REPRODUCTIVE ENDOCRINOLOGY

PHYSIOLOGY, PATHOPHYSIOLOGY AND CLINICAL MANAGEMENT

YEN
JAFFE

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SAMUEL S. C. YEN

Professor and Chairman, Department of Reproductive Medicine,
University of California, San Diego, School of Medicine,
La Jolla, California;
Director of Clinical Services in Obstetrics and Gynecology,
University of California Medical Center, San Diego,
San Diego, California

ROBERT B. JAFFE

Professor and Chairman, Department of Obstetrics, Gynecology
and Reproductive Sciences;
Director, Reproductive Endocrinology Center,
University of California, San Francisco, School of Medicine,
San Francisco, California

1978

W. B. SAUNDERS COMPANY
Philadelphia / London / Toronto

W. B. Saunders Company: West Washington Square
Philadelphia, PA 19105

1 St. Anne's Road
Eastbourne, East Sussex BN21 3UN, England

1 Goldthorne Avenue
Toronto, Ontario M8Z 5T9, Canada

Reproductive Endocrinology

ISBN 0-7216-9625-2

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

This book is dedicated to our wives, Kathryn and Evelyn.

And to all those investigators and clinicians who have contributed to our understanding of the endocrine control of reproductive processes.

CONTRIBUTOR LIST

TOM P. BARDEN, M.D.,

Professor of Obstetrics and Gynecology, University of Cincinnati College of Medicine, Cincinnati, Ohio

C. WAYNE BARDIN, M.D.,

Professor of Medicine, The Pennsylvania State University, and Chief, Division of Endocrinology, The Milton S. Hershey Medical Center, Hershey, Pennsylvania

KURT BENIRSCHKE, M.D.,

Professor of Pathology and Reproductive Medicine in Residence, and Chairman, Department of Pathology, University of California Medical Center, La Jolla, California

GERARD NOEL BURROW, M.D.,

Professor of Medicine, University of Toronto, and Director, Division of Endocrinology and Metabolism, Toronto General Hospital, Toronto, Ontario, Canada

KEVIN J. CATT, M.D., Ph.D.,

Chief, Endocrinology and Reproduction Research Branch, National Institute of Child Health and Human Development, N.I.H., Bethesda, Maryland

ROBERT H. GLASS, M.D.,

Associate Professor, Department of Obstetrics, Gynecology, and Reproductive Sciences, University of California, San Francisco, School of Medicine, San Francisco, California

MELVIN M. GRUMBACH, M.D.,

Professor and Chairman, Department of Pediatrics, University of California, San Francisco, School of Medicine, San Francisco, California

MILAN R. HENZL, M.D., Ph.D.,

Assistant Clinical Professor, Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, School of Medicine, and Section Head, Reproductive Physiology, Syntex Research, Palo Alto, California

MORTIMER B. LIPSETT, M.D.,

Director, Clinical Center, National Institutes of Health, Bethesda, Maryland

ROBERT Y. MOORE, M.D., Ph.D.,

Professor, Department of Neurosciences, University of California, San Diego, School of Medicine, La Jolla, California

JOHN G. PIERCE, Ph.D.,

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

ROBERT W. REBAR, M.D.,

Assistant Professor of Reproductive Medicine, University of California, San Diego, School of Medicine, San Diego, California

GRIFF T. ROSS, M.D., Ph.D.,

Deputy Director, The Clinical Center, National Institutes of Health, Bethesda, Maryland

PAUL T. RUSSELL, Ph.D.,

Associate Professor of Research Obstetrics and Gynecology, University of Cincinnati College of Medicine, Cincinnati, Ohio

JAMES R. SCHREIBER, M.D.,

Assistant Professor, Department of Reproductive Medicine, University of California, San Diego, School of Medicine, La Jolla, California

DENNIS M. STYNE, M.D.,

Assistant Professor, Department of Pediatrics, University of California, San Francisco, School of Medicine, San Francisco, California

JUDITH L. VAITUKAITIS, M.D.,

Professor of Medicine, Boston University School of Medicine, and Head, Section of Endocrinology and Metabolism, Boston City Hospital, Boston, Massachusetts

FOREWORD

Over the past decade, the combined research efforts of biologists, chemists, and clinical investigators have yielded an extraordinary understanding of the fundamental mechanisms involved in the neuroendocrine control of human reproductive processes. Professors Yen and Jaffe have exploited this still-burgeoning knowledge and have produced a textbook that can be both analytic and, in places, holistic in its approaches. Normal function, as well as dysfunction, is analyzed in terms of physiologic, cellular, and molecular mechanisms, so the book represents a synthesis of laboratory and clinical science. The author-editors and the contributing authors are all recognized experts in their respective fields; the book thus contains up-to-date material, both factual and conceptual.

