CONCEPTUALIZATION OF ENDOCRINE FUNCTION OF THE GASTROINTESTINAL TRACT

ABSTRACT:

The endocrine and gastrointestinal systems (GIT) are integrated into a well-coordinated complex to meet the body's metabolic needs. 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 examples of 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, Crohn's disease, Zollinger-Ellison Syndrome, 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.

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.

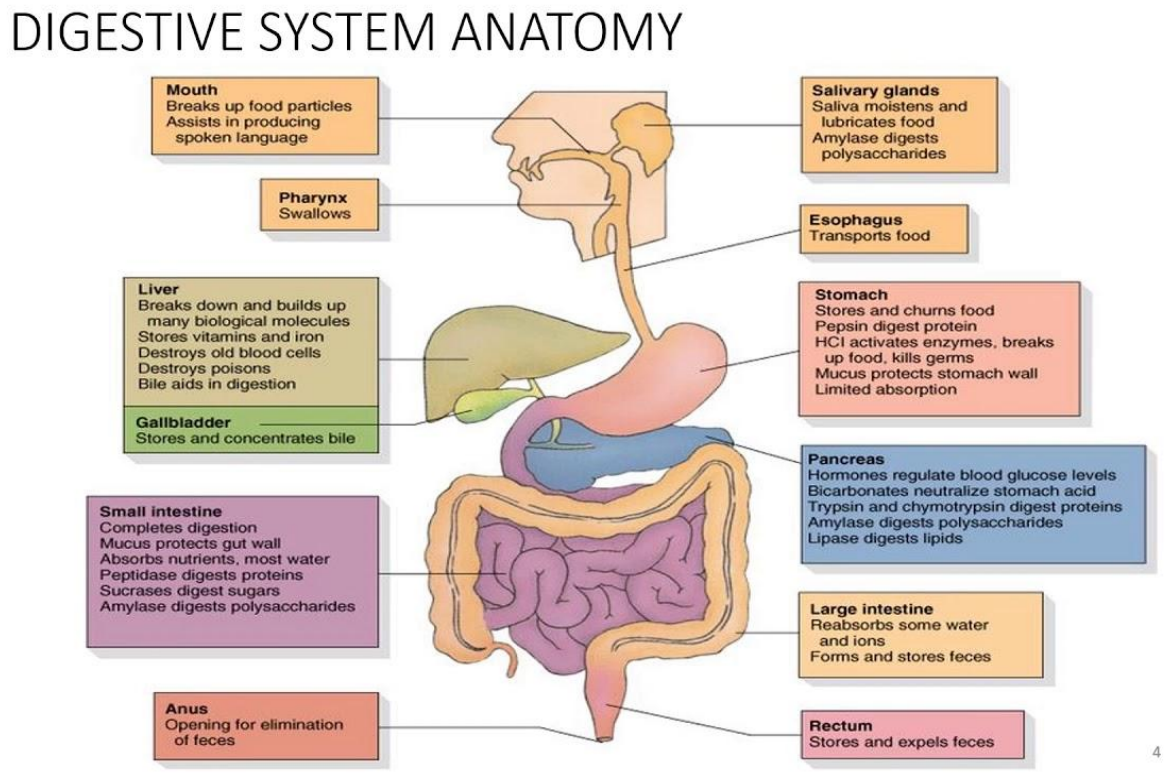

Fig 1a: The schematic of GIT and functions.

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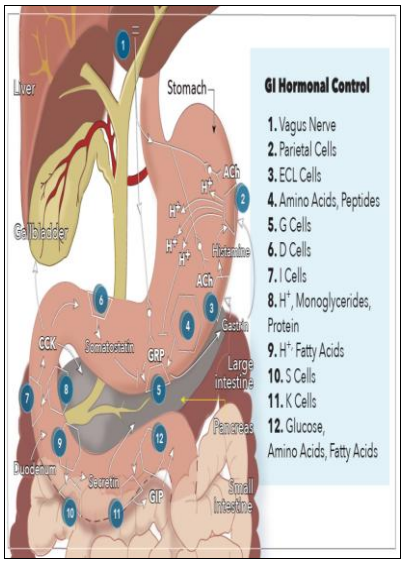

