

THE THYROID

a fundamental and clinical text

editors
SIDNEY C. WERNER
SIDNEY H. INGBAR

FOURTH EDITION

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MEDICAL DEPARTMENT
HARPER & ROW, PUBLISHERS
HAGERSTOWN, MARYLAND
NEW YORK, SAN FRANCISCO, LONDON

DRUG DOSAGE

The authors and publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

78 79 80 81 82 83 10 9 8 7 6 5 4 3 2

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The Thyroid, Third Edition, is available in a Spanish translation

Library of Congress Cataloging in Publication Data

Werner, Sidney C ed.
The thyroid.

Includes bibliographies and index.

1. Thyroid gland—Diseases. 2. Thyroid gland. I. Ingbar, Sidney H., joint ed. II. Title. [DNLM: 1. Thyroid diseases. 2. Thyroid gland. WK200 T5455]

RC655.W4 1978 616.4'4 77-22611
ISBN 0-06-142678-4

Contributors

RAYMOND D. ADAMS, M.D., D.Sc., M.D. (HON.), A.M. (HON.)

Sections in Ch. 39, 47

Chief, Neurology Service and Director of The John F. Kennedy, Jr. Memorial Laboratories, Massachusetts General Hospital; Bullard Professor of Neuropathology, Harvard Medical School, Boston; Director, Eunice K. Shriver Research Institute, Waltham, Massachusetts

H. VERDAIN BARNES, M.D.

Ch. 13

Associate Professor of Medicine and Pediatrics; Director of Adolescent Medicine, University of Iowa College of Medicine, Iowa City, Iowa

DAVID V. BECKER, M.D.

Ch. 18

Professor of Medicine and Radiology; Director, Division of Nuclear Medicine, Departments of Radiology and Medicine, The New York Hospital-Cornell Medical Center, New York, New York

HENRIK H. BENDIXEN, M.D.

Section in Ch. 30

Professor and Chairman, Department of Anesthesiology, Columbia University, New York, New York

STANLEY E. BRADLEY, M.D., A.B.I.M.

Sections in Ch. 38, 46

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

LEWIS E. BRAVERMAN, M.D.

Section in Ch. 27

Professor of Medicine and Chairman, Division of Endocrinology and Metabolism, Department of Medicine, University of Massachusetts Medical School, Worcester, Massachusetts

GERARD N. BURROW, M.D., F.A.C.P., F.R.C.P. (C)

Section in Ch. 49

Professor of Medicine; Honorary Professor, Banting and Best Department of Medicine Research, University of Toronto; Director, Division of Endocrinology and Metabolism, Toronto General Hospital, Toronto, Ontario, Canada

RALPH R. CAVALIERI, M.D.

Section in Ch. 15

Associate Professor, Departments of Medicine and Radiology, University of California, San Francisco, School of Medicine; Chief, Nuclear Medicine Service, Veterans Administration Hospital, San Francisco, California

INDER JIT CHOPRA, M.D.

Ch. 6

Associate Professor of Medicine, Department of Medicine, Center for the Health Sciences, University of California, Los Angeles, School of Medicine, Los Angeles, California

NICHOLAS P. CHRISTY, M.D.

Sections in Ch. 42, 47

Director, Medical Service, Department of Medicine, The Roosevelt Hospital; Professor of Medicine, Columbia University College of Physicians and Surgeons, New York, New York

D. JACKSON COLEMAN, M.D.*Section in Ch. 35*

Assistant Professor of Clinical Ophthalmology, Department of Ophthalmology, Columbia University College of Physicians and Surgeons, New York, New York

PAUL J. DAVIS, M.D.*Section in Ch. 12*

Professor of Medicine; Head, Endocrinology Division, Department of Medicine, Medical School of the State University of New York at Buffalo, Buffalo, New York

