DIGESTION AND ABSORPTION

Chunmei Xia, Ph.D
Department of Physiology and Pathophysiology
cmxia@fudan.edu.cn
Contact number: 021-54237612-805
We require:

- carbohydrates (mainly glucose)
- proteins (essential amino acids)
- fats (but Western diet fats too high)
- vitamins
- minerals

Intake (normally 3000-6000 kcal per day & depends on

Geography

Occupation
Digestive System Organization

- **The GI tract** (gastrointestinal tract)
  - The muscular alimentary canal
    - Mouth
    - Pharynx
    - Esophagus
    - Stomach
    - Small intestine
    - Large intestine
    - Anus

- **The accessory digestive organs**
  - Supply secretions contributing to the breakdown of food
    - Teeth & tongue
    - Salivary glands
    - Gallbladder
    - Liver
    - Pancreas
Main function

1. Digestion of food and absorption of nutrients are accomplished in a long tube connected to the external world at both ends.

2. Secretion and motility of “the tube” are major themes in understanding the gut.
The Digestive Process

• **Ingestion**
  – Taking in food through the mouth

• **Propulsion** (movement of food)
  – Swallowing
  – Peristalsis – propulsion by alternate contraction & relaxation

• **Mechanical digestion**
  – Chewing
  – Churning in stomach
  – Mixing by segmentation

• **Chemical digestion**
  – By secreted enzymes: see later

• **Absorption**
  – Transport of digested end products into blood and lymph in wall of canal

• **Defecation**
  – Elimination of indigestible substances from body as feces
Histology/organization of the Gut Wall

From esophagus to anus, GI tract has the same basic arrangement of tissues.

There are 4 layers that can be distinguished

- Mucosa
- Submucosa
- Muscularis
- Serosa
Layers of Gut Wall

- **Intramural plexus**
  - Myenteric plexus
  - Submucosal plexus

- **Gland in submucosa**

- **Duct from gland**

- **Lymph nodule**

- **Mucosa**
  - Mucous epithelium
  - Lamina propria
  - Muscularis mucosae

- **Submucosa**

- **Muscularis**
  - Circular muscle layer
  - Longitudinal muscle layer

- **Serosa**
  - Connective tissue layer
  - Peritoneum

- **Blood vessels**
- **Nerve**
- **Mesentery**
I REGULATION OF GASTROINTESTINAL TRACT FUNCTIONS
## Endocrine Cell and gut hormone

<table>
<thead>
<tr>
<th>Cell</th>
<th>Hormone</th>
<th>Site</th>
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</thead>
<tbody>
<tr>
<td>G</td>
<td>Gastrin (G)</td>
<td>autumn, duodenum</td>
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<tr>
<td>I</td>
<td>Cholecystokinin (CCK)</td>
<td>duodenum, jejunum</td>
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<tr>
<td>S</td>
<td>Secretin</td>
<td>duodenum, jejunum</td>
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<tr>
<td>D</td>
<td>Somatostatin (SS)</td>
<td>Stomach, duodenum, pancreas, colon</td>
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<tr>
<td>L</td>
<td>Enteroglucagon</td>
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<tr>
<td>PP</td>
<td>Pancreatic polrpeptide (PP)</td>
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<td>EC1</td>
<td>Substance P (SP)</td>
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<tr>
<td>D1</td>
<td>VIP</td>
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<td>ileum</td>
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<tr>
<td>B</td>
<td>insulin</td>
<td>pancreas</td>
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<tr>
<td>A</td>
<td>glucagon</td>
<td>pancreas</td>
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<tr>
<td>K</td>
<td>Gastric inhibitory polypeptide (GIP)</td>
<td>duodenum, jejunum</td>
</tr>
</tbody>
</table>
Types of secretion

Endocrine

Paracrine

Neurocrine
Function of GI hormones

1. Regulate the secretion and motility of GI tract
   - Gastrin $\rightarrow$ HCl secretion, gastric emptying

2. Trophic action
   - Gastrin $\rightarrow$ stomach and duodenum mucosa

3. Regulate the release of other hormones
   - GIP $\rightarrow$ insulin
   - SS $\rightarrow$ gastrin
CONTROL OF DIGESTIVE FUNCTIONS
BY NERVOUS SYSTEM

