Digestion and Intestinal Absorption

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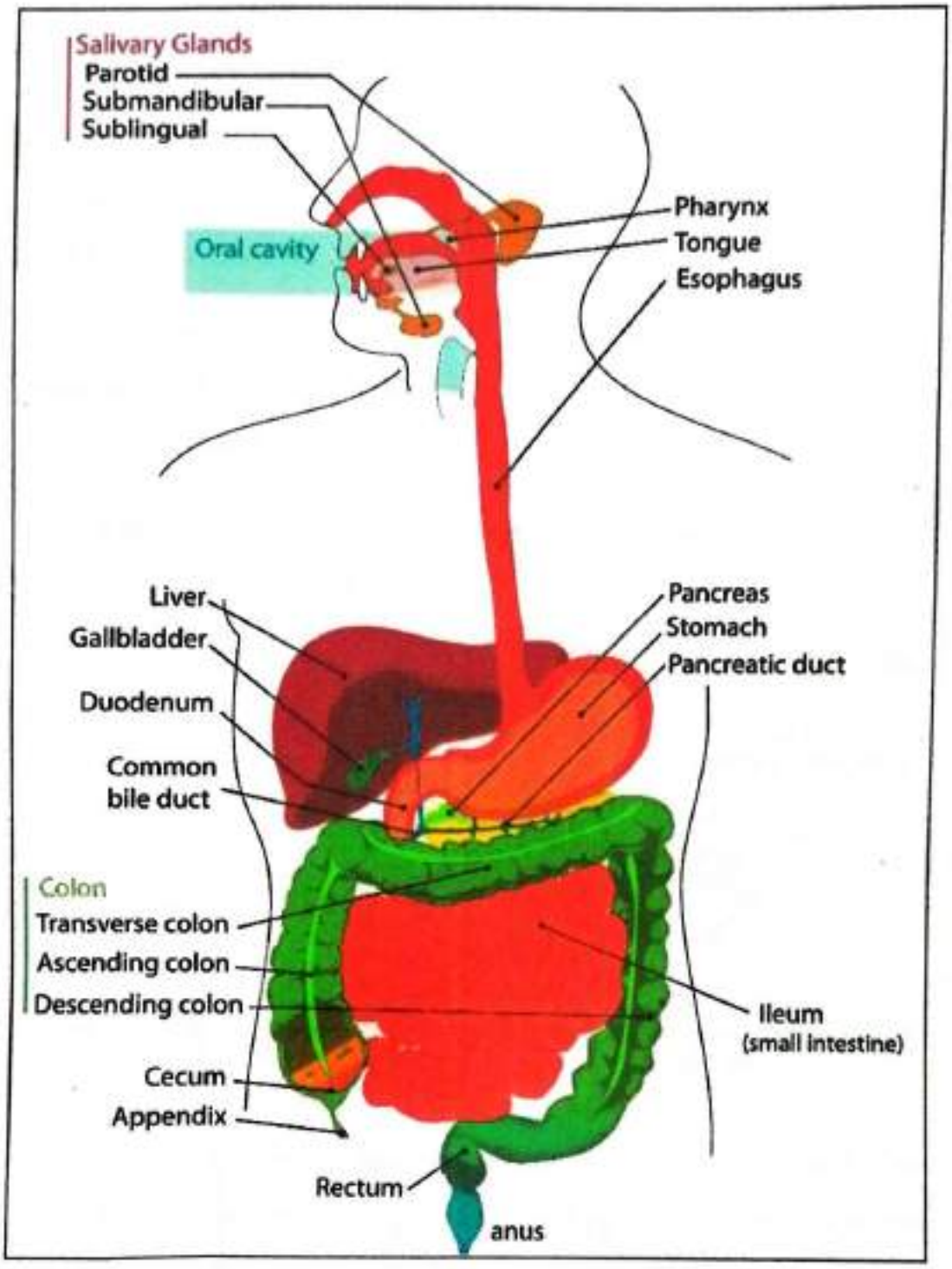


