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# Conceptualization of Endocrine Function of the Gastrointestinal Tract

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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## ABSTRACT

The gastrointestinal systems (GIT) and endocrine systems are integrated into a well-coordinated complex to meet the metabolic needs of the body. The endocrine functions and possible dysfunctions are less emphasized in the medical curriculum. Hormones are synthesized and released by different segments of the GIT to perform specific functions. The main sites of synthesis and secretion are the stomach and intestines. The hormones of the GIT are categorized as paracrine, neurocrine, and endocrine.

Cholecystokinin (CCK), gastrin, secretin, glucose-dependent insulinotropic peptide or gastrin inhibitory peptide (GIP), and motilin are Endocrine hormones. Somatostatin and histamine are examples of Paracrine hormones. Enkephalins, vasoactive intestinal peptides (VIP), and gastrin-releasing peptides (GRP) are examples of neurocrine hormones. An additional three work together as paracrine and endocrine hormones Glucagon-like peptide [GLP-1], pancreatic polypeptide, and peptide-YY. Villikinin from Brunner's gland of the duodenum, duocrinin from intestinal mucosa, and parotin are a few others rarely discussed in most literature. Gastrointestinal tract hormones play crucial roles in providing satiety, maintaining hormonal secretion and inhibition, and breaking down proteins, fats, and carbohydrates into simple molecules for absorption. There are documented manifestations of hypersecretion or hyposecretion of these hormones. Likewise, known medical conditions can subsequently lead to GIT hormone dysfunction.

Gastric Outlet Obstruction, Somastinoma, celiac disease, Zollinger-Ellison Syndrome, Crohn's

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disease, ulcerative colitis, tropical sprue, intestinal resection, pancreatic insufficiency, gastric ulcers, infective diarrhea, and Inflammatory bowel disease(IBS) are few known documented medical conditions that lead to GIT hormonal dysfunctions. The Article aims to reiterate the endocrine function and dysfunction of the GIT. The review article is part of an integrative learning process for students.

*Keywords: Endocrine hormones; gastrointestinal tracts; gastrointestinal hormones; zollinger-ellison syndrome; gastric ulcers; inflammatory bowel disease.*

## ABBREVIATIONS

*AIMAH : ACTH-Independent Macronodular Adrenal Hyperplasia;*
*BBS : Bombesin;*
*CCK : Cholecystokinin;*
*EPI : Exocrine Pancreatic Insufficiency;*
*GIP : Gastrin-Inhibiting Peptide;*
*GIT : Gastrointestinal Tract;*
*GRP : Gastrin-Releasing Peptide;*
*HCl : Hydrochloric Acid (Acid);*
*PPIs : Proton Pump Inhibitors;*

## 1. INTRODUCTION

The Gastrointestinal system, also known as the alimentary tract, is essential for maintaining life. We must ingest appropriate nutrients for proper energy release, growth, and cell repair. The GI tract and its hormonal interplay is a thought-provoking phenomenon that obscures truth-seekers/readers' understanding concerning the GI mechanism of action. This Article explores the entirety of the tract and the hormones required in this specific system.