Fig 1b: Schematic showing sites of GI hormones.
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The gastrointestinal tract or the alimentary canal is the region or the pathway of the digestive system that spans from the mouth to the anus. The human GI tract consists of the esophagus, stomach, intestines, and upper & lower tract. The tract may also be divided into foregut, midgut, and hindgut, indicating their embryological origin. In addition, the complete human digestive system comprises the gastrointestinal tract and the accessory organs of digestion(the tongue, salivary glands, pancreas, liver, and gallbladder). The human GI tract is about nine meters (30 feet) long at autopsy. It is considerably shorter in the living body because the intestines are tubes lined by smooth muscles that maintain constant muscle contraction and relaxation in a peristaltic process.[1][2]

Peristalsis pushes solid and liquid food through the GI tract and then mixes the contents within each organ. The muscle behind the food contracts squeezes the food forward, and relaxes to allow the food to move with the help of the muscle in front of the food. The duodenum serves a mixing function as it combines digestive secretions from the pancreas and liver with the contents expelled from the stomach. The start of the jejunum is marked by a sharp bend, the duodenojejunal flexure. Most digestion and absorption occur in the jejunum. The final portion, the ileum, is the most extended segment and empties into the caecum at the ileocecal junction. [1]The small intestine performs most of the digestion and absorption of nutrients. 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. The absorption of water, salts, sugar, and vitamins also occurs in the large intestine. [1][2]

The mode of delivery of substances to their target cells determines the classification of GI hormones as endocrine, paracrine, and neurocrine. Enteroendocrine cells secrete endocrine hormone directly into the bloodstream, passing from the portal to the systemic circulation, before being delivered to target cells with receptor-specificity for the hormone. The five GI hormones that qualify as endocrines hormones are gastrin, cholecystokinin (CCK), secretin, glucose-dependent insulinotropic peptide (GIP), and motilin. Enteroendocrine cells also secrete paracrine hormones, but they diffuse through the extracellular space to act locally on target tissues and not enter the systemic circulation. Two examples of paracrine hormones are somatostatin and histamine. Additionally, some hormones may operate via endocrine and paracrine mechanisms. These "candidate" hormones are glucagon-like peptide-1 (GLP-1), pancreatic polypeptide, and peptide YY. Lastly, neurocrine hormones get secreted by postganglionic non-cholinergic neurons of the enteric nervous system. Three neurocrine hormones with significant physiologic functions in the gut are vasoactive intestinal peptide (VIP), gastrin release peptide (GRP), and enkephalins. [1]

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 is produced by the stomach, especially when one is hungry. It acts on the hypothalamus to stimulate feeding. This action counteracts the inhibition of feeding by leptin and Pyy 3-36. [3]

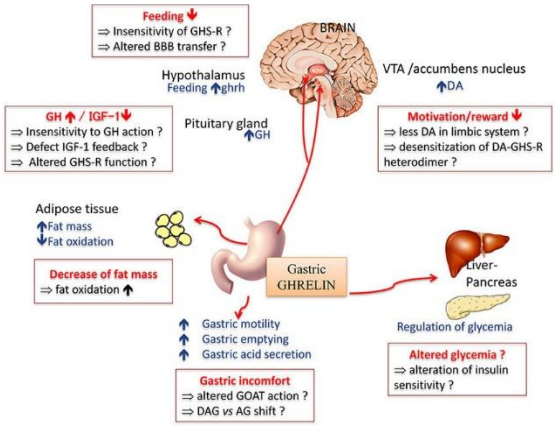

Fig1c: Schematic showing the activities of GHRELIN.