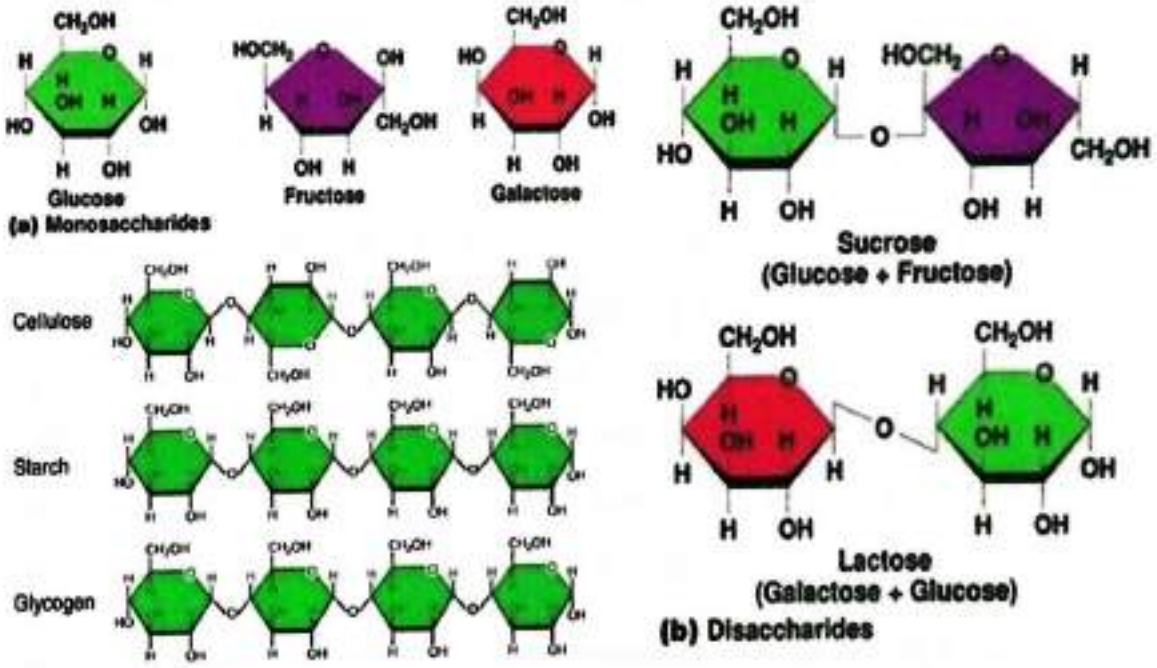
Anatomy of the digestive tract and associated organs.

The Strategy of Digestion

1- Carbohydrates

Dietary carbohydrate may take a number of forms. In most real meals (as opposed to the pure glucose loads studied in many experimental situations) there is a mixture of simple sugars, oligosaccharides, and complex carbohydrates.

Of the complex carbohydrates, some will be readily digestible starch, composed of the straight-chain amylose and the branching amylopectin, together with very small amounts of glycogen in animal tissues.



There are other types of starch which are resistant to digestion in the small intestine but fully digested in the large intestine; they are referred to as resistant starch. Their chemical structure is identical to more easily digestible starch, but the polysaccharide chains are in a semicrystalline state that makes the bonds inaccessible to the usual enzymes of starch

digestion. The remaining, less digestible, carbohydrate is referred to as non-starch polysaccharide or more generally as dietary fiber.

Cellulose, one of the main components of the non-starch polysaccharide fraction. The digestible carbohydrates are, for the most part, absorbed from the small intestine in the form of monosaccharides.

The strategy of the digestive process, then, is to have them in that form as they reach the small intestine. Digestion of dietary carbohydrate to monosaccharide units takes place in two stages: **luminal digestion** – digestion occurring in the intestinal lumen – and **membrane digestion**, the hydrolysis of certain small oligosaccharides by enzymes forming part of the microvillus membrane, the absorptive surface of the cells lining the small intestine.

2- Fats

The majority of dietary fat is in the form of triacylglycerol, together with some cholesterol and small amounts of other lipids such as phospholipids. Fat-soluble vitamins are ingested with other foods. Some are taken in as relatively water-soluble precursors, or provitamins, such as carotene in carrots and other vegetables. Others, such as vitamin D, are taken in with fatty foods and absorbed with the fat.

The digestion and absorption of fat necessitates that the fat is made accessible to the enzymes which break it down for digestion. This is achieved by emulsification – formation of microscopic droplets in which the ratio of surface area (where enzymes can act) to mass is very large. Thus, in considering the digestion and absorption of fat, we are concerned both with physicochemical changes and with enzymatic processes.

3- Proteins and Amino Acids

Protein in the diet may take many forms. For the most part, this makes little difference to its handling in the digestive process; proteins are hydrolyzed to free amino acids and dipeptides for absorption.

Stages of Digestion

Three phases of digestion:

(a) Cephalic (or nervous).

(b) Gastric.

(c) Intestinal.

(a) Cephalic Phase:

Starts immediately after taking food. It is a reflex process involving both conditioned and unconditioned reflexes. The juice secreted is called appetite juice. It is constant in composition and does not vary with the nature of food. In man it is small in amount but is important.

(b) Gastric Phase:

Starts half an hour after the entry of food in the stomach. The stimulus is chemical. The chemical substance is manufactured by the pyloric mucous membrane from some products of protein digestion and is known as gastrin. Gastrin enters blood stream carried to the gastric glands and stimulates their secretion independent of all nerves.

Largest quantity of gastric juice is secreted during this phase. This part of gastric juice varies in quality and quantity with the nature of food. Proteins increase both the amount and the HCl content. Fats inhibit both.

Bread stimulates a secretion having the greatest digestive power. Water, coffee, spices stimulate.

(c) Intestinal Phase:

Starts when food enters the duodenum. It is small in amount and is independent of nerves; consequently, the stimulus is chemical but its exact nature is not known. Presence of fat in the duodenum inhibits gastric secretion. This, according to Ivy, is due to the liberation of an inhibitory hormone from the intestine called enterogastrone.

The three phases are closely interrelated. Cephalic phase initiates appetite juice, which digests the proteins partly. Form these products of digestion gastrin are manufactured which initiates the second phase. After this when gastric digestion has proceeded to the required stage, stomach empties into duodenum and thereby intestinal phase starts. Thus each phase initiates the next.