ROBERT M. DAY, M.D.*Sections in Ch. 35, 46*

Clinical Professor of Ophthalmology, Department of Ophthalmology, Columbia University College of Physicians and Surgeons; Attending Ophthalmologist, The Presbyterian Hospital in the City of New York, New York

ISRAEL DONIACH, M.D., F.R.C.P., F.R.C.PATH.*Ch. 14*

Professor Emeritus, University of London; Honorary Consulting Morbid Anatomist, The London Hospital, London, England

HAROLD EDELHOCH, PH.D.*Section in Ch. 3*

Scientist, Clinical Endocrinology Branch, National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health, Bethesda, Maryland

CHARLES J. EDMONDS, M.D., F.R.C.P.*Section in Ch. 29*

Consultant Physician, Department of Medicine, University College and Northwick Park Hospitals; Member, Senior Scientific Staff, Medical Research Council Clinical Research Centre, Northwick Park Hospital, London, England

ANDRÉ MARIE ERMANS, M.D.*Section in Ch. 27*

Associate Professor, Department of Nuclear Medicine, Free University of Brussels, Brussels, Belgium

CALVIN EZRIN, M.D., F.R.C.P.(C), F.A.C.P.*Section in Ch. 9*

Clinical Professor of Medicine, Department of Medicine, Cedars-Sinai Medical Center and University of California, Los Angeles, California; Professor, Department of Medicine; Associate Professor, Department of Pathology, University of Toronto, Faculty of Medicine; Director, Medical-Endocrine Clinic, Toronto General Hospital, Toronto, Ontario, Canada

CARL R. FEIND, M.D.*Sections in Ch. 21, 44**Ch. 22*

Associate Professor of Clinical Surgery, Columbia University College of Physicians and Surgeons, New York, New York

PETER FELS, M.A., F.R.C.S., D.O.*Sections in Ch. 35*

Consultant Ophthalmologist, Moorfields Eye Hospital; Senior Lecturer in Ophthalmology, Institute of Ophthalmology, University of London, England

JAMES B. FIELD, M.D.*Section in Ch. 9*

Professor of Medicine; Head, Division of Endocrinology and Metabolism; Director, Clinical Research Unit, Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

CONTRIBUTORS

DELBERT A. FISHER, M.D.*Ch. 20, 43, 48*

Professor of Pediatrics and Medicine, Departments of Pediatrics and Medicine,
University of California, Los Angeles, School of Medicine, Los Angeles, California

IRWIN M. FREEDBERG, M.D.*Sections in Ch. 34, 46*

Professor of Dermatology, Department of Dermatology, Harvard Medical School; Chief
of Dermatologic Services, Beth Israel Hospital and Children's Hospital Medical
Center, Boston, Massachusetts

VALERIE ANNE GALTON, PH.D.*Section in Ch. 12*

Professor of Physiology, Department of Physiology, Dartmouth Medical School, Hanover, New Hampshire

STEVEN R. GOLDRING, M.D.*Sections in Ch. 39, 47*

Research Fellow in Medicine, Department of Medicine, Harvard Medical School; Clinical
and Research Fellow in Medicine, Department of Medicine, Massachusetts General Hospital;
Assistant to the Chairman, Department of Medicine, New England Deaconess Hospital, Boston,
Massachusetts

AUBREY GORBMAN, PH.D.*Section in Ch. 2*

Professor of Zoology, Department of Zoology, University of Washington, Seattle, Washington

WILLIAM L. GREEN, M.D.*Ch. 4*

Associate Professor, Department of Medicine, University of Washington School of Medicine;
Associate Director, Division of Endocrinology, Harborview Medical Center, Seattle, Washington

ROBERT I. GREGERMAN, M.D.*Section in Ch. 12*

Chief, Endocrinology Section, Clinical Physiology Branch, National Institute
on Aging, National Institutes of Health at Baltimore City Hospitals; Head,
Endocrinology Division, Baltimore City Hospitals; Associate Professor of Medicine,
Johns Hopkins University School of Medicine, Baltimore, Maryland