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

Gastrin Releasing Peptide

It is produced by the G cells in the 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

Gastrin is a linear peptide synthesized as a preprohormone. It is post-translationally cleaved to form a family of peptides with identical carboxyterminal. Receptors of Gastrin are found on parietal cells, and enterochromaffin-like cells (ECL) also bear gastrin receptors. Recent evidence indicates that this ECL may be the most crucial target of gastrin in regulating acid secretion. [3][8]

Gastrin release is primarily stimulated by vagal and gastrin-releasing peptides (GRP). The secondary stimulant is the ingestion of peptides, gastric distention, amino acids, and an elevated stomach pH. Conversely, decreased stomach pH and somatostatin

inhibition of paracrine lead to decreased gastrin release. [2][4][5]

The main functions of gastrin are enhancing Gastric motility, hydrochloric acid stomach secretion, and gastric mucosal growth enhancement is gastrin's primary role. [5]

Urogastrone

The stomach secretes urogastrone to reduce gastric acid secretion and increase oxyntic gland growth. Its stimulus is not yet known. [3][26]

Bombesin

Bombesin is homologous to the gastrin-releasing peptide (G cells). It is mediated by gastrin in the antrum and regulates the release of GI hormones. [3][26]

Intestine

The intestine is composed 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 member of the gastrin/cholecystokinin family of peptide hormones and is very similar in structure to gastrin, sharing the same 5 C-terminal amino acids. This hormone is found on chromosome 3. It is produced by the I-cell of the duodenum and jejunum. CCK plays essential physiological roles as a neuropeptide in the central nervous system and a peptide hormone in the gut. I-cells are concentrated in the proximal small intestine, which secret CCK into the blood upon the ingestion of food. The physiological actions of CCK include stimulating pancreatic secretion and gallbladder contraction, regulating gastric emptying, and induction of satiety. [3][7][12][25]

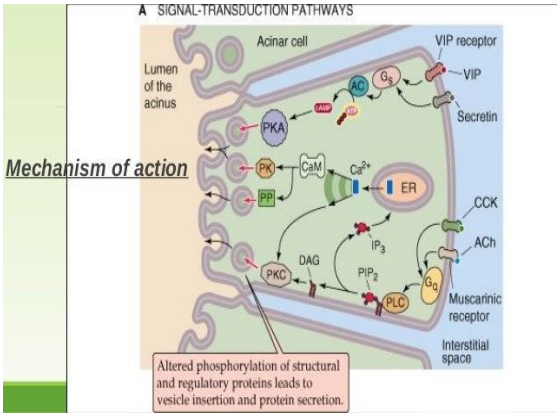

Fig 2: Signal transduction pathways of CCK

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

Secretin

It is initially synthesized as a 120 amino acid precursor protein, prosecretin. This precursor contains an N-terminal signal peptide, spacer, secretin (residues 28–54), and a 72-amino acid C-terminal peptide. It is produced 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. [6]

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. It can inhibit gastric acid secretion and stimulate the production of gastric and colonic mucus. [3][16]

Motilin

Motilin is a 22-amino-acid peptide synthesized in the duodenal and jejunal mucosae endocrine cells (Mo cells). Motilin is the hormone that is cyclically released during the fasted state and is released by the entero-endocrine cells (Mo cells) in the upper small intestine. Motilin stimulates gastric and small intestine motility, causing undigested food in these regions to move into the large intestine. [3][27]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][24]

Peptide-YY

This hormone is produced in the L cells in the distal portion of the small intestine on chromosome 17. 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

It is produced by the K cells of the duodenum and the upper jejunum. It is located on chromosome 17. Its stimuli include glucose, amino acids, and fatty acids. It inhibits gastric acid secretion and stimulates insulin secretion. [3][9]

Glucagon-like peptide

It is secreted by the L cells in the small intestine and colon and partly by the rectum. Its stimuli include glucose and fats. It inhibits gastric motility and encourages insulin release. [3][26]

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 functions to relax the lower esophageal sphincter and fundus of the stomach. It also stimulates biliary and pancreatic secretions. [10][13]

Bulbogastrone

It is a candidate hormone secreted in the duodenum. It reduces gastric acid secretion and is stimulated by gastrin. [5][26]