Digestive Juices	Digestive Enzymes	Hormones
The digestive juices are the secretions of the digestive tract that break down food.	A digestive enzyme helps in the breakdown of food into smaller particles that can be absorbed by the body.	Hormones carry messages from glands to cells to maintain chemical levels in the bloodstream.
Gastric juice is a nearly colorless, strongly acidic liquid secreted by the gastric glands.	Food-dissolving ingredients of gastric juices are the digestive enzymes pepsin and rennin, which break down proteins, and hydrochloric acid.	Presence of hormones acts as a catalyst for other chemical changes at the cellular level necessary for growth, development, and energy.

1- The Mouth

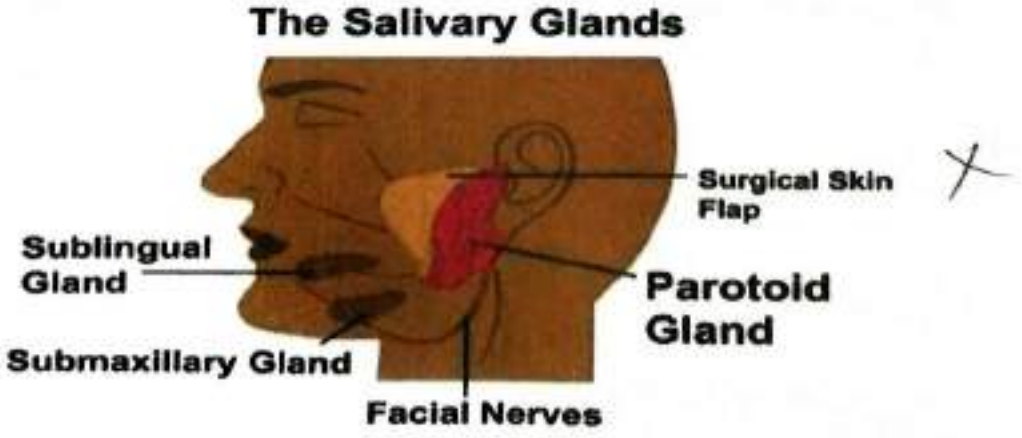
The process of digestion and preparation for the absorption of food may begin even before food enters the mouth. The cephalic phase represents the brain's anticipation of food, through the sight or smell or even thought of food; it is reinforced by the taste of

food in the mouth. Cephalic stimulation of the flow of saliva occurs through activation of the parasympathetic nervous supply to the salivary glands.

Stimulation of gastric juice secretion also occurs, and there is cephalic-phase secretion of insulin, showing the control of insulin secretion by the nervous system. The presence of food in the mouth stimulates nerve receptors both mechanically and chemically, through taste receptors, to reinforce the stimulus to saliva production. The taste receptors, expressed in specialized taste sensory cells, are mostly G-protein coupled receptors; there are also ion channels. Saliva is produced in pairs of glands which are located along the line of the jaw: the parotid, submandibular, and sublingual.

There are two types of salivary glands:

- serous glands: These glands produce a secretion rich in water, electrolytes, and enzymes. A great example of a serous oral gland is the parotid gland.
- Mixed glands: These glands have both serous cells and mucous cells, and include sublingual and submandibular glands. Their secretion is mucinous and high in viscosity.