NICHOLAS S. HALMI, M.D.*Section in Ch. 2*

Professor of Endocrinology, Departments of Anatomy and Physiology-Biophysics, University
of Iowa, Iowa City, Iowa

WYLIE C. HEMBREE, M.D.*Sections in Ch. 40, 47*

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

VICTOR HERBERT, M.D., J.D.*Ch. 41**Section in Ch. 47*

Vice Chairman and Professor of Medicine, State University of New York Downstate Medical
Center; Chief of Medicine, Brooklyn Veterans Administration Hospital, Brooklyn,
New York

JEROME M. HERSHMAN, M.D.*Ch. 33*

Professor, Department of Medicine, University of California, Los Angeles: Chief,
Department of Endocrinology, Wadsworth Veterans Administration Hospital, Los Angeles, California

ROBERT M. HUI, M.D.*Sections in Ch. 37, 46*

Professor of Clinical Otolaryngology and Former Acting Chairman, Department
of Otolaryngology, Columbia University College of Physicians and Surgeons, New York, New York

SIDNEY H. INGBAR, M.D.*Ch. 10**Section in Ch. 42*

Professor of Medicine, Harvard Medical School; Director, Thorndike Laboratory of Harvard Medical School at the Beth Israel Hospital, Boston, Massachusetts

NORMAN B. JAVITT, M.D., PH.D.*Sections in Ch. 37, 46*

Professor of Medicine; Head, Division of Gastroenterology, New York Hospital-Cornell Medical Center, New York, New York

PHILIP M. JOHNSON, M.D.*Section in Ch. 15*

Professor of Radiology, Department of Radiology, Columbia University College of Physicians and Surgeons; Director of Nuclear Medicine, The Presbyterian Hospital in the City of New York, New York

EUGENE C. JORGENSEN, PH.D.*Section in Ch. 7*

Professor of Chemistry and Pharmaceutical Chemistry; Associate Dean, School of Pharmacy, University of California, San Francisco, California

F. DAVID KITCHIN, M.D., F.R.C.P.*Ch. 25*

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

LEONARD D. KOHN, M.D.*Sections in Ch. 34, 46*

Chief, Section on Biochemistry of Cell Regulation, Laboratory of Biochemical Pharmacology, National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health, Bethesda, Maryland

STEPHEN M. KRANE, M.D.*Sections in Ch. 39, 47*

Professor, Department of Medicine, Harvard Medical School; Physician and Chief, Arthritis Unit, Massachusetts General Hospital, Boston, Massachusetts

LEWIS LANDSBERG, M.D.*Sections in Ch. 42, 47*

Assistant Professor of Medicine, Harvard Medical School; Associate Chief, Department of Medicine, Beth Israel Hospital, Boston, Massachusetts

P. REED LARSEN, M.D.*Ch. 16*

Head, Thyroid Unit, Department of Medicine, Peter Bent Brigham Hospital; Associate Professor of Medicine, Harvard Medical School, Boston, Massachusetts

JOHN N. LOEB, M.D.*Sections in Ch. 38, 46*

Professor of Medicine, Columbia University College of Physicians and Surgeons; Associate Attending Physician, The Presbyterian Hospital in the City of New York; Adjunct Associate Professor, The Rockefeller University, New York, New York

WILLIAM A. MEISSNER, M.D.*Ch. 24*

Professor of Pathology, Department of Pathology, New England Deaconess Hospital, Harvard Medical School, Boston, Massachusetts

ARNE MELANDER, M.D., PH.D.*Ch. 11*

(Acting) Professor and Chief, Department of Clinical Pharmacology, University of Lund, Lund, Sweden

S. H. NGAI, M.D.*Section in Ch. 30*

Professor, Department of Anesthesiology and Pharmacology, Columbia University College of Physicians and Surgeons; Attending Anesthesiologist, The Presbyterian Hospital in the City of New York, New York

