Physiology of Gastrointestinal Tract
Segments of the GI tract

and Sphincters
GI Track Functions

1. Ingestion
2. Digestion
3. Absorption
4. Defecation
There are two stages of digestion

1. **Mechanical digestion** is physical breakdown of food into smaller particles that helps chemical digestion. It is achieved by the cutting and grinding actions of the teeth and the contractions of the stomach and small intestine.

2. **Chemical digestion** is a series of catabolic reactions that breaks down large carbohydrate, lipid, and protein food macromolecules into smaller molecules that are used by body cells. It is achieved by the enzymes (GI tract and accessory organs secretions, intestinal brush border).
Digestion requires

1. **Motility** - muscular contractions that break up food, mix it with digestive juices and propel it through the canal

2. **Secretion** of enzymes, peptides, and other products that carry out or regulate digestion
Layers of the GI tract

From the esophagus to the anus, the tube consists of concentrically arranged layers of muscle, nervous and mucosal tissue.

- Mucosa with epithelial cells (Secretion & absorption)
- Muscularis mucosa
- Submucosal plexus
- Submucosa
- Circular muscle (Contraction – a decrease in diameter)
- Myenteric plexus
- Longitudinal muscle (Contraction – shortening)
- Serosa
Neurol Control of GI - 1. Enteric Nervous System

- Composed of
  - Myenteric (Auerbach`s) plexus
  - Submucosal (Meissner`s) plexus

- Neurotransmitters released by the nerve endings: Acetylocholine, norepinephrine, serotonin, dopamine, cholecystokinin, somatostatin, VIP, bombesin, enkephalis.

- Lies in the wall of GI tract from the esophagus to the anus
- Coordinates and relays information
- Can function by its own – local reflexes (within GI tract)
- Affected by extrinsic nerves (parasympathetic or sympathetic systems can enhance or inhibit it`s functions)
  - Composed of
    - Myenteric (Auerbach`s) plexus
    - Submucosal (Meissner`s) plexus
1. Enteric Nervous System

- **Myenteric plexus** controls muscle activity along the GI tract
  - Increases muscle activity
    - Increased „tone“ of the gut wall
    - Increased intensity of the rhythmical contractions
    - Increased velocity of conduction of excitatory waves along the gut wall
  - Inhibits (relaxes) sphincters (LES, pyloric, ileocecal) via VIP

- **Submucosal plexus** – controls local GI secretion, blood flow, and contraction of the submucosal muscle
Parasympathetic Innervation

- Cranial – via vagus
  Vagal innervation of GI tract extends from the esophagus to the level of the transverse colon
- Sacral – via pelvic nerves to the distal part of large intestine

- The postganglionic fibres are located in the enteric NS
- Stimulation of the parasympathetic nerves increases activity of the enteric NS (and GI functions)

Sympathetic Innervation

- Begins in the spinal cord (Th5-S2)
- Postganglionic nerves innervate all GI tract
- Stimulation of the sympathetic nerves inhibits activity of the enteric NS (and GI functions)
Neural Control of the GI Tract

- The Enteric Nervous System
- The Autonomic Nervous System
Control of GI – *Electrical Activity of GI Smooth Muscle*

- **Unitary smooth muscle in the GI tract** (except the pharynx, upper 1/3 esophagus, external anal sphincter)

- **Intrinsic electrical activity**
  Caused by changes in Na⁺ conductance of pacemaker cells (interstitial cells of Cajal)

- **Rhythmical changes in resting membrane potential** - *slow waves*
  - Fixed frequency
  - Cyclic depolarization increases the probability that action potential will occur

- **Spike (action) potentials** occur at the tops of the slow wave when threshold (-40mV) is reached.
  - Initiate (followed by) phasic muscle contraction
  - Modified by neural and hormonal factors
    (number is increased by parasympathetics and decreased by sympathetics)

- **Baseline level of the resting membrane potential** can be changed by
  - Stretching, acetylcholine, parasympathetics, some GI hormones → depolarization → smooth muscle more excitable
  - Norepinephrine, epinephrine, sympathetics → hyperpolarization → smooth muscle less excitable
Control of GI Functions

Neural Reflexes:
- Enteric NS
- Autonomic NS

GI Peptides:
- Gastrin
- CCK
- Secretin
- GIP
Control of GI Functions

Neural Reflexes

- Control secretion and/or motility
- Stimulatory or inhibitory
- Named with anatomical origin of reflex (prefix) followed by the name of GI segment in which the outcome is found

„gastroileal reflex”
GI Reflexes

The chyme is stopped before the ileocecal sphincter until the person eats next meal

- **The gastroileal reflex**
  (the presence of food in the stomach causes increased peristalsis in the ileum and relaxation of the ileocecal sphincter - via extrinsic ANS and possibly by gastrin).

- **The gastrocolic reflex**
  (the presence of food in the stomach stimulates mass movements in the colon - via parasympathetic nerves, CCK, and gastrin).
Control of GI Functions
Neural Reflexes

1. Local - integrated entirely within the enteric NS

- secondary esophageal peristalsis, intestinal segmentation, migrating motor complexes
- Unaffected by vagotomy

Initiated by
- Distension
- Chemical substances
- Irritation of the mucosa

Afferent fibers carry information from chemo-, mechanoreceptors.
2. Long (parasympathetic) and local (enteric NS)

- Peristalsis of caudad stomach (decreased but not abolished by vagotomy)
- From the gut wall to the brain stem or the spinal cord and back to the GI tract (gastroileal reflex, defecation reflex)

Initiated by:
- Distension
- Chemical substances
- Irritation of the mucosa

Afferent fibers carry information from chemo- and mechanoreceptors.
Control of GI Functions
Neural Reflexes

3. Sympathetic and local (enteric NS)

- From the gut wall to the prevertebral (sympathetic) ganglia and back to the GI tract

(Intestino-intestinal (colocolic) reflex- distension of a segment of intestine causes relaxation of the remaining intestine)

Initiated by
- Distension
- Chemical substances
- Irritation of the mucosa

Afferent fibers carry information from chemo-, mechanoreceptors
Control of GI Functions

Neural Reflexes:
- Enteric NS
- Autonomic NS

GI Piptptides:
- GASTRIN
- CCK
- SECRETIN
- GIP
Segment: Mouth

- In the mouth, food is chewed, reduced to small particles, mixed with saliva, and formed into a bolus in preparation for swallowing.