1. Autonomic nervous system (ANS) is divided into
   - Parasympathetic
   - Sympathetic

2. Enteric nervous system: ENS
Innervation of the GI tract

Intrinsic (or enteric) nervous system

Extrinsic nervous system
1. The autonomic nervous system

**Sympathetic system:**
- Noradrenaline

**EFFECTS**
- $\beta(+) $
- $\alpha (+) $
- $\beta2 (-) $
- $\beta_{1/2} (-) $
- $\alpha (+) $

**ACTION**
- Gut secretions (+)
- Gut sphincters (-)
- Pancreas (+)
- Rectum (+) defaecation

**Parasympathetic system:**
- Acetylcholine (Ach)

**EFFECTS**
- Salivary glands (+)
- Gut wall (+)
- Gut sphincters (-)
- Gut secretions (+)
- Pancreas (+)
- Rectum (+) defaecation

**ACTION**
- Adrenal medulla
- Salivary glands
- Gut blood vessels
- Gut wall, sphincters
- Cranial nerves

Adrenal medulla

Salivary glands (+)
CONTROL OF DIGESTIVE FUNCTIONS BY NERVOUS SYSTEM

Parasympathetic Nerves:
• Located in brain stem & sacral region
• Projection to the G.I. are preganglionic efferents
• Vagus & pelvic nerves
• Vagus nerves synapse with neurons of ENS in esophagus, stomach, small intestine, colon, gall bladder & pancreas
• Pelvic nerves synapse with ENS in large intestine
• Neurotransmitter is Ach
CONTROL OF DIGESTIVE FUNCTIONS BY NERVOUS SYSTEM

- Sympathetic nerves:
  - Located in thoracic & lumbar regions
  - Neurotransmitter is NE
  - NE increases sphincter tension
  - Inactivate the motility
Innervation of the GI tract

To prevertebral ganglia, spinal cord, and brain stem

Sympathetic
(mainly post-ganglionic)

Parasympathetic
(preganglionic)

Myenteric Plexus

Submucosal Plexus

Epithelium

Sensory Neurons
Innervation of the GI tract

2. Intrinsic (enteric) nerve plexuses

**Located**

in the submucosa (submucosal or Meissner’s plexus) and between circular and longitudinal muscle layers (myenteric or Auerbach’s plexus)

**Control**

Motility - Myenteric plexus

Secretion - Submucosal plexus

through release of neurotransmitters

Excitatory - Acetylcholine, Substance P

Inhibitory - VIP, nitric oxide

Excitatory - Acetylcholine
The enteric nervous system

- Myenteric plexus
- Circular muscle
- Deep muscular plexus
- Submucosal plexus
- Submucosal artery
- Longitudinal muscle
- MUCOSA
- Muscularis mucosa
Intrinsic (or enteric) nervous system
The enteric nervous system coordinates digestion, secretion, motility to optimize nutrient absorption.

Its activity is modified by information from the CNS from local chemical and mechanical sensors.
Gastrointestinal reflex

Reflex control of gut activity

CNS

Parasympathetic and sympathetic efferents

Myenteric plexus ↔ Submucosal plexus

Parasympathetic and sympathetic efferents

Splanchnic and vagal afferents

Local afferents

Chemoreceptors mechanoreceptors in gut wall

Gut wall muscle
Endocrine cells
Secretory cells
Blood vessel

Local efferents
II GASTROINTESTINAL SMOOTH MUSCLE
Musculature of the GI tract

> All smooth muscle except:

> Upper third oesophagus – striated

> Middle third of oesophagus – mixed

> External anal sphincter – striated

> Areas of striated muscle are areas that are under conscious control
General Functional characteristics

1. Lower excitability, slower contraction and relaxation
2. Higher extensibility
3. Tonic contraction
4. Autorhythmicity
5. More sensitive to stretch, chemicals, cold and warm stimulation but not to electric stimulation
Slow Waves & Action potentials are Forms of Electrical Activity in GI Muscles

1. Resting potential

2. Slow wave or basic electric rhythm
   The smooth muscle membrane slowly depolarizes and repolarizes in a cyclic fashion