JOHN T. NICOLOFF, M.D.*Ch. 5*

Professor of Medicine, Department of Medicine, University of Southern California School of Medicine, Los Angeles, California

JOHN G. PIERCE, PH.D.*Section in Ch. 9*

Professor and Vice Chairman, Department of Biological Chemistry, University of California, Los Angeles, School of Medicine, Los Angeles, California

JAMES A. PITTMAN, JR., M.D.*Section in Ch. 47*

Professor of Medicine and Dean, Department of Medicine, University of Alabama School of Medicine, Birmingham, Alabama

JOSEPH E. RALL, M.D., PH.D.*Section in Ch. 7*

Director, Intramural Research Programs, National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health, Bethesda, Maryland

SEYMOUR REICHLIN, M.D., PH.D.*Ch. 8*

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

BUCK A. RHODES, PH.D.*Ch. 13*

Director of Radiopharmacy, Professor of Pharmacy, College of Pharmacy; Professor of Radiology, The University of New Mexico School of Medicine, Albuquerque, New Mexico

RICHARD S. RIVLIN, M.D.*Sections in Ch. 38, 46*

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

JACOB ROBBINS, M.D.*Section in Ch. 3*

Chief, Clinical Endocrinology Branch, National Institute of Arthritis, Metabolism and Digestive Diseases, National Institutes of Health, Bethesda, Maryland

WILLIAM M. ROGERS, PH.D.*Section in Ch. 21*

(deceased)

N. PAUL ROSMAN, M.D., C.M., F.R.C.P. (C)*Sections in Ch. 39, 47*

Professor of Pediatrics and Neurology; Director of Pediatric Neurology; Associate Director of Pediatrics, Boston University School of Medicine, Boston City Hospital, Boston, Massachusetts

GEORGE E. SHAMBAUGH, III, M.D.*Section in Ch. 7*

Associate Professor, Department of Medicine, Northwestern University Medical School, Chicago, Illinois

C. LYNN SKELTON, M.D.*Sections in Ch. 36, 46*

Head, Division of Cardiology, Department of Internal Medicine, Ochsner Clinic, New Orleans, Louisiana

MARY E. SMITH, B.A.*Section in Ch. 35*

Research Assistant, Department of Ophthalmology, Columbia University College of Physicians and Surgeons, New York, New York

DAVID H. SOLOMON, M.D.*Section in Ch. 44*

Professor and Chairman, Department of Medicine, University of California, Los Angeles, School of Medicine, Los Angeles, California

EDMUND H. SONNENBLICK, M.D.*Sections in Ch. 36, 46*

Professor of Medicine; Chief, Division of Cardiology, Department of Medicine, Albert Einstein College of Medicine, Bronx, New York

ALVIN TAUROG, PH.D.*Section in Ch. 3*

Professor of Pharmacology, Department of Pharmacology, University of Texas Health Science Center at Dallas, Texas

SELWYN TAYLOR, M.D., F.R.C.S.*Section in Ch. 26*

Surgeon and Senior Lecturer in Surgery, Royal Postgraduate Medical School, Hammersmith Hospital, London, England

THOMAS B. TOMASI, JR., M.D., PH.D.*Section in Ch. 32*

Professor of Immunology; Professor of Medicine; Chairman, Department of Immunology, Mayo Clinic-Foundation, Mayo Medical School, Rochester, Minnesota

C. DOMINIQUE TORAN-ALLERAND, M.D.*Section in Ch. 21*

Assistant Professor, International Institute for the Study of Human Reproduction and Department of Neurology, Columbia University College of Physicians and Surgeons, New York, New York

GERARD M. TURINO, M.D.*Sections in Ch. 36, 46*

Professor of Medicine, Department of Medicine, Columbia University College of Physicians and Surgeons; Attending Physician, Department of Medicine, The Presbyterian Hospital in the City of New York, New York