- Functions:
  - Food intake, taste,
  - Chewing,
  - Mechanical and chemical digestion,
  - Swallowing,
  - Speech,
  - Respiration
Saliva

- High volume (1L / day),
- pH: 6.0 – 7.0
- Hypotonicity

Content:
1. Water 97-99,5%: moistens food and dissolves food for tasting
2. Mucus: lubricates and binds food into bolus (not secreted by the parotid glands)
3. Ptyalin (α-Amylase): starts breakdown of starch in the mouth
Saliva

4. Lingual lipase – activated by stomach acid

5. Factors that destroy bacteria: lysozyme (enzyme) and thiocyanate

4. Bicarbonate (HCO₃⁻) - buffering action - neutralizes acidic food

5. Electrolytes (basal conditions):
   - Low concentration of Na⁺ and Cl⁻
     (10%-15% that of plasma)
   - High concentration of K⁺ and HCO₃⁻
     7 times that of plasma
     3 times that of plasma
Saliva – Regulation of Secretion

**FIGURE 6-6** Regulation of salivary secretion. ACh = acetylcholine; cAMP = cyclic adenosine monophosphate; IP$_3$ = inositol 1,4,5-triphosphate; NE = norepinephrine.
Deglutition

is allowed by saliva and 22 muscles of mouth, pharynx and esophagus

1. Voluntary stage
Deglutition - 2. Pharyngeal Stage

- Stimulation of epithelial swallowing receptors (around the opening of the pharynx)
- **Swallowing reflex**
  - Subsequent contractions of pharyngeal muscles

1) Transmission of signals via the sensory fibres of the 5th and 9th cranial nerves
2) to **the swallowing center** (medulla, lower pons)
3) Transmission of motor signals by the 5th, 9th, 10th, and 12th cranial nerves to the pharynx and upper esophagus.
Deglutition

2. Pharyngeal Stage (less than 6 s)
   - a reflex act initiated by the voluntary movement of the bolus towards the pharynx

   a. Soft-palate is pulled upward closing off the nasopharynx
   b. Palatoglossal and palatopharyngeal arches are pulled medially forming a sagittal slit with the fauces.
   c. Vocal cords close
Deglutition

2. Pharyngeal Stage:

c. Larynx is pulled upward and anteriorly, and epiglottis goes backward over larynx to close off the opening of the larynx

d. Upward movement of larynx pulls up and enlarges the opening to the esophagus.

e. Upper esophageal sphincter relaxes and the bolus can enter the esophagus.

f. Muscular wall of the pharynx contracts to propel the bolus into the esophagus.
Peristalsis pushes the bolus down the esophagus.

**Primary peristalsis** - A continuation of the peristaltic wave that begins in the pharynx (passes to the stomach in 8-10 seconds)

- Food movement accelerated by the effect of gravity (5-8 seconds)
Lower esophageal sphincter (LES)

- Tonically contracted
  (intraluminal pressure – 30 mm Hg)
  in the resting state

- Effected by GI peptides
Deglutition – 3. Esophageal Stage

- As the bolus approaches the end of esophagus, LES relaxes - **vagally mediated (VIP) reflex relaxation**
Esophageal Motility

**Secondary peristalsis**

- Local reflex
- Clears the esophagus of any remaining food
- Localized response to irritation or distention
Gastroesophageal Reflux Disease (GERD)

CAUSES = incompetent LES

- Because of the acidic nature of gastric contents, GERD is associated with esophageal pain (heartburn), esophageal ulcers, and increased risk of esophageal cancer.

- It is aggravated by conditions in which the LES is forced up into the thorax, such as in hiatal hernia and pregnancy.
GI Tract Functions: Stomach

**Stomach:**
- Storage of the food
- Mixing of food with gastric juices → *chyme* (semidigested food)
- Regulation (slowing) of chyme emptying into the duodenum

**Anatomic division:**
- The fundus, body, and antrum
Physiologic division:

- The orad portion (fundus, proximal body)
- The caudad portion (distal body, antrum)
Receptive Relaxation of the Orad Stomach

The orad portion

- Receives and accommodates the food
- Characterized by low-intensity tonic contractions
- but no slow wave activity (no phasic contractions)

Accommodation:

Food stretches the stomach wall → via a vagovagal reflex → stomach relaxes to accommodate the ingested food (receptive accommodation)

- Increase in volume up to 0.8-1.5 L with small increase in intragastric pressure
**Contractile Activity of the Cauded Stomach**

*The cauded portion*
- Mixes the food with gastric secretion
- Propels chyme into the duodenum
- *Slow wave activity* and phasic contractions

- **Mixing (peristaltic) waves**
  - Begin in mid- to upper portion of the stomach
  - Move toward the antrum
  - Frequency of 3-5 times/min
  - Initiated by wall basic electrical rhythm
    - Electrical slow waves
    - Action potential → contraction

- *Normal tonic contraction of the pyloric sphincter prevents duodenogastric reflux.*
Gastric Secretion (pH: 1.0 – 3.5)