Such a text is long overdue. It will prove to be unusually informative and useful to all students of human biology; it will be particularly valuable to those whose careers or goals include either the creation or the clinical application of new knowledge concerning the neuroendocrine control of human reproduction.

ROGER GUILLEMIN, M.D., Ph.D.
Nobel Laureate for Medicine, 1977
The Salk Institute
La Jolla, California

PREFACE

Among those biomedical fields in which a virtual explosion of new knowledge and understanding has occurred over the past decade, the physiology and pathophysiology of reproductive processes are prime examples. The neural and endocrine regulation of reproduction has been explored with new and sophisticated methods and with increasing comprehension of the important factors involved in the control of this important function. By extrapolation from animal models, as well as by direct investigation involving humans, new light has been shed on the operation of the human reproductive system in both health and disease.

The planning of a book embodying these advances began in July, 1976, when the author-editors were Visiting Scholars at the Villa Serbelloni, an elegant conference and study center operated under the auspices of the Rockefeller Foundation in the picturesque environment of Lake Como, Italy. An outline of this book was completed there, contributing authors were identified, and the writing of several chapters was begun.

Our overall purpose is to provide contemporary factual information and new understanding of human reproductive processes. We attempted to keep in mind the needs of students and investigators in reproductive endocrinology and biology, as well as the needs of clinicians who face the problem of diagnosing and treating reproductive dysfunction. To accomplish these purposes, our authors' expert knowledge ranges from the clinical and systemic to the cellular and molecular. Thus, whenever possible, cellular or molecular mechanisms for normal or disturbed function are presented.

The elements of the reproductive system with which we deal most extensively are various parts of the brain, the pituitary gland, and the gonads. Each of these obviously is a separate and distinguishable component of the system. However, not only are they intimately associated to form an integrated system for periodically releasing germ cells and hormones but, in addition, they have a number of common mechanistic features. We hope that these similarities and integrated modes of action will impress the reader as they have impressed us, and that some readers will be provoked into continued, deeper study of this intriguing field.

The contributing authors were chosen for recognized authority in their respective areas and for their ability to transmit information in a manner we think is lucid and interesting. The lists of references are not intended to be exhaustive but do include key articles and reviews.

Our task as editors was greatly facilitated by the help and cooperation of the contributing authors. We also wish to express our appreciation to Marcia Finkle, Leslie Muga, Alana Schilling, and Rae Feinstein, our secretaries, whose capable assistance helped overcome the few trying problems we met. My (S.Y.) special thanks to Dr. Allen Lein for his critical review of and suggestions for several of my chapters. The editors are grateful to the staff of the W. B. Saunders Company, particularly John Hanley for his confidence, encouragement, and courtesies, which made the preparation of this book a satisfying experience.

The information in this book is at the cutting edge of contemporary reproductive endocrinology. If the book assists the clinician, excites and teaches the student and investigator, and lends deeper understanding of the control of reproductive processes, it will have served its purpose.

S. S. C. YEN
R. B. JAFFE

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PART I

ENDOCRINE REGULATION OF THE REPRODUCTIVE SYSTEM

1

NEUROENDOCRINE REGULATION OF REPRODUCTION

ROBERT Y. MOORE

INTRODUCTION

The purpose of this chapter is to provide a review of the neural basis of neuroendocrine regulation. During the early part of this century the sciences of endocrinology and neurobiology developed rapidly but largely independently. In endocrinology, the unifying concept is that of the hormone: a substance secreted by an endocrine organ into the blood to have effects upon a distinct tissue or tissues. The major unifying concept in neurobiology is the neuron doctrine: the view that the nervous system is composed of individual functional units, nerve cells, which are distinct and separate cellular entities. Early functional research on the neuron emphasized the unique capacity of these cells to transmit information rapidly and reliably over long distances by the mechanism termed the action potential or nerve impulse.