ROBERT D. UTIGER, M.D.*Ch. 19**Section in Ch. 9*

Professor of Medicine, Department of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

RAYMOND L. VANDE WIELE, M.D.*Sections in Ch. 40, 47*

Professor and Chairman, Department of Obstetrics and Gynecology, Columbia University College of Physicians and Surgeons, New York, New York

ROBERT VOLPÉ, M.D., F.R.C.P. (C)*Ch. 50**Sections in Ch. 51*

Professor, Department of Medicine, University of Toronto; Physician-in-Chief, The Wellesley Hospital, Toronto, Ontario, Canada

HENRY NICHOLAS WAGNER, JR., M.D.*Ch. 13*

Professor, Departments of Medicine, Radiology and Radiation Health, The Johns Hopkins Medical Institutions, Baltimore, Maryland

CHIU-AN WANG, M.D.*Sections in Ch. 26, 29**Ch. 28*

Associate Clinical Professor of Surgery, Harvard Medical School; Visiting Surgeon, Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts

HERBERT WEINER, M.D.*Sections in Ch. 32, 39, 47*

Professor of Psychiatry and Neuroscience; Chairman, Department of Psychiatry, Albert Einstein College of Medicine, Bronx, New York

I. BERNARD WEINSTEIN, M.D.*Ch. 25*

Professor of Medicine, Department of Medicine and Institute of Cancer Research, Columbia University College of Physicians and Surgeons, New York, New York

SIDNEY C. WERNER, M.D., D.SC. (MED.)*Ch. 1, 23, 31, 45**Sections in Ch. 21, 26, 29, 32, 35, 44, 49, 51*

Professor Emeritus of Clinical Medicine, Department of Medicine, Columbia University College of Physicians and Surgeons; Consultant (Medicine), The Presbyterian Hospital in the City of New York, New York ; Visiting Professor, Department of Medicine, University of Arizona Medical Center, Tucson, Arizona

KENNETH A. WOEBER, M.D.*Ch. 17*

Professor of Medicine, University of California, San Francisco, School of Medicine; Chief, Department of Medicine, Mount Zion Hospital and Medical Center, San Francisco, California

Preface to the Fourth Edition

The efforts from edition to edition to stem the growth of *The Thyroid* have once again been unavailing, in good part from the need to provide new and necessary background material from other fields. An example is the increasing importance of the immune system: evidence accumulates that perturbation therein is related pathogenetically to Graves' disease and lymphocytic thyroiditis. In consequence, this edition is a virtually new book.

Much has changed in the basic science chapters. Comparative Anatomy of the Thyroid has become Comparative Anatomy and Physiology. The chapter on development of the human thyroid now comprises both structure and function, including that of the suprathyroidal control mechanisms. The thyroid hormone analogues and the effects of spatial configuration upon the binding of the thyroid hormone molecules to cell membrane receptor sites have received detailed attention, as have the current hypotheses concerning the action of the thyroid hormone at the cellular level subsequent to binding. Although a final answer for the last remains elusive, the light at the end of the tunnel may be in sight.

The unfolding of the mechanisms by which the hypothalamus and anterior hypophysis control thyroid function has had its impact upon the clinic. Apart from the recognition that hyper- and hypothyroidism may result from excessive or decreased functioning of these control areas, new diagnostic procedures have blossomed. Radioimmunoassay (RIA) introduced to quantitate pituitary thyrotropin is now employed to quantitate the thyroid hormones as well as their metabolites and precursors. RIA for hypothalamic thyrotropin-releasing hormone remains a research tool.

In turn, RIA is meeting competition. Cell membrane radio-receptor assay methods permit detection of TSH and also of the thyroid-stimulating immunoglobulins present in Graves' disease. Sensitivity of the receptor method is considerably greater than that of RIA, but the technique presents more of a problem than does RIA.

