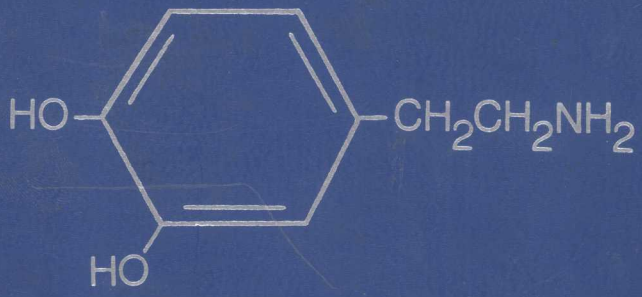
HORMONE-SECRETING PITUITARY TUMORS

James R. Givens, editor



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HORMONE-SECRETING PITUITARY TUMORS

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Based on the proceedings of the Sixth Annual Symposium on Gynecologic Endocrinology held March 5–7, 1981 at the University of Tennessee, Memphis, Tennessee

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Dedication

ANNE PAPPENHEIMER FORBES, M.D.

THIS VOLUME is dedicated to Dr. Anne Pappenheimer Forbes for her outstanding contributions to the science of endocrinology. After obtaining A.B. and M.D. degrees from Radcliffe College and the Columbia University College of Physicians and Surgeons, respectively, Dr. Forbes became a pediatric house officer in the Johns Hopkins Hospital. A succession of appointments in the Massachusetts General Hospital and in the Harvard Medical School followed, culminating in her promotion to the rank of Clinical Professor of Medicine.

In the Massachusetts General Hospital, Dr. Forbes first became associated with Dr. Fuller Albright and, as his health worsened, she became not only useful but indispensable to him. It was she who su-

pervised the workup of the endocrine cases he attracted from all over the world, and who translated the resulting therapeutic recommendations to his patients. At the same time Dr. Forbes, who with her husband was rearing a family of five children, permitted herself only the briefest of absences from her work. In the course of this arduous but rich apprenticeship, she achieved the refinement of clinical skill that distinguished her ever afterward.

To energy and clinical ability was added a capacity for rigorous thinking. The latter quality, so brilliantly exemplified by Dr. Albright, was systematically inculcated in his trainees. The marshalling of clinical evidence in a manner that permits the systematic testing of hypotheses is discernible in all of Dr. Forbes' work and is well illustrated by the deduction that prolactin (a then uncharacterized human hormone) must be hypersecreted in the syndrome of galactorrhea, amenorrhea and low urinary FSH. She published this remarkable finding in the memorable monograph, "Syndrome characterized by galactorrhea, amenorrhea and low urinary FSH: Comparison with acromegaly and normal lactation" (Forbes A.P., Henneman P.H., Griswold G.C., Albright F.: *J. Clin. Endocrinol. Metab.* 14:265, 1954).

While Dr. Forbes' scholarly contributions to endocrinology reflect her long association with Dr. Albright, they are by no means limited to it. Following his enforced retirement and subsequent death, she remarked that she had ingested "enough calcium for a lifetime." With characteristic imaginativeness, she struck out in new directions. Among the findings that resulted were a demonstration of the frequency of autoimmune disease in patients with gonadal dysgenesis, the existence of ovarian autoantibodies in certain patients with secondary amenorrhea, and the presence of anti-kidney antibodies in the serum of patients with primary tumors of the liver or kidney.

Schooled to abhor shoddy thinking, Dr. Forbes brought discipline as well as integrity to experimentation, colored by such qualities as wit, humaneness, and unfailing kindness to patients. Her students, fellows and colleagues savor her distinction, recognizing the improbability of encountering her like again.

JANET W. MCARTHUR, M.D.

Preface

THIS VOLUME represents the proceedings of the "Functioning Pituitary Tumors: Diagnosis and Treatment" symposium, which was sponsored by the Baptist Memorial Hospital, Memphis, Tennessee, in cooperation with the Pituitary Foundation of America, Inc., and the University of Tennessee College of Medicine. The symposium was held March 5–7, 1981, in the Frank S. Groner Education Center of the Baptist Memorial Hospital in Memphis. The speakers submitted prepared manuscripts of their presentations for publication. The panel discussions are edited transcriptions.

