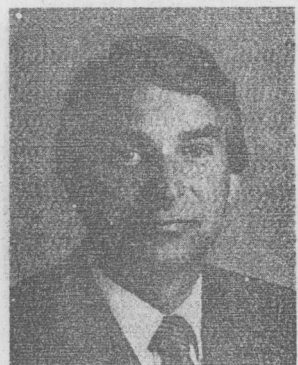
The Anterior Pituitary



William J. Kovacs

Associate Professor of Medicine, Vanderbilt University School of Medicine, Nashville

The Adrenal Cortex



Guenter J. Krejs

Professor and Chairman, Department of Medicine, Karl Franzens University, Graz, Austria

Non-Insulin-Secreting Tumors of the Gastroenteropancreatic System



Lewis Landsberg

Cutter Professor and Chairman, Department of Medicine, and Director, Center for Endocrinology, Metabolism and Nutrition, Northwestern University Medical School, Chicago

Catecholamines and the Adrenal Medulla



P. Reed Larsen

Professor of Medicine, Harvard Medical School, Boston

The Thyroid Gland



Marc E. Lippman

Professor of Medicine and Pharmacology and Director, Vincent T. Lombardi Cancer Research Center, Georgetown University Medical School, Washington, DC

Endocrine-Responsive Cancers of Humans



Paul C. MacDonald

Professor, Cecil H. and Ida Green Center for Reproductive Biology Sciences, Departments of Obstetrics-Gynecology and Biochemistry, The University of Texas Southwestern Medical Center at Dallas

Endocrinological Changes of Pregnancy



Stephen J. Marx

Chief, Mineral Metabolism Section, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda

*Parathyroid Hormone, Calcitonin, and the Calciferols
Metabolic Bone Disease*



Boyd E. Metzger

Professor of Medicine and Acting Chief, Section of Endocrinology, Metabolism and Nutrition, Northwestern University Medical School, Chicago

Metabolic Changes in Pregnancy



John A. Oates

Professor of Medicine and Pharmacology and Chairman, Department of Medicine, Vanderbilt University School of Medicine, Nashville

*Disorders of Vasodilator Hormones: The Carcinoid Syndrome
and Mastocytosis*



William D. Odell

Professor of Medicine and Physiology and Chairman, Department of Internal Medicine, University of Utah School of Medicine, Salt Lake City

Humoral Manifestations of Cancer



Bert W. O'Malley

Professor and Chairman, Department of Cell Biology, Baylor College of Medicine, Houston

Mechanisms of Action of Steroid Hormones

xii CONTRIBUTORS



David N. Orth

Professor of Medicine, Professor of Molecular Physiology and Biophysics, and Director, Division of Endocrinology, Vanderbilt University School of Medicine, Nashville

The Adrenal Cortex



Charles Y. C. Pak

Professor of Medicine, The University of Texas Southwestern Medical Center at Dallas

Kidney Stones



W. Brian Reeves

Assistant Professor of Internal Medicine, Division of Nephrology, University of Arkansas College of Medicine, Little Rock

The Posterior Pituitary and Water Metabolism



Seymour Reichlin

Professor of Medicine, Tufts University School of Medicine; Chief, Endocrine Division, New England Medical Center, Boston

Neuroendocrinology



L. Jackson Roberts II

Professor of Pharmacology and Medicine, Vanderbilt University School of Medicine, Nashville

Disorders of Vasodilator Hormones: The Carcinoid Syndrome and Mastocytosis



William T. Schrader

Professor of Cell Biology, Baylor College of Medicine, Houston

Mechanisms of Action of Steroid Hormones



Evan R. Simpson

Professor, Cecil H. and Ida Green Center for Reproductive Biology Sciences, Departments of Obstetrics-Gynecology and Biochemistry, The University of Texas Southwestern Medical Center at Dallas

Endocrinological Changes of Pregnancy



Robert J. Smith

Associate Professor of Medicine, Harvard Medical School; Assistant Director of Research, Head of Section on Metabolism, Joslin Diabetes Center, Boston

Mechanism of Action of Hormones That Act at the Cell Surface



Allen M. Spiegel

Chief, Molecular Pathophysiology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda

*Parathyroid Hormone, Calcitonin, and the Calciferols
Metabolic Bone Disease*



Dennis M. Styne

Professor and Chairman of Pediatrics, University of California, Davis

Puberty: Ontogeny, Neuroendocrinology, Physiology, and Disorders



Sandra M. Swain

Assistant Professor of Medicine and Director, Comprehensive Breast Center, Vincent T. Lombardi Cancer Research Center, Georgetown University Medical School, Washington, DC

Endocrine-Responsive Cancers of Humans



Michael O. Thorner

Kenneth R. Crispell Professor of Medicine and Head, Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Virginia Medical School, Charlottesville

The Anterior Pituitary



Louis E. Underwood

Professor of Pediatrics, University of North Carolina at Chapel Hill

Normal and Aberrant Growth



Roger H. Unger

Touchstone/West Distinguished Chair in Diabetes Research and Director, Gifford Laboratories for Diabetes Research, The University of Texas Southwestern Medical Center at Dallas; Senior Medical Investigator, Department of Veterans Affairs Medical Center, Dallas

Diabetes Mellitus



Mary Lee Vance

Associate Professor of Medicine, University of Virginia Medical School, Charlottesville

The Anterior Pituitary



Judson J. Van Wyk

Kenan Professor of Pediatrics, University of North Carolina at Chapel Hill

Normal and Aberrant Growth



Bruce D. Weintraub

Chief, Molecular, Cellular and Nutritional Endocrinology Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda

Radioreceptor and Other Functional Hormone Assays



Jean D. Wilson

Charles C. Sprague Professor of Internal Medicine, The University of Texas Southwestern Medical Center at Dallas

*Disorders of the Testes and the Male Reproductive Tract
Endocrine Disorders of the Breast*



Rosalyn S. Yalow

Solomon A. Berson Distinguished Professor-at-Large, Mt. Sinai School of Medicine of City University of New York; Senior Medical Investigator, Department of Veterans Affairs Medical Center, Bronx

Radioimmunoassay of Hormones



James B. Young

Professor of Medicine, Northwestern University Medical School, Chicago

Catecholamines and the Adrenal Medulla

PREFACE

The aim of *Williams Textbook of Endocrinology* continues to be to serve as a bridge between basic science and clinical endocrinology. This aim was clearly formulated in the preface to the first edition:

The rapidity and extent of advances in endocrinology have made it increasingly difficult for the student and physician to take full advantage of information available for the understanding, diagnosis and treatment of clinical disorders. It is the realization of these difficulties that prompted the writing of this book. The main objective is to provide a condensed and authoritative discussion of the management of clinical endocrinopathies, based upon the application of fundamental information obtained from chemical and physiologic investigations.

Since the publication of the seventh edition, endocrinology has continued to change. The impact of molecular and cell biology has been to radically transform our understanding of endocrine physiology and endocrine pathology. Today in the approach to disease—no less than in basic endocrine science—the focus is more on how hormones act than on factors that influence hormone levels. Moreover, the recognition that many chemical mediators behave like hormones, even though they act by autocrine or paracrine mechanisms rather than via the circulation, has vastly broadened the scope of endocrinology. The technological change in clinical medicine, especially the imaging revolution, has given new power to diagnosis that was unknown at the time of the last edition and has expanded the therapeutic repertoire.

The eighth edition of *Williams Textbook of Endocrinology* has been carefully planned to reflect the rapidly advancing elements of modern endocrinology. Molecular biology and cell biology are in evidence in essentially every chapter. The introductory chapters on hormone action, which are rich with diagrams, make the basic principles readily understandable both to beginning students and to clinicians who trained before the new science appeared. We have also added new chapters on fetal endocrinology and on puberty and its disorders.