The impact of conceptual change has also been felt in the more purely clinical part of the book (Part III). The instance of immunology has already been stated. Additionally, renewed interest in the connective tissues has arisen, especially in view of their relation to the pathogenesis of the eye changes per se of Graves' disease. Ideas about management of the various thyroid diseases have been changing. This is particularly true of those chronically contentious areas, nontoxic nodular goiter, thyroid cancer, and the thyroid irradiated in infancy and youth.

As the volume increases in size, the division of editorial responsibilities initiated in the third edition is found again in this one. Sidney Ingbar shepherded the basic and diagnostic parts (I and II) of the volume, and the senior editor the clinical part (III). Special competency accounts for the appearance of many new authors in this edition. On the other hand, some former authors are no longer contributors because of shifts in interest within or without the thyroid field. The passing of one author, Dr. William Rogers, is recorded with sincere regret. He was associated with *The Thyroid* from its beginning, and his elegant chapter on anomalous development of the thyroid has been retained.

The Editors wish to express their gratitude to those readers of the third edition who took time out to make suggestions, point out errors and misprints, or offer praise or adverse criticism. Their comments proved helpful in making corrections for a second printing of that edition, as well as in the planning for this one.

As in the previous editions, gaps in information have been identified. Hopefully, this will intrigue some reader(s) to rise to the challenge. Whether this process was

responsible or not, the record for resolution of such problems from one edition to the next continues to be high.

Besides the contributors and the staff of the Medical Department of Harper and Row concerned with this edition, the senior editor is indebted to Mrs. Helen C. Smith for her patience in typing and retyping most of the manuscripts in Part III. He particularly wishes to take this opportunity to thank his wife for her forbearance for the fourth time as she became deserted for the book. There was too little time for the family anyway, and that too little too often reached the vanishing point.

S.C.W.
S.H.I.

Preface to the First Edition

This book is intended for those who must deal with the problems of thyroid function and thyroid disease in man. It is designed for use in the clinic and in the basic science laboratory connected with the clinic. The information made available has been brought together from widely diverse sources, and in some instances is reported here for the first time. Many subjects have been presented both in broad outline and in more comprehensive detail to meet differing requirements. It has been planned to provide sufficient documentation to satisfy most needs and, for more exhaustive requirements, to provide a bibliography adequate enough to initiate a search of the literature.

The introduction of a book into a field of clinical medicine today requires considerable justification. In the thyroid field particularly, there already is a profusion of books including the almost classic works of Means in this country and of Joll in England, recently and capably revised by Rundle. Nevertheless, the recent growth of medical knowledge in general, and about the thyroid in particular, appears to have created need for a new volume constructed on a somewhat different basis from those of previous works.

Barry Wood has compared the growth of medical information to that of bacteria. Bacteria show a lag at the beginning of growth and then multiply at a logarithmic rate. Wood considers the growth of current-day medicine to have reached the logarithmic phase. The accumulation of data about the thyroid provides a good example of this acceleration. One author of a recent review claims to have unearthed 3000 new references pertaining to the gland and published during the single year before he wrote his article. The *Quarterly Cumulative Index Medicus* offers about 7800 references to the thyroid in the past decade. More than this, the thyroid field is permeated by contributions from the cardiologist, neurologist, muscle physiologist, and many others, bringing the highly unique technics of their particular specialties to bear on the subject.

It is evident that the ability of any one individual to follow progress in all directions at once has all but vanished. As a consequence, marked subspecialization of interest has developed and advances have come to depend upon the interchange of information among many specialists, each providing his own orientation.

This trend has suggested that the information in a book about the healthy and diseased thyroid should also be subjected to the process of sifting and appraising through many eyes. The various specialists present material with which they have had direct experience and the editor functions as the overseer to provide orientation and preserve the inherent orderliness of the entire subject. The total clinical and research experience made available in this way exceeds that of one person alone. Each topic can be subjected to the critique of a man who has worked intensively with the problem. Finally, a book of this sort can be readily kept current, because of the authors' continuing contact with investigation and the fact that there are no large sections to be rewritten by any one individual.