1. **The Oxyntic (Gastric) Glands**
   - The proximal 80% of the stomach (fundus, body)
   - **Mucus**: lubricates and protects the stomach mucosa
   - **Hydrochloric acid (parietal cells)**
     - Destroys pathogens,
     - Dissolves food particles
     - Converts ferric ions (Fe$^{3+}$) to ferrous ions (Fe$^{2+}$)
     - Indirectly (?) stimulates secretion of pepsinogen
     - Activates pepsinogen and
     - Creates a highly acid medium for pepsin (pepsin – optimal pH -1.8-3.5)
   - **Intrinsic factor (parietal cells)**
   - **Pepsinogen (chief cells)** - inactive form of the proteolytic enzyme – pepsin
   - **Histamine** (enterochromaffin-like cells – ECL cells)
Gastric Secretion (pH: 1.0 – 3.5)

2. The Pyloric Glands
   - The distal 20% of the stomach (antral portion)

   - Gastrin (G cells) – stimulate gastric secretion

   - Mucus
   - Pepsinogen
<table>
<thead>
<tr>
<th>Secretory Cells</th>
<th>Secretion</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucous neck cells</td>
<td>Mucus</td>
<td>Protects mucosa from HCl and enzymes</td>
</tr>
<tr>
<td>Parietal cells</td>
<td>Hydrochloric acid</td>
<td>Activates pepsin and lingual lipase; helps liquefy food; reduces dietary iron to usable form (Fe^{2+}); destroys ingested pathogens</td>
</tr>
<tr>
<td></td>
<td>Intrinsic factor</td>
<td>Enables small intestine to absorb vitamin B_{12}</td>
</tr>
<tr>
<td>Chief cells</td>
<td>Pepsinogen</td>
<td>Converted to pepsin, which digests protein</td>
</tr>
<tr>
<td></td>
<td>Rennin</td>
<td>Coagulates milk proteins in infant stomach; not secreted in adults</td>
</tr>
<tr>
<td></td>
<td>Gastric lipase</td>
<td>Digests fats in infant stomach; not secreted in adults</td>
</tr>
<tr>
<td>Enteroendocrine cells</td>
<td>Gastrin</td>
<td>Stimulates gastric glands to secrete HCl and enzymes; stimulates intestinal motility; relaxes ileocecal valve</td>
</tr>
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<td></td>
<td>Serotonin</td>
<td>Stimulates gastric motility</td>
</tr>
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<td></td>
<td>Histamine</td>
<td>Stimulates HCl secretion</td>
</tr>
<tr>
<td></td>
<td>Somatostatin</td>
<td>Inhibits gastric secretion and motility; delays emptying of stomach; inhibits secretion by pancreas; inhibits gallbladder contraction and bile secretion; reduces blood circulation and nutrient absorption in small intestine</td>
</tr>
</tbody>
</table>

Rennin - not to be confused with renin, the enzyme secreted by the kidneys
Actions of Gastrin

- Contracts LES
- Stimulates gastric motility,
- Relaxes pyloric sphincter
- Enhances intestinal motility, relaxes ileocecal sphincter (gastroileal reflex)
- Stimulates insulin secretion (only after ingestion of proteins)
  - Hypergastrinemia (gastrin-producing pancreatic tumors) is associated with gastric hyperplasia and gastric acid hypersecretion
Release of Gastrin

Stimulatory factors:

- **Simulation of the vagus nerve**
  (in the case of G cells, the postganglionic nerve endings release GRP not Acetylcholine)

- **Distension of the stomach**

- **Proteins (digestion products)**
  (amino acids: phenylalanine & tryptophan act directly on the G cells)

- **Blood-borne:** adrenaline, calcium

Inhibitory factors:

- **Acid** - a negative feedback effect
  (both via a direct action on the G cells and via stimulation of somatostatin secretion)

- **Somatostatin**
Regulation of HCl Secretion by the Parietal Cells

- Controlled by both endocrine and nervous signals

**Diagram Description:**

- **Vagus** stimulation
- **GRP** (Gastrin Releasing Peptide) via G cells
- **ACh** (Acetylcholine) via ECL cells

**Key Receptors and Signals:**

- **$M_3$** receptor
- **CCK$_B$** receptor
- **H$_2$** receptor

**Agents and Effects:**

- **Atropine** blocks **ACh**
- **Cimetidine** blocks **Histamine**
- **Somatostatin** inhibits secretion
- **Prostaglandins** activate secretion

**Key Enzyme:**

- **H$_+$,K$_+$-ATPase**

**Agents that stimulate and inhibit H$^+$ secretion by gastric parietal cells:**

- **ACh** = acetylcholine
- **cAMP** = cyclic adenosine monophosphate
- **CCK** = cholecystokinin
- **ECL** = enterochromaffin-like
- **IP$_3$** = inositol 1,4,5-triphosphate
- **M** = muscarinic

**Figure 6-9**

[Diagram showing the regulation of HCl secretion by the parietal cells with various signaling pathways and agents.]
Protection of the stomach

1. **Mucous coat** — thick alkaline mucus resists the action of acid and enzymes.

2. **Epithelial cell replacement** — these cells live only 3 to 6 days and are then digested with the food.

