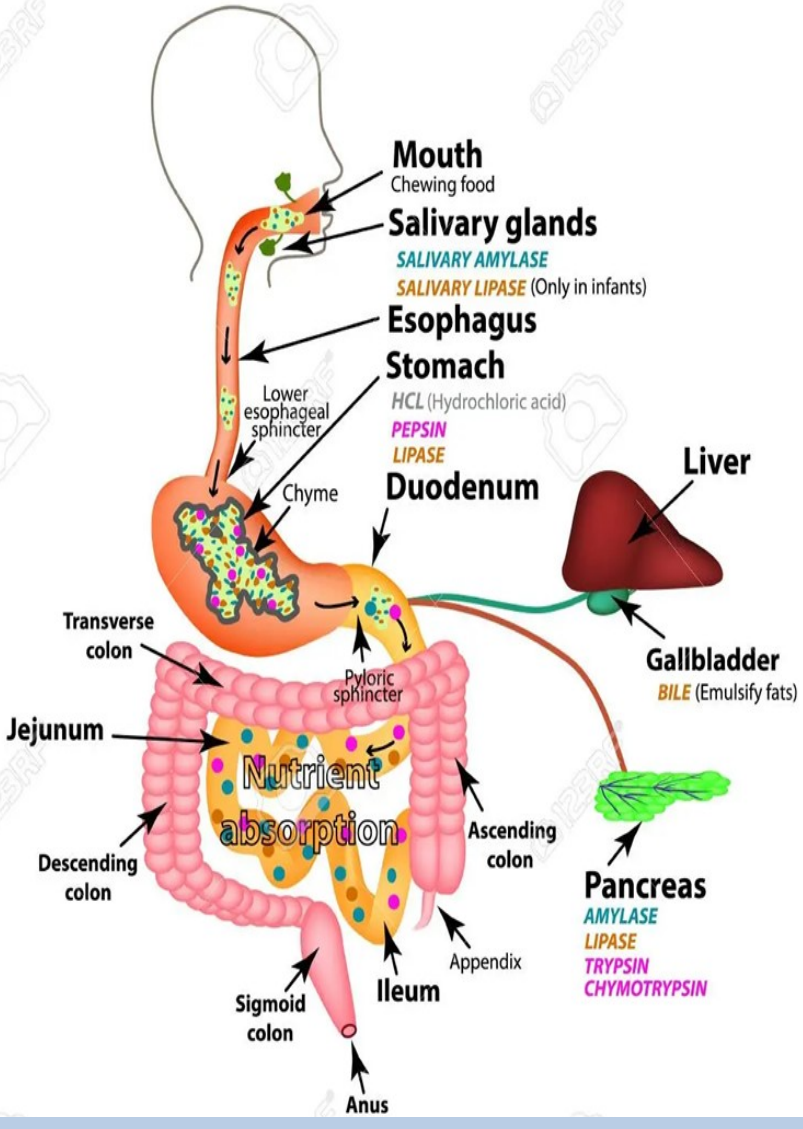
Al-Mustaqbal University
College of Pharmacy
2nd stage
Physiology
Lecture: 1

Gastrointestinal Physiology
Chapter 25
GIT secretions

Dr. Weaam J. Abbas

Outline

- General overview
- Secretion of Saliva
- Gastric Secretion
- Pancreatic Secretion
- Biliary Secretion
- Gastrointestinal Regulation



Overview of Gastrointestinal Function & Regulation

- ✓ **The primary function** of the gastrointestinal tract is to serve as a portal whereby nutrients and water can be absorbed into the body. The meal is mixed with a variety of secretions that arise from both the gastrointestinal tract itself and organs that drain into it, such as the pancreas, gallbladder, and salivary glands.
- ✓ The parts of the gastrointestinal tract that are encountered by the meal or its residues include, in order, the mouth, esophagus, stomach, duodenum, jejunum, ileum, cecum, colon, rectum, and anus.

Overview of Gastrointestinal Function & Regulation

- Throughout the length of the intestine, glandular structures deliver secretions into the lumen, particularly in the stomach and mouth.

- Also important in the process of digestion are secretions from the pancreas and the biliary system of the liver.
- **The intestine itself also has a very substantial surface area, which is important for its absorptive function**

SALIVARY SECRETION

The first secretion encountered when food is ingested is saliva. Saliva is produced by three pairs of salivary glands (the **parotid, submandibular, and sublingual glands)** that drain into the oral cavity.

It has a number of organic constituents that serve to initiate digestion (particularly of starch, mediated by amylase) and which also protect the oral cavity from bacteria (such as immunoglobulin A and lysozyme).

Secretions of the three glands differ in their relative proportion **of proteinaceous and mucinous** components, which results from the relative number of serous and mucous salivary acinar cells, respectively.

Saliva is also hypotonic compared with plasma and **alkaline;**

the latter feature is important to neutralize any gastric secretions that reflux into the esophagus.