Every effort has been made to make available sufficient basic and clinical knowledge to satisfy curiosity about either of these aspects. For example, sections on the fundamental properties of radioiodine that permit the use of the isotope and on the instrumentation that facilitates such use are presented as well as a discussion of the clinical application. Most basic sections are separated from the clinical material, but are incorporated with it where this has seemed reasonable.

The fundamental aspects of thyroid function in man and the mechanisms which control the activity of the gland; the biochemistry of the hormone; and histology and comparative anatomy make up Part I. The mechanisms of action of the anti-

thyroid drugs are included because of the intimate relationship of their effects to the problems of basic physiology.

Part II presents the laboratory methods which supplement the clinical appraisal of thyroid secretory activity. The presentations of the basic principles involved in radioiodine usage and the instrumentation which is employed are included within the laboratory section and are available here for later reference when the therapeutic as well as diagnostic uses of the isotope are considered.

The diseases of the thyroid are considered in Part III. The disorders first described are those in which the level of thyroid hormone in the circulation and tissues is within normal limits—euthyroidism. After this come the derangements in which hormone levels are increased—toxic goiter or hyperthyroidism—or decreased—hypothyroidism or myxedema. The effects of hyperthyroidism and of hypothyroidism upon the individual body systems have been subjected to fairly detailed analysis.

The plan to arrange disease by functional categories breaks down in relation to inflammations of the thyroid including the peculiar composite entity, chronic thyroiditis. Inflammations of the thyroid tend to inactivate the gland but chronic thyroiditis is almost as often associated with evidence of hyperthyroidism as with hypothyroidism. The inflammations have been placed under a separate heading on this account.

Before the disease states are presented, several important preliminary subjects are considered in PART III. The normal and abnormal developments of the gland are described, together with the surgical anatomy and a method of physical examination that is an essential procedure because of the accessibility of the thyroid to this approach. The pathology is presented in its entirety in the introductory sections and is not dispersed among the various diseases. A concept of change in thyroid disease emerges in this way which could not otherwise become evident.

A major goal throughout the volume has been to assess the validity of the facts on which current information or procedure is based. Corroborative information is often documented beyond reasonable doubt, but too often is based only on speculation or custom or is wanting altogether. The fact that a critical appraisal has been accomplished is a tribute to the contributors. The world today, as in the past, is threatened by prejudice, of which racial, social, and economic prejudices are but a few. Equally influential, but less well recognized, is the prejudice of “experience,” derived from uncritical or uncontrolled observation, from the word of an “authority,” or from emotional bias.* Fortunately there are those who are willing to give time and effort to seek out and correct such distortions of the truth.

Considerable aid has come to the editor from several sources. Dr. John Stanbury has been particularly helpful. The members of the Thyroid Clinic at the Presbyterian Hospital need recognition for their influence upon the formulation of many of the views presented herein. Credit must be given to the patience and forbearance of the many contributors who tolerated changes in style and length of manuscript in the interest of creating an integrated volume out of a series of individual essays. The editor's wife has acted as guardian of clarity, upon the thesis that even the layman should be able to read and understand a well-written article. Miss Anne Powell, of the librarian staff at P. & S., was extremely generous with her time. Finally, Mrs. R. Levine and Mrs. K. Sorensen were more than patient with the secretarial details.

Sidney C. Werner

New York City

* “Conviction is by no means devoid of emotion but it is a disciplined and differentiated emotion, pointed to the removal of a realistic obstacle. By contrast, the emotion behind prejudice is diffused and overgeneralized, saturating unrelated objects.”—GORDON W. ALLPORT: *The Nature of Prejudice*.