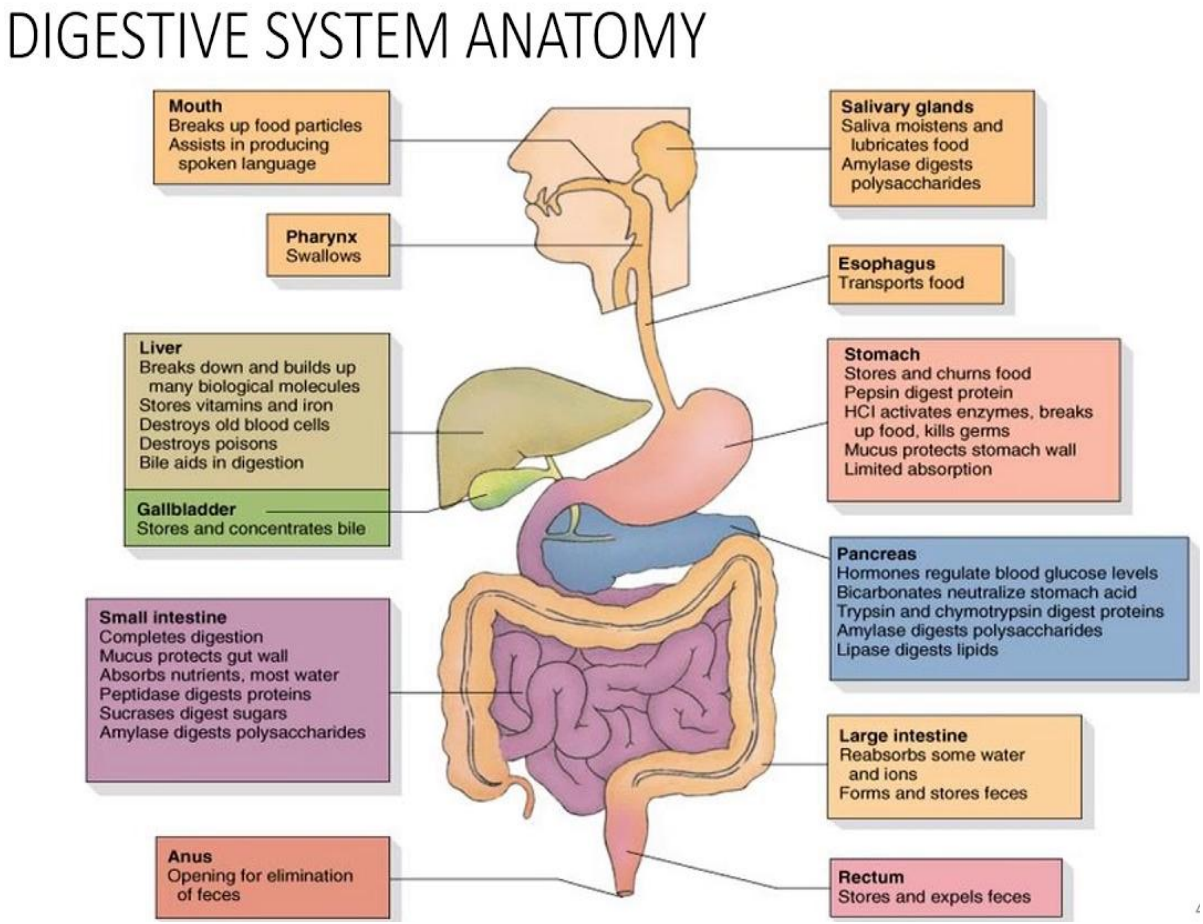


**Fig. 1a. The schematic of GIT and functions**
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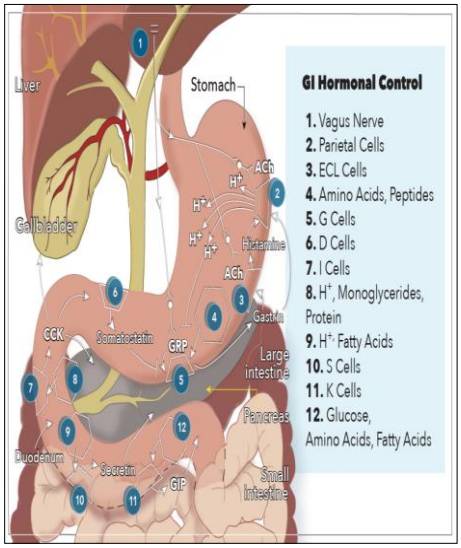


**Fig. 1b. Schematic showing sites of GI hormones**

*Source:https://www.ncbi.nlm.nih.gov/books/NBK537284/ Humphries] - StatPearls - NCBI Bookshelf (nih.gov)*

The gastrointestinal tract is the region or the pathway of the digestive system that spans from the buccal cavity to the anal region. The human GI tract consists of the esophagus, stomach, intestines, and upper & lower tract. The GIT is further divided embryologically into foregut, midgut, and hindgut. In addition, the whole digestive system comprises the gastrointestinal tract and the accessory organs of digestion ( Salivary glands, tongue, liver, gallbladder and pancreas). The GI tract is nine meters (30 feet) at autopsy and shorter in the living body because the intestines are lined by smooth muscles that constantly maintain muscle contraction and relaxation in a peristaltic process [1,2]

In the GIT, the peristalsis process pushes food through the tract, then mixes the contents within each organ. Food is moved forward by the muscle behind during contraction and relaxes to allow the food to move with the help of the muscle distal to the food. Mixing of the food from the stomach with digestive secretion from the liver and pancreas is done in the duodenum. Most digestion and absorption occur in the jejunum. The most extended segment is the final segment called the ileum, and at the ileocecal junction, the content in the ileum is emptied into the caecum [1]. Nutrients digestion and absorption mostly happen in the small intestine. The accumulation of unabsorbed materials forming feces takes place in the large intestine. It also aids some digestion by bacteria responsible for forming intestinal gas. Water, Salts, vitamins, sugar, and water are absorbed in the large intestine.

The mode of delivery of substances to their target cells determines the classification of GI hormones as endocrine, paracrine, and neurocrine. Endocrine hormones are directly secreted by the enteroendocrine cells into the bloodstream via the portal system into the systemic circulation and delivered to the hormone-sensitive receptor target cells. Five GI hormones referred to as endocrine GI hormones are; cholecystokinin (CCK), gastrin, motilin, glucose-dependent insulinotropic peptide (GIP), and secretin. In the extracellular space, the paracrine hormones secreted from enteroendocrine cells diffuse and act locally on the target space but do not enter systemic circulation, e.g., somatostatin and histamine. Peptide YY, glucagon-like peptide-1 (GLP-1), and pancreatic polypeptide are a few hormones that act via the endocrine and pancreatic mechanisms. In the enteric nervous system, the postganglionic non-cholinergic neurons secrete neurocrine hormones. It is noteworthy that neurocrine hormones with physiologic functions in the gut are enkephalins, gastrin release peptides (VIP), and vasoactive intestinal peptides (VIP).

## 2. OVERVIEW OF THE ANATOMY AND PHYSIOLOGY

The main sites of hormone synthesis and secretion are in the stomach and intestines.

There is no secretion of exocrine hormones by the mouth, pharynx, esophagus, rectum, and anus.

**Stomach:** The GI tract is the most dilated part, having a capacity of 1000-1500ml in the adult. It is located at the L1-L2 vertebrae at the upper left side of the abdomen, inferior to the diaphragm. It functions to store masses of food and secretes hydrochloric acid, mucus, and digestive enzymes required to break down and digest the food [2].

**GHRELIN:** This hormone is produced when hungry in the stomach. It stimulates feeding by acting on the hypothalamus. Pyy 3-36 and leptin(from fat cells) counteract this action [3].

**Gastrin Releasing Peptide:** It is produced by the G cells in the stomach antrum and duodenum with its genetic location on chromosome 17. The stimuli for its release are protein (phenylalanine, tryptophan) and stomach distention (from eating). It functions to stimulate gastrin release in the stomach [2,3].

**Gastrin:** It is a peptide (linear) synthesized as a preprohormone. It is post-translationally cleaved to form a family of peptides with identical carboxyterminal. Receptors are found on parietal cells and enterochromaffin-like cells (ECL). Recent evidence suggests that the most crucial target of gastrin in regulating acid secretion may be ECL [3,4].