3. **Tight junctions** — that prevent gastric juice from seeping between them and digesting the connective tissue.
Small Intestine

1. **Duodenum:**
   shortest region, about 25cm

   a. *Continues the digestion of carbohydrates, proteins, and lipids*  
      Begins the digestion of nucleic acids

   b. *Gets the digestive fluids from the pancreas and liver* via the hepatopancreatic ampulla

   c. *Secretes intestinal hormones*
Pancreas

- Head, body, and tail
- Connected to the duodenum via
  - The pancreatic duct (duct of Wirsung)
  - Accessory duct (duct of Santorini)
Pancreas – Exocrine Part

• **Acinar cells**
  Produce a small volume of initial pancreatic secretion rich in digestive enzymes

• **Ductal cells**
  (ductules, larger ducts)
  Secrete large volume of watery solution of sodium bicarbonate
Pancreatic Juice

- High volume (1.2L - 1.5L daily)
- pH – 8.0-8.3, isotonicity
- **Zymogens and digestive enzymes**
  - Much lower Cl⁻ conc. than plasma
  - The same Na⁺ and K⁺ conc. than plasma
  - **Much higher HCO₃⁻ conc. than plasma** (up to 145 mEq/l)

Sodium bicarbonate secretion serves to neutralize the acidic chyme emptied from stomach

- inhibit further digestive activity of the gastric juices (at the pH >5, pepsin is denaturated)
- protects the intestinal mucosa
- provides a pH for action of the pancreatic digestive enzymes (7.0 - 8.0)
## Exocrine Secretions of the Pancreas

### Zymogens and digestive enzymes

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<td><strong>Zymogens</strong></td>
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### Enzymes

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<td>Pancreatic amylase</td>
<td>Digests starch</td>
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<tr>
<td>Pancreatic lipase</td>
<td>Digests fat</td>
</tr>
<tr>
<td>Ribonuclease</td>
<td>Digests RNA</td>
</tr>
<tr>
<td>Deoxyribonuclease</td>
<td>Digests DNA</td>
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Pancreatic proteolytic enzymes become activated only after they are secreted into the intestinal tract!!!
Activation of Pancreatic Proteases in the Small Intestine
## Exocrine Secretions of the Pancreas

### Zymogens and digestive enzymes

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<td>Deoxyribonuclease</td>
<td>Digests DNA</td>
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Gastrin - Cholecystokinin (CCK) (Family of GI Peptides)

- Five identical amino acids
- Do not share any actions at normal, physiological concentrations
- Identical actions at high, pharmacological concentrations
Cholecystokinin (CCK)

The principal stimuli for CCK release:

- fats
- proteins

(I cells of the duodenal and jejunal mucosa)
Cholecystokinin (CCK)

(I cells of the duodenal and jejunal mucosa secrete CCK)
Cholecystokinin is the only GI hormone that inhibits gastric emptying – keeps the stomach full for a long time.

A breakfast containing fat and protein „stick with you” better than that containing mostly carbohydrates.
Control of Gastric Emptying

**Stimulatory Gastric Factors**
- Stretching
- Isotonic content
- Gastrin

1. Increase antral peristalsis (pressure -50-70 cmH2O)
1. Relax pyloric sphincter

**Inhibitory Duodenal Factors**
- Increasing the volume, fat content, acidity, or osmolarity of the lumen of the small intestine
- Elicits inhibitory neural enterogastric reflex & hormonal feedback mechanisms (CCK)

1. Decrease antral peristalsis
2. Increase pyloric sphincter tone

Promotes Gastric Emptying  Inhibits
Secretin
Secreted by (S) Cells in the duodenum and jejunum

**Stimulus:**
Acid chyme in small intestine causes secretion of secretin (pH less than 4.5 - 5.0)

**Action**

1. Parasympathetic impulses along vagus (X) nerves
2. Stimulate secretion of pancreatic enzymes
3. Stimulates secretion of pancreatic juice rich in bicarbonate ions
4. Stimulates secretion of pancreatic juice rich in digestive enzymes
5. Secretin
6. CCK
7. Blood

Pancreatic Fluid (HCO₃⁻) Secretion
Gastric Acid Secretion
Hepatic HCO₃⁻ Secretion
Pancreatic Growth
Neural and Hormonal Control of the Pancreas

**Secretin:**
acidity in intestine causes increased sodium bicarbonate release

**Cholecystokinin (CCK):**
small peptides, amino acids, and fatty acids cause increased digestive enzyme release

**Acetylocholine (Vagus)**
The Intestine: An Unknown Organ

- 100,000 billion bacteria
- 60 to 70% of our immune cells
- 100 million neurons
- Surface of approximately 300 m²
Small Intestine

1. **Duodenum:**
   shortest region, about 25cm
   
   a. *Continues the digestion of carbohydrates, proteins, and lipids*
   Begins the digestion of nucleic acids
   
   b. *Gets the digestive fluids from the pancreas and liver* via the hepatopancreatic ampulla
   
   c. *Secretes intestinal hormones*
2. **Jejunum**:  
   Middle region  
   a. Continues and completes the digestion of carbohydrates, proteins, lipids, and nucleic acids  
   b. Begins the absorption of carbohydrates, proteins, and water-soluble vitamins  

3. **Ileum**  
   final, longest region  
   a. Involved in absorption of majority produced by digestion.
Functions of the Small Intestine Mucosa - 1

Digestion

- Contact digestion

*The brush border* increases the absorptive surface area of the small intestine and contains brush border enzymes – they are not released into the lumen and the chyme must contact the brush border for digestion to happen- contact digestion.
Functions of the Small Intestine Mucosa - 2 Absorption

Absorptive area of the intestinal mucosa is increased 600 times

1. The mucosa of the small intestine has **folds** (of Kerckring) that increase the surface area of the mucosa about **threelfold**.

