Endocrine Influences on the Gastrointestinal Tract

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In recent years, there has been a growing body of evidence suggesting that the gastrointestinal tract, particularly the stomach, may be influenced by endocrine as well as neurogenic factors. In this article, present knowledge regarding some endocrine effects upon the stomach in humans and animals will be reviewed and their significance in peptic ulcer disease evaluated. The hypothalamus and the pituitary, adrenal, and parathyroid glands, as well as their relationship to the Zollinger-Ellison syndrome, will be considered.

Recent studies suggest that stress may be mediated to the stomach not only by the vagus nerve but by a solely hormonal mechanism acting through the hypothalamic-pituitary-adrenal pathway, independent of the vagus nerve and gastric antrum. Thus, the gastric and peptic glands may be integrated into the general endocrine system.

The hypothalamus was described by Cannon as the seat of primitive human emotions. An intact hypothalamus is essential for the transmission of stimuli of emotional origin to the pituitary. Leonardo de Vinci located the soul in the vicinity of the hypothalamus. A number of systemic stress factors (anoxia, shock, pain, infections, burns, trauma, and the like) or physical stimuli (muscular exertion, fatigue, temperature changes), as well as chronic emotional stress (rage, fear, anxiety, frustration), may induce the hypothalamus to secrete a humoral substance that stimulates the pituitary gland to secrete corticotropin (adrenocorticotropic hormone); this pattern is part of the general adaptation syndrome. Corticotropin, in turn, activates the adrenal cortex to release a number of steroid hormones, including cortisone and cortisone-like compounds.

Gastrointestinal ulceration with hemorrhage or perforation is an integral part of the alarm reaction. The repeated administration of corti-
cotropin simulates certain forms of stress since both corticotropin and stress may produce an increase in the output of adrenal corticoids that can be measured in the blood and urine.

The adrenal cortex may have a dual role in the gastric responses to stress, according to the “permissive” concept and the “conditioned” theory of hormonal activity. The adrenal cortex may function as an agent that “permits” a gastric response to occur and without which the response could not occur. In its second role the adrenal cortex is postulated to have a more directive function, controlling the levels of adrenal cortical hormone attained and thereby the extent of the gastric response. Excess adrenal hormone may sensitize the stomach to respond more readily, or stress itself may “condition” the stomach to respond to adrenal hormone. It would therefore appear that the adrenal steroids may sensitize the stomach to ulcerogenic influences or to other factors yet to be determined, or that the stress itself may cause the stomach to respond abnormally to the adrenal hormones.

STRESS PATHWAYS FROM HYPOTHALAMUS TO STOMACH

Results of recent studies suggest that there are two routes by which stress may be relayed from the hypothalamus to the stomach: (1) a neurogenic one involving the cerebral cortex, the anterior hypothalamus, and the vagus nerve; and (2) a hormonal mechanism mediated through the posterior hypothalamus, pituitary gland, and adrenal cortex.

**Neurogenic Pathway**

The neurogenic transmission is by way of the anterior hypothalamus to the vagal centers and the vagus nerve. Direct electrical stimulation of the anterior hypothalamus in animals produces a prompt increase in gastric secretion of hydrochloric acid within 30–60 min. that is abolished by vagotomy. Insulin hypoglycemia also induces a prompt gastric hypersecretion in animals and that is attributed to anterior hypothalamic and vagal stimulation.

**Hormonal Pathway**

A second hormonal phase of gastric secretion mediated through the adrenal cortex to the stomach by way of the hypothalamus and pituitary gland was postulated in 1950 on the basis of observations in man of an increase in gastric hydrochloric acid and pepsin secretion during prolonged corticotrophic hormone stimulation—an increase unaffected by vagotomy but requiring an intact adrenal gland. It was suggested