Gastrin release is primarily stimulated by vagal and gastrin-releasing peptides (GRP). Amino acid gastric distention, an elevated stomach pH, and ingestion of peptides act as secondary stimulants. Conversely, decreased stomach pH and somatostatin inhibition of paracrine lead to decreased gastrin release [2,5,6].

The main functions of gastrin are enhancing Gastric motility, hydrochloric acid stomach secretion, and gastric mucosal growth enhancement is gastrin's primary role [6].

**Urogastrone:** The stomach secretes urogastrone to reduce gastric acid secretion and increase oxyntic gland growth. Its stimulus is not yet known [3,7].

**Bombesin:** Bombesin is homologous to the gastrin-releasing peptide (G cells). Mediated by gastrin in the antrum, it functions to regulate GIT hormone release [3,7].

**Intestine:** It composes of the small and large intestines. These are also divided into regions known as the duodenum, jejunum, ileum, cecum, and colons.

**Cholecystokinin (CCK):** CCK is a peptide hormone in the same family as gastrin hormones with a similar structure, sharing the same 5 C-terminal amino acids. This hormone is found on chromosome 3. The I-cell of the duodenum and jejunum produces it. In the CNS, it plays essential physiological roles as a neuropeptide and, in the gut, a peptide hormone. The proximal small intestine has a concentrated amount of I-cells, and upon digestion, it secretes CCK into the blood. Induction of satiety, regulating gastric emptying, pancreatic secretions, and stimulating gallbladder contraction are some of CCK's physiological actions [3,8-10].

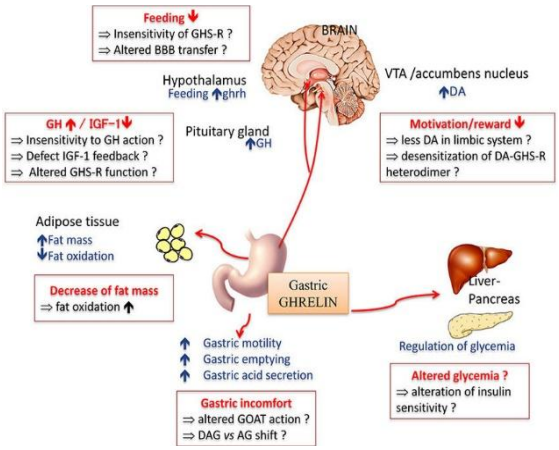


**Fig. 1c. Schematic showing the activities of GHRELIN**

*Source:https://www.researchgate.net/figure/Main-physiological-effects-of-the-orexigenic-hormone-ghrelin-In-anorexia-nervosa-some_fig8_304622614*

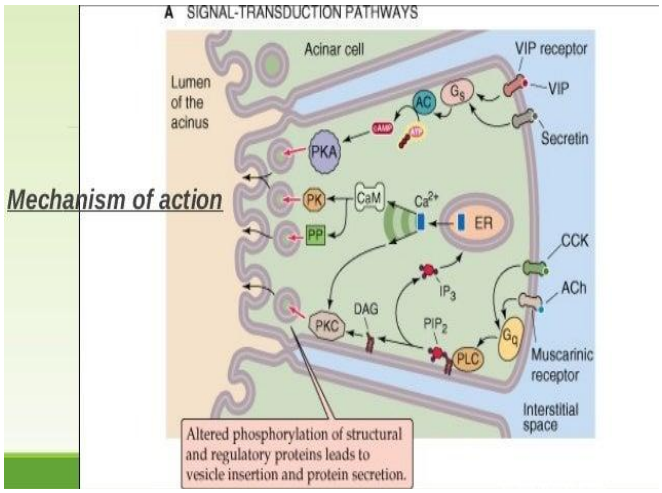


**Fig. 2. Signal transduction pathways of CCK**

*Source: https://image.slidesharecdn.com/min-metabolism-140901135656-phpapp02/95/git-hormones-25-638.jpg?cb=1409579900*

**Secretin:** It is synthesized as pro-secretin, a 120 amino acid precursor protein containing an N-terminal signal peptide, spacer, secretin (residues 28–54), and a 72-amino acid C-terminal peptide by the S cells of the duodenum and in smaller numbers by the jejunum. It is mainly stimulated in response to the arrival of gastric contents that decrease the duodenal pH to a range between 2 to 4.5. Secretin increases bicarbonate and pancreatic fluid secretion to neutralize the acid. It may also function to increase hepatic bile secretion [11].

**Serotonin:** Serotonin is a monoamine neurotransmitter. Peripheral serotonin is produced in all regions of the GIT by enterochromaffin (EC) cells which produce about 90% of the total body serotonin. Stimulate the production of gastric and colonic mucus and gastric acid secretion inhibition [3,12].

**Motilin:** It is a peptide with 22-amino-acid, synthesized in the duodenal and jejunal mucosae endocrine cells (Mo cells). Enter-endocrine cells (Mo cells) in the upper small intestine release motilin during the fasting state. Gastric and small intestine motility is stimulated by motilin, helping undigested food in these regions to move into the large intestine [3,13]. They are the reason for "growling" sounds in the stomach.

**Neurotensin:** Neurotensin is synthesized and released by the jejunum and ileum N-cells. It is stimulated by the presence of fats and gastrin-releasing peptides. Its principal function is stimulating pancreatic and biliary secretions while suppressing the small intestine's motility [3,14].

**Peptide-YY:** L cells in the distal portion of the small intestine on chromosome 17 produce this hormone. It exists as a 36-chain amino acid. The presence of fats and protein stimulates it. It inhibits acid and pepsin secretion from the stomach and the exocrine function of the pancreas [3].

**Gastrin Inhibiting Hormone (GIH):** The K cells of the duodenum and the upper jejunum produce this hormone. It is located on chromosome 17. Its stimuli include glucose, amino acids, and fatty acids. It inhibits the secretion of gastric acid and stimulates insulin secretion [3,15].