2. The **millions of villi** enhance the absorptive surface area by perhaps another **tenfold**.

3. Each intestinal epithelial cell in the villus is characterized by a **brush border** (has about 1000 **microvilli**), and increasing the area another **twentyfold**.
Villi
Villus

- Each villus contains a central lacteal for absorption into the lymph, an artery, a vein, and blood capillaries, so that dissolved materials can be sent directly into the portal circulation.
Functions of the Small Intestine Mucosa – 3

Secretion

- **Duodenum**
  - Large amounts of alkaline mucus produced by Brunner`s glands
    - Inhibited by sympathetic stimulation
      (50% of peptic ulcers)

- **Small Intestine**
  - 1 to 2 L of intestinal juice per day
  - Contains water, electrolytes, and almost no enzymes, that are found in the brush border
  - pH – 7.5 – 8.0
  - Produced by enterocytes in the crypts of Lieberkühn
  - Absorbed by the villi
  - Local regulation of secretion (enteric nervous reflexes)
Functions of the Small Intestine Mucosa - 4

Secretion of Peptides

- Vasoactive Intestinal Peptide (VIP)
- Encephalins
  - Stimulate contraction of the sphincters
  - Inhibit intestinal secretion
- Hormones
  - Secretin
  - CCK
  - Glucose Dependent Insulinotropic Peptide (GLIP)

Hormones, Paracrines, and Neurocrines

FIGURE 6-2 Gastrointestinal hormones, paracrines, and neurocrines.
Secretin

- 27-amino acid residues
- Secreted by enteroendocrine (S) cells in the duodenum and jejunum

**Secretin Family of GI Peptides**

- This family has segments in which there are amino acid sequences identical to those found in secretin
  - Glucose dependent insulinotropic peptide (GLIP)
  - Glucagon
  - Vasoactive intestinal peptide (VIP)

- An overlap of peptide receptor interaction, but each peptide has a much greater potency when it reacts with its own receptor
Glucose-dependent Insulinotropic Peptide (GLIP)

- A linear peptide (42 amino acid residues)
- Homologues to secretin and glucagon
- Secreted by K cells (duodenum and jejunum)

- The only GI hormone released by all three major nutrients: fats (fatty acids), proteins (amino acids), and carbohydrates (glucose)

- Actions:
  - Strong stimulator of insulin release
  - Inhibits gastric secretion and motility
Vasoactive Intestinal Peptide (VIP)

- 28 amino acid residues
- Homologues to secretin
- released from nerve endings in the mucosa and smooth muscle of the GI tract
- Found in brain and ANS nerves

**Actions:**

- Stimulates intestinal and pancreatic secretion of electrolites \((\text{HCO}_3^-)\) and water
  (VIP-oma may cause severe diarrhea – pancreatic cholera)
- Relaxes GI smooth muscle (including sphincters)
- Dilates peripheral blood vessels
- Inhibits gastric secretion
SOMATOSTATIN

Secretion:
- by D cells in the GI tract in response to H+ in the lumen
- Inhibited by vagus

Action - It inhibits
- release of GI peptides
- GI secretions (gastric and pancreatic juices)
- contraction of the gallbladder
- motility of GI tract
GI Motility

• The term GI motility refers to the motor activity (i.e., contractions) of the GI muscles.
• Functions:
  - transport of ingested food
  - mixing of ingested food with the digestive secretions
  - regulation of rate at which material moves from proximal to distal segments
  - preventing of reflux
GI Phasic Contraction: Segmentation

- Segmentation (mixing) contractions
  - Occur at intervals along the intestine
  - As one set of segmentation contractions relaxes, a new set often begins at new points between the previous contractions.
  - The back-and-forth movement causes mixing the chyme with the digestive secretions, exposes the mucosal absorptive surface to the luminal contents and helps move chyme along the tract.

- Determined by slow waves
- Amplified by excitation from the myenteric nervous plexus
- Up to 12/min – duodenum and upper jejunum, up to 8-9 – terminal ileum)
GI Phasic Contraction: Peristalsis

- Peristalsis is a propulsive reflex activity that involves both circular and longitudinal muscle layers, that is coordinated by the enteric NS.

- Propels the chyme caudally.

- Small intestine - 0.5 to 2.0 cm/sec, net movement of chyme - 1 cm/min

- Occurs in the esophagus, the distal stomach, small and large intestines.

  - Peristaltic contractions are increased after a meal by:
    - stretching of the stomach wall (gastroileal, gastrocolic reflexes)
    - stretching the gut wall
    - hormonal factors (gastrin, CCK, motilin)
Anatomy of Large Intestine

- Include the **cecum**, **colon**, **rectum**, and **anal canal**.
- **1.25 m** long, diameter from **8 - 9 cm** (cecum) to **2 - 3 cm** (the sigmoid colon)
- Ascending & descending colon are retroperitoneal
- Hanging inferior to the cecum is the **appendix**.
  - Inflammation of the appendix is called **appendicitis**.
  - A ruptured appendix can result in gangrene or peritonitis, which can be life-threatening conditions.
Control of Ileocecal Sphincter

- **Colonoileal reflex** – inhibits ileal peristalsis and contracts ileocecal sphincter

- **Ileocecal reflex** – increases ileal peristalsis and relaxes ileocecal sphincter

- **Gastroileal reflex**
  (food in the stomach causes increased peristalsis in the ileum and relaxation of the ileocecal sphincter)
Mixing movements – „Haustrations”
- Contraction of the circular muscle (2.5 cm)
- Contraction of the longitudinal muscle (arranged in 3 strips – teniae coli)
- Exposure of chyme to the surface area – absorption of water and electrolytes
- Slow propulsive effect (8-15 hours)

Propulsive (mass) movements
- Begin in the transverse colon as a constrictive ring followed by a contraction of 20 cm of the colon
- 1-3 times a day
- Enhanced by gastro(duodeno)colic reflexes

- Proximal half – absorption of water electrolytes: Na⁺, Cl⁻, vitamin K

- Distal half – storage
The Mucosa of the Large Intestine Functions

1. **Secretion** *(pH of 7.5 - 8.0)*
   - 200 ml per day
   - Mucus that lubricates colon and protects mucosa
   - Sodium bicarbonate
   - Regulation:
     - Direct stimulation
     - Local nervous reflexes
     - Stimulation of pelvic (parasympathetic) nerves

2. **Absorption**
   - **Absorptive cells:** Maintains water balance, solidifies feces, absorbs vitamins and some ions

Extreme parasympathetic stimulation → secretion of large amounts of mucus → bowel movement every 30 minutes
Absorption & Feces Formation in the Large Intestine

- Large intestin takes about 12 to 24 hours to reduce the residue of a meal to feces
- Bacterial fermentation converts
  - undigested carbohydrates into carbon dioxide & methane gas
  - undigested proteins into simpler substances (indoles) - odor
  - turn bilirubin into simpler substances that produce color

- *Feces* consist of undigested parts of food, water, inorganic salts, epithelial cells, bacteria, and products of bacterial decomposition.