3. Action potential

4. Relationship to contraction
Cells and Electrical Events in the Muscularis

**Structures**

- Interstitial cells of Cajal
- Smooth muscle cells
- Autonomic axon

**Functions**

- Production of slow waves
- Conduction of slow waves to smooth muscle
- Depolarization and opening of Ca\(^2+\) channels, production of action potentials
- Neural input to ICC and smooth muscle
Slow waves in GI smooth muscle

- Unknown cause
- Responsible for triggering AP in G.I.
- Interstitial cells of Cajal, ICCs (pacemaker)
  Myenteric border
  Submucosa border
- Occur at different frequency
  stomach (3/min)
  small intestine (duodenum, 12-18/min)
  ileum & colon (6-10/min)
- May or may not accompanied by AP
Electrical activity and muscle contraction

- Factors that depolarize the membrane:
  - Stretching of the muscle
  - Ach
  - Parasympathetic stimulation
  - Hormonal stimulation

- Factors that hyperpolarize the membrane:
  - Norepinephrine
  - Sympathetic stimulation
Membrane potentials in intestinal smooth muscle. Note the slow waves, the spike potentials, total depolarization, and hyperpolarization, all of which occur under different physiologic conditions of the intestine.
GI motility

There are many types of contractions in different areas of the GI tract.

Some muscles contract and relax in seconds – Phasic Contractions

-Peristalsis and Segmentation

Some maintain contractions over minutes or hours – Tonic Contractions

-Sphincter
III GASTRIC MOTILITY
Major Function of Gastric Motility

- To serve as a reservoir
- To break food into small particles and mix food with gastric secretions
- To empty gastric contents into the duodenum at a controlled rate
1. Anatomy and innervation of the Stomach
Stomach Anatomy

- Esophagus
- Fundus
- Lesser curvature
- Internal folds—rugae
- Body
- Duodenum
- Pyloric sphincter
- Pyloric antrum
- Greater curvature
The stomach can be divided into three anatomic regions (A) and two functional regions (B)

A

Fundus
Pylorus
Antrum
Corpus

B

Gastric pump
Phasic contractions

Gastric reservoir
Tonic contractions
Functional Anatomy of Stomach

Fundus
- Storage

Body
- Storage
- Mucus
- HCl
- Pepsinogen
- Intrinsic factor

Antrum
- Mixing/Grinding
- Gastrin
2. Responses to Gastric Filling – Receptive Relaxation
Receptive relaxation

During chewing and swallowing food, the stimulation of food to the receptors in mouth, pharynx, and esophagus reflexly causes the smooth muscle of the fundus and body of the stomach to relax,

This process allows the stomach to accommodate a large amounts of food and fluid.
The relaxation of the gastric reservoir is mainly regulated by reflexes.

receptive, adaptive and feedback-relaxation
3. Peristalsis of the Gut and Gastric Emptying
Gastric Motility

Peristaltic waves: Body → Antrum

Body
Thin muscle → weak contraction
→ No mixing

Antrum
Thick muscle → powerful contraction
A  Mixing
B  Contraction of pyloric sphincter →
1  Only small quantity of gastric content (chyme) entering duodenum
2  Further mixing as antral contents forced back towards body
The contraction of the gastric pump three phases:
A: phase of propulsion,
B: phase of emptying,
C: phase of retropulsion and grinding
Control of gastric motility

Vagovagal reflex – fundal relaxation

Myenteric plexus – slow waves – contraction

Parasympathetic and Gastrin – increase contraction force and frequency

Sympathetic – decrease contraction force and frequency
Gastric emptying

1. Def.

The process by which the chyme is expelled from the stomach into the duodenum is called the gastric emptying.