Salivary secretion

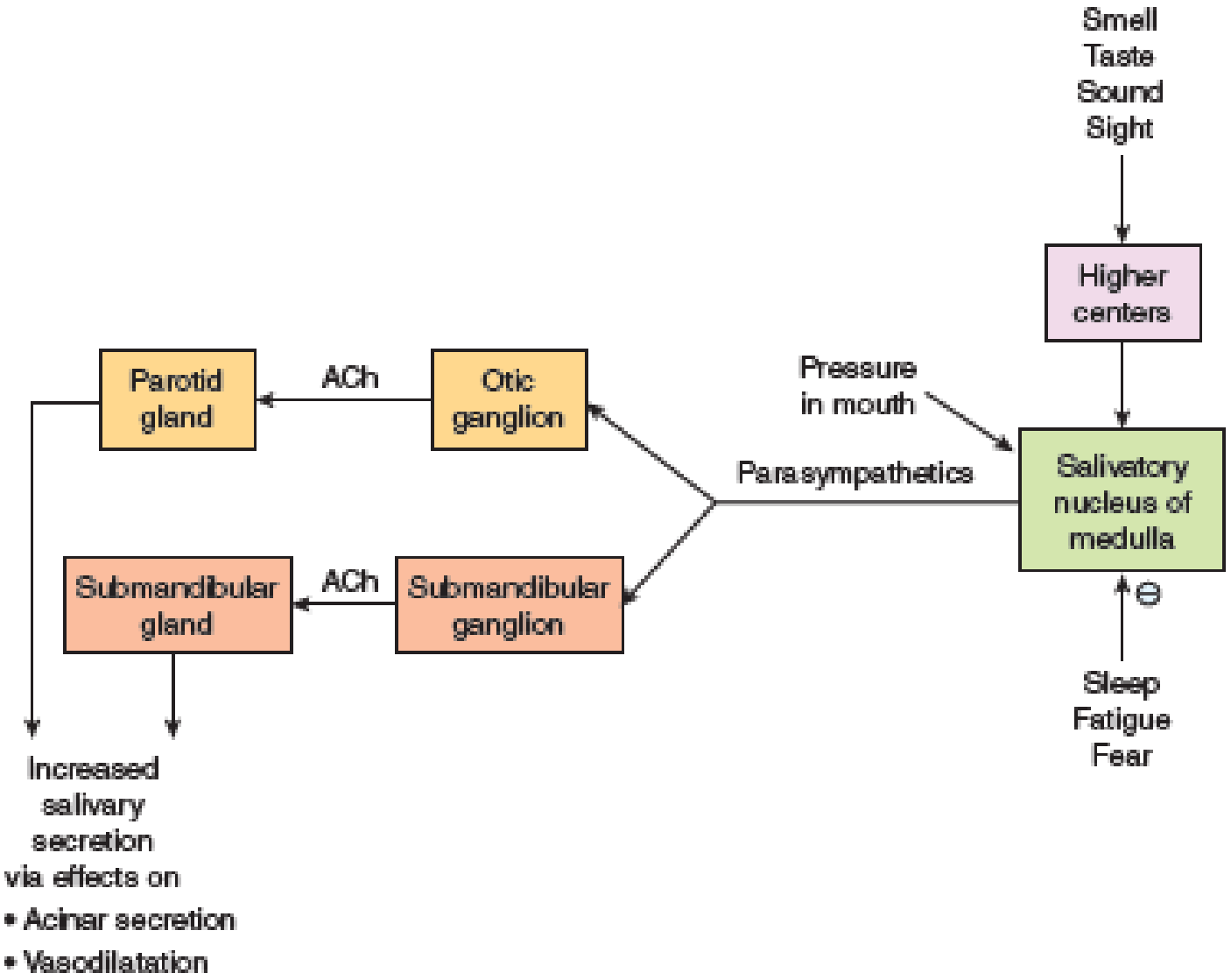
Salivary secretion is almost entirely controlled by ***neural influences,*** *with the* ***parasympathetic*** *branch of the autonomic nervous system* ***playing the most prominent role.***

Sympathetic input ***slightly*** *modifies the composition of saliva (particularly by increasing proteinaceous content), but has* ***little influence*** *on volume.*

Saliva performs a number of important functions:

it facilitates swallowing, keeps the mouth moist, serves as a solvent for the molecules that stimulate the taste buds, aids speech by facilitating movements of the lips and tongue, and keeps the mouth and teeth clean

Regulation of saliva secretion



GASTRIC SECRETION (Stomach)

Food is **stored** in the stomach; mixed with acid, mucus, and pepsin; and released at a controlled, steady rate into the duodenum.