**Glucagon-Like Peptide (GIP):** L cells in the small intestine and colon and partly by the rectum secrete GIP. Its stimuli include glucose and fats. It inhibits gastric motility and encourages insulin release [3,7].

**Vasoactive intestinal peptide:** Enteric nerves commonly produce it. This hormone is located on chromosome 6. The pattern of stimulation for this hormone is not yet known. It helps to relax the lower esophageal sphincter and fundus of the stomach. It also stimulates biliary and pancreatic secretions [16,17].

**Bulbogastrone:** It is a candidate hormone secreted in the duodenum. It reduces gastric acid secretion and is stimulated by gastrin [5,7].

**Table 1. Summary of GIT hormones**

| Hormone | Source | Target | Action |
|---|---|---|---|
| Cholecystokinin | I cells in duodenum and jejunum and neurons in ileum and colon | Pancreas<br>Galbladder | ↑ Enzyme secretion<br>↑ Contraction |
| Gastric inhibitory peptide | K cells in duodenum and cjunum | Pancreas | Exocrine: ↓ fluid absorption<br>Endocrine: ↑ T insulin release |
| Gastrin | G cells, antrum of stomach | Parietal cells in body of stomach | ↑ $H^+$ Section |
| Gastrin-releasing peptide | Vagal nerve endings | G cells in antrum of stomach | ↑ Gastrin release |
| Guanylin | ileum and colon | Small and large intestine | ↑ Fluid absorption |
| Motilin | Endocrine cells in upper GI tract | Esophageal sphincter Stomach Duodenum | ↑ Smooth musde contraction |
| Neurotensin | Endocrine cells widespread in GI tract | Intestinal smooth musde | Vasoactive stimulation of histamine release |
| Peptide YY | Endocrine cells in ileum and colon | stomach<br>Pancreas | ↓ Vagally mediated acid secretion<br>↓ Enzyme and fluid secretion |
| Secretin | S cell in small intestine | Pancreas<br>stomach | ↑ $HCO_3$ and fluid secretion by pancreatic ducts<br>↓ Gastric acid secretion |
| Somatostatin | D cells of stomach and duodenum, & cells of pancreatic islets | stomach<br>Intestine<br><br><br>Pancreas<br><br>Liver | ↓ Gastrin release<br>↑ Flusid. absorption secretion<br>↑ Smooth musde contraction<br>↓ Endocrine/exdonne secretions<br>↓ Bile flow |
| Substance P<br>VIP | Entenc neurons<br>ENS neurons | Entenc neurons<br>Small intestine<br><br><br>Pancreas | Neurotransmitter<br>↓ Smooth musde relaxation<br>↑ Secretion by small intestine<br>↑ Secretion by pancreas |

*Source:https://doctorlib.info/physiology/medical-physiology-molecular/medical-physiologymolecular.files/image1030.jpg*

## 3. PATHOPHYSIOLOGY

### 3.1 Gastrin

#### 3.1.1 Hypersecretion of gastrin

**Zollinger-Ellison Syndrome (ZES):** Hypersecretion of Gastrin usually occurs in disorder known as ZES (Gastrinoma). Relatively rare syndrome associated with peptic ulcers caused by a gastrin-secreting neuroendocrine tumor or multiple tumors (Gastrinoma) of the pancreas or duodenum. Gastrin secretion increase causes excessive gastric acid secretion, leading to gastric and duodenal ulcers with abdominal pain, gastroesophageal reflux, and diarrhea [4,12].

The incidence of gastrinoma is 0.5-2 per million annually. Patients in this category are diagnosed between 20 and 50 years. There is lower incidence in females. Approximately 80% of gastrinomas are sporadic, but 20-30% occur associated with Multiple Endocrine Neoplasia type 1 (MEN1). Duodenal gastrinomas occur in about 50% - 88% of patients with sporadic (ZES) and 70% - 100% of patients with ZES associated with MEN1. Duodenal gastrinomas are predominantly found in the first part of the duodenum. Compared with pancreatic gastrinomas, duodenal gastrinomas are usually small (<1 cm), are often multiple, and have a low metastasize change to the liver at diagnosis (0 to 10 versus 22 to 35%). Gastrinomas arise in non-pancreatic in about 5-15% of patients, duodenal

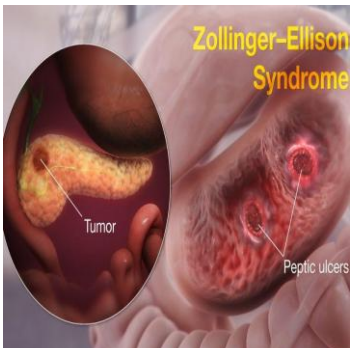


**Fig. 3. Zollinger-Ellison Syndrome [Source]**

non-abdominal (stomach, peripancreatic lymph nodes, liver, bile duct, ovary), and extra-abdominal (heart, small cell lung cancer) locations [18,19]. Manifestations of ZE syndrome are ulcers refractory to standard treatment, multiple ulcers, giant ulcers greater than 2 cm in size, recurrent ulcers symptomatology, ulcers with unexplained diarrhea, positive family history of ulcers, hypercalcemic symptoms and signs and duodenal ulcer that is unrelated to *H.pylori* infection or nonsteroidal anti-inflammatory drug(NSAIDs) usage.

**Helicobacter pylori infection:** This is a gram-negative bacteria that can colonize the stomach and cause ulcers. Some people with an H. Pylori infection may also have high stomach acid [4,20].

**Gastric outlet obstruction:** In any medical condition, stomach acid secretion will increase in folds when the path leading from the stomach to the small intestine is blocked or in cases of intestinal resection, blockage, or a short bowel syndrome [4,21-23].

