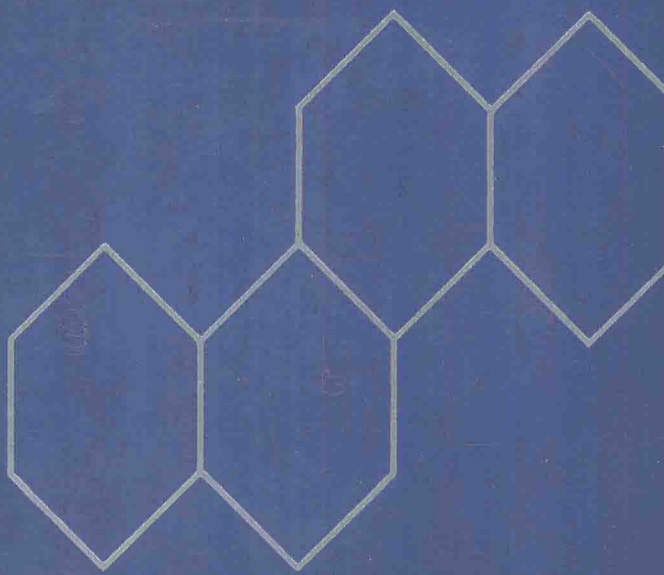
ENDOCRINE CAUSES OF MENSTRUAL DISORDERS

James R. Givens, editor



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GYNECOLOGIC ENDOCRINOLOGY (1977)

Dedication

THE PROCEEDINGS of the first University of Tennessee symposium on gynecologic endocrinology were dedicated to the pioneer clinical endocrinologist, Dr. E. B. Astwood. The second symposium is dedicated to Roy O. Greep, Ph.D., a neighbor, close friend, and collaborator of Dr. Astwood.

Roy Greep was a farm boy from Kansas who left his plough in Longford, Kansas and attended Kansas State College, where he received his B.S. degree. He transferred to the University of Wisconsin where he received a Master's Degree. That was the time of the "Great Depression," and also a time when dust storms made Kansas intolerable. He married and stayed at the University of Wisconsin, where his first piece of research, for his Ph.D. degree, showed that follicle-stimulating hormone and thyroid-stimulating hormone could be separated. He joined the staff at Harvard where he advanced from lecturer in anat-

omy and physiology to professor and dean of the dental school. He has been editor of prestigious journals and has received many scientific awards of merit, as well as having been president of the Endocrine Society. Dr. Greep has received honorary degrees from Harvard, the University of Buffalo, Kansas State College, and the University of Sheffield (England).

Some years ago he gave up the position as dean to become director of the Laboratory for Reproductive Biology and Medicine, at the Harvard School of Public Health, from which he retired recently. He presided at the International Endocrine Congress in Hamburg last summer. He is now in charge of a worldwide study of reproduction and human welfare financed by the Ford Foundation.

Dr. Greep is a warm, mild-mannered man who speaks as little as possible. However, when he speaks, it is worth listening, contemplating and enjoying. Dr. Greep is one man who has helped to make Harvard what it is, and also one of the scientists who has made the science of endocrinology what it is.

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Preface

THIS VOLUME presents the proceedings of the University of Tennessee second annual symposium on gynecologic endocrinology, which was titled "Endocrine Causes of Menstrual Disorders." The symposium was held March 16–18, 1977, in Memphis, and was sponsored by the Division of Reproductive Medicine of the Department of Obstetrics and Gynecology. The authors submitted prepared manuscripts. Several panel discussions were part of the program and the edited transcriptions are contained herein.

Disordered menstruation is a common medical problem. The purpose of the symposium was to discuss the various derangements of the endocrine system that cause menstrual abnormalities. The endocrine events that lead to menstruation consist of a number of exquisitely and finely balanced phenomena. The first portion of the program was devoted to a definition of the normal menstrual cycle and the associated hormonal events. Following this introduction, central nervous system, pituitary, ovarian and adrenal disorders that produce abnormalities in menstruation were considered in sequential fashion. This volume is arranged similarly.