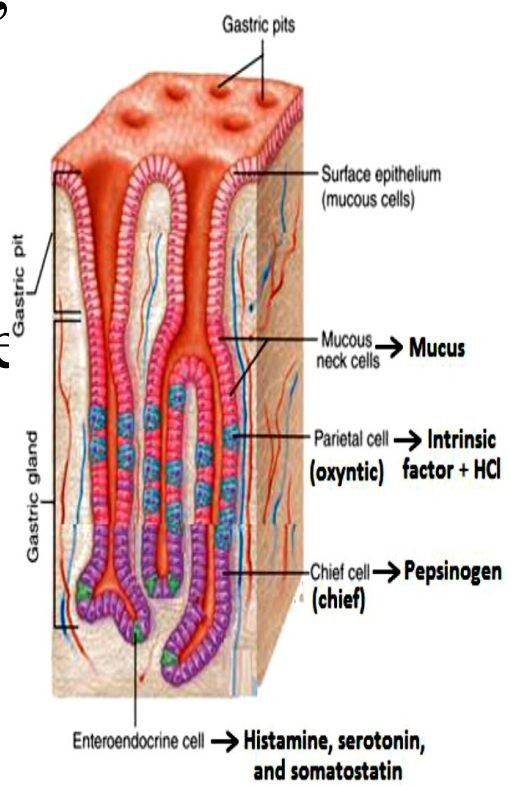
The stomach also adds a significant volume of digestive juices to the meal.

Like salivary secretion, the stomach readies itself to receive the meal before it is actually taken in, during the so-called **cephalic phase** that can be influenced by food preferences. Subsequently, there is **a gastric phase** of secretion that is quantitatively the most significant, and finally an **intestinal phase** once the meal has left the stomach. Each phase is closely regulated by both local and distant triggers.

GASTRIC SECRETION (Stomach)

The gastric secretions arise from glands in the wall of the stomach that drain into its lumen, and also from the surface cells that secrete primarily mucus and bicarbonate to protect the stomach from digesting itself. Gastric secretion adds about **2.5 L/day** to the intestinal contents. The most characteristic secretions derive from the glands in the fundus or body of the stomach.

These contain the distinctive ***parietal cells,*** **which secrete *hydrochloric acid* and *intrinsic factor* and chief cells, which produce pepsinogens and gastric lipase .**



للاطلاع فقط

Gastric Secretion

- **The acid secreted by parietal cells serves to sterilize the meal and also to begin the hydrolysis of dietary macromolecules**.
- Intrinsic factor is important for the later absorption of vitamin B12, or cobalamin. Pepsinogen is the precursor of pepsin, which initiates protein digestion.
- **Lipase** similarly begins the digestion of dietary fats.

TABLE 25–1 Contents of normal gastric juice (fasting state).

Cations: Na^+, K^+, Mg^{2+}, H^+ (pH approximately 3.0)
Anions: Cl^-, HPO_4^{2-}, SO_4^{2-}
Pepsins
Lipase
Mucus
Intrinsic factor

GASTRIC SECRETION (Stomach)

There are three primary stimuli of gastric secretion, each with a specific role to play in matching the rate of secretion to functional requirements:

1- Gastrin is a hormone that is released by G cells in the antrum of the stomach both in response to a specific neurotransmitter released from enteric nerve endings, known as gastrin-releasing peptide (GRP).

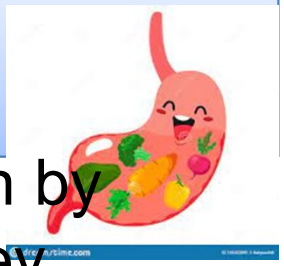
2- **Histamine** is also a trigger of parietal cell secretion, via binding to H2- receptors.

3- Finally, parietal and chief cells can also be stimulated by acetylcholine, released from enteric nerve endings in the fundus.

GASTRIC SECRETION (Stomach)

Gastric secretion that occurs during the **cephalic phase** is defined as being activated predominantly by vagal input. Once the meal is swallowed, on the other hand, meal constituents trigger substantial release of **gastrin** and the physical presence of the meal also distends the stomach and activates stretch receptors, which provoke a "vago-vagal" as well as local reflexes that further amplify secretion during the **gastric phase**. The presence of the meal also **buffers** gastric acidity that would otherwise serve as **a feedback** inhibitory signal to shut off secretion secondary to the release of **somatostatin**,

GASTRIC SECRETION (Stomach)



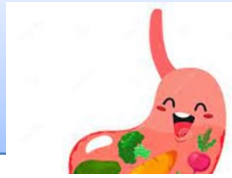
which inhibits both G and ECL cells as well as secretion by parietal cells themselves. This probably represents a key mechanism whereby gastric secretion is terminated after the meal moves from the stomach into the small intestine.

The Gastric parietal cells are packed with mitochondria that supply energy to drive the apical H+,K+-ATPase, or proton pump, that moves H+ ions out of the parietal cell against a concentration gradient of more than a million-fold..