Investigative procedures that may be helpful are blood tests(complete blood count, Fasting gastrin test, and secretin stimulation test in ZES, Imaging study, and endoscopy (scintigraphy, MRI, and CT scan) to locate and determine the size of gastrinoma.
Hypersecretion is usually managed by injecting drugs into the tumor to relieve cancer symptoms and chemotherapy to reduce tumor growth. A triple therapy regimen for eradication of H.Pylori, comprising a proton pump inhibitor and two antibacterial, and sometimes surgery may be recommended, such as removing gastrinomas in people with Zollinger-Ellison syndrome [4].

**Hyposecretion of Gastrin:** Gastrin levels are rarely low, but when they occur, the condition can increase the risk of infection in the digestive system and interfere with the functions of the stomach. [14,20].

## 3.2 Somatostatin

**Hypersecretion of Somatostatin:** Hormones simultaneously produced by somatostatin are insulin, gastrin, glucagon, VIP, corticotropin, calcitonin, and pancreatic polypeptide. An autosomal dominant disorder, neurofibromatosis is characterized by abnormalities of growth and differentiation of the nervous system, which may be associated with duodenal somatostatinomas. 93% of Somatostatinoma cases occur randomly, and 7% of cases are seen with multiple endocrine neoplasia type 1 (MEN 1) syndromes. Pancreatic, parathyroid, and pituitary neoplasms are involved in MEN1. The duodenal form of somatostatinomas is associated with pheochromocytoma and neurofibromatosis. Risk factors can also include Von Hippel-Lindau disease and tuberous sclerosis. [13,19,20].

Somatostatinoma may present with pain in the abdomen (most common symptom), diabetes, unexplained weight loss, gallstones, steatorrhea or fatty stools, bowel obstruction, diarrhea, Jaundice, or yellowing skin.

Investigative measures that can be useful are endoscopic ultrasound, CT scan, Octreoscan (a radioactive scan using $^{111}$Indium isotope), and MRI. Management of somatostatinoma involves surgical procedures and antineoplastic agents.

## 3.3 Cholecystokinin (CCK)

**Hypersecretion of CCK:** The higher the CCK level, the higher the effectiveness of quick gastric emptying occurring. The increased excitatory effect of uprisen CCK on the small and large

intestine leads to bowel movement and improves the pyloric sphincter's tension. Increased anxiety and panic attacks have been associated with cholecystokinin [9].

CCK is a known trophic factor in the growth of pancreatic cells. Pancreatic tumors proliferation can be accentuated by CCK. Recent studies have shown that CCK enhances the induction of pancreatic carcinogenesis and has growth-promoting actions cancers, especially pancreatic carcinomas [24,25]

**Hyposecretion of CCK:** Reduced feelings of fullness and difficulty in losing weight in very obese people may be due to a low level of CCK.

Obesity dampens the effect of CCK, which means vagal afferent neurons are insensitive to CCK. Reduced effect on satiety and a lot of obese people mostly complain about feeling hungry is due to reduced expression of CCK. Diminished expression of the CCK-1 receptor with high-fat diet consumption increases ghrelin plasma levels. Due to this, food intake increases by dampening satiety peptide cocaine and amphetamine-regulated transcript's (CART) expression in vagal afferent neurons. It takes part in metabolic regulation and lipid absorption [7,21]. To reduce weight gain, the inactivation of the signaling pathway of CCK is linked. Inactivation increases energy expenditure and lowers energy extraction [21].

## 3.4 Secretin

**Hypersecretion of Secretin:** Pancreatic secretion is controlled by hormonal and neural mechanisms. CCK and secretin collectively play an essential role in its regulation. The acid in the duodenum leads to secretin secretion, causing duct cells to release water and bicarbonate. The release of pancreatic enzymes is stimulated by acinar cells, and CCK's secretion is stimulated by the presence of fat and protein in the small intestine. Excess secretin has adverse effects of nausea, abdominal pain, flushing, and vomiting in 5% of patients. In secretin administration, acute pancreatitis is a contraindication [16].

A common cause of hypersecretion is Exocrine Pancreatic Insufficiency (EPI). EPI is not usually recorded because it has multiple possible causes; its prevalence and demographics cannot be established with certainty. According to a German study, an age-adjusted prevalence of 8 per 100,000 for males and 2 per 100,000 for women is the most common cause of EPI; EPI prevalence in most developed countries is closely related to these numbers. No other reliable data are currently available.
Clinical manifestations include steatorrhea, weight loss, flatulence, and abdominal pain.

**Hyposecretion of Secretin:** Untreated adult celiac disease or achlorhydria has been found in patients with blood secretin levels below normal (hyposecretinemia). Exogenous duodenal acidification or after a mixed meal has failed to increase the secretin concentration in patients with celiac disease. In contrast, patients with achlorhydria have reduced secretin levels after a mixed meal. However, the response to duodenal acidification remains normal [20].

## 3.5 Gastric Inhibiting Hormone (GIH or GIP)

**Hypersecretion of GIH:** GIP's hyposecretion or hypersecretion is less associated with these diseases' pathogenesis, but its secretion is altered in these diseases.

**Type 2 Diabetes Mellites:** Pathological glucose intolerance has an abnormal incretin effect. In a dose-dependent incretin response to oral glucose demonstration, low GIP level was noted in type-2 diabetes mellitus patients or GIP beta-cell resistance compared to healthy individuals. Incretins contribute post meals,70% of insulin response. This reduced effect of incretin is responsible for glucose intolerance in diabetics [15].

**Obesity:** Obesity and lipid metabolism is GIP's vital role. In GIP secretion, fat is a significant stimulant, and in obesity, K-cell hyperplasia and elevated GIP levels are observed. Inhibition of lipolysis and stimulation of lipogenesis is done by GIP(anabolic hormone) [15,20].