2. Control

1) stomach: stimulating factor, neuronal and hormonal

2) duodenum: inhibiting factor

   entero-gastric reflex, hormones
Control of Gastric emptying

Stimulating factors in stomach

– Presence of food

– Gastrin
Control of gastric emptying

- Central nervous system
- Vagal afferent fibers
- Increased gastric emptying
- Gastrin
- Distention of gastric wall
- Gastric nerve plexus
- Vagal efferent fibers
Control of Gastric emptying

Inhibitory effects in duodenum and jejunum – through reflexes and hormones

Inhibitory reflexes – direct – myenteric plexus

    indirect – via extrinsic nerves

Neural reflexes stimulated by:

Distension, irritation, acidity, high osmolarity, protein/fat

Fats and acids also stimulate release of humoral factors which reduce gastric emptying

Cholecystokinin (CCK), stimulated by fats

Secretin, stimulated by acids
Enterogastric Reflex

Regulates the rate at which chyme leaves the stomach

1. Duodenum fills with chyme
2. Sensory stretch receptors are stimulated
3. Sensory nerve impulses travel to central nervous system
4. Nerve impulses inhibit peristalsis in stomach wall
“Quality” of food regulates gastric emptying
4. Vomiting

- Emesis
- Stretching, toxins, alcohol, spicy foods, and drugs may stimulate this.
- Emetic Center of the Medulla
- Diaphragm and abdominal wall contract
- Cardiac sphincter relaxes.
- Soft palate rises
IV MOTILITY OF THE SMALL INTESTINE
Function of Intestinal Motility

(1) To **mix chyme** with digestive secretion

(2) To bring fresh chyme into **contact with the absorptive surface** of the microvilli

(3) To **propel chyme toward** the colon
Types of small intestinal movement

1. Tonic contraction: the base of the other contractions

2. Segmentation contractions
   (1) def.
   When a portion of the small intestine becomes distended with chyme,
   the stretch of the intestinal wall elicits a rhythmical contraction and relaxation of localized circular muscles spaced at intervals along the intestine,
   (2) function:
   mix the chyme with the digestive juice
   increase its exposure to the mucosal surface
Types of small intestinal movement

3. Peristalsis: propels the small intestinal contents towards the large intestines
   peristaltic rush: initiated by the harmful stimulation

4. MMC (migrating motor complex):
   Occurs during fasting state
Segmentation: mix contents to promote digestion & absorption

Segmental contractions are responsible for mixing

No net forward movement
Peristalsis

- Distinctive pattern of smooth muscle contractions that propels foodstuffs distally through the esophagus and intestines

- Mediated by . . .
  - Local, intrinsic nervous system
  - Ex: peristalsis is not affected to any significant degree by vagotomy or sympathectomy
Peristalsis: movement along the tract

Peristaltic contractions are responsible for forward movement

Time zero

Contraction

Bolus

Receiving segment

Seconds later

Bolus moves forward

Direction of movement
Peristalsis of the small intestine

http://medweb.bham.ac.uk/research/toescu/Teaching/OverviewGITY2.html
Control of Intestinal Motility – Neuronal

Mixing – segmentation

Frequency set by slow waves (12/minute duodunum)
additional control: myenteric plexus

Propulsion – peristalsis

Local reflex – stretch causes relaxation distal and contraction proximal

Moves bolus through intestines

Intestino-intestinal reflex – extrinsic nerves
Local stretch in one area inhibits contraction in rest of bowel
Control of Intestinal Motility – Hormonal

Gastrin
CCK
5-HT
Motilin

+ motility --

Secretin
Glucagon
VIP
GIP
Ileocecal Valve

• What it is
  – Opening to large intestines

• Function:
  • (1) prevent the repulsion
  • (2) control the emptying
  • normally closed.
  • Gastro-ileal reflex: enhances ileal emptying after eating.
• The hormone gastrin relaxes ileocecal sphincter
  – Short-range peristalsis in terminal ileum and distension relaxes IC sphincter
  – small amount of chyme is squirted into the cecum.
• Distension of cecum contracts IC sphincter.
V. GASTROINTESTINAL MOTILITY DURING FASTING STATE
Gastric motility on fasting

“Migrating Motor Complex, MMC”

• Occurs during fasting
• To clear undigested food particles
• Peristaltic contractions sweep down stomach and duodenum – pylorus relaxes
• Pattern of contraction approx. every 90 min
• Slow peristaltic waves sweeping whole of GI tract
• Thought to be controlled by motilin
MMC (migrating motor complex)

- Phase I: Almost have no contractions 40-60 min
- Phase II: have contractions, only have few 30-45 min
- Phase III: have continuous contractions 5-10 min

- Originates simultaneously at the stomach and duodenum
- Migrates within 90 to 120 minutes along the small intestine
Importance of MMC