- The average person expels about 500ml of flatus per day; flatus is composed of nitrogen (N2), CO2, H2, CH4, H2S and indoles and skatoles)

- Indoles, skatoles and H2S produce the odor of flatus and feces
Defecation – Rectosphincteric reflex

- Mediated by the local enteric NS
- Distension of the rectum initiates peristaltic waves and relaxes the internal anal sphincter
- Enhanced by parasympathetic defecation reflex via spinal cord
- Associated by closure of the glottis and contractions of the abdominal muscles.
- The external anal sphincter can be voluntarily controlled (except in infants) to allow or postpone defecation.

**Figure 25.31 Neural Control of Defecation.** (1) Filling of the rectum with feces stimulates stretch receptors, which transmit impulses to the spinal cord. (2) A spinal reflex stimulates contractions of the rectum and relaxation of the internal anal sphincter. (3) Defecation normally does not occur unless voluntary impulses relax the external anal sphincter.
Overview of Intestinal Absorption

- Absorption is the transport of solute and water from the gut lumen, across the intestinal epithelium, into the lymph or venous blood. Basic mechanisms of absorption involve simple diffusion, facilitated diffusion, and active transport.

- Most absorption takes place in the small intestine. The average daily (small) intestinal absorption consists of:
  - Several hundreds gram of carbohydrates
  - 50-100 grams of amino acids,
  - 100 grams of fat
  - 50-100 grams of electrolytes
  - 7-8 L of water.

- Colon is able to absorb additional water and ions
Overview of fluid intake and secretion compared to fluid absorption by the digestive tract

- **Fluid intake and secretion:**
  - 7.0 L is secreted
  - 2.0 L is ingested
  - A total fluid input = 9.0 L.

- **GI fluid absorption:**
  - the small intestine - about 8.0 L
  - the colon – 0.9 L

- **Fluid loss in the feces** – 0.1 L

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Overview of fluid intake and secretion compared to fluid absorption by the digestive tract

<table>
<thead>
<tr>
<th>Daily Secretion of Intestinal Juices</th>
<th>Daily Volume (ml)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saliva</td>
<td>1000</td>
<td>6.0–7.0</td>
</tr>
<tr>
<td>Gastric secretion</td>
<td>1500</td>
<td>1.0–3.5</td>
</tr>
<tr>
<td>Pancreatic secretion</td>
<td>1000</td>
<td>8.0–8.3</td>
</tr>
<tr>
<td>Bile</td>
<td>1000</td>
<td>7.8</td>
</tr>
<tr>
<td>Small intestine secretion</td>
<td>1800</td>
<td>7.5–8.0</td>
</tr>
<tr>
<td>Brunner’s gland secretion</td>
<td>200</td>
<td>8.0–8.9</td>
</tr>
<tr>
<td>Large intestinal secretion</td>
<td>200</td>
<td>7.5–8.0</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>6700</strong></td>
<td></td>
</tr>
</tbody>
</table>
Carbohydrates

- Dietary sources of carbohydrates:
  - starch
  - sucrose (table sugar)
  - lactose (milk sugar)
  - others (amylose, dextrins, glycogen, lactic acid, pyruvic acid, alcohol)

- Unavailable carbohydrates: indigestible oligosaccharides (e.g., raffinose) and dietary fiber (cellulose and hemicellulose).

These carbohydrates are not digested in the small intestine. They pass to the colon, where they are fermented by bacterial enzymes. Fermentation products include:
  - carbon dioxide & methane gas
  - acids (acetic, propionic, butyric acid)
Carbohydrates - digestion

Starches
- Mouth – 5%
- Stomach – 1 hour – at pH > 4
- Duodenum – 15-30 min

Maltose and 3-9 glucose polymers
- Ptyalin (saliva) - 20-40%
- Pancreatic α-amylase (50-80%)

Glucose
- 80% of final products of carbohydrates digestion
- (fructose – 10%, galactose – 10%)

Contact digestion
Brush border
(Small intestine)

Maltase and α-dextrinase
(Sucrase and lactase)
## Carbohydrates - Enzymatic Digestion

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Source</th>
<th>Substrate</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amylase</td>
<td>Salivary glands, Pancreas</td>
<td>Starches</td>
<td>Maltose, Dextrins</td>
</tr>
<tr>
<td>Dextrinase</td>
<td>Brush Border cells</td>
<td>Dextrins</td>
<td>Glucose</td>
</tr>
<tr>
<td>Maltase</td>
<td>Brush Border cells</td>
<td>Maltose</td>
<td>Glucose</td>
</tr>
<tr>
<td>Sucrase</td>
<td>Brush Border cells</td>
<td>Sucrose (cane sugar)</td>
<td>Glucose, Fructose</td>
</tr>
<tr>
<td>Lactase</td>
<td>Brush Border cells</td>
<td>Lactose (milk sugar)</td>
<td>Glucose, Galactose</td>
</tr>
</tbody>
</table>
Carbohydrates – Absorption

- The initial active transport of Na+ through the basolateral membrane generates a Na+ gradient across the epithelial cell providing motive force for glucose transport.
Figure 25.26  Starch Digestion in the Small Intestine. Pancreatic amylase digests starch into maltose and small oligosaccharides. Brush border enzymes digest these to glucose, which is absorbed by the epithelial cells.
Proteins – Digestion & Absorption

- **Proteins**
  - **Stomach**
  - **Duodenum**

- **Polypeptides**
  - **Pepsin**
  - **Pancreatic proteases**
  - **Aminopeptidases**
  - **Dipeptidases**

- **Di(Tri)peptides**
- **Amino Acids**

- **Cell membrane**
  - \( H^+ \)-dependent cotransport
  - \( Na^+ \)-dependent cotransport

- **Cytoplasmatic Peptidases**
Mouth

No digestion occurs.