**Food-Induced Cushing Syndrome:** Food-induced Cushing syndrome or ACTH-independent macronodular adrenal hyperplasia (AIMAH) can be caused by cortisol hypersecretion after mixed meals, as GIP acts like ACTH. The adrenal cortex (the zona fasciculata) contains GIP-receptors. GIP concentration increases in the blood following a meal, which causes an increase in cortisol even in the presence of low ACTH. Somatostatin analog (octreotide) is used in the treatment of AIMAH [15].

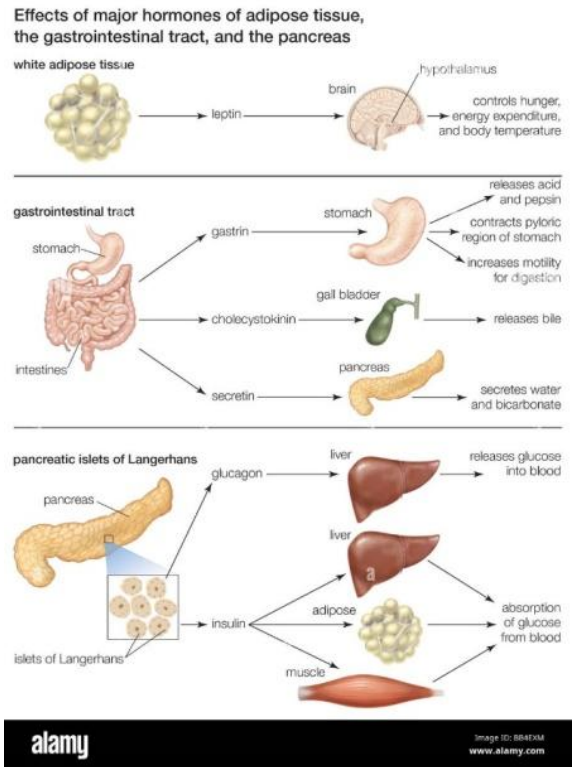


**Fig. 4. Schematic showing the relationship between adipose tissues and major hormones**
*Source:https://c8.alamy.com/comp/BB4EXM/the-major-hormones-of-adipose-tissue-the-gastrointestinal-tract-and-BB4EXM.jpg*

## 4. ASSOCIATED DISEASES

**Celiac's Disease:** The failure of GIP and secretin release in patients with untreated coeliac disease. These hormones are localized to the area of maximum mucosal damage [20]. Pancreatic hormones diminished response to intraduodenal stimuli has been reported to be due to failure of CCK release [10].

Blood motilin level rises a little above average in steatorrhea, whereas enterglucagon level is significantly raised. The other GI hormones are not significantly affected.

**Tropical Sprue (Malabsorption):** In an observational study of 8 patients with severe tropical sprue, there is a significant decrease in GIP and insulin release. Tropical sprue is associated with a delayed and impaired blood glucose elevation. In contrast, however, plasma motilin and enteroglucan levels are significantly elevated, with the latter rising a little further after a test breakfast. The pattern of hormonal changes differs from coeliac disease, reflecting the different pathophysiological processes and the greater gut area involved in tropical malabsorption. Neurotensin, pancreatic polypeptide and gastrin responses are similar [15,25].

**Crohn's Disease:** Fourteen patients with Crohn's disease were part of an experimental study. After the test breakfast, there was an increase in the release of the upper small intestinal hormone GIP. Despite augmented pancreatic polypeptide response, the most significant response showed by motilin. In Crohn's disease patients, the level of plasma enteroglucagon when fasting and after-meal response are more significant than usual but lower in magnitude than in coeliac disease [20].

**Ulcerative Colitis:** After breakfast, there was a normal GIP response in 24 ulcerative colitis patients and high basal plasma motilin levels. An adjusted gastrin response might be secondary to hypochlorhydria or possibly due to loss of some colonic gastric inhibitory substance secondary to the pathological damage. Enteroglucagon and pancreatic polypeptide showed a moderately raised response in Crohn's disease [20].

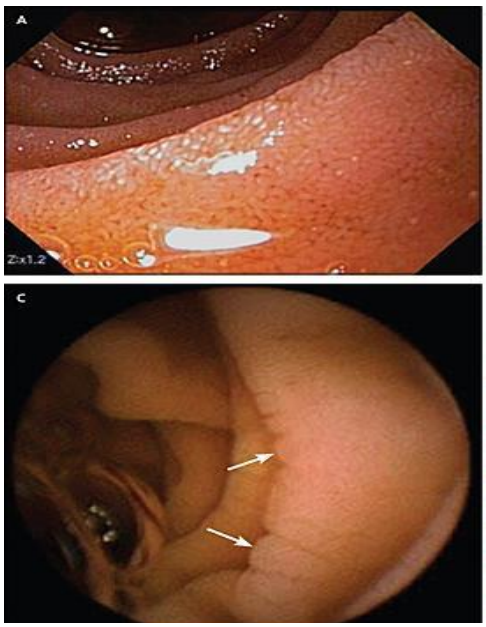

**Fig. 5. Gross & Histological appearance of Celiac Disease [Source]**

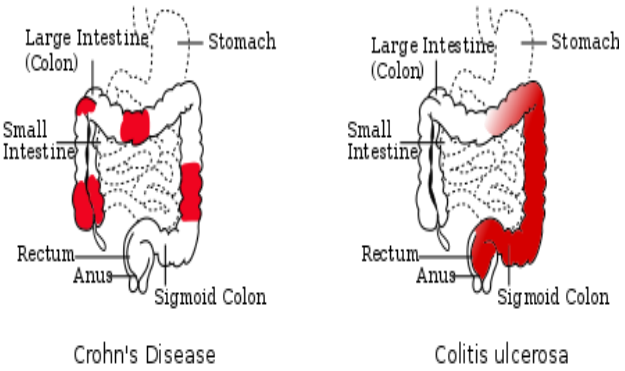


**Fig. 6. Side-by-side comparison of Crohn's Disease and Ulcerative Colitis [Source]**

**Infective Diarrhea:** The responses of pancreatic polypeptide and GIP are normal. In contrast, gastrin, motilin, and enteroglucagon have augmented responses. Compensatory mechanisms occurring in the gut to diarrhea may be related, as diarrhea abates, basal blood motilin levels fall in parallel [26].

