Gastrointestinal Physiology

Secretion
Fig. 24.26

INGESTED AND SECRETED

Saliva (1 liter)
Ingestion of liquids (2.3 liters)
Gastric juice (2 liters)
Bile (1 liter)
Pancreatic juice (2 liters)
Intestinal juice (1 liter)

Total ingested and secreted = 9.3 liters

Small intestine (8.3 liters)
Large intestine (0.9 liters)

Total absorbed = 9.2 liters

Excreted in feces (0.1 liter)

Fluid balance in GI tract
Functions

Provided by secretory glands which serve 2 functions:

- Digestive enzymes.
- Lubrication and protection of the mucosa.
Types of secretory structures

The types of secretory glands:
- Single-cell secretory glands (goblet cells).
- Pits that represent invaginations of the epithelium in the submucosa in small intestine are known as crypts of Lieberkühn.
- Complex glands: in stomach and duodenum.
- Organs: salivary, pancreas and liver. Located outside the tubular structure of the GI.
Control of secretion

Neural Control

ENS:
ANS:

Parasympathetic:

Sympathetic:
- moderate increase →
- it reduces secretion by reducing blood flow.
Hormonal regulation

Some hormones are secreted by the presence of food or other local changes in the digestive organs.
Salivary Secretions
<table>
<thead>
<tr>
<th>Name of Gland</th>
<th>Type of Saliva</th>
<th>% of Total Saliva Secreted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Submandibular</td>
<td>Mucous-serous</td>
<td>70</td>
</tr>
<tr>
<td>Parotid</td>
<td>Serous</td>
<td>25</td>
</tr>
<tr>
<td>Sublingual</td>
<td>Mucous</td>
<td>5</td>
</tr>
</tbody>
</table>
Capillaries around acinar cells

PRIMARY SECRETION BY ACINAR CELLS

Capillaries around ducts

SECONDARY MODIFICATION IN DUCTS

Arterial blood

Venous blood

Saliva

\( H_2O \), \( Na^+ \), \( Cl^- \)

\( K^+ \), \( Cl^- \)

\( Na^+ \)

Urea

\( HCO_3^- \)

Amino Acids

\( I^- \)

\( Na^+ \), \( K^+ \), \( Cl^- \)

Glucose

\( H_2O \) and \( HCO_3^- \)
Mechanism of Secretion

- **Active transport of Cl-** at the basal portion of the membrane.
- Increase in negativity of membrane potential which attract the positive ion (Na+).
- Increase osmotic pressure inside the cell >> pull water inside >> increase hydrostatic pressure.
- This increase results in **minute ruptures at the luminal part** of the membrane which causes flushing of water,
Primary Secretion
- Amylase
- Mucus
- Extracellular fluid

Na⁺ active absorption
Cl⁻ passive absorption
K⁺ active secretion
HCO₃⁻ secretion
PRIMARY SECRETION BY ACINAR CELLS

Capillaries around acinar cells

Arterial blood

Capillaries around ducts

Venous blood

SECONDARY MODIFICATION IN DUCTS

H₂O  Na⁺  Cl⁻

K⁺  Cl⁻  Na⁺

H₂O  Urea

HCO₃⁻  Amino Acids

I⁻  Glucose

H₂O and HCO₃⁻

Saliva
Changes in Composition in Final Saliva

↓ the Na+ and Cl⁻ concentration to the 1/10 of their plasma concentration

↑ 7 folds increase in K+ concentration.

↑ HCO₃⁻ concentration also increases 2-3 times.
Rate of Secretion

The amount of salivary secretion is about 1500ml/day.

Resting secretion rate 0.025-0.5ml/min (during basal conditions).

The pH = 7.0
DURING MAXIMAL STIMULATION

The primary saliva increasing 20 folds.
- Flow rate of saliva is increased
PH=8
Saliva

Concentration mEq/L

Flow ml/min

- Na⁺
- HCO₃⁻
- Cl⁻
- K⁺
Control of salivary Secretion

Autonomic nervous system.
- Both sympathetic and parasympathetic increase salivation but by different mechanisms
- **parasympathetic** increase water and electrolyte secretion.
- **Sympathetic** increase mucin synthesis.
An increase in the sympathetic activity → reduces salivation
Control of salivary Secretion

Aldosterone:

Salivation is increased by:
- **Unconditioned** salivary reflex (dental procedures).
- **Conditioned** salivary reflex (learned response).
Functions of Saliva

- Saliva begins **digestion** of carbohydrates in the mouth:
  
  **Amylase** that breaks polysaccharide into maltose (disaccharide consists of 2 glucose).

- **Facilitate swallowing** by:
  
  Moistening the food particles.