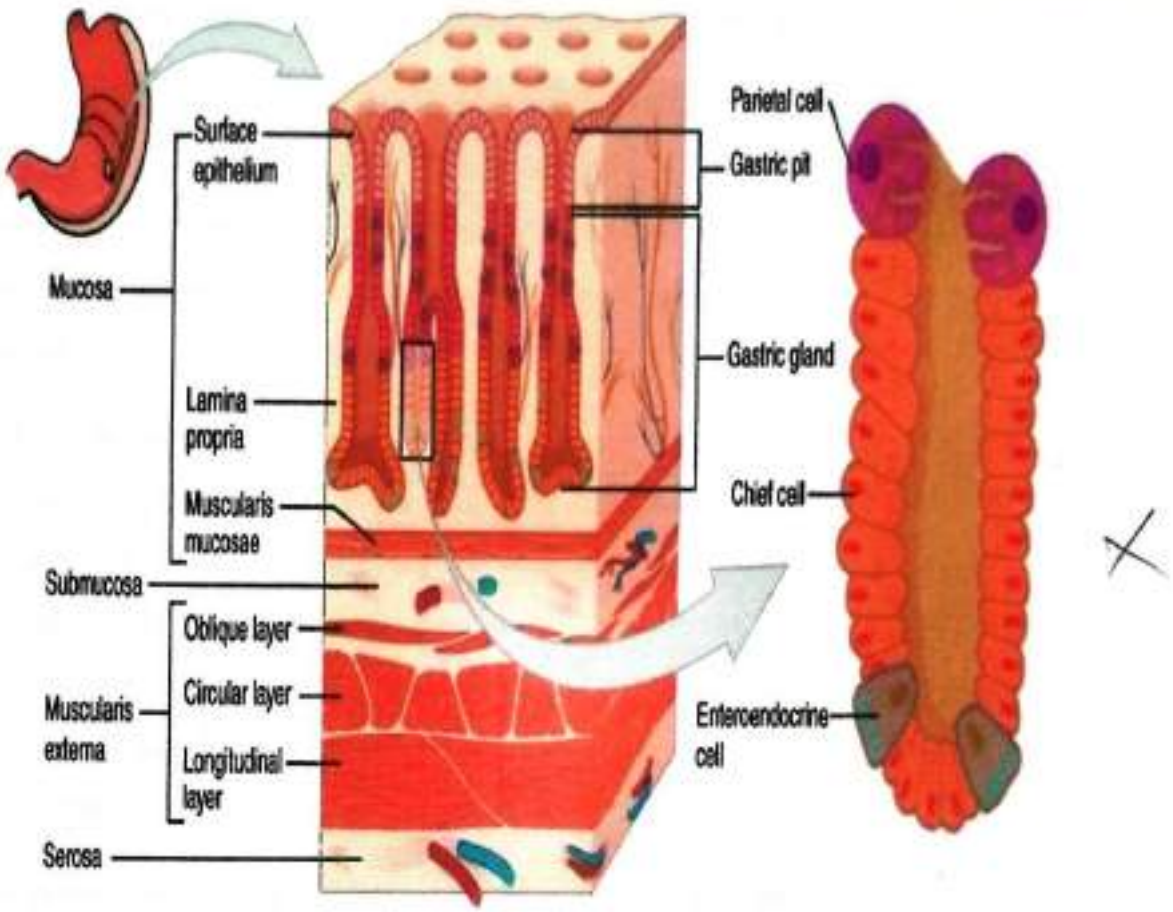


2- The Stomach

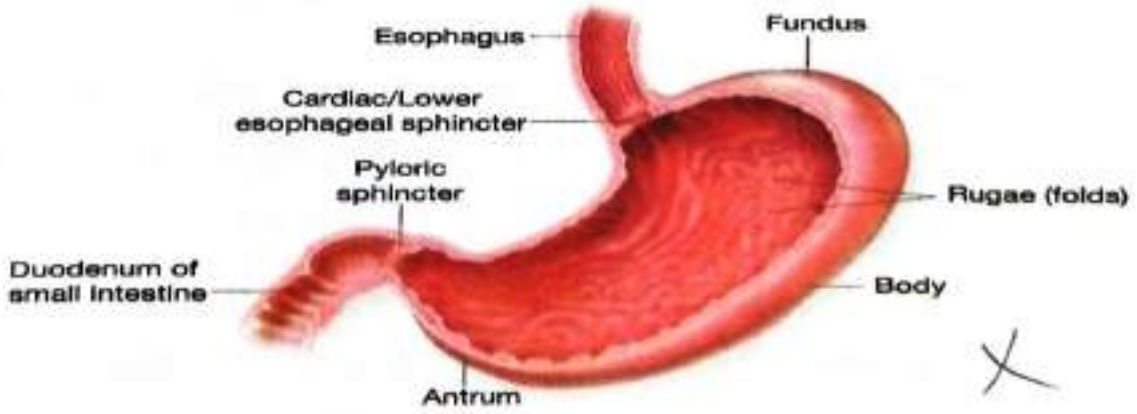
After swallowing, the chewed food is propelled rapidly, in a matter of seconds, through the esophagus to enter the stomach. The stomach is a distensible muscular sac, about 25 cm long, with a volume of around 50 ml when empty, but which can expand to hold up to 1.5 litres or more. Its muscular walls are made of three layers of smooth muscle running in different directions, giving the stomach the ability to churn food around and physically break it up further and mix it with the stomach's own digestive juices.

The cells of the epithelium (inner lining) of the stomach produce both mucus and an alkaline, bicarbonate-containing fluid, which protect them from attack by the stomach's own acidic digestive juices. Interspersed with these cells are many millions of small holes, visible microscopically; these are the openings of the gastric pits or gastric glands.

The gastric pits are lined with further epithelial, mucus-secreting cells but also contain specialized cells secreting different substances: the parietal or oxyntic cells secreting HCl (hydrochloric acid), and the chief cells, also known as zymogenic or peptic cells, which secrete proteins, particularly the pro-enzyme pepsinogen. The oxyntic cells also secrete the glycoprotein known as intrinsic factor, which is necessary for absorption of vitamin B12.



Secretions and movements of the stomach are controlled by the **vagus nerve** and the **sympathetic nervous system**; emotional stress can alter normal stomach functions.



Regulation of Digestive Processes in the Stomach

The control of acid secretion is summarized in (Figure below) Secretion of HCl is stimulated by three factors acting at specific receptors on the basolateral membrane of parietal cells: **acetylcholine**, the parasympathetic neurotransmitter; **histamine**; and the peptide hormone **gastrin**.

Maximal acid production is only achieved when all three signals are present; any one of the three will only give weak stimulation of acid production. Cellular signaling is achieved by elevation of cAMP concentrations, which brings about translocation of the proton pump enzyme that secretes acid to the apical cell membrane. The proton pump is an "ATPase" that splits ATP to derive the energy needed for acid secretion.