The first section of the book deals with the basic physiology of pituitary function, including neuroendocrine control of pituitary function, modulation of hypothalamic function by opioid and other peptides, and metabolic effects of neuroendocrine peptides. The second section describes the pretreatment hormonal evaluation of the patient. Also discussed in this section are the histopathology of pituitary tumors, as well as their radiologic therapy. The next several sessions of symposium (reproduced in sequential order in this volume) dealt with the diagnosis and management of Cushing's disease, acromegaly and prolactin-secreting tumors.

A particularly enlightening aspect of the program was the definition and clinical features of the amenorrhea-galactorrhea syndrome provided by Dr. Anne Forbes, to whom this volume is dedicated.

Considerable interest was generated by "The Great Debate," which examined the pros and cons of medical vs. surgical treatment of prolactin-secreting tumors. Proposing the medical therapeutic approach was Gordon M. Besser, M.D., and speaking in favor of the surgical treatment was George Tindall, M.D.

The last sections of the book concern the posttreatment evaluation of the pituitary patient and the complications and failures attending surgical management. Also included in this section is a discussion of the treatment of children with pituitary tumors and a review of pituitary tumor epidemiology.

The cooperation and support of the Postgraduate Education Department of the Baptist Memorial Hospital under the able direction of Dr. Kenneth Burch, with the efficient assistance of Ms. Anne Wallace are gratefully acknowledged. The skillful assistance of Gabriela Radulescu and the staff at Year Book Medical Publishers was again essential to the success of this publication. The expert secretarial assistance of Jeanette Austin is gratefully appreciated.

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Contents

Neuroendocrinology of Pituitary Regulation

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THE FACT THAT ALL ANTERIOR PITUITARY SECRETIONS are under the control of the hypothalamus has important implications for understanding of the pathogenesis and manifestations of adenoma of the pituitary. New findings that reveal the high incidence of clinically silent adenomas, and the embarrassing inaccuracy of current radiologic techniques for the diagnosis of prolactinoma, the most common pituitary adenoma, have further emphasized the importance of physiologic studies for the identification of pituitary disorder. This chapter reviews current concepts of the nature of the hypothalamic-pituitary control mechanism, and the physiologic basis of neuroendocrine strategies for the clinical evaluation of pituitary adenomas. These topical areas have been recently summarized in comprehensive monographs and reviews.[1–13]

The Concept of Neurosecretion

Central to the understanding of neural control of the pituitary is the concept of neurosecretion.[14–18] As currently defined, neurosecretion refers to the synthesis and release of chemical substances by neurons (Fig 1). When so defined, it is apparent that virtually all neurons are neurosecretory. Some, like cholinergic neurons, synthesize

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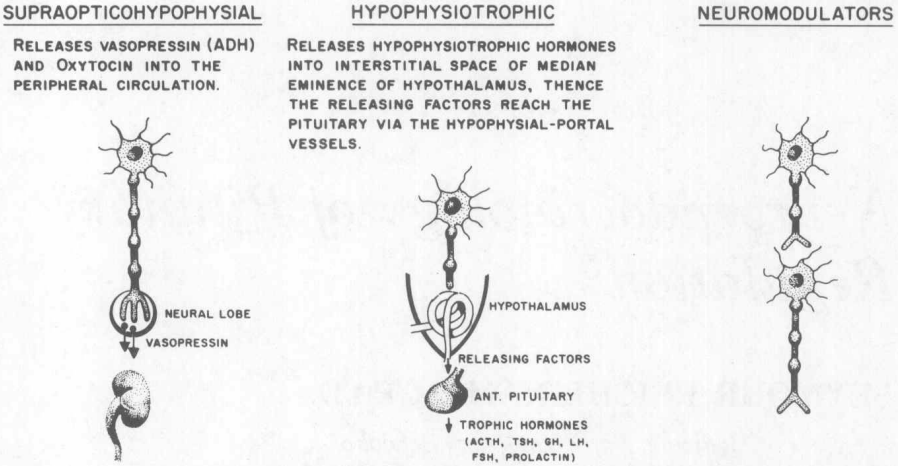


Fig 1.—Schema of neurosecretory, peptidergic neurons involved in pituitary regulation and neuromodulation. (From Reichlin S., in Williams R.H. (ed): *Textbook of Endocrinology*. Philadelphia: W.B. Saunders Co. In press. Used by permission.)