  Lubrication
Functions of Saliva

- Antibacterial actions:
  Lysozyme: an enzyme that lyses or destroys certain bacteria.

- oral hygiene
  keeping mouth and teeth clean by the constant flow and secretion of IgA which helps in the destruction of bacteria
Functions of Saliva

- Solvent for molecules that stimulate taste buds.
- Aids speech.
- Bicharbonate neutralizes acids → preventing caries
Esophageal secretion

- Simple mucus glands and solitary cells (mucoid character) help in lubrication and protection.

- Compound mucus glands near the esophago-gastric junction and protect the esophagus from reflux.
Gastric Secretions
Histology of the Stomach: Layers of the Stomach and the Stomach Mucosa, Fig# 24.12a-b

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Mechanism of HCl Secretion
Biochemical Balance Among the Stomach, Pancreas, and Small Intestine

- Digestive-tract lumen
  - Stomach parietal cell
    - $H^+ + Cl^-$
    - $CO_2 + H_2O$ → $H_2CO_3$ → $H^+ + HCO_3^-$
  - Pancreatic duct cell
    - $Na^+ + HCO_3^-$
    - $HCO_3^- + Na^+$
  - Intestinal epithelial cell
    - $Na^+ + Cl^-$ and $H^+ + HCO_3^-$
    - $H_2CO_3$ → $CO_2 + H_2O$
Functions of HCl

- Conversion of pepsinogen to pepsin
- Helps in the decomposition of connective tissue.
- Defense (killing most microorganisms ingested with food).
Secretion of pepsinogen

Secreted by peptic (chief) and mucos cells.
- Optimal activity at pH (1.8-3.5).

**Function:**
- Pepsin cleaves the peptide linkage protein → into smaller peptide fragments.
Mucus secreting cells

- pH ~ 2 in gastric juice
- Mucus layer
- pH ~ 7 at cell surface
- Mucus droplets
- Gastric mucus cell
- $\text{HCO}_3^-$

Capillary
Mucus secreting cells

Function:

- Lubricating functions.
- Protect the mucosa from the chemical injury by:
  - Preventing the activity of the proteolytic enzymes to act on the mucosa
  - Neutralizing HCl by its alkaline character.
Gastrin Secretion

Secreted by G cells
stimulated by:
  - gastric distention.
  - presence of proteins in chyme.
  - vagal stimulation.

Functions:
  - Increases HCl and pepsinogen secretion.
  - trophic effect on gastric mucosa to maintain growth of mucosal cells.
Secretion of Intrinsic factor

Is secreted by parietal cells (oxyntic cells).

Essential for B12 absorption
Control of Gastric Secretion
Neural Control

ENS: Ach neurons $\rightarrow$ parietal and peptic cells.
ANS (Parasympathetic): vagal activation during cephalic and gastric phases (via long arc reflex)
Neural Control

ANS (Parasympathetic): vagal activation during cephalaic and gastric phases (via long arc reflex)

- **enteric excitatory** neurons to release Ach.

- enteric neurons $\rightarrow$ enterochromaffin-like cells $\rightarrow$ Histamine.

- enteric neurons that release GRP $\rightarrow$ Gastrin Releasing Peptide $\rightarrow$ G Cells $\rightarrow$ Gastrin.
Control of Gastric Secretion

Hormonal control

**Gastrin** → parietal cells → increase HCl secretion.

Gastrin stimulate CCK-B receptor on oxyntic cells to secrete HCl.

This receptor can also be activated by CCK (cholecystokinin).
Control of Gastric Secretion

Paracrine

Histamine (secreted by enterochromaffin-like cells) \(\rightarrow\) H2 receptors on parietal cells \(\rightarrow\) increased cAMP \(\rightarrow\) increased HCl secretion.

Somatostatin (SS) \(\rightarrow\) SS receptors on parietal cells decrease cAMP \(\rightarrow\) decrease HCl secretion.
Role of HCl in controlling secretion

- HCl acts indirectly by initiating enteric reflexes that causes an increase in pepsinogen secretion by peptic cell.

- Excess of acids
- causes feed back inhibition of gastric secretions by 2 ways:
  * Reduction of gastrin release
  * Initiation of inhibitory reflexes.