Stomach

Pepsin (▲) hydrolyzes certain peptide bonds, breaking protein down into smaller polypeptides.

Small intestine

Actions of pancreatic enzymes

Trypsin (▲) and chymotrypsin (▲) hydrolyze other peptide bonds, breaking polypeptides down into smaller oligopeptides.

Carboxypeptidase (▲) removes one amino acid at a time from the carboxyl (−COOH) end of an oligopeptide.

Small intestine

Actions of brush border enzymes (contact digestion)

Carboxypeptidase (▲) of the brush border continues to remove amino acids from the carboxyl (−COOH) end.

Aminopeptidase (▲) of the brush border removes one amino acid at a time from the amino (−NH₂) end.

Dipeptidase (▲) splits dipeptides (▲) into separate amino acids (●).
<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Source</th>
<th>Substrate</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pepsin</td>
<td>Chief Cells</td>
<td>Proteins</td>
<td>Peptides</td>
</tr>
<tr>
<td>Pepsinogen (HCl)</td>
<td>Chief Cells</td>
<td>Proteins</td>
<td></td>
</tr>
<tr>
<td>Trypsin</td>
<td>Acinar Cells</td>
<td>Proteins</td>
<td>Peptides</td>
</tr>
<tr>
<td>Trypsinogen</td>
<td>Acinar Cells</td>
<td>Proteins</td>
<td>Peptides</td>
</tr>
<tr>
<td>(enterokinase)</td>
<td></td>
<td></td>
<td>Amino acids</td>
</tr>
<tr>
<td>Chymotrypsin</td>
<td>Acinar Cells</td>
<td>Proteins</td>
<td>Peptides</td>
</tr>
<tr>
<td>Chymotrypsinogen (Trypsin)</td>
<td>Acinar Cells</td>
<td>Proteins</td>
<td>Peptides</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Amino acids</td>
</tr>
</tbody>
</table>
## Enzymatic Digestion of Proteins

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Source</th>
<th>Substrate</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elastase</td>
<td>Acinar Cells</td>
<td>Proteins</td>
<td>Peptides amino acids</td>
</tr>
<tr>
<td>Proelastase (Trypsin)</td>
<td>Acinar Cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carboxypeptidase</td>
<td>Acinar cells</td>
<td>Terminal AA on the carboxyl end</td>
<td>Amino acids</td>
</tr>
<tr>
<td>Procarboxypeptidase</td>
<td>Acinar cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Trypsin)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterokinase</td>
<td>Brush Border</td>
<td>Trypsinogen</td>
<td>Trypsin</td>
</tr>
<tr>
<td>Enzyme</td>
<td>Source</td>
<td>Substrate</td>
<td>Product</td>
</tr>
<tr>
<td>-----------------</td>
<td>--------------</td>
<td>----------------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>Aminopeptidase</td>
<td>Brush Border</td>
<td>Terminal AA at the amino end</td>
<td>Amino acids</td>
</tr>
<tr>
<td>Dipeptidase</td>
<td>Brush Border</td>
<td>Dipeptides</td>
<td>Amino Acids</td>
</tr>
</tbody>
</table>
Lipids

Dietary sources:

- Triglycerides (neutral fat)
- Small amounts of phospholipids, cholesterol, and cholesterol esters
- About 90% of fatty acids in triglycerides are long-chain fatty acids (16 to 18 carbons) saturated or unsaturated. The remaining 10% are medium or short-chain fatty acids

- Absorbed long chain fatty acids are re-esterified to TG and released in the form of chylomicrones into the lymphatics (thoracic duct).
- Absorbed fatty acids which contain less than 10-12 carbons are more water soluble and diffuse into the capillary blood.
- Begins in the stomach
- Occurs mainly in the duodenum
- Increases the total surface area of the fat 1000 fold

**Enzymes for fat digestion:**
- Pancreatic lipase, phospholipase A₂
- Cholesterol esterase

Micelles are soluble in chyme

Intestinal cells absorb lipids from micelles, resynthesize triglycerides, and package triglycerides, cholesterol, and phospholipids into protein-coated chylomicrons.

Golgi complex packages chylomicrons into secretory vesicles; chylomicrons are released from basal cell membrane by exocytosis and enter the lacteal (lymphatic capillary) of the villus.
Lipids – digestion

- **Lingual Lipase**
  - secreted by glands located at the root of the tongue and the parotid glands,
  - Active in stomach, digests less than 10% of TG
  - more specific for medium fatty acids (more important in the digestion of milk fat in the newborn).

- **Gastric Lipase**
  - secreted by cells of the fundic stomach
  - important during the neonatal period (when pancreatic lipase is not yet very active and milk fat must be digested)
  - not secreted in the adults
## Enzymatic Digestion of Lipids

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Source</th>
<th>Substrate</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipase</td>
<td>Tongue (Lingual)</td>
<td>Triglycerides</td>
<td>Fatty acids monoglycerides</td>
</tr>
<tr>
<td>Lipase</td>
<td>Stomach (gastric)</td>
<td>Milk butterfats</td>
<td>Fatty acids monoglycerides</td>
</tr>
<tr>
<td>Lipase</td>
<td>Pancreas (pancreatic)</td>
<td>Triglycerides</td>
<td>Fatty acids monoglycerides</td>
</tr>
</tbody>
</table>
(a) Mechanisms for movement of nutrients through epithelial cells of the villi

(b) Movement of absorbed nutrients into the blood lymph
Most water-soluble vitamins are absorbed by Na\(^+\)-dependent cotransport mechanism.