**Pancreatic Insufficiency:** In another study, compared to the reduced secretion in coeliac disease and acute tropical sprue, the GIP secretion was normal in the patients. Mucosal damage is responsible for malabsorption. The gastrin response was low, but the motilin and enteroglucagon responses raised. However, the increased enteroglucagon release was much less than that associated with the atrophic small intestinal mucosa, whereas it is higher in pancreatic insufficiency.

The failure of pancreatic polypeptide release following the test breakfast is a major finding in patients with pancreatic insufficiency [26]. This probably reflects the extensive damage to pancreatic tissue as the pancreatic polypeptide cells are scattered throughout the pancreatic parenchyma.

**Intestinal Resection:** The site and the length of the intestines surgically resected determines the effects on the hormones. The loss of absorptive area can lead to severe malabsorption, even when only a short length of distal ileum has been resected (for example, failure of vitamin B12 and bile salt absorption).There is villous hypertrophy of the mucosa epithelium in segmental small intestine resection [21]. A humoral agent probably stimulates this compensatory mechanism, possibly enteroglucagon. Patients

studied have undergone varying degrees of gut resection for several different pathological states [20]. Crohn's disease is the primary reason for the patient's surgery, in which one and two meters of terminal ileum are resected. In Crohn's disease and ulcerative colitis, partial resection of the ascending or transverse colon or both can be done. Neoplasia, trauma, and post-radiation fibrosis are other indications for bowel resection.
Partial ileal and colonic resection effects on gastrin secretion are not significant, same as pancreatic polypeptide, GIP, and neurotensin responses. Gastrin and pancreatic polypeptide post-breakfast release are higher than normal in both groups of patients. Elevated gastrin levels after intestinal resection have been reported [22,23]. The GIP and neurotensin responses, in contrast, were similar to normal in these patients. There was, however, difference in the responses of motilin and enteroglucagon between the two groups. The group of patients with partial colon resection had only mildly raised motilin responses and a somewhat decreased enteroglucagon level. Those with partial resection of the ileum had a greatly augmented motilin response and a substantially increased release of enteroglucagon [21,22].

**Irritable Bowel Syndrome (IBS):** This common diagnosis excludes demonstrable organic disease and is usually considered a 'functional' disorder. An intestinal motility abnormality has been described [14], and the release of gut hormones being postulated as a possible etiological factor [17].

In a study of forty -two patients with IBS, confirmed with thorough investigations and no organic disease found. Nineteen had abdominal pain and increased bowel frequency, Eleven had constipation and abdominal pain, and twelve of them had normal bowel function and abdominal pain. In contrast to all other disease groups studied, these patients had entirely normal responses to the measured gut hormones [9,14,17].

**Gastric (Peptic) Ulcers:** Enhanced HCl (acid) secretion resulting from increased parietal cell stimulation (Gastrin in gastremia), decreased PGE2 secretion resulting in; a. Increased HCl secretion b. Decreased mucus production (such as aspirin-induced) results in HCl's epithelial-cell damage and enhanced vagal activity (cholinergic stimulation and enhanced histamine secretion) [4,18].

**Gastric-Related Peptide (GRP) and Cancer:** This is a homolog of bombesin (BBS). BBS peptides have a broad spectrum of biological effects on the GIT, pancreatic cells and CNS. In addition to their actions as neurotransmitters in CNS, these peptides stimulate the contraction of smooth muscle in the GIT and the release of various GI hormones like Gastrin, somatostatin, CCK, pancreatic polypeptide, insulin, enteroglucagon, pancreatic glucagon, and GIP as well as the pancreatic exocrine hormones. [8,12].

Several studies have shown that BBS can be a growth factor in colon cancer cells in recent years. GRP receptor mRNAs are known to be present in gastric cancer cell lines. Hence, in general, the effect of these peptides in GI cancer is stimulatory. However, they may also repress the growth of some specific cell types [14,27].

## 5. CONCLUSION

Naturally, most medical students and health workers assume the GIT does not have a primary endocrine function. As a result, primary endocrine dysfunctions are not usually associated with the GIT. The GIT is one of the body's largest reservoirs of endocrine hormones, with the least understood physiological function of most hormones. The function of the GIT is inherently known to break down food, process them mechanically and biochemically with the assistance of non-GIT endocrine hormones and create absorptive surfaces for functional nutrients [13]. The alimentary canals produce hormones, and any form of derangement can lead to myriads of manifestations ranging from mild subtle to severe life-threatening manifestations.

There is a broad range of etiology of GI hormonal imbalances, leading to hypo or hypersecretion of hormones by the intestines, mainly in the stomach, duodenum, and jejunum. However, these hormones can also fluctuate throughout life as we grow older or with changes like obesity and conditions such as infection, metabolic, postsurgical, immunological, or genetic diseases and cancers.

GIT response to meals in the lumen is critical to understanding the metabolic effects of functional foods and their relationship to the hormones secreted, with each hormone having specific effects on digestive functions. Changes in plasma hormone concentrations after a meal related to changes in digestive function

encourage a natural correlation. Therefore, it is necessary to relate changes in endogenous hormone concentrations to digestive function.