The secretion of protons is also accompanied by the release of equivalent numbers of **bicarbonate** ions into the bloodstream, which are later used to neutralize gastric acidity once its function is complete

(Cephalic phase Gastric phase Intestinal phase)

Clinical case of stomach



CLINICAL BOX 25–1

Peptic Ulcer Disease

Gastric and duodenal ulceration in humans is related primarily to a breakdown of the barrier that normally prevents irritation and autodigestion of the mucosa by the gastric secretions. Infection with the bacterium *Helicobacter pylori* disrupts this barrier, as do aspirin and other nonsteroidal anti-inflammatory drugs (NSAIDs), which inhibit the production of prostaglandins and consequently decrease mucus and HCO_3^- secretion. The NSAIDs are widely used to combat pain and treat arthritis. An additional cause of ulceration is prolonged excess secretion of acid. An example of this is the ulcers that occur in the **Zollinger–Ellison syndrome.** This syndrome is seen in patients with gastrinomas. These tumors can occur in the stomach and duodenum, but most of them are found in the pancreas. The gastrin causes prolonged hypersecretion of acid, severe ulcers are produced.

THERAPEUTIC HIGHLIGHTS

Gastric and duodenal ulcers can be given a chance to he by inhibition of acid secretion with drugs such as omepra zole and related drugs that inhibit H^+–K^+ ATPase ("proto pump inhibitors"). If present, *H. pylori* can be eradicate with antibiotics, and NSAID-induced ulcers can be treate by stopping the NSAID or, when this is not advisable, b treatment with the prostaglandin agonist misoprosto Gastrinomas can sometimes be removed surgically.

Pancreatic Secretion

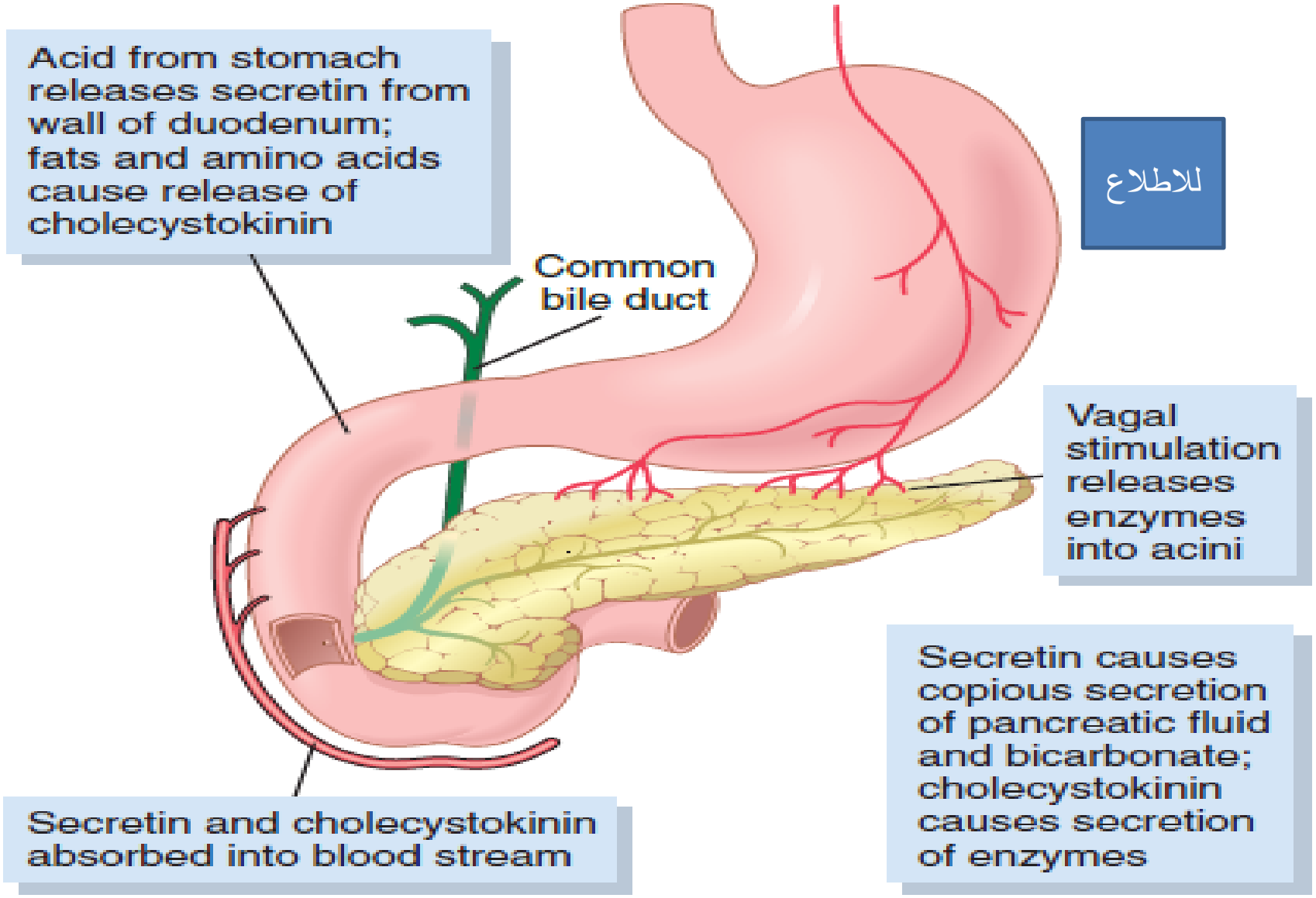


Figure 65-10. Regulation of pancreatic secretion.