In organizing this edition, we faced the special problem of the dual system of laboratory unit nomenclature within the United States. Since 1988, virtually all medical journals have used the International System of Units (SI units) for clinical laboratory values, whereas most hospital laboratories in the United States have used conventional units. Thus one system is used in the medical literature and another in the hospital. We decided to use both systems in the text: SI units are given first and the conventional units follow in parentheses for all measurements except blood pressure, which is given only in millimeters of mercury; energy value of food, which is given in kilocalories; and quantities for which the numbers are the same in both systems (e.g., nanomoles per liter or milliequivalents per liter for sodium concentration and international units per liter or milli-international units per milliliter for luteinizing hormone). In most instances the conversion between SI and conventional units is straightforward. In other cases the optimal way to convert from one system to the other is not clear-cut because there are different ways to express values in both systems. It is imperative that each reader consult his or her own laboratory for normal values. Readers must be alert to units, not only in our text, but also in clinical practice.

A striking feature of this textbook has always been the fact that the contributors are at the forefronts of their disciplines, thereby ensuring the freshness of each edition. This feature remains true for the current edition. Those who wrote in previous editions have devoted an immense effort to updating material, and the new contributors have expended an equal or greater effort in formulating new chapters. Neither task is easy, and to our authors we say thank you.

The book could not have been edited without the dedicated help of the co-workers in our offices—Christy K. Gonzales, Brenda H. Hennis, and Rita A. Koger. We acknowledge the special contributions made by Judith Gandy, our manuscript editor at the W. B. Saunders Company. Her remarkable attention to detail and her pursuit of excellence have had a major impact on the editors and on the book.

JEAN D. WILSON
DANIEL W. FOSTER

The aim of *Williams Textbook of Endocrinology* continues to be to serve as a bridge between basic science and clinical endocrinology. This aim was clearly formulated in the preface to the first edition.

The rapidity and extent of changes in endocrinology have made it increasingly difficult for the student and clinician to stay fully abreast of information available for the understanding of the endocrine system. The need for a text which is both comprehensive and up-to-date in the field of endocrinology is more acute than ever. The new edition is intended to provide a comprehensive and authoritative presentation of the endocrinology of clinical endocrinology, based upon the application of fundamental information obtained from chemical and physiological investigations.

Since the publication of the seventh edition, endocrinology has continued to change. The impact of molecular and cell biology has been to radically transform our understanding of endocrine physiology and endocrine pathology. Today in the approach to disease—no less than in basic endocrine research—the focus is more on how hormones act than on factors that influence hormone levels. Moreover, the recognition that many clinical mechanisms involve the hormones, even though they are not endocrine or paracrine mechanisms, rather than via the circulation, has vastly broadened the scope of endocrinology. The technological change in clinical medicine, especially the imaging revolution, has given new power to diagnosis that was unknown in the time of the last edition and has expanded the therapeutic repertoire.

The eighth edition of *Williams Textbook of Endocrinology* has been carefully planned to reflect the rapidly advancing elements of modern endocrinology. Molecular biology and cell biology are in evidence in essentially every chapter. The introductory chapters on hormone action, which are rich with diagrams, make the basic principles readily understandable both to beginning students and to clinicians who trained before the new science appeared. We have also added new chapters on both endocrinology and on puberty and its disorders.

In organizing this edition, we faced the special problem of the dual system of laboratory units and nomenclature within the United States. Since 1958, virtually all medical journals have used the International System of Units (SI units) for clinical laboratory values, whereas most hospital laboratories in the United States have used conventional units. Thus one system is used in the medical literature and another in the hospital. We decided to use both systems in the text. SI units are given first, and the conventional units follow in parentheses for all measurements except blood pressure, which is given only in millimeters of mercury, energy value of food, which is given in kilocalories, and quantities for which the numbers are the same in both systems (e.g., nanomoles per liter or milliequivalents per liter for sodium concentration and international units per liter or milliequivalents per liter for parathyroid hormone). In most instances the conversion between SI and conventional units is straightforward. In other cases the optimal way to convert from one system to the other is not clear, or because there are different ways to express values in both systems. It is imperative that each reader consult his or her own laboratory for correct values. Readers must be alert to units, not only in our text, but also in clinical practice.

A special feature of this textbook has always been the fact that the contributors are in the forefront of their specialties, thereby ensuring the freshness of each edition. This feature remains true for the current edition. Those who wrote in previous editions have devoted an immense effort to updating material, and the new contributors have expanded in equal or greater effort in formulating new chapters. Neither task is easy, and to our authors we say thank you.