1. Sweep the contents of the small intestine towards the colon
   Housekeeper of the small intestine

2. Inhibit the migration of colonic bacteria into the terminal ileum
VI MOTILITY OF THE COLON
Large intestine

• Functions
  – Absorption of water and electrolytes
  – Storage of feces
  – In non-ruminant herbivores, fermentative digestion and absorption of nutrients

• Motility patterns
  – mixing (form hastrations)
  – propulsive (mass movements)
Segmentation in large intestine

- Haustration: (modified form of segmentation in which intense, local contraction of circular muscle causes large intestine to appear to bulge into sacs)
Mass movement

• Occurs in colon

• Period of intense propulsive activity that moves entire contents of colon distally toward rectum
  – Contractions progress for long distance such that long length of colon contracts as a unit
  – Entry of fecal matter into rectum triggers defecation reflex
Mass Movement
Defecation

Defecation Reflex initiated when rectal walls stretch

⇒ parasympathetic reflex

⇒ walls of the sigmoid colon and the rectum to contract & relaxation of the anal sphincter

⇒ External sphincter control is voluntary control

⇒ If defecation is delayed: the reflex stops until the next mass movement
Gastrointestinal Secretions and absorption

Chunmei Xia, Ph.D
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Exocrine of the GI

Composition

Function
A. Digest food
B. Dilute the food into iso-osmotic fluid
C. Provide a favorable pH for the digestive enzymes
D. Provide mucus for lubrication and protection of all parts of the alimentary tract

Regulation

Ingest c. 2000 ml/day
0.1 L/d water excreted

Saliva 1.5 L/d pH 6.8-7.0
Ingest 2 L/d water

Gastric secretion 2 L/d, pH 1.5-3

Bile 0.5 L/d pH 7.8-8.0

Pancreatic juice 1.5 L/d pH 8.0-8.4

Intestinal secretion 1.5 L/d pH 7.8-8.0

Small intestine absorbs 8.5 L/d

Colon absorbs 0.4-1 L/d
1. Gastric secretion
Functional Anatomy of Stomach

**Fundus**
- Storage

**Body**
- Storage
- Mucus
- HCl
- Pepsinogen
- Intrinsic factor

**Antrum**
- Mixing/Grinding
- Gastrin
II.1 Gastric gland cells

1. Oxyntic gland
   - Parietal cell
   - Chief cell
   - Mucous neck cell

2. Pyloric gland
   - Mucus cell

3. Cardiac gland
   - Mucus cell

4. Endocrine cells (G, D, ECL)
   - ECL: enterochromaffin-like cell
Exocrine gland cells of gastric pits

- Synthesize and secrete the HCl acid responsible for the acidic pH in the gastric lumen.
- Synthesize and secrete the protease precursor known as pepsinogen.
- Produce alkaline mucus that covers mucosa layer.
- Synthesize and secrete the HCl acid responsible for the acidic pH in the gastric lumen.

Gland region

Gastric lumen

Gastric pit

Mucous neck cells

Chief cell

Parietal cells

Muscularis mucosa
II.2 Composition and function of gastric secretions

1. HCl

- converts pepsinogen to pepsin for chemical digestion
- provides optimal pH environment for pepsin
- destroys some bacteria
- stimulates the small intestinal mucosa to release secretin and CCK
- promotes the absorption of $\text{Ca}^{2+}$ and $\text{Fe}^{2+}$ in small intestine
Composition and function of gastric secretions

2. **Pepsinogen** (precursor of pepsin)
   - digestion of proteins

3. **Mucus**
   - forms a protective barrier: Mucus-bicarbonate barrier

4. **Intrinsic factor**
   - combines with vitamin $B_{12}$ to make it absorbable
HCl secretion

Parietal cell - secreting

Tubulovesicles fuse with canalculus, increased surface area and numbers of $\text{H}^+\text{K}^+\text{ATPase}$ increases acid secretion into lumen of gut.