Pancreatic Secretion

- **PANCREATIC SECRETION**: The pancreatic juice contains enzymes that are of major importance in digestion . Its secretion is controlled in part by a reflex mechanism and in part by the **gastrointestinal hormones secretin and cholecystokinin** (CCK). Granules containing the digestive enzymes **(zymogen granules)** are formed in the cell and discharged by exocytosis from the apexes of the cells into the lumens of the pancreatic ducts.
- About **1500** mL of pancreatic juice is secreted per day.
- Bile and intestinal juices are also neutral or alkaline, and these three secretions **neutralize** the gastric acid, raising the pH of the duodenal contents to **6.0–7.0**.
- The **pancreatic juice** also contains a range of digestive enzymes, but most of these are released in **inactive forms** and **only activated** when they reach the intestinal lumen

Pancreatic Secretion

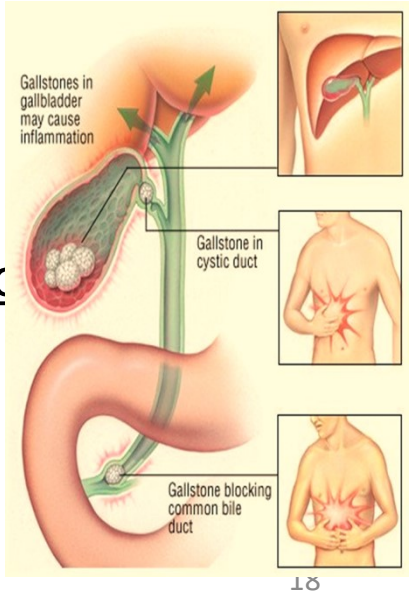
- The enzymes are activated following proteolytic cleavage by **trypsin**, itself a pancreatic protease that is released as an inactive precursor(**trypsinogen**).
- The potential danger of the release into the pancreas of a small amount of trypsin is apparent; the resulting chain reaction would produce active enzyme that could digest the pancreas.
- It is therefore not surprising that the pancreas also normally secretes a trypsin inhibitor. Secretion of pancreatic juice is primarily under **hormonal control**

BILIARY SECRETION:

- An additional secretion important for gastrointestinal function, **bile**, arises from the liver.
- The bile acids contained therein are important in the **digestion and absorption of fats**.
- **Bile** is also the only route by which the body can dispose of cholesterol—either in its native form, or following conversion to **bile acids**.
- **Bile** is made up of **the bile acids**,

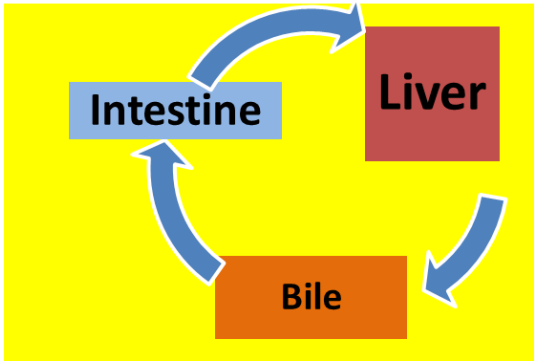
+ **bile pigments,** and other substances dissolved in an alkaline electrolyte solution that resembles pancreatic juic

- About **500 mL** is secreted per day.



BILIARY SECRETION:

- Some of the components of the bile are reabsorbed in the intestine and then excreted again by the liver **(enterohepatic circulation)**.
- The glucuronides of the **bile pigments**, bilirubin and biliverdin, are responsible for the golden yellow **color of bile**. When considering **bile** as a digestive secretion, it is the bile acids that represent the most important components.
- They are synthesized from cholesterol and secreted into the bile.



GASTROINTESTINAL REGULATION

The various functions of the gastrointestinal tract, including secretion, digestion, and absorption , and motility must be regulated in an integrated way to ensure efficient assimilation of nutrients after a meal. There are three main modalities for gastrointestinal regulation that operate in a complementary fashion to ensure that function is **appropriate**

First, endocrine regulation is mediated by the release of hormones by triggers associated with the meal. These hormones travel through the bloodstream to change the activity of a distant segment of the gastrointestinal tract, an organ draining into it (eg, the pancreas), or both

Second, some similar mediators are not sufficiently stable to persist in the bloodstream, but instead alter the function of cells in the local area where they are released, in a paracrine fashion.

Finally, the intestinal system is endowed with extensive neural connections. These include connections to the central nervous system (extrinsic innervation), but also the activity of a largely autonomous enteric nervous system that comprises both sensory and secretomotor neurons.

GASTRIN:

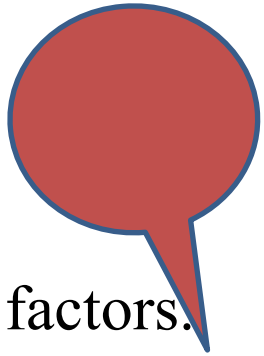
is produced by cells called G cells in the antral portion of the gastric mucosa.