This maintains the pH from falling below 3.
Summary of Control

- Cephalic phase
- Gastric phase
- Intestinal phase
3 phases of control of gastric secretions

- Cephalic phase: stimuli before food reaching the stomach via parasympathetic NS
- Gastric phase: Food in stomach
  - Distension and the presence of proteins local and long reflexes increased gastric secretion.
  - Caffeine and alcohol also stimulate acid secretions via ENS, ANS and Hormones
- Intestinal phase:
  - Excitatory
  - Inhibitory
Intestinal Secretions
Enlarged Villus Showing Lacteal, Capillaries and Intestinal Gland, Fig# 24.23b

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Small Intestinal Secretions

(1500ml/day)
- Cells of mucosal epithelium secrete mucus, water and electrolytes.
Tubular glands (crypts of Leiberkuhn) secrete serous secretion.
Small Intestinal Secretions

Regulation

Neural mechanisms (mediated by Ach and VIP.

Hormonal:

Secretin: increases duodenal secretion.
Colonic secretions

- Mostly mucus secretion
- Small amount of serous secretions which is high in K+ and HCO3-.
Pancreatic Secretions
Exocrine portion

- Enzymes: secreted by acinar cells.
- Water and bicarbonate are secreted by duct cells.
Schematic Representation of Exocrine and Endocrine Portions of the Pancreas

- Bile duct from liver
- Duodenum
- Stomach
- Hormones (insulin, glucagon)
- Blood
- Duct cells secrete aqueous NaHCO₃ solution
- Acinar cells secrete digestive enzymes
- Exocrine portion of pancreas (Acinar and duct cells)
- Endocrine portion of pancreas (Islets of Langerhans)

The glandular portions of the pancreas are grossly exaggerated.

Acetate 148 (Figure 16-16)

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Pancreas and Duodenum (1)

- Cystic duct
- Common hepatic duct
- Common bile duct
- Pancreatic duct
- Duodenum
- Tail of pancreas
- Hepatopancreatic ampulla
- Head of pancreas
- Hepatopancreatic sphincter
Enzyme Secretion by acinar cells
Protelytic enzymes:

- **Trypsin** *(ogen)*: activated by **enterokinase** from the duodenum acts as (endopeptidase. As long as this enzyme is in pancreas remains inactive by trypsin inhibitor.

- **Chemotrypsin**(ogen): activated by trypsin and acts as endopeptidase.

- **(Pro) carboxypeptidase**: activated by trypsin and acts as exopeptidase.
Enzyme for Digestion of Carbohydrates

Pancreatic amylase:
secreted as active enzyme to convert
Starch (polysaccharide) $\rightarrow$ disaccharides.
Lipolytic enzymes

- **Lipase** that split
Triglycerides $\rightarrow$ monglyceride + free fatty acids.
Their activity requires an oil/water interface, bile salts (secreted by liver) and other co-lipase secreted by the pancreas.

- **Phospholipase**.

- **Cholesterol ester hydroxylase**.
Water and bicarbonate secretion by duct cells.
Control of pancreatic secretion:
- Neural
- Hormonal
Neural Control

- **Parasympathetic:**
  Vagal stimulation $\rightarrow$ enteric nervous system $\rightarrow$ release of Ach, VIP, and GRP (Gastrin releasing peptide).

- **Sympathetic:** indirect inhibition via vasoconstriction
Hormonal Control

- **Secretin** (duodenal mucosa) → blood → ductal cells → increase water and HCO₃⁻ secretion.

- **CCK (Cholecystokinin):**
  * → CCK-A receptors (acinar cells) → enzyme secretion.
  * → vago-vagal reflex to stimulate enzyme secretions.
Hormonal Control

- **Pancreatic polypeptide**: inhibits the release of enzymes by its inhibitory effect
  *- Inhibits Ach release from enteric nervous system.
  *- Inhibits vagal output of the CNS.
Control of pancreatic secretion:
- Cephalic phase
- Gastric phase
- Intestinal phase
3 phases of control of pancreatic secretions

Cephalic phase: sight, smell, taste or hearing. Mediated by vagus.

Gastric phase: Distension. Mediated by vagus.

Intestinal phase: Aminoacids (aa), Fatty acids, H+, Distension. Mediated by CCK, secretin, enteropancreatic reflexes, other hormones.
Liver Secretions
Liver functions

- Metabolic processing: Process all nutrients after their absorption.
- Detoxification of body wastes, hormones, drugs, and other foreign bodies.
- Synthesis of plasma proteins, including clotting factors (their synthesis requires vit. K), hormone transporters.
- Storage organ of glycogen, iron (ferritin), copper, and vitamins.
- Removal of bacteria and foreign materials by reticuloendothelial cells (Kupffer cells).
- Excretion of cholesterol and bilirubin.
Bile secretion

- Bile acts as detergent to emulsify lipids and make them soluble.

