Hormonal Control of Gastrointestinal Motility

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The motor responses of the gastrointestinal tract to a meal are tuned to provide the optimal conditions for digestion and absorption of food. Hormones released from the mucosa of the intestinal tract play an important role in regulating and integrating the various motor events which occur. Complex feedbacks, both nervous and humoral, control the release of intestinal hormones and also modify their actions. Preliminary studies suggest that abnormalities in the secretion or action of various gastrointestinal hormones may play an important role in the production of motor disorders of the gastrointestinal tract.

The orderly digestion and absorption of food is brought about by a series of complex and interdependent events effected by the autonomic nervous system and various hormones released when a meal is eaten. The nature of the interaction between regulating nervous and humoral factors, between secretion into and movement along the gut, and between absorption and metabolism of ingested foodstuffs, is so extremely complicated that only the most sophisticated of investigative techniques can do more than study a few of the many factors concerned at any one time (1–5). It is clear, however, that the orderly assimilation of a meal is in large part dependent on optimal rates of gastric emptying and of small-intestinal transit, and that the changes in motor activity after food, seen at all levels of the gastrointestinal tract from the lower esophagus downwards, are markedly influenced by gastrointestinal hormones.

The intestinal hormones whose motor effects on the gut have been most extensively studied are gastrin (6–9), secretin, and cholecystokinin (10–16), and these will be the only ones whose actions are considered in any detail in this review. A number of other humoral agents have been isolated from the intestinal mucosa, notably motilin (17, 18), gastric inhibitory polypeptide (GIP) (19, 20), vasoactive intestinal peptide (VIP) (21, 22) and enteroglucagon (23). It is not possible at present to assess any physiologic importance their motor actions on the gut may have, because not enough information is yet available about these peptides. Various nonpeptide substances also have potentially important motor actions on the gastrointestinal tract (eg, prostaglandins, 5-hydroxytryptamine), but these will not be discussed at length here. Excellent recent summaries of their actions are available (24–26).

EFFECT OF TRANSIT OF MEALS ON HORMONE RELEASE

The total amount of a gastrointestinal hormone released after food will depend on the number of hormone-secreting cells stimulated and on the potency of the stimulus for release of that hormone. It will also depend (as will the pattern of release) on the length of time food and food products remain in contact with hormone-secreting cells. Rapid gastric emptying is thus likely to result in an increased rate of release of hormones from the small-intestinal mucosa. Similarly, substances transported along a
greater than usual length of small intestine, either because of rapid small-intestinal transit or because they are relatively poorly absorbed, may release greater amounts of secretin and cholecystokinin. For example, the cholecystokinin-releasing effect of the poorly absorbed saline purgative magnesium sulphate, given as an oral bolus, is relatively more marked (27, 28) than its effect when given by perfusion over a limited length of small intestine (29), possibly because the Mg and SO₄ ions taken as a bolus stimulate a greater length of small intestine. In contrast, amino acids such as L-phenylalanine or L-tryptophan are rapidly absorbed in the upper jejunum, so that, although probably at least as potent as Mg SO₄ as CCK-releasing agents, they do not come into contact with as many CCK cells.

Because both secretin and CCK are released from a considerable length of the small intestine (appreciable amounts of each being demonstrable as far down as the ileum) (14, 16, 30–35), the small intestine is able to act as an integrator for the release of both CCK and secretin (16, 30). Entry into the duodenum of a large bolus of gastric contents will thus evoke a relatively larger volume of hormone-mediated secretions from the pancreas, small intestine, and biliary tract than that produced by a small bolus. The motor responses will similarly be tailored to the amount of food entering the intestine in a given time.

** PATTERNS OF HORMONE RELEASE **

After a mixed meal, intestinal hormones are released into the blood very quickly. Levels of immunoreactive gastrin, cholecystokinin, and secretin rise rapidly, and usually reach a peak within 20–40 minutes after the oral ingestion of a liquid meal, falling thereafter. Although the timing of the response may vary somewhat (for example peak levels of cholecystokinin occur much later after a fatty or solid meal than after aminoacid solutions (16)), the pattern appears to be similar for each of the hormones so far studied. This physiologic response, of a rapid rise in hormone levels to a peak followed by a fall, is difficult to mimic under experimental circumstances and is not produced either by rapid intravenous injections or by prolonged infusions of a hormone. This may be important, as the motor effect of some hormones appears to be influenced by the rate at which they reach the target organ (36, 37). A further complication is that both gastrin (38–46) and cholecystokinin (47–50) are present in the body in various forms with similar biologic activity but differing in properties such as their potency, half-life in the blood, and the degree to which they are recognized by immunoassays. These points are made to emphasize that apparently clearcut results seen in well-designed experiments may not truly reflect the complex events that occur after a meal is eaten.

The interaction of various neuroendocrine factors on the function of the gut is also extremely complicated: not only do the hormones interact at the receptor site (51, 52), but their release is influenced by other hormones (53–57) and by nervous factors (5, 58, 59).

**THE NORMAL PROGRESS OF FOOD THROUGH THE GASTROINTESTINAL TRACT**

The patterns of release of gastrin, secretin, and cholecystokinin are affected by the rate of gastric emptying, which in turn is influenced by each hormone (see below). These factors interact with each other and with nervous influences in such a way as to produce, after a short initial period, a steady delivery of gastric contents into, and a steady flow along the intestine, permitting optimal mixing with digestive juices, digestion, and absorption. These processes have been described in elegant detail by Lagerlöf, Johansson, and Ekelund (1–3). The ingestion of a mixed meal containing carbohydrate, fat, and protein is followed by two distinctive phases. The period immediately after ingestion of the meal is characterized by relatively rapid gastric emptying, a rapid flow of the initial part of the meal through the upper small intestine, and a