Hormone	Source	Target	Action
Cholecystokinin	I cells in duodenum and jejunum and neurons in ileum and colon	Pancreas	↑ Enzyme secretion
		Gallbladder	↑ Contraction
Gastric inhibitory peptide	K cells in duodenum and jejunum	Pancreas	Exocrine: ↓ fluid absorption Endocrine: ↑ insulin release
Gastrin	G cells, antrum of stomach	Parietal cells in body of stomach	↑ H^+ secretion
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 muscle contraction
Neurotensin	Endocrine cells, widespread in GI tract	Intestinal smooth muscle	Vasoactive stimulation of histamine release
Peptide YY	Endocrine cells in ileum and colon	Stomach	↓ Vagally mediated acid secretion
		Pancreas	↓ Enzyme and fluid secretion
Secretin	S cells in small intestine	Pancreas	↑ HCO_3^- and fluid secretion by pancreatic ducts
		Stomach	↓ Gastric acid secretion
Somatostatin	D cells of stomach and duodenum, δ cells of pancreatic islets	Stomach	↓ Gastrin release
		Intestine	↑ Fluid absorption/ ↓ secretion ↑ Smooth muscle contraction
		Pancreas	↓ Endocrine/exocrine secretions
		Liver	↓ Bile flow
Substance P	Enteric neurons	Enteric neurons	Neurotransmitter
VIP	ENS neurons	Small intestine	↓ Smooth muscle relaxation ↑ Secretion by small intestine
		Pancreas	↑ Secretion by pancreas

Table 1: Summary of GIT hormones

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

PATHOPHYSIOLOGY

Gastrin

Hypersecretion of Gastrin

Zollinger-Ellison Syndrome:

Hypersecretion of Gastrin usually occurs in disorder known as Zollinger-Ellison Syndrome (gastrinoma). It is a rare syndrome associated with peptic ulcers caused by a gastrin-secreting neuroendocrine tumor or multiple tumors (gastrinoma) of the pancreas or duodenum. Increased gastrin secretion causes excess gastric acid secretion, resulting in gastric and duodenal ulcers, gastroesophageal reflux, abdominal pain, and diarrhea. [8][16]

The annual incidence of gastrinoma is 0.5-2 per million population. Most patients in this category are diagnosed between 20 and 50 years, with a higher incidence in males than 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. As 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 percent). In 5 -15% of patients, gastrinomas arise in non-pancreatic, non-duodenal abdominal (stomach, peripancreatic lymph nodes, liver, bile duct, ovary), and extra-abdominal (heart, small cell lung cancer) locations. [11][17]

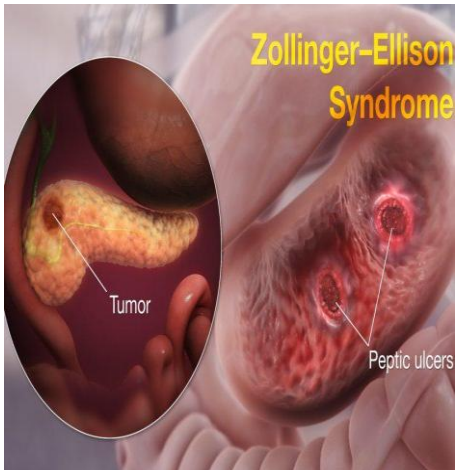

Fig 3: Zollinger-Ellison Syndrome [Source]

Manifestations of ZE syndrome are ulcers refractory to standard therapy or multiple ulcers, giant ulcers larger than 2 cm, recurrent ulcers, ulcers with unexplained diarrhea, strong family history of ulcers, hypercalcemic symptoms and signs and duodenal ulcer that is not related to *Helicobacter pylori* infection or nonsteroidal anti-inflammatory drug usage.

Helicobacter pylori infection:

H. pylori 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. [8][14]

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. [8][21][22][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, chemotherapy to reduce tumor growth, a triple therapy regimen for eradication of 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. [8]

Hyposecretion of Gastrin

Low gastrin levels are rare, but when they occur, the condition can increase the risk of infection in the digestive system and limit the stomach's ability to absorb nutrients. [14][24]

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. [14][17][27]

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.