Gastrin has a **variety of actions**, but its principal physiologic actions are

1-stimulation of gastric acid

2-pepsin secretion

3-stimulation of the growth of the mucosa of the stomach and small and large intestines (trophic action).



Gastrin secretion is affected by

1- The contents of the stomach,

2-The rate of discharge of the vagus nerves, and blood borne factors.

3-Increased by the presence of the products of **protein digestion** in the stomach, particularly **amino acids**, which act directly on the G cells

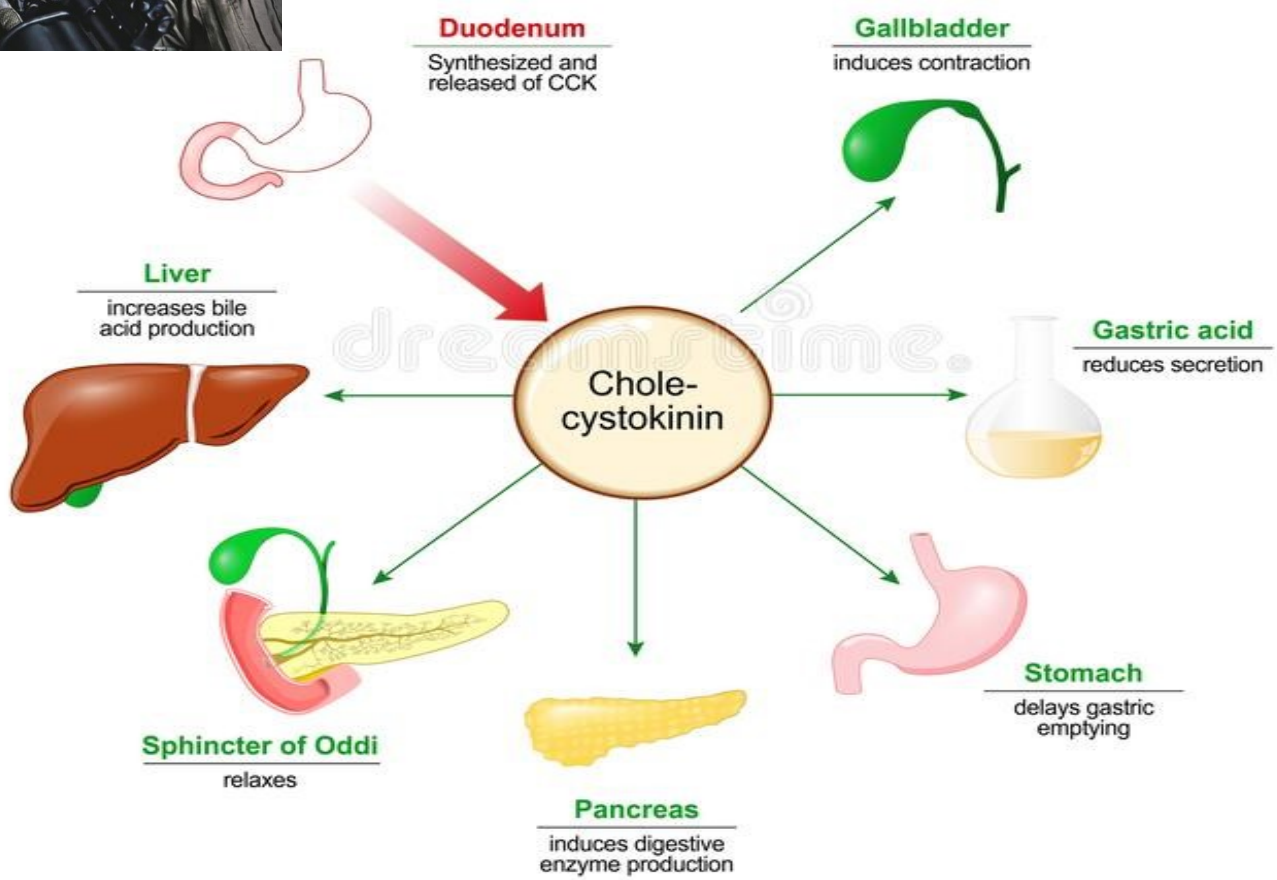
GASTRIN:

Acid in the antrum
inhibits gastrin secretion,
partly by a direct action on G cells and partly by release of **somatostatin,**
(a relatively potent inhibitor of gastrin secretion.)
The effect of acid is the basis of **–ve feedback** loop regulating gastrin secretion.
(Increased secretion of the hormone ↑ acid secretion, but the acid then feeds back to ↓ further gastrin secretion.)

TABLE 25–6 Stimuli that affect gastrin secretion.