Acetylcholine; is the chief neurotransmitter of the parasympathetic nervous system, the part of the autonomic nervous system that contracts smooth muscles, dilates blood vessels, increases bodily secretions, and slows heart rate.

In the body of the stomach, the vagal nerves release acetylcholine(ACh) which stimulates parietal cell H+ secretion and histamine secretion from ECL cells.

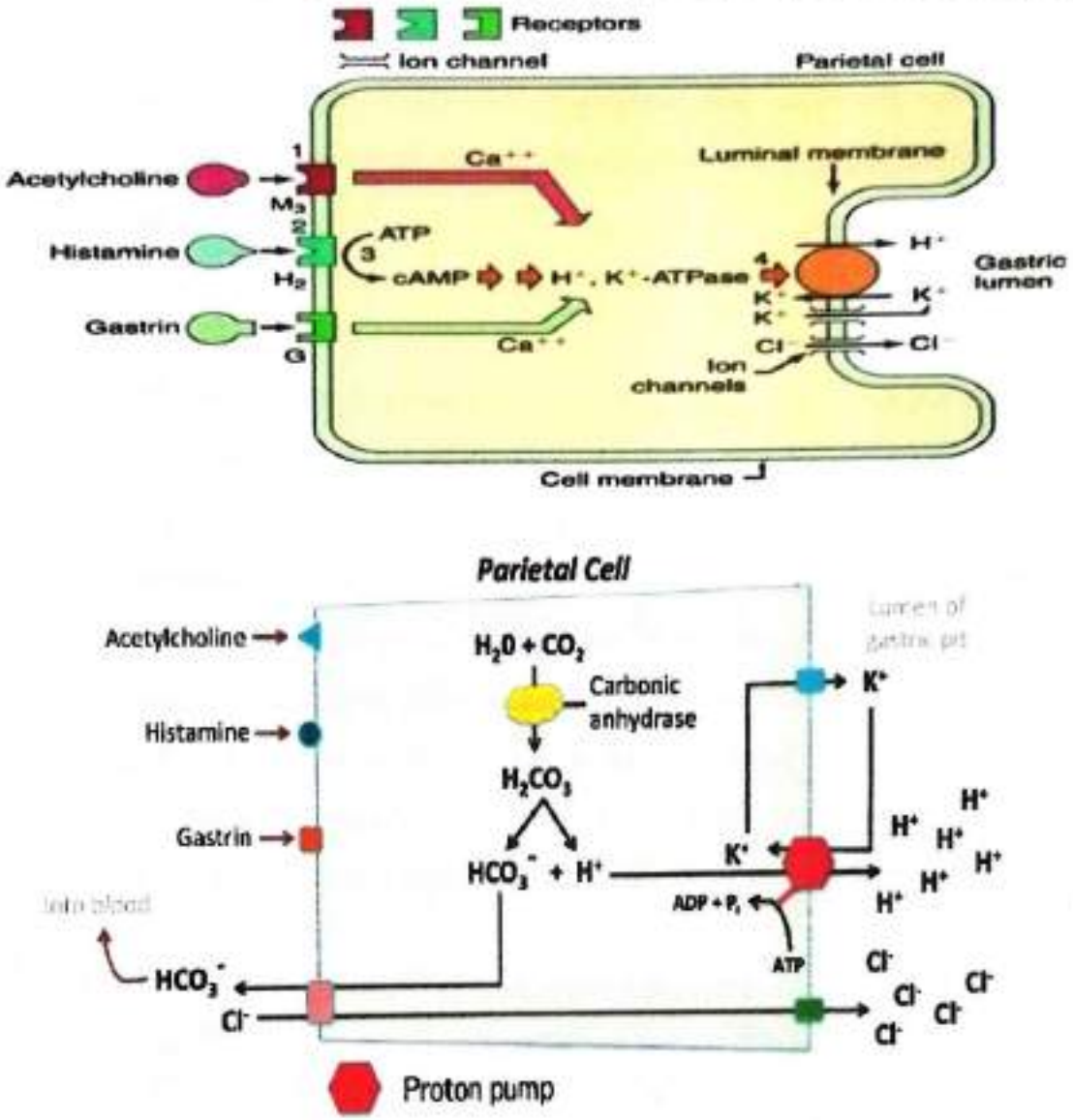
Histamine is released from cells in the stomach wall in response to food in the stomach. It acts locally, on nearby cells; it is thus not a true hormone, but acts in a paracrine manner.

The parasympathetic nervous system is activated during digestion, as noted earlier, by the taste, smell, and sight of food; when food enters the stomach, distension of its walls activates stretch receptors which send signals to the brain, which in turn causes further activation of the

parasympathetic nervous system (the vagus nerve), and enhances acid secretion. A traditional surgical treatment for gastric ulcers was to sever the vagus nerve, thus removing one stimulus for acid secretion.

Gastrin, the third regulator of acid secretion, is produced by enteroendocrine cells, a general term for cells in the gastrointestinal tract that secrete hormones. The cells that secrete gastrin are known as G cells. Gastrin is a true hormone; it is released from these cells into the bloodstream and circulates in the bloodstream. There is no apparent short cut for it, although the cells it affects are near to the cells secreting it. The release of gastrin is stimulated by a number of factors arising from the food in the stomach: some amino acids and peptides released from partially digested protein in the stomach, caffeine, calcium, and alcohol. In addition, stimulation of gastrin secretion is reinforced by the parasympathetic nervous system, activated during the digestive process. Gastrin acts directly on the parietal cells to stimulate acid secretion.