Cholecystokinin (CCK)

Hypersecretion of CCK

High levels of CCK can increase the effectiveness of how fast gastric emptying occurs. It increases the excitatory effect on the small and large intestine, leading to movement in the bowels or improving the pyloric sphincter's tension. Increased anxiety and panic attacks have been associated with cholecystokinin. [12]

In a primary-care study from the UK, BN's overall age- and sex-adjusted incidence rate decreased during the second half of the 1990s from 12.2 per 100,000 person-years in 1993 to 6.6 per 100,000 person-years in 2000. However, the incidence rate of BN in women

aged 10–19 years remained relatively stable at around 40 per 100,000 person-years in 1993 and 2000. Several studies suggest that the age at onset of BN is decreasing. In a sample of 793 Italian BN patients referred to an eating disorders outpatient unit between 1985 and 2008, subjects born in 1970–1972 had a mean age at onset of 18.5 years, compared to 17.1 years in subjects born between 1979–1981. It is unclear whether this reflects an earlier age at onset or relatively earlier detection of BN cases. [18][19[20]

CCK is a well-established trophic factor in pancreatic growth. It is therefore believed that CCK may affect the proliferation of pancreatic tumors. Recent studies have shown that CCK enhances the induction of pancreatic carcinogenesis and has growth-promoting actions on GI cancers, especially pancreatic carcinomas. [18][20]

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 the expression of satiety peptide cocaine and amphetamine-regulated transcript (CART) in vagal afferent neurons. It is also involved in metabolic regulation and lipid absorption. [21][26] They link the inactivation of the CCK signaling pathway to reduced weight gain. Inactivation increases energy expenditure and lowers energy extraction. [21]

Secretin

Hypersecretion of Secretin

Pancreatic secretion is controlled by hormonal and neural mechanisms. Secretin and CCK play a significant role in 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. [10]

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. [14]

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 demonstrating a dose-dependent incretin response to oral glucose, type-2 diabetes mellitus patients have reduced levels of GIP or beta-cell resistance to GIP compared to healthy individuals. Incretins contribute post meals,70% of insulin response. This reduced incretin effect is responsible for the glucose intolerance seen in diabetics. [9]

Obesity

Obesity and lipid metabolism is GIP's vital role. Fat is a potent stimulant in GIP secretion, and in obesity, K-cell hyperplasia and increased GIP levels are observed. Inhibition of lipolysis and stimulation of lipogenesis is done by GIP(anabolic hormone). [9][14]

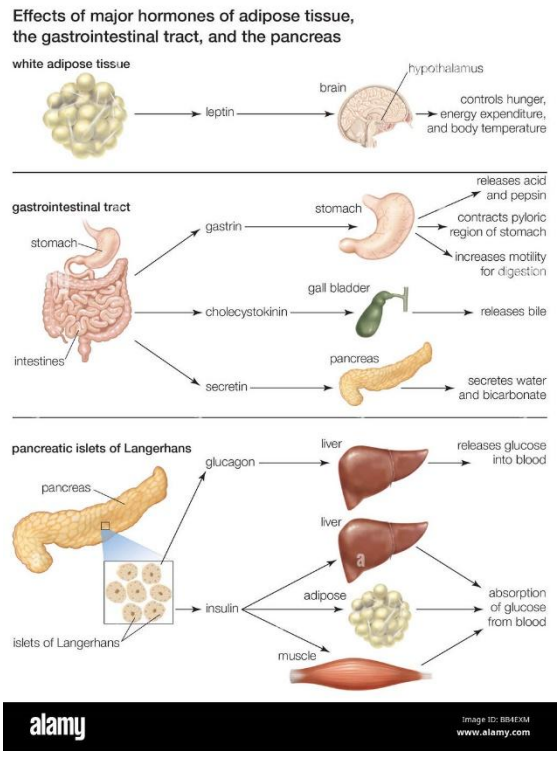

Fig 4: Schematic showing the relationship between adipose tissues and major hormones.