Assessing digestive function in groups with altered circulating concentrations of gastrointestinal hormones would be valuable. The elevated plasma concentrations of these hormones in patients with gastrointestinal cause poor digestive function, which results in poor nutritional status [13]. These hormones are established to have metabolic effects beyond the GIT. Gastrointestinal endocrinology is beginning to reveal the complexity of hormonal involvement in indigestion [13]. More research work needs to be done.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

## REFERENCES


1. Parikh A, Thevenin C. Physiology, gastrointestinal hormonal control. StatPearls [Internet]. 2021 May 9; 2022.
2. Daniels IR, Allum WH. The anatomy and physiology of the stomach. Upper gastrointestinal surgery. Springer specialist surgery series. In: London: Springer [article]; 2005.
3. Wittert GA, Fraser R, Morley JE. The endocrine system of the gastrointestinal tract. In: Conn PM, Melmed S, editors. Endocrinology. Totowa, NJ: Humana Press [article]; 1997.
4. Seladi-Schulman J. High stomach acid symptoms: side effects, causes & treatment. Healthline, Healthline Media; May 11; 2020 [article].
5. Rao JN, Wang JY. Regulation of gastrointestinal mucosal growth. San Rafael, (CA): Morgan & Claypool Life Sciences; 2010. Role of GI Hormones on Gut Mucosal Growth [article].
6. Gastrin. Pathophysiology of the Endocrine System. Colorado State University [article].
7. Kim ND. “Chapter 7 Gastrointestinal Hormones.” [Article].
8. Rehfeld JF. Cholecystokinin and the hormone concept. Endocr Connect. March 2021;10(3):R139-50 [article]. DOI: 10.1530/EC-21-0025, PMID 33640870.
9. Bradwejn J, Koszycki D. Cholecystokinin and panic disorder: Past and future clinical research strategies. Scand J Clin Lab Invest Suppl. 2001;234:19-27 [article], PMID 11713976.
10. DiMagno EP, Go WL, Summerskill WHJ. Impaired cholecystokinin-pancreozymins secretion, intraluminal dilution, and maldigestion of fat in sprue. Gastroenterology. 1972;63(1):25-32. DOI: 10.1016/S0016-5085(19)33344-X, PMID 5055745.
11. Afroze S, Meng F, Jensen K, McDaniel K, Rahal K, Onori P et al. The physiological roles of secretin and its receptor. Ann Transl Med. 2013;1(3):29. DOI: 10.3978/j.issn.2305-5839.2012.12.01, PMID 25332973.
12. Track NS. The gastrointestinal endocrine system. Can Med Assoc J. 1980;122(3):287-92. PMID 6989456.
13. Schneeman BO. Gastrointestinal physiology and functions. Br J Nutr. 2002;88(S2);Suppl 2:S159-63. DOI: 10.1079/BJN2002681, PMID 12495458.
14. Misiewicz JJ. Muscular disorders of the colon. Br J Hosp Med. 1974;11:191-202.
15. Gupta K, Raja A. Physiology, gastric inhibitory peptide. StatPearls [Internet]. In: Treasure Island, (FL): StatPearls Publishing; Updated 2021 September. 2022;28. [article].
16. Samer Al-Kaade MD. Exocrine pancreatic insufficiency. Practice Essentials, Anatomy, Pathophysiology, Medscape; August 12; 2021 [article]. Harvey RF. The irritable bowel syndrome; hormonal influences. Clin Gastroenterol. 1977;6(3):631-41. DOI: 10.1016/S0300-5089(21)00180-2, PMID 923141.
17. Bergsland E. Zollinger-Ellison syndrome (gastrinoma): Clinical manifestations and diagnosis Feldman M, Grover S, UpToDate, editors; November 30, 2021 [article].
18. Schneeman BO. Gastrointestinal physiology and functions. Br J Nutr. 2002;88(S2);Suppl 2:S159-63.

DOI:10.1079/BJN2002681, PMID 12495458.

19. Besterman HS. Gut hormones in gastrointestinal disease journal of clinical pathology. 1978;8:76-84 (Ass. Clin. Path.).
20. Porus RL. Epithelial hyperplasia following massive small bowel resection in man. Gastroenterology. 1965;48:753-7.
DOI:10.1016/S0016-5085(65)80064-6, PMID 14300172.
21. Osborne MP, Frederick PL, Sizer JS, Blair D, Cole P, Thum W. Mechanism of gastric hypersecretion following massive intestinal resection: clinical and experimental observations. Ann Surg. 1966;164(4):622-34.
DOI:10.1097/00000658-196610000-00009, PMID 5924784.
22. Straus E, Gerson CD, Yalow RS. Hypersecretion of gastrin is associated with short bowel syndrome. Gastroenterology. 1974;66(2):175-80.
DOI: 10.1016/S0016-5085(74)80100-9, PMID 4810910.
23. Marx M, Gomez G, Lonovics J, Thompson JC. Cholecystokinin. In: Thompson JC, Greeley Jr GH, Rayford PL, Townsend CM Jr, editors Gastrointestinal endocrinology. New York: McGraw-Hill. 1987;213-22.
24. Axelson J, Ihse I, Håkanson R. Pancreatic cancer: the role of cholecystokinin? Scand J Gastroenterol. 1992;27(12):993-8.
DOI: 10.3109/00365529209028128, PMID 1475628.
25. Adrian TE, Besterman HS, Mallinson CN, Garalotis C, Bloom SR. Impaired pancreatic polypeptide release in chronic pancreatitis with steatorrhea. Gut. 1979;20(2):98-101.
DOI: 10.1136/gut.20.2.98, PMID 428832.
26. Rehfeld JF, van Solinge WW. The tumor biology of gastrin and cholecystokinin. Adv Cancer Res. 1994;63:295-347.
DOI:10.1016/s0065-230x(08)60403-0, PMID 8036989.
27. Samer Al-Kaade MD. Exocrine pancreatic insufficiency. Practice Essentials, Anatomy, Pathophysiology, Medscape; August 12; 2021 [article].



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