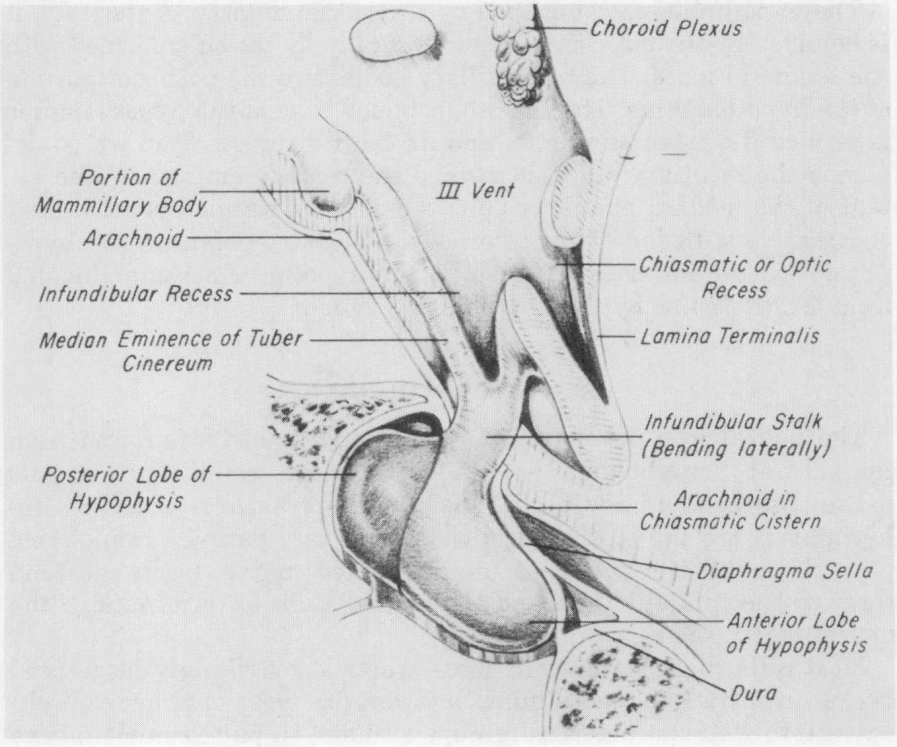
acetylcholine by enzymatic processes and release their product at presynaptic nerve endings that may terminate on other nerve cells, glandular cells, or muscle cells. Other kinds of neurons may synthesize and release into synapses neurotransmitters, such as norepinephrine, glutamic acid, and γ-aminobutyric acid. Other kinds of neurosecretory neurons may release their product into the blood. Such neurosecretions can be referred to as neurohormones because they satisfy the classic description of a hormone as a substance arising in one structure to influence the activity of another structure at a more remote site. Most of the neurons involved in pituitary regulation are neurohormone-secretory because they release their secretory products (vasopressin and oxytocin, the secretions of the neurohypophysis) directly into the general bloodstream or into the specialized (hypophysial-portal) blood supply that links the hypothalamus and anterior pituitary.

The bulk of neurons involved directly in pituitary gland regulation secrete polypeptides, and for this reason they are called peptidergic neurons. But at least one bioamine, dopamine, is involved in anterior pituitary regulation. All cells giving rise to neurosecretions that ultimately impinge upon the pituitary are themselves influenced by other neurons—some aminergic, some peptidergic. To understand how these interactions are brought about it is necessary to consider the physical structure of the hypothalamus and pituitary.

Anatomy of the Hypothalamic-Pituitary Unit

The pituitary gland is divided into a glandular portion (adenohypophysis, anterior lobe, pars distalis), intermediate lobe (pars intermedia), and a neural lobe (posterior pituitary, infundibular process) that is a direct downgrowth of tissue from the base of the hypothalamus (Fig 2). The intermediate lobe is rudimentary in man, making up less than 0.8% of total weight. A significant number of intermediate-lobe cells are diffusely distributed in the adenohypophysis and neural lobe of man. The neurohypohysis consists of specialized tissue at the base of the hypothalamus, together with the neural stalk and lobe. The neurohypophysial portion of the hypothalamus forms the base of the third ventricle. Viewed grossly, this region resembles a funnel, and was given the name infundibulum (Latin for funnel) by early anatomists. Indeed, a funnel function was assigned to this re-

Fig 2.—Sagittal view of the human hypothalamic-pituitary unit illustrating the anatomical relationships between optic chiasm and pituitary stalk. (From Post K.D., et al. (eds): *The Pituitary Adenoma.* New York: Plenum Medical Book Co., 1980. Used by permission.)



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