The secretion of gastrin is inhibited by too high an acidity in the stomach; when the pH falls below about 2 (the optimum for the action of pepsin) gastrin secretion declines. This seems to be brought about by release from adjacent cells of the 14-amino acid peptide somatostatin. Somatostatin is a widespread inhibitor of peptide hormone secretion: it is found throughout the intestine, in the brain and in the pancreas, and, when given intravenously, will inhibit the secretion of many peptide hormones, including growth hormone, gastrin, insulin, and glucagon.



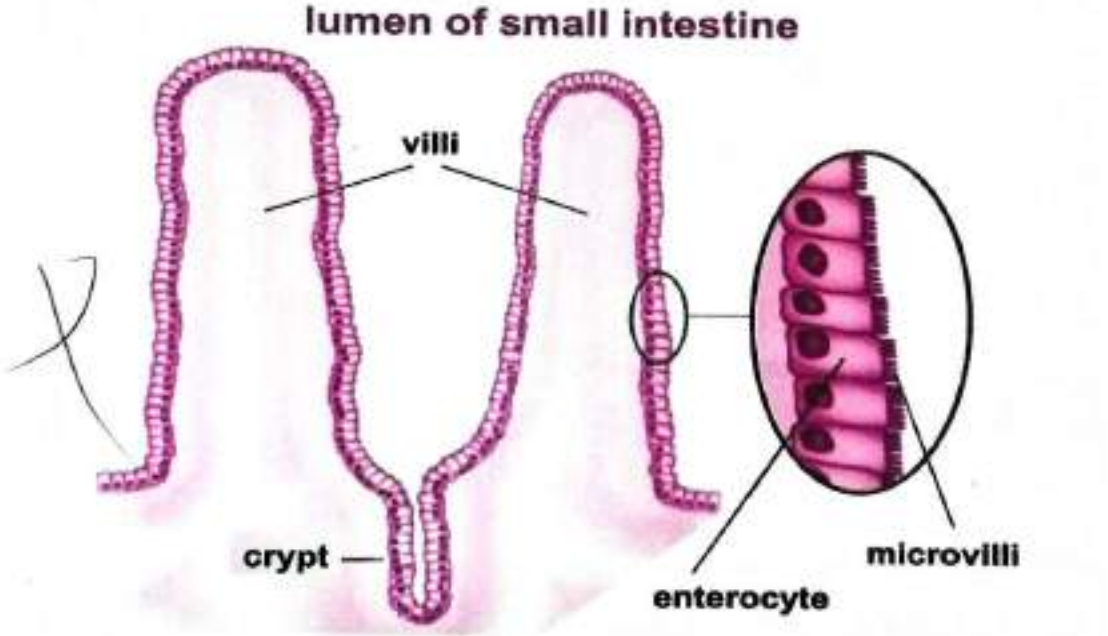
The mechanism of HCL secretion

2- The Small Intestine

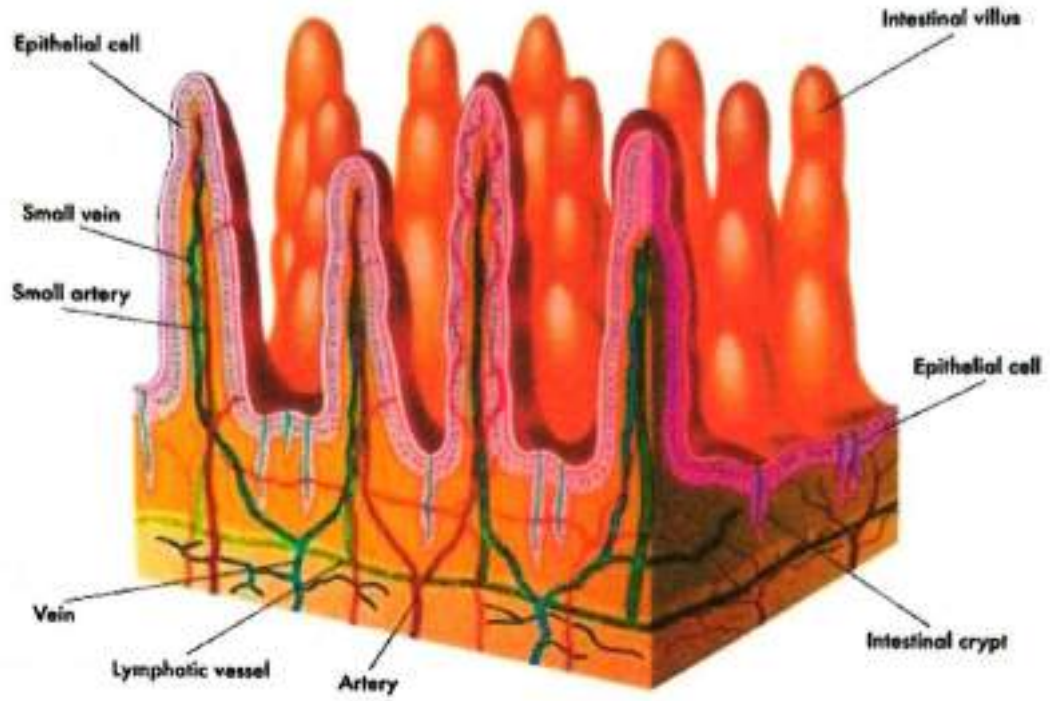
The small intestine is often said to be about 6 m (20 feet) long. The small intestine, like all parts of the intestine, has layers of smooth muscle running lengthways and around its circumference. The inner surface, or mucosal layer, is folded into finger-like projections (villi). This increases the surface area, to a total of about 300 m2; this surface area is where absorption takes place. The surface area is increased still further by the presence of the