- B12 is absorbed in a complex with the intrinsic factor produced by the parietal cells of the stomach mucosa.
- Fat-soluble vitamins (ADEK) are incorporated into micelles and absorbed along with other lipid.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Pancreatitis</td>
<td>Severe pancreatic inflammation perhaps caused by trauma leading to leakage of pancreatic enzymes into parenchyma, where they digest tissue and cause inflammation and hemorrhage.</td>
</tr>
<tr>
<td>Appendicitis</td>
<td>Inflammation of the vermiform appendix, with swelling, pain, and sometimes gangrene, perforation, and peritonitis.</td>
</tr>
<tr>
<td>Ascites</td>
<td>Accumulation of serous fluid in the peritoneal cavity, often causing extreme distension of the abdomen. Most often caused by cirrhosis of the liver (see chapter 26) and frequently associated with alcoholism. The diseased liver “weeps” fluid into the abdomen. About 25% of people who develop ascites as a consequence of cirrhosis die within one year.</td>
</tr>
<tr>
<td>Cancers</td>
<td>Digestive system is subject to cancer especially of the esophagus, stomach, colon, liver, and pancreas, with colon and pancreatic cancer being among the leading causes of cancer death in the United States.</td>
</tr>
<tr>
<td>Crohn Disease</td>
<td>Inflammation of small and large intestines, similar to ulcerative colitis. Produces granular lesions and fibrosis of intestine, diarrhea, and lower abdominal pain. Often hereditary.</td>
</tr>
<tr>
<td>Diverticulitis</td>
<td>Presence of inflamed herniations (outpocketings, diverticula) of the colon, caused especially by low-fiber diets. Diverticula may rupture, leading to peritonitis.</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>Difficulty swallowing. Can result from esophageal obstructions (tumors, constrictions) or impaired peristalsis (due to neuromuscular disorders).</td>
</tr>
<tr>
<td>Hiatal Hernia</td>
<td>Protrusion of part of the stomach into the thoracic cavity, where the negative thoracic pressure may cause it to balloon. Often causes gastroesophageal reflux (especially when a person is supine) and esophagitis (inflammation of the esophagus).</td>
</tr>
<tr>
<td>Ulcerative Colitis</td>
<td>Chronic inflammation resulting in ulceration of the large intestine, especially the sigmoid colon and rectum. Tends to be hereditary but exact causes are not well known.</td>
</tr>
</tbody>
</table>
Absorption of Ions - Sodium

- 25-35 g of Na\(^+\) is daily absorbed

- The motive power for Na\(^+\) absorption is provided by **active transport of Na\(^+\) out of the cells** through the basolateral membranes by the Na\(^+\)-K\(^+\) pump (ATPase)

- Na\(^+\) moves across the luminal membrane from the lumen into the cells **down its electrochemical gradient** by
  - passive diffusion (Na\(^+\) channels)
  - Na\(^+\)-glucose or Na\(^+\)-amino acids cotransport (also with bile salts, water-soluble vitamins)
  - Na\(^+\)-Cl\(^-\) cotransport
  - Na\(^+\)-H\(^+\) exchange

- Small intestine – mainly via cotransport and exchange mechanisms
- Large intestine – mainly via passive diffusion
- Aldosterone stimulates Na\(^+\) (Cl\(^-\), water) absorption.
Absorption of Water

- Water is transported from the chyme into the paracellular spaces by diffusion, down a large osmotic gradient (osmosis).

- The jejunum absorbs more water than the ileum, but the colon is the most efficient water-absorbing segment of the gut.

- Hyperosmococity of chyme causes water to move in the opposite direction.

*Figure 65–8*

Absorption of sodium through the intestinal epithelium. Note also osmotic absorption of water—that is, water “follows” sodium through the epithelial membrane.
Absorption of Ions - Chloride

Cl⁻ absorption accompanies Na⁺ absorption by

- **Passive diffusion** (Cl⁻ follows Na⁺)
- Na⁺- Cl⁻ cotransport
- Cl⁻- HCO₃⁻ exchange

- Duodenum, jejunum – mainly via diffusion
- Ileum, large intestine – mainly via Cl⁻-HCO₃⁻ exchange

(alkaline bicarbonates neutralize acidic products formed by bacteria)
Absorption of potassium

• absorption of potassium from the diet is passive and does not require any specific mechanism;

• absorption takes place in the small intestine (especially lower jejunum) as long as the concentration in intestine contents is higher than that in the blood
Intestinal Absorption of Bile Acids

The ileum is the principal site of bile acid absorption. Bile acids cross the brush-border plasma membrane by simple diffusion or active transport.

- The active process is a secondary active transport powered by a Na+ gradient across the brush-border plasma membrane. Na+ is cotransported with bile acids. Conjugated bile acids (bile salts) are substrates for active absorption.

- Deconjugated bile acids are less polar and can be absorbed by simple diffusion. Absorbed bile acids leave the intestinal cell via the basolateral membrane and enter the portal circulation. Hepatocytes take up the bile acids and reconjugate most deconjugated bile acids.
NUTRIENT ABSORPTION in the SMALL INTESTINE

- Duodenum and Upper Jejunum: most minerals (except sodium, chloride, and potassium)
- Jejunum and Upper Ileum: carbohydrates, amino acids, water-soluble vitamins
- Jejunum: lipids and fat-soluble vitamins
- Terminal Ileum: Vitamin B12
NUTRIENT ABSORPTION in the SMALL INTESTINE

• Water-soluble nutrients are absorbed directly into the bloodstream

• Fat-soluble lipid compounds are absorbed into the lymph rather than the blood