Since neurons are morphologically separate entities, it was evident that some further mechanism must exist to accomplish the necessary transfer of information from one neuron to another or from a neuron to an effector cell. For some time it was assumed that this process, like the nerve impulse, is essentially a bioelectric phenomenon. Over a

number of years, however, painstaking work, pioneered by Loewi and Dale, conclusively established that the transmission of information from nerve to muscle which results in muscle contraction requires release of a chemical, acetylcholine, from the nerve onto the muscle. The point of functional contact is termed the synapse and the process is termed chemical transmission at the synapse.

It is now evident that nearly all synapses in the mammalian peripheral and central nervous systems use chemical transmission. Thus, one of the major advances in neurobiology has been the demonstration that nerve cells have two basic functions: one to transfer information rapidly along cell processes using a bioelectric phenomenon, and the second to transmit information to other nerve cells and effector cells by the secretion of a specific chemical.

During the period in which the concept of chemical transmission was developed and established, another neuronal function was discovered that brought neurobiology and endocrinology inextricably together and led to the development of the burgeoning field now called neuroendocrinology. This function is the process of neurosecretion, in which the neuron secretes a substance into the blood stream rather than at a synaptic junction. Neurosecretion was first demonstrated in fish by E. Scharrer (cf. Scharrer and Scharrer[1] for review) but was not clearly shown in mammals until the late 1940s. Then the work of Bargmann and Scharrer[2] provided the essential evidence that the posterior, or neural, lobe of the pituitary did not function as a self-contained, hormone-producing gland but instead stored and released neurohypophyseal hormones produced by the neurons of the supraoptic and paraventricular hypothalamic nuclei of the hypothalamus and transported along their axons in the supraopticohypophyseal tract to the neural lobe.

These discoveries occurred during a period in which it was becoming increasingly apparent that the regulation of pituitary function, hence the function of target endocrine organs involved both in feedback influences of the target organ hormones on the pituitary and in a variety of environmental and hormonal influences, is mediated by the central nervous system. Thus, the concepts of feedback regulation of pituitary function became much more complex because of the introduction of the central nervous system into the regulatory mechanisms (Fig. 1–1). The necessity of recogniz-

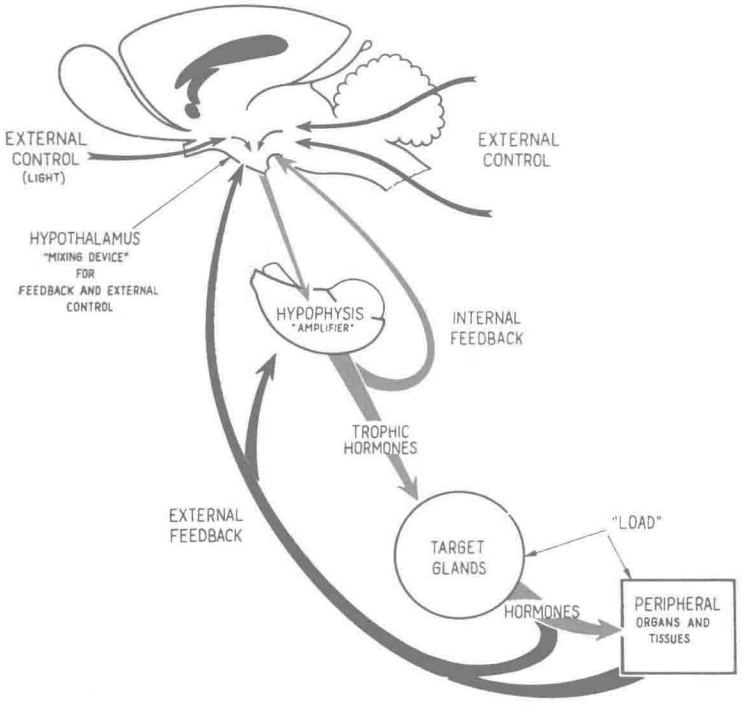

Figure 1–1. General principles of feedback control in the endocrine system. (Reproduced from Szentagothai et al.[4])