Source: https://c8.alamy.com/comp/BB4EXM/the-major-hormones-of-adipose-tissue-the-gastrointestinal-tract-and-BB4EXM.jpg

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 zona fasciculate of the adrenal cortex contains GIP-R. Following a meal, GIP concentration increases in the blood, which causes an increase in cortisol even in the presence of low ACTH. Treatment of AIMAH involves the use of somatostatin analogs such as octreotide. [9]

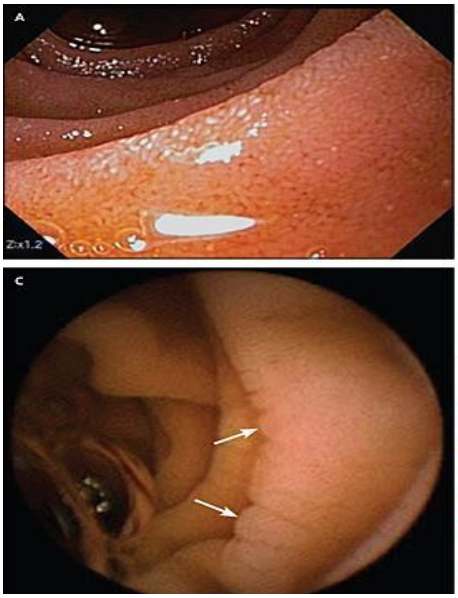

Fig 5: Gross & Histological appearance of Celiac Disease. [Source]

ASSOCIATED DISEASES

CELIAC'S DISEASE

There is the relative failure of GIP and secretin release in patients with untreated coeliac disease, two hormones -localized to the area of maximal mucosal damage in coeliac disease [14]. Pancreatic endocrine and exocrine diminished response to intraduodenal stimuli has been reported to be due to failure of CCK release. [25]
In their studies, the release of gastrin and pancreatic polypeptide, whose tissues of origin are unaffected, was entirely normal. Plasma motilin levels were slightly above average, following a tendency for this peptide to be raised in steatorrhea conditions. Plasma enterglucagon levels, in contrast, were significantly raised.

TROPICAL SPRUE (MALABSORPTION)

Eight patients with severe tropical sprue were studied. A significant diminution of GIP and insulin release was associated with a delayed and impaired rise in blood glucose. In contrast, however, plasma motilin levels were significantly raised. Basal plasma enteroglucagon concentrations were higher than expected, with only a small further rise after the test breakfast. This pattern differs from coeliac disease, possibly reflecting the different pathophysiological processes and the greater gut area involved in tropical malabsorption. Neurotensin, gastrin, and pancreatic polypeptide responses were similar to normal. [15][25]

CROHN'S DISEASE

In an experiment studying fourteen patients with Crohn's disease, it was discovered that there was an increase in the release of the upper small intestinal hormone GIP after the test breakfast. In contrast to the poor rise in coeliac disease and acute tropical sprue. 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. [14]

ULCERATIVE COLITIS

After breakfast, there was a normal GIP response in 24 ulcerative colitis patients and high basal plasma motilin levels. An augmented gastrin response might be secondary to hypochlorhydria (acid studies were not performed) 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. [14]

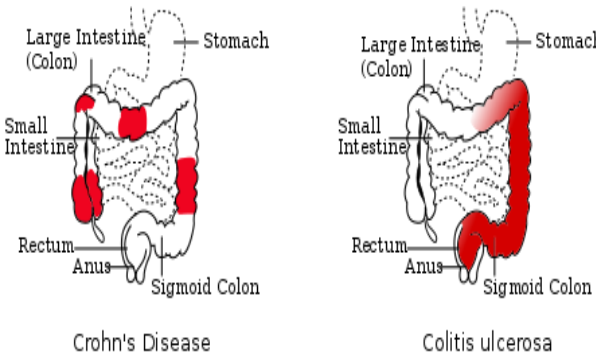

Fig 6: Side-by-side comparison of Crohn's Disease and Ulcerative Colitis [Source]