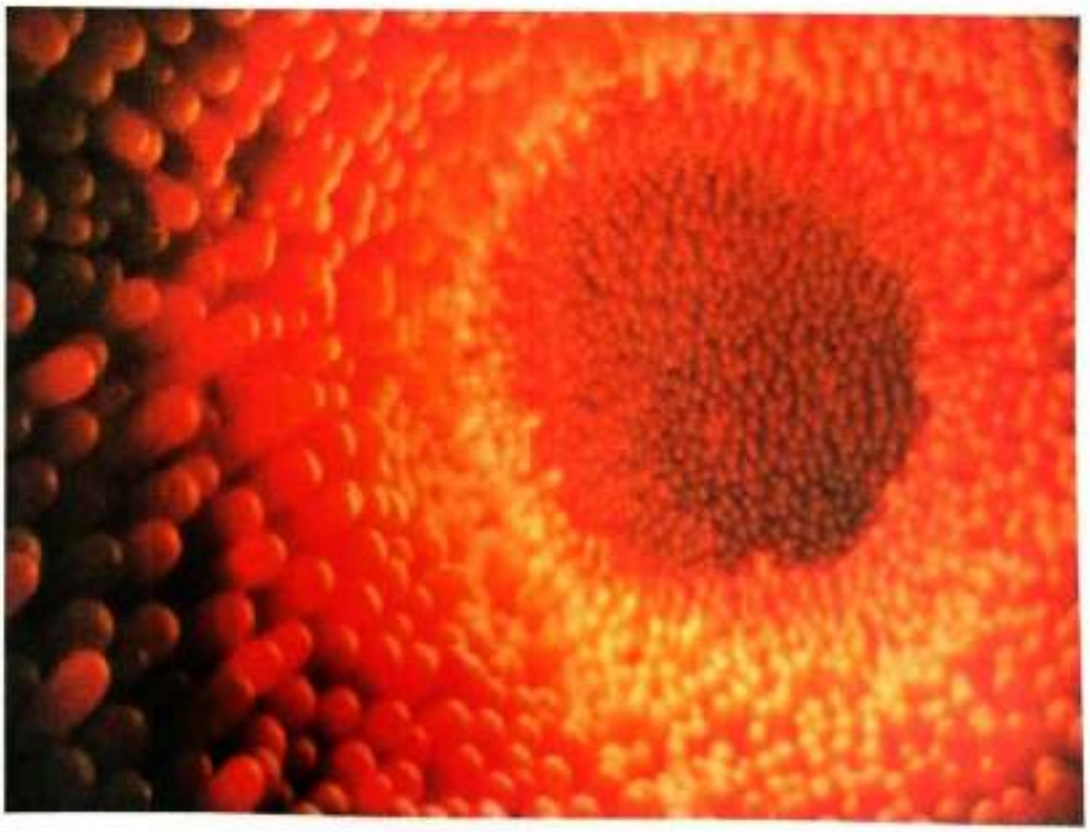
brush border. Each cell making up the surface of a villus has its own microscopic finger-like projections, the microvilli, giving a brush-like appearance under the electron microscope. There are around 2000–4000 microvilli per cell. The presence of the microvilli increases the surface area about a further 30-fold.

There are four important sources of digestive agents in the **small intestine**: the **gall bladder**, which provides the bile salts necessary for emulsification of fat; the **exocrine pancreas**, which provides bicarbonate to neutralize the acidic chyme entering through the pylorus and a **mixture of digestive enzymes**; secretory cells in glands located throughout the small intestinal wall which produce an isotonic, neutral, mucuscontaining juice; and the brush border membrane, in which are incorporated several digestive enzymes. These, and the other digestive juices, are summarized in Table 1,2.