The cooperation and willingness of the faculty to meet a number of deadlines is gratefully acknowledged. Appreciation is expressed to Dr. Preston V. Dilts, Jr., chairman of the Department of Obstetrics and Gynecology, for continued support and encouragement in the conducting of this symposium. The expert assistance of Ms. Bernie Mizell in every phase of the preparation of the symposium and its publication is also acknowledged. The transcription of the panel discussions was made possible through the secretarial assistance of Ms. Gail Adams and Ms. Marty Nance. The professional editorial skills of Ms. Mary Konstant and other members of the staff of Year Book Medical Publishers made the publication of the proceedings a much easier task.

James R. Givens, M.D.

Memphis
February 1978

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Normal Events

Maturational Changes in the Hypothalamic-Pituitary Axis during Puberty

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MY REMARKS will serve as an introduction to the program since I will review some of the basic concepts that have evolved over the years that have become useful in endocrinology. The discussion will be built around the framework of the changes in the reproductive system of the fetus, the child, the pubertal child and the adolescent.

Starting during fetal life and continuing throughout childhood and adulthood, the normal female has a very active and well-controlled neuroendocrine function. Gonadotropin levels are measurable in plasma during childhood; thus the child is not in a "cocoon," as was thought as recently as 10–15 years ago. During a subsequent period, gonadotropin levels rise and they then become "managed", resulting in the capacity for reproduction. In order to understand how these events come about, we have to understand some of the basic mechanisms involved in the neuroendocrine control of reproduction. These are similar to neuroendocrine mechanisms involved in many of the other vegetative functions of the body. It is worthwhile emphasizing that everyone is under these same controls and that even now, moment to moment, we are managing our metabolism and our endocrine system using these mechanisms. Since the controls are generally a feedback loop type of system, it is possible to break in at one place and follow it back

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through the circuit. I have chosen to do so using the central nervous system as a reference point.

An important role in reproductive neuroendocrine function is played by the lower portion of the diencephalon, the hypothalamus, which receives a colossal amount of information by means of external cues such as temperature, light, noises and odors. It receives messages from portions of the central nervous system; it generates its own messages and also receives messages through the blood-vascular system. All of these data are filtered into the neural network and are translated, after proper data reduction, into a message. The message takes the form of neurochemicals which are then passed down the pituitary-portal vessels to the anterior pituitary gland. The portal system is absolutely necessary since there is no direct tissue connection between the anterior pituitary and the central nervous system.

The pituitary receives the messages. Since these are either in the form of neurotransmitters or protein hormones (polypeptides) they are received at the cell surface and function by triggering events previously programmed inside the anterior pituitary cell. This results in the release and, directly or indirectly, the subsequent manufacture of pituitary tropins. The characteristic pattern of this release function is episodic. In this case, the gonadotropins are released in pulses. The tropins then reach the blood-vascular system. They have no specific binding protein in the blood.

When the gonadotropins LH (luteinizing hormone) or FSH (follicle-stimulating hormone) find a cell upon which to act, the following sequence occurs: the protein hormone, by its molecular shape and electric charge, appears to have a certain configuration. A portion of the cell membrane containing a "receptor" recognizes this configuration. If the receptor is specific enough in its ability to recognize the specific configurations, it is a "specific receptor." The joining of the membrane-bound receptor and the hormone triggers a series of steps that is available to apparently all mammalian cells and seems designed to carry the message of contact at the cell membrane. This activates the intracellular machinery. Some mechanisms which interweave cell membranes with intracellular function involve the prostaglandins and the adenyl cyclase:protein kinase system. If the cell receiving the message from the protein hormone is programmed to be a steroid-secreting cell, the message turns on the enzymatic machinery in the cell to modulate the manufacture of steroids. The steroid product will depend on whether it is an adrenal cell, a gonadal cell or some other steroid-producing cell.

For example, a precursor such as acetate or cholesterol is started