Gastrointestinal Physiology
Digestion and Absorption
Definition

• **Digestion**: Food is dissolved and broken down.

  **Physical digestion**: Propulsion and mixing of food by muscle in the alimentary tract.

  **Chemical digestion**: Secreting digestive solution into the alimentary tract.

• **Absorption**: The digestive products is moved from the lumen of alimentary tract across a layer of epithelial cells and enter the blood and lymph.
Functions of the digestive system

- **Digestion and absorption**
  - Motility: physical digestion, propels food through the digestive system, elimination
  - Secretion: chemical digestion
  - Absorption: passage of the molecules into the body

- **Immune function**

- **Endocrine function**
Anatomy —

Components of the digestive system:

Gastrointestinal (GI) tract plus the accessory organs
Structure of the alimentary canal

- **Tunics**
  - Serosa
  - Muscularis (outer layer)
  - Muscularis (inner)
  - Submucosa
  - Mucosa

- mesentery
Histology

- Esophagus
- Stomach
- Small Intestine
- Large Intestine
The gut wall has a layered organization, with the absorptive cells lining the lumen and neural and muscular components below. Blood and lymph vasculature is abundant.
Mechanical digestion —
smooth muscle
General properties of gastrointestinal smooth muscle

- Low excitability
- High distensibility
- Tonic contraction
- Autorhythmicity
- High sensitivity to temperature, stretch and chemical stimulation
Electrophysiological properties of gastrointestinal smooth muscle

- **Membrane resting potential (RP)**
  - -50~-60 mV

- **Slow wave** (basic electrical rhythm, BER)
  - The spontaneous rhythmic fluctuation of the RP.
  - Initiated in the interstitial cells of Cajal (ICC).
  - Due to rhythmic changes in Na⁺-K⁺ pump activity.
  - Frequency: 3~12 cpm.

- **Spike potential (AP)**: Ca²⁺ influx & K⁺ efflux.
Rhythmic waves of smooth muscle contraction in the gut are the result of waves of action potentials moving along via gap junctions.
Normal **BER frequencies** of gastrointestinal system

BER not generated by nervous activity
Neural control of gastrointestinal function

• Autonomic nervous system (extrinsic)
• Enteric nervous system (intrinsic)
- **Enteric nervous system**
  - Myenteric plexus
    (Auerbach’s plexus)
  - Submucosal plexus
    (Meissner’s plexus)

- **Neurotransmitters** secreted by enteric neurons
  - Ach, NE, ATP, serotonin, dopamine, cholecystokinin, substance P, vasoactive intestinal polypeptide, somatostatin, leu-enkephalin, met-enkephalin, bombesin, etc.
Function

- Myenteric plexus: control over GI motility
- Submucous plexus: regulate blood flow and control secretion
Organization of the enteric nervous system.
For simplification, the myenteric and submucous plexuses have been combined. The sites of some known transmitters are shown, as are sites of synaptic excitation (+) and inhibition (−). NE = noradrenaline (norepinephrine); ACh = acetylcholine.

The submucosal (Meissner's) plexus is in the submucosal layer. The myenteric (Auerbach's) plexus is between the longitudinal (outermost) and circular muscle layers of the wall of the alimentary tract. Each plexus is composed of small autonomic ganglia, with interconnecting strands of unmyelinated axons.
To prevertebral ganglia, spinal cord, and brain stem

Sympathetic (mainly postganglionic)

Parasympathetic (preganglionic)

Sensory Neurons

Myenteric Plexus

Submucosal Plexus

Epithelium
Gastrointestinal reflexes

- Reflexes that are integrated entirely within the enteric nervous system
- Reflexes from the gut to the spinal cord or brain stem and then back to the gastrointestinal tract
Gastrointestinal hormones
(Gastrointestinal peptide)

• The hormones synthesized by a large number of endocrine cells (APUD) within the gastrointestinal tract.