INFECTIVE DIARRHEA

The responses of pancreatic polypeptide and GIP were normal. In contrast, gastrin, motilin, and enteroglucagon were augmented responses. Compensatory mechanisms occurring in the gut to diarrhea may be related. As diarrhea abated, basal motilin levels fell in parallel. [15]

PANCREATIC INSUFFICIENCY

Compared to the diminished release in coeliac disease and acute tropical sprue, the GIP response was normal in these patients. The malabsorption is secondary to mucosal damage. The gastrin response was diminished, but the motilin and enteroglucagon responses increased. However, the increased enteroglucagon release was much less than that associated with the atrophic small intestinal mucosa. This is much greater in patients with pancreatic insufficiency.

The most striking finding in patients with pancreatic insufficiency was the gross failure of pancreatic polypeptide release following the test breakfast [15]. This probably reflects the extensive damage to pancreatic tissue as the pancreatic polypeptide cells are scattered throughout the pancreatic parenchyma.

INTESTINAL RESECTION

The subsequent effects of surgical removal of a length of intestine depend on the site and the length of gut resected. The loss of absorptive area may give rise 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). After small intestinal resection, there is villous hypertrophy of the mucosa of the remainder [21]. A humoral agent probably stimulates this compensatory mechanism, possibly enteroglucagon. We have studied patients who have undergone varying degrees of gut resection for several different pathological states [14]. The most standard indication for

surgery was Crohn's disease, when most patients had between one and two meters of terminal ileum resected. Partial resection of the ascending or transverse colon or both was carried out for Crohn's disease or ulcerative colitis. Neoplasia, trauma, and post-radiation fibrosis were fewer common reasons.

There was no significant difference between partial ileal and partial colonic resection effects in Gastrin, pancreatic polypeptide, GIP, and neurotensin responses. The post-breakfast release of both gastrin and pancreatic polypeptide was greater than normal in both groups of patients. Raised gastrin levels after intestinal resection have been reported by others [23], which may be relevant to gastric acid hypersecretion in these patients [22]. The GIP and neurotensin responses, in contrast, were similar to normal. There was, however, a striking difference in the responses of motilin and enteroglucagon between the two groups of patients. The patients with partial colon resection had only mildly raised motilin responses and a somewhat decreased enteroglucagon release. 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. Abnormalities of intestinal motility have been described [24], and abnormal gut hormone release has been postulated as an etiological factor [13].
A total of 42 patients with IBS were studied.

Nineteen had abdominal pain and frequency of bowel action, 11 had pain and constipation, and 12 had pain but normal bowel function. All had been thoroughly investigated, and no organic disease was found. In contrast to all other disease groups studied, these patients had entirely normal responses to the measured gut hormones. [12][13][24]

GASTRIC (PEPTIC) ULCERS

Enhanced HCl 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; enhanced vagal (cholinergic stimulation; enhanced histamine secretion).[8][11]

GASTRIC-RELATED PEPTIDE (GRP) AND CANCER

This is a homolog of bombesin (BBS). Peptides of the BBS have a broad spectrum of biological effects on the GIT, pancreas, 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- Gastrin, somatostatin, CCK, pancreatic polypeptide, insulin, enteroglucagon, pancreatic glucagon, and GIP as well as the exocrine secretion in the pancreas. [7][16]

Several studies have shown that BBS may be a growth factor in colon cancer cells in recent years. GRP receptor mRNAs are present in gastric cancer cell lines.

Hence, in general, the effect of these peptides in GI cancer is stimulatory. However, they also inhibit the growth of some specific cell types. [19][24]

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. [27] 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. [27]. These hormones are established to have metabolic effects beyond the GIT. Gastrointestinal endocrinology is beginning to reveal the complexity of hormonal involvement in indigestion. [27] More research work needs to be done.

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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
PPIs – Proton Pump Inhibitors