Contents

Contributors	xix
Preface to the Fourth Edition	xxvii
Preface to the First Edition	xxix
PART I The Normal Thyroid	1
I HISTORICAL RESUMÉ	3
<i>Sidney C. Werner</i>	
SECTION A Structure, Function and Chemistry	7
2 ANATOMY	
ANATOMY AND HISTOCHEMISTRY	9
<i>Nicholas S. Halmi</i>	
COMPARATIVE ANATOMY AND PHYSIOLOGY	22
<i>Aubrey Gorbman</i>	
3 THYROID HORMONE SYNTHESIS AND RELEASE	
HORMONE SYNTHESIS: THYROID IODINE METABOLISM	31
<i>Alvin Taurog</i>	
THYROGLOBULIN: CHEMISTRY AND BIOSYNTHESIS	62
<i>Harold Edelhoch, Jacob Robbins</i>	
4 MECHANISMS OF ACTION OF ANTITHYROID COMPOUNDS	77
<i>William L. Green</i>	
5 THYROID HORMONE TRANSPORT AND METABOLISM: PATHOPHYSIOLOGIC IMPLICATIONS	88
<i>John T. Nicoloff</i>	
6 NATURE, SOURCE AND BIOLOGIC SIGNIFICANCE OF THYROID HORMONES IN BLOOD	100
<i>Inderjit Chopra</i>	

7

CHEMISTRY AND ACTIONS OF THYROID HORMONE

BIOLOGIC AND CELLULAR EFFECTS

115

*George E. Shambaugh, III*THYROID HORMONE STRUCTURE-FUNCTION
RELATIONSHIPS

125

*Eugene C. Jorgensen*MECHANISM OF ACTION OF T_4

138

*Joseph E. Rall*SECTION B Regulatory Influences on
Thyroid Function

149

8

NEUROENDOCRINE CONTROL

151

Seymour Reichlin

9

PITUITARY THYROTROPIN

EMBRYOLOGY AND ANATOMY OF THE THYROTROPIN-
SECRETING CELL (THYROTROPH)

174

Calvin Ezrin

CHEMISTRY

179

John G. Pierce

MECHANISM OF ACTION

185

James B. Field

ASSAY AND SECRETORY PHYSIOLOGY IN MAN

196

Robert D. Utiger

10

EFFECTS OF IODINE: AUTOREGULATION OF THE THYROID

206

Sidney H. Ingbar

11

SYMPATHETIC NERVOUS-ADRENAL MEDULLARY SYSTEM

216

Arne Melander

12

EFFECTS OF INTRINSIC AND EXTRINSIC VARIABLES ON
THYROID HORMONE ECONOMY

223

INTRINSIC PHYSIOLOGIC VARIABLES AND
NONTHYROID ILLNESS*Robert I. Gregerman, Paul J. Davis*

CONTENTS		ix
ENVIRONMENTAL EFFECTS		247
Valerie Anne Galton		
PART II	Laboratory Assessment of Thyroid Function	253
SECTION A	Radioisotopes and Direct Tests of Thyroid Function	255
13	RADIATION PHYSICS <i>H. Verdain Barnes, Buck A. Rhodes, Henry Nicholas Wagner, Jr.</i>	257
14	BIOLOGIC EFFECTS OF RADIATION ON THE THYROID <i>Israel Doniach</i>	274
15	ISOTOPIC TESTS QUANTITATIVE IN VIVO TESTS <i>Ralph R. Cavalieri</i> THYROID AND WHOLE-BODY SCANNING <i>Philip M. Johnson</i>	284 297
SECTION B	Tests of Thyroid Hormones in Blood	319
16	THYROID HORMONE CONCENTRATIONS <i>P. Reed Larsen</i>	321
17	TESTS OF THYROID HORMONE TRANSPORT <i>Kenneth A. Woeber</i>	338
SECTION C	Tests of Peripheral Thyroid Hormone Action	345
18	METABOLIC INDICES <i>David V. Becker</i>	347