Stimuli that increase gastrin secretion
Luminal
Peptides and amino acids
Distention
Neural
Increased vagal discharge via GRP
Bloodborne
Calcium
Epinephrine
Stimuli that inhibit gastrin secretion
Luminal
Acid
Somatostatin
Bloodborne
Secretin, GIP, VIP, glucagon, calcitonin

Cholecystokinin



Cholecystokinin(CCK):

- CCK is secreted by endocrine cells known as I cell in the mucosa of the upper small intestine.
- **The most important action** is to be

✓ The stimulation of pancreatic enzyme secretion;

✓ The contraction of the gallbladder (the action for which it was named);

✓ Relaxation of the sphincter of Oddi (which allows both bile and pancreatic juice to flow into the intestinal lumen.)

In addition to its secretion by I cells, CCK is found in

- nerves in the distal ileum and colon. It is also found in neurons in the brain, especially the cerebral cortex, and in nerves in many parts of the body.

Cholecystokinin(CCK):

- In the brain, it may be involved in the **regulation of food intake**, and it appears to be related to the production of **anxiety and analgesia**. In **addition to its primary actions,**
- **CCK augments the action of secretin in producing secretion of an alkaline pancreatic juice.**
- **It also inhibits gastric emptying,**
- **exerts a trophic effect on the pancreas,**
- **enhance the motility of the small intestine and colon**.
- The secretion of CCK is increased by contact of the intestinal mucosa with the products of digestion, particularly peptides and amino acids
- Because the bile and pancreatic juice that enter the duodenum in response to CCK enhance the digestion of protein and fat, and the products of this digestion stimulate further CCK secretion, a sort of positive feedback operates in the control of CCK secretion

SECRETIN:

- **Secretin** is secreted by S cells that are located deep in the glands of the mucosa of the upper portion of the small intestine.
- Only one form of secretin has been isolated, and any fragments of the molecule that have been tested to date are inactive. Its half life is about 5 min, but little is known about its metabolism.
- **Secretin function**
- increases the secretion of **bicarbonate** by the duct cells of the pancreas and biliary tract. It thus causes the secretion of a watery, alkaline pancreatic juice.
- augments the action of **CCK** in producing pancreatic secretion of digestive enzymes.
- decreases gastric acid secretion and may cause **contraction of the pyloric sphincter.**.

SECRETIN:

- **The secretion of secretin is increased by**

❖ the products of protein digestion

❖ acid bathing the mucosa of the upper small intestine.

(**The release of secretin by acid is another example of feedback control**)

Secretin causes alkaline pancreatic juice to flood into the duodenum, **neutralizing** the acid from the stomach and thus inhibiting further secretion of the hormone.

Gastric Inhibitory Peptide(GIP):

- is produced by K cells in the mucosa of the duodenum and jejunum.
- Its secretion is **stimulated** by **glucose and fat** in the duodenum, and because in large doses it **inhibits** gastric secretion and motility, **it was named gastric inhibitory peptide.**
- In the meantime, it was found that **GIP** stimulates **insulin secretion.** Gastrin, CCK, secretin, and glucagon also have this effect,
- but **GIP** is the **only one** of these that stimulates insulin secretion when administered at blood levels comparable to those produced by oral glucose. For this reason, it is often called glucose-dependent insulino tropic peptide..

MOTILIN:

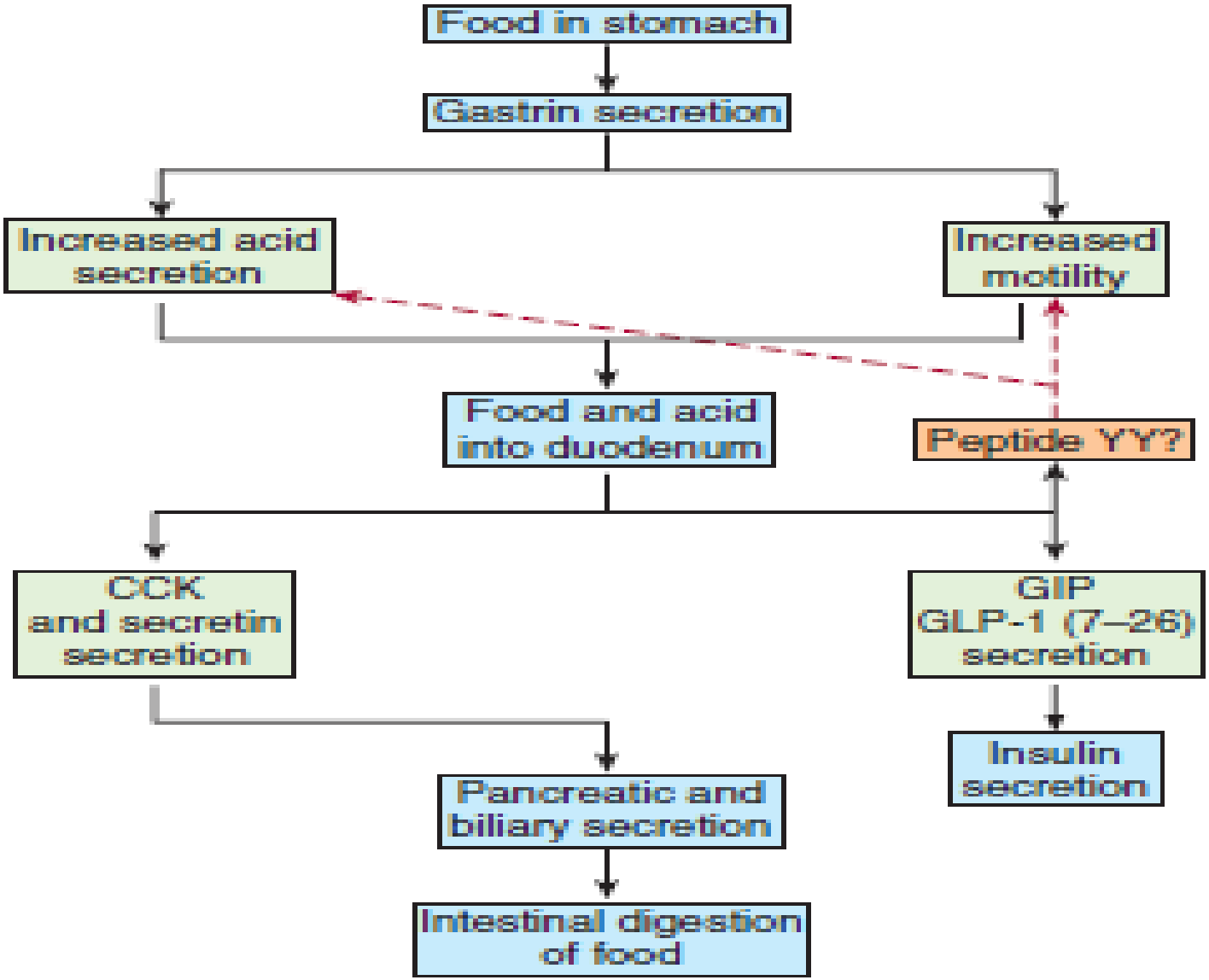
- Motilin is a polypeptide containing 22 amino acid residues that is secreted by **enterochromaffin cells and Mo cells in the stomach, small intestine, and colon.**

- It acts on G-protein–coupled receptors on enteric neurons in the duodenum and colon and produces **contractio**n of smooth muscle in the stomach and intestines in the period between meals.

SOMATOSTATIN:

- **Somatostatin,** the growth hormone–inhibiting hormone originally isolated from the hypothalamus, is secreted as **a paracrine by D cells in the pancreatic** islets and by similar D cells in the gastrointestinal mucosa.
- It exists in tissues in two forms, somatostatin 14 and somatostatin 28, and both are secreted.
- Somatostatin **inhibits** the secretion of gastrin, VIP, GIP, secretin, and motilin. Its secretion is **stimulated** by acid in the lumen, and it probably acts in a paracrine fashion to mediate the inhibition of gastrin secretion produced by acid.
- It also **inhibits** **pancreatic exocrine secretion; gastric acid secretion and motility; gallbladder contraction; and the absorption of glucose, amino acids, and triglycerides.**

Action of GIT hormones in regulating digestion and utilization of ingested nutrients.



OTHER GASTROINTESTINAL PEPTIDES:

Ghrelin

is secreted primarily by the **stomach** and appears to play an important role in the **central control of food intake** .

It also **stimulates growth hormone** secretion by acting directly on receptors in the pituitary.

Substance P

is found in endocrine and nerve cells in the gastrointestinal tract and may enter the circulation.

It **increases the motility of the small intestine**

THE ENTERIC NERVOUS SYSTEM

- Two major networks of nerve fibers are intrinsic to the gastrointestinal tract:

1-The **myenteric plexus** (Auerbach plexus), between the outer longitudinal and middle circular muscle layers,

2-the **submucous plexus** (Meissner plexus), between the middle circular layer and the mucosa . Collectively, these neurons constitute the

(enteric nervous system).

The system contains about 100 million sensory neurons,interneurons, and motor neurons in humans as many as are found in the whole spinal cord that is concerned with the regulation of gastrointestinal function.

THE ENTERIC NERVOUS SYSTEM

- It is sometimes referred to as the "**little brain**" for this reason.
- It is connected to the CNS by **parasympathetic** and sympathetic fibers but can function autonomously without these connections .
- **The myenteric plexus** innervates the longitudinal and circular smooth muscle layers and is concerned primarily with motor control, whereas the

submucous plexus innervates the glandular epithelium, intestinal endocrine cells, and submucosal blood vessels and is primarily involved in the control of intestinal secretion..

THE ENTERIC NERVOUS SYSTEM

- The **neurotransmitters in** the system include **acetylcholine, the amines norepinephrine and serotonin, the amino acid γ-aminobutyrate (GABA), the purine adenosine triphosphate (ATP), the gases NO and CO, and many different peptides and polypeptides.**
- Some of these peptides also act in a paracrine fashion, and some enter the bloodstream, becoming hormones.