INTERRUPTION OF THE PITUITARY STALK IN THE PATIENT WITH MAMMARY CANCER*

GEORGE EHNI, M.D., AND NYLENE E. ECKLES, M.D.

The University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, Texas

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The hypothesis that maintained interruption of the hypophysial portal vessels of the human pituitary stalk is physiologically equivalent in all observable respects to excision of the pituitary gland has been put to test in a series of 17 women with metastasized cancer of the breast. Used as indicators of hypophysial activity were a variety of tests of the functional state of tissues subservient to the hypophysis, response of the patient's cancer to the intervention, and gross and histologic examination of tissue removed during life and at necropsy.

Our conviction that the hypothesis was valid and that no ethical problem would arise through submission of patients with far advanced breast cancer to the operation in question derived from historical, physiological, anatomical and clinical sources. In 1907 Paulesco reported observations on dogs submitted to section of the stalk and regarded this as tantamount to hypophysectomy. Three years later Crowe, Cushing and Homans duplicated Paulesco's observations, explaining that whereas the neural lobe derives its blood supply from an artery entering at its posterior pole the anterior lobe depends upon small vessels passing down the stalk which do not anastomose with the supply to the neural lobe, as had been shown by Herring. They likened the stalk-section state to that following removal of the gland and immediate implantation elsewhere in the body—a view that requires no modification 48 years later! In 1911 Dandy and Goetsch reported confirmation of Herring's finding of the separateness of blood supply to the anterior and posterior lobes but had distinct reservations that mere transection of the stalk would inevitably necrose the anterior lobe. They believed that some vascular supply derived from dural attachments, which in the dog are slight, and that a collateral circulation between the anterior and posterior lobe through the pars intermedia might exist. In their hands, application of a clip to the stalk was not followed by pituitary deficiency or degeneration and they believed that those who had observed such a consequence had inadvertently damaged a small part of the pars intermedia where such anastomosis was believed to exist. Dandy and Goetsch seem to have been tantalizingly close to a discovery not made until 25 years later by Wislocki and King (who described the

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portal nature of at least part of the adenohypophysial blood supply) when they observed that arterial injection of material bearing granules too large to pass capillaries failed to fill the sinusoids of the anterior lobe because of stoppage in the capillaries of the stalk. They recognized that the anterior lobe was not directly supplied by systemic arteries and decided that these vessels break up into capillaries in the stalk before they reach the hypophysial substance and that these capillaries then empty into the sinusoids. The first report of interruption of the pituitary stalk in man was given by Dandy and Goetsch. The patient was Dr. Cushing’s and the result was necrosis of the pars distalis. This was described more fully by Dr. Cushing a year later.

After it was established that the pars distalis was devoid of a competent nerve supply, though under control of the nervous system in its gonadotrophic, adrenocorticotrophic, thyrotrophic, lactogenic and other functions, the hypophysial portal vessels came under investigation as the avenue for transmission of humoral signals from the median eminence and stalk to the gland. Their role in functionally linking the pars distalis to the nervous system has been confirmed in all species studied. Fortunately, in view of the great numbers of such reports, several surveys exist. The striking regenerative capacity of these vessels of the stalk following simple section makes necessary the interposition of a competent mechanical barrier or the taking of other steps to prevent their resumption of function. This capability probably explains well known instances, such as that described by Dandy, in which little or no endocrinologic abnormality save polyuria was observed following division of the stalk.

Strong anatomical support for the hypothesis exists in the findings of Xuereb, Prichard and Daniel that, though arteries derived from the carotid traverse the pars distalis, no artery of any sort supplies blood to this structure and that all the blood in the pituitary sinusoids flows down the portal vessels after having first passed through capillaries in the median eminence and stalk. They suggested that the postpartum necrosis of the anterior pituitary gland described by Sheehan was the result of obstruction by thrombosis of the portal vessels in the stalk and lower infundibular stem. It was, of course, this very result that we hoped to attain for our patients.

Most importantly, there was the personal experience of one of us in producing an intense hypopituitary state in a male patient of Dr. J. B. Trunnell with prostatic cancer who was subjected to pituitary-stalk interruption on December 7, 1955 (before the series here reported was begun) at the suggestion of Drs. Claude Fortier and Roger Guillemin.

**MATERIAL**

The majority of patients chosen for this study (Table 1) had been treated at the M.D. Anderson Hospital over a considerable period of time with hormones, irradiation, ovariectomy and, in 2 cases, adrenalectomy. Some (Cases B, D, E, G, L, M) were newly seen by us in a such far-advanced stage of disease that hypophysial interference rather than a single endocrine attack was