Bile is composed of **bile salts**, water & electrolytes, cholesterol, phospholipids and wastes intended for excretion, (bilirubin).
Liver functions

- Metabolic processing: Process all nutrients after their absorption.
- Detoxification of body wastes, hormones, drugs, and other foreign bodies.
- Synthesis of plasma proteins, including clotting factors (their synthesis requires vit. K), hormone transporters.
- Storage organ of glycogen, iron (ferritin), copper, and vitamins.
- Removal of bacteria and foreign materials by reticuloendothelial cells (Kupffer cells).
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Excretion of bilirubin in the bile

Bilirubin results from the catabolism of hemoglobin $\rightarrow$ Heme + Globin
Heme ring $\rightarrow$ iron + biliverdin
Biliverdin $\rightarrow$ bilirubin secreted with bile as conjugated (glucoronide, sulfate, other substances).
bilirubin

Bilirubin (by bacterial action) \(\rightarrow\) urobilinogen \(\rightarrow\) reabsorbed and secreted in urine (urobilin).

Or in feces \(\rightarrow\) stercobilin.

Jaundice is cause by large quantity of bilirubin in the extracellular space.
Bile formation

- Bile salts are synthesized by the liver, concentrated in the gallbladder and modified in the lumen.

- Synthesized as primary bile acids from cholesterol (\textit{cholic} and \textit{chenodeoxycholic acid})
Bile salts

Bile acids $\rightarrow$ Conjugated to Glycine or Taurine $\rightarrow$ Bile salts
Bile

- Between meals, bile $\rightarrow$ gallbladder where it is stored. The epithelium of the gallbladder removes water and electrolytes $\rightarrow$ 5-20 fold concentration of bile.
Histology of the Liver, Fig# 24.19a-b
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1. Parasympathetic impulses along vagus nerves (cranial nerve X) stimulate bile production by liver.

2. Fatty acids and amino acids in chyme entering the duodenum stimulate secretion of cholecystokinin (CCK) into blood. Acidic chyme entering duodenum stimulates secretion of secretin into blood.

3. CCK causes contraction of gallbladder.

4. Secretin enhances flow of bile rich in $\text{HCO}_3^-$ from liver.
<table>
<thead>
<tr>
<th></th>
<th>LIVER BILE</th>
<th>GALLBLADDER BILE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>97.5 gm/dl</td>
<td>92 gm/dl</td>
</tr>
<tr>
<td>Bile Salts</td>
<td>1.1 gm/dl</td>
<td>6 gm/dl</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>0.04 gm/dl</td>
<td>0.3 gm/dl</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>0.1 gm/dl</td>
<td>0.3 to 0.9 gm/dl</td>
</tr>
<tr>
<td>Fatty Acids</td>
<td>0.12 gm/dl</td>
<td>0.3 to 1.2 gm/dl</td>
</tr>
<tr>
<td>Lecithin</td>
<td>0.04 gm/dl</td>
<td>0.3 gm/dl</td>
</tr>
<tr>
<td>Na⁺</td>
<td>145 mEq/liter</td>
<td>130 mEq/liter</td>
</tr>
<tr>
<td>K⁺</td>
<td>5 mEq/liter</td>
<td>12 mEq/liter</td>
</tr>
<tr>
<td>Ca⁺⁺</td>
<td>5 mEq/liter</td>
<td>23 mEq/liter</td>
</tr>
<tr>
<td>Cl⁻</td>
<td>100 mEq/liter</td>
<td>25 mEq/liter</td>
</tr>
<tr>
<td>HCO₃⁻</td>
<td>28 mEq/liter</td>
<td>10 mEq/liter</td>
</tr>
</tbody>
</table>
Enterohepatic circulation
Modification in the intestine

Modified to secondary bile acid:

Cholic acid $\rightarrow$ deoxycholic acid.

Chenodeoxycholic acid $\rightarrow$ lithocholic acid
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Bile salts

Glucose
Amino Acids
Secondary Solutes

Inorganic Ions
($HCO_3^-$)

$H_2O$

Secretin

Somatostatin

Inorganic Ions
($HCO_3^-$)

$H_2O$

Bile Duct

Bile