• Brain-gut peptide

• Physiological functions
  – Control of the digestive function
  – Control of the release of other hormones
  – Trophic action
Gastrointestinal hormones

• Four main types
  – Gastrin
  – Secretin
  – Cholecystokinin (CCK)
  – Gastric inhibitory peptide (GIP)
(1) **Gastrin**: Synthesized in G cells;
   - Regulator gastric acid secretion
   - Proliferation of gastric epithelium

(2) **Cholecystokinin**: I cells in the duodenum and jejunum
   - Contraction of the gallbladder
   - Inhibits stomach motility
   - Stimulates secretion of pancreatic enzymes

(3) **Secretin**: Secreted by S cells in the duodenum and jejunum
   - Inhibits the motility of gastrointestinal tract
   - Stimulates secretion of water and bicarbonate from pancreas

(4) **Gastric inhibitory peptide**: K cells in the duodenum, jejunum
   - Inhibits gastric secretion and motility.
   - Potentiates release of insulin in response to elevated blood glucose.
Splanchnic circulation

Hepatic portal system

Liver

Hepatic portal vein

Superior mesenteric

gastroepiploic

Ascending colon

Splenic flexure

Descending colon

Sigmoid colon
Blood supply to the intestines through the mesenteric web
Microvasculature of the intestinal villus
Digestion in mouth

Physical digestion:
Masticated (chewed) by teeth; mixed by tongue

Functions:
1. Breaking large pieces into small pieces, resulting in an increase in surface area which is where digestive enzymes work.
2. Softening of food and transformation into a size conducive to swallowing.
3. Lubrication of food by impregnating it with saliva.
Chemical digestion by saliva

1000 ml/d, pH 6.0~7.0
Composition of saliva
– H$_2$O
– Na$^+$, Cl$^-$, K$^+$, HCO$_3^-$
– Mucus (containing mucin)
– Amylase
– lysozyme, …

Function:
• Moisten and Lubricate food
• Dissolve food
• Antibacterial action: lysozyme
• Initiates starch digestion: amylase
The swallowing reflex is coordinated by the medulla oblongata, which stimulates the appropriate sequence of contraction and relaxation in the participating skeletal muscle, sphincters, and smooth muscle groups.
Deglutition — Esophagus peristalsis

Peristaltic waves:
Progressive wave of muscle contraction

Heartburn
Gastroesophageal reflux
Digestion in the stomach
The three-layered muscularis causes compression and churning of contents.

The gastroesophageal region has a functional but not a structural sphincter.
Gastric juice

- **Properties**
  - pH 0.9~1.5
  - 1.5~2.5 L/day

- **Major components**
  - Hydrochloric acid
  - Pepsinogen
  - Mucus
  - Intrinsic factor
Hydrochloric acid

• Secreted by the parietal cells

• Output
  – Basal: 0~5 mmol/h
  – Maximal: 20~25 mmol/h

Mechanism

• HCl is actively secreted against a concentration gradient by H+/K+ ATPase or "proton pump"
H2 receptor antagonist

M-type receptor antagonist

Omeprazole

Parietal cell

H^+ / K^+ - ATPase

Acid secretion

Gastrin

Histamine

ACh

Somatostatin

Second messengers

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• Role of HCl

  – Acid sterilization
  – Activation of pepsinogen
  – Promotion of secretin secretion
  – Beneficial to absorption of iron and calcium
(2) **Pepsinogen**

- **MW:** 42,500
- Secreted by the chief cells as an inactive form.
- Activated initially by H\(^+\) ions and then by active pepsin, autocatalytic activation.
- Active *pepsin* (MW: 35,000)
(3) Mucus

- Secreted by the epithelial cells all over the mucosa and by the neck mucus cells in the upper portion of the gastric glands and pyloric glands.
- A layer $\sim 500 \, \mu\text{m}$ thick composed chiefly of mucins.
- Protection of the tissue from Mechanical damage by food particles and H+ damage.
Mucus-HCO$_3^-$ barrier

Protecting the epithelium from acid and pepsin insults by trapping HCO$_3^-$ in mucus layer to buffer chemically insulates.
If the mucus-$\text{HCO}_3^-$ barrier is weak?
(4) **Intrinsic factor**

- A high molecular weight glycoprotein which synthesized and secreted by the parietal cells.
- The intrinsic factor binds to Vit B$_{12}$ and facilitates its absorption.
(5) other enzymes

- Gastric lipase
- Gastric amylase
- Gelatinase
Regulation of gastric secretion

- Basic factors that stimulate gastric secretion
  - Acetylcholine (+ all secretory cells)
  - Gastrin (+ parietal cells)
  - Histamine (+ parietal cells)
• **Nervous regulation**