INTESTINAL VILLUS





The Digestive Enzymes

Enzyme Category	Enzyme Name	Source	Substrate	Product
Salivary Enzymes	Lingual lipase	Lingual glands	Triglycerides	Free fatty acids, and mono- and diglycerides
Salivary Enzymes	Salivary amylase	Salivary glands	Polysaccharides	Disaccharides and trisaccharides
Gastric enzymes	Gastric lipase	Chief cells	Triglycerides	Fatty acids and monoacylglycerides
Gastric enzymes	Pepsin*	Chief cells	Proteins	Peptides
Brush border enzymes	α-Dextrinase	Small intestine	α-Dextrins	Glucose
Brush border enzymes	Enteropeptidase	Small intestine	Trypsinogen	Trypsin
Brush border enzymes	Lactase	Small intestine	Lactose	Glucose and galactose
Brush border enzymes	Maltase	Small intestine	Maltose	Glucose
Brush border enzymes	Nucleosidases and phosphatases	Small intestine	Nucleotides	Phosphates, nitrogenous bases, and pentoses
Brush border enzymes	Peptidases	Small intestine	Aminopeptidase: amino acids at the amino end of peptides Dipeptidase: dipeptides	Aminopeptidase: amino acids and peptides Dipeptidase: amino acids
Brush border enzymes	Sucrase	Small intestine	Sucrose	Glucose and fructose
Pancreatic enzymes	Carboxy-peptidase*	Pancreatic acinar cells	Amino acids at the carboxyl end of peptides	Amino acids and peptides
Pancreatic enzymes	Chymotrypsin*	Pancreatic acinar cells	Proteins	Peptides
Pancreatic enzymes	Elastase*	Pancreatic acinar cells	Proteins	Peptides
Pancreatic enzymes	Pancreatic amylase	Pancreatic acinar cells	Polysaccharides (starches)	α-Dextrins, disaccharides (maltose), trisaccharides (maltotriose)
Pancreatic enzymes	Pancreatic lipase	Pancreatic acinar cells	Triglycerides that have been emulsified by bile salts	Fatty acids and monoacylglycerides
Pancreatic enzymes	Trypsin*	Pancreatic acinar cells	Proteins	Peptides

GASTRIC JUICE
VERSUS
PANCREATIC JUICE

GASTRIC JUICE	PANCREATIC JUICE
A thin, clear, virtually colorless acid fluid secreted by the stomach glands and active in promoting digestion	A clear, alkaline digestive fluid secreted by the pancreas
Secreted by gastric glands	Secreted by exocrine glands
Acidic	Alkaline
Contains pepsin, hydrochloric acid, intrinsic factor, mucus, and water	Contains bicarbonate, trypsinogen, chymotrypsinogen, elastase, carboxypeptidase, pancreatic lipase, nucleases, and amylase
Main role is to digest proteins	Main role is to digest carbohydrates and fat
Secretion is stimulated by a hormone called gastrin	Secretion is stimulated by secretin and pancreozymin

The presence of chyme in the duodenum activates receptors in its walls via both stretch and chemical effects. These receptors trigger the **enterogastric reflex**, in which the brain reduces parasympathetic activity (one of the main stimulants of gastric secretion and gastric contraction) and increases sympathetic nervous stimulation of the pyloric sphincter,

which causes it to contract; these effects combine to retain food in the stomach and reduce the loading of the small intestine until it is ready for more. Acidity in the duodenum also causes the secretion of secretin.

Secretin gets its name from its effects on pancreatic secretion, but it has an additional effect in inhibiting gastric contractions and secretion; these effects are reinforced by other hormones, cholecystokinin and gastric inhibitory peptide (GIP), both also secreted in response to distension of the duodenum and the presence of acidic chyme.

Two of these hormones, **secretin** and **cholecystokinin**, also have important effects on digestive enzyme secretion. Secretin stimulates the exocrine pancreas to produce a fluid which is high in bicarbonate.

Cholecystokinin stimulates the exocrine pancreas to produce a digestive juice which is relatively lower in bicarbonate but higher in enzyme content. The name cholecystokinin, however, relates to its effect on the gall bladder: it causes the gall bladder to contract, releasing its contents via the common bile duct into the duodenum. (At one time there were thought to be two separate hormones, known as pancreozymin, responsible for stimulation of pancreatic juice secretion, and cholecystokinin, acting on the gall bladder. Now they are known to be one and the same.

Digestive hormones in the GI tract

HORMONE	LOCALIZATION	MAIN PHYSIOLOGIC ACTIONS
Gastrin	Gastric antrum, duodenum (G cells)	-stimulate secretion of gastric acid and intrinsic factor from parietal cells -stimulate secretion of pepsinogen from chief cells -promotes gastric and intestinal motility, mucosal growth
Cholecystokinin (CCK)	Duodenum, jejunum (I cells)	-stimulate gallbladder contraction -stimulates release of pancreatic enzymes -relaxes sphincter of Oddi for release of bile and enzymes -role in inducing satiety
Secretin	Duodenum, jejunum (S cells)	-stimulate secretion of HCO_3 from pancreas -inhibits gastrin and gastric acid secretion
Vasoactive intestinal peptide (VIP)	Enteric nerves	-increases water and electrolyte secretion from pancreas and gut -relaxes smooth muscles (via nitric oxide) of the gut
Gastric inhibitory polypeptide (GIP)	Duodenum, jejunum (K cells)	-reduces gastric acid secretion and intestinal motility -stimulates insulin release
Motilin	Throughout the gut (Mo cells and ECL cells)	-increases small bowel motility (MMC during fasting) and gastric emptying
Somatostatin	Stomach, small intestine, and pancreas (D cells)	-inhibits secretion and action of many hormones, including all of the above

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