  – ‘Short’ reflex pathways

    • ‘Short’ excitatory reflexes: mediated by cholinergic neurons in the plexuses

    • ‘Short’ inhibitory reflexes: mediated by non-adrenergic non-cholinergic (NANC) neurons

  – ‘Long’ autonomic pathways

    • ‘Long’ excitatory reflexes: parasympathetic

    • ‘Long’ inhibitory pathways: sympathetic
**Humoral regulation**

<table>
<thead>
<tr>
<th>Excitatory</th>
<th>Inhibitory</th>
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<tbody>
<tr>
<td>ACh</td>
<td>Somatostatin</td>
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<tr>
<td>Histamine</td>
<td>Secretin</td>
</tr>
<tr>
<td>Gastrin</td>
<td>5-hydroxytryptamine (5-HT)</td>
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<td></td>
<td>Prostaglandin</td>
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Phases of gastric secretion

- Cephalic phase
- Gastric phase
- Intestinal phase
Cephalic phase via vagus

Parasympathetics excite pepsin and acid production

Gastric phase:
1. Local nervous secretory reflexes
2. Vagal reflexes
3. Gastrin stimulation

Intestinal phase:
1. Nervous mechanisms
2. Hormonal mechanisms
Control of gastric secretion

Phases of gastric secretion

Gastric secretion

Cephalic
- 30% of total secretion
  - Food! thought, smell, sight, taste
    - Central pathways
      - Vagus nerve - ACh
      - Gastrin-releasing peptide (GRP) also

Gastric
- 60% of total secretion
  - Mechanical (distention) & amino acids
    - GI reflexes
      - Short - myenteric
      - Long - central
        (ACh, gastrin & histamine)

Intestinal
- 10% of total secretion
  - Digestion products in s. intestine
    (protein, lipid, pH, osmolarity)
  - Enterogastrones
    - Gastrin - increase secretion
    - Secretin - decr.
    - CCK - decr.
    - GIP - decr.
Inhibition of gastric secretion

Inhibition of gastric secretion by intestinal factors is presumably to slow the release of chyme from the stomach when the small intestine is already filled or overactive.

Mechanism

- Reverse enterogastric reflex: initiated by the presence of food in the small intestine
- Secretin secretion: stimulated by the presence of acid, fat, protein breakdown products, hyperosmotic or hypo-osmotic fluids, or any irritating factors in the upper small intestine.
Motor function — physical digestion

Proximal stomach
- cardia
- fundus
- corpus (body)

Distal stomach
- antrum
- pylorus
- pyloric sphincter
Motor function of the stomach

• **Receptive relaxation**
  – Storage function (1.0~1.5 L)
  – Vago-vagal reflex

• **Peristalsis**
  – BER in the stomach
Contractions in the empty stomach

• Migrating Motor Complex (MMC)
  – Periodic waves of contraction, which move along the gastrointestinal tract from stomach to colon
  – Purpose of this activity: to ‘sweep’ debris out of the digestive tract during the interdigestive period
  – MMCs can lead to hunger contractions, which are associated with discomfort, referred to as ‘hunger pains’
Emptying of the stomach

• Emptying rate
  – Fluid > viscous
  – Small particle > large particle
  – Isosmotic > hyper- & hypo-osmotic
  – Carbohydrates > Protein > Fat
  – Regular meal 4〜6 hrs
• Regulation of stomach emptying
  – Gastric factors that promote emptying
    • Gastric food volume
    • Gastrin
  – Duodenal factors that inhibit stomach emptying
    • Enterogastric nervous reflexes
    • Fat
    • Cholecystokinin
Neuronal and hormonal Control of GASTRIC emptying

- Ingested Food
  - Vagal Stimulatory
  - Gastric Distension
    - Intrinsic Neural Reflex EXCITATORY
- Vagal Inhibitory
  - Hormonal regulation (INHIBITION)
    - GIP
    - Gastrin
    - CCK
    - Secretin
    - Carbohydrates
    - Amino acids
    - Fat
    - pH
    - (osmolarity esp., hyper-)
- Intrinsic Neural Reflex INHIBITION
- STOMACH
  - Gastric Emptying
  - DUODENUM
- Local Reflexes (Myenteric plexus)
  - ILEO-GASTRIC
- MechanoReceptors:
  - Distension
- ChemoReceptors:
Thank you!