Acid secretion is against a 3 million fold concentration gradient

$[\text{H}^+]$ inside $= 4 \times 10^{-8}\text{M}$

$[\text{H}^+]$ outside $= 0.1\text{M}$

NEEDS ENERGY
HCl secretion

- H⁺ source is carbonic anhydrase
  \[ \text{H}_2\text{O} + \text{CO}_2 \rightarrow \text{H}_2\text{CO}_3 \]
- H⁺ is pumped out via H⁺/K⁺ ATPase
- Lots of mitochondria to generate the ATP required
- \( \text{HCO}_3^- \) passes into the plasma in exchange for Cl⁻
- Cl⁻ is secreted into the lumen
Gastric secretions

- **Pepsinogen**
  Inactive precursor of pepsin which initiates protein digestion
  Is not necessary for complete digestion of dietary protein – pancreatic enzymes are sufficient
  Active only when the pH < 3.5
Gastric secretions

- **Mucus**

  Physical/chemical barrier to attack by gastric juice

  Stimulated by:
  - Ach
  - Mechanical Stim
  - Chemicals (ethanol)

  If breached e.g. hypersecretion of acid - ulceration

pH<2

pH7

$\text{HCO}_3^-$
Gastric Mucus-Bicarbonate Barrier

Stomach lumen with gastric juice (pH ~ 2)

The mucus layer is a physical barrier

\[ \text{HCO}_3^- \]

Bicarbonate is a chemical barrier that neutralizes acid

\[ \text{HCO}_3^- \]

pH ~ 7 at cell surface

Mucus droplets

Gastric mucus cell

Capillary
Gastric Mucus-bicarbonate barrier

The insoluble mucus and bicarbonate construct a barrier

- prevent hydrogen ions from diffusing to the mucosal layer
- protect the stomach mucosa from injury by hydrochloric acid and pepsin,
Intrinsic Factor

• Only gastric secretion that is essential for health

• Secreted from parietal cells in humans, chief cells in other species

• Forms a complex with vitamin $B_{12}$ in the gut

• The complex is resistant to digestion and therefore enables absorption of vitamin $B_{12}$

• Lack of intrinsic factor causes Vit $B_{12}$ deficiency (pernicious anaemia) – as all the Vit $B_{12}$ is digested and therefore can not be absorbed
Control of Gastric Acid Secretion

Gastric acid secretion is controlled by three mechanisms:

• Neurocrine (vagus/local reflexes)
• Endocrine (gastrin)
• Paracrine (histamine)
Endocrine gland cells of gastric pits

- Stimulates acid secretion
- Inhibits:
  - acid secretion
  - gastrin and pepsin release
  - pancreatic exocrine secretions

Stimulates acid secretion
Regulation of Gastric Secretions

The important stimulatory signals

Autonomic nerves
  • Release ACh
    • Stimulates smooth muscle contraction
    • stimulates Chief, Parietal, ECL and G cells

Gastrin
  • Stimulates Chief, Parietal, ECL cells

Histamin
  • Stimulates Parietal cells

Protein products such as peptides
Stimulates G-cells

Acids
  • Stimulate D cells
Endogenous substances regulating gastric secretion

When all three stimulators are present, acid secretion is maximally stimulated.

Ach, gastrin & histamine act synergistically.
Gastric secretion during digesting food

Cephalic phase via vagus

Parasympathetics excite pepsin and acid production

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

Intestinal phase:
1. Nervous mechanisms
2. Hormonal mechanisms
Gastric secretion in the digestive phase

Cephalic phase

Mechanisms:

- Conditioned & Unconditioned reflex
- Vagal efferent & with Gastrin secretion through gastrin-releasing peptide (GRP)

Experiment: Sham feeding by Pavlov

Characteristics:

- Large quantity (30%)
- High acidity & digestive power
Cephalic Phase

- Unconditioned and conditioned reflex
- Only occurs when we want food
- Depression dampens this reflex
- Large amount of HCL and pepsinogen, high digestive ability
Experiment of Sham feeding by Pavlov
Cephalic Phase

Taste or smell of food
Tactile sensation
in mouth

1. Medulla oblongata
2. Vagus nerves
3. Stomach
4. Gastrin
5. Circulation

Secretions stimulated
Mechanisms Stimulating Gastric Acid Secretion in Cephasic Phase

Sight, smell, taste of food → Vagus nerve → ACh → G cells → Gastrin → Histamine → ECL cells → Gastrin/ACh → GRP → G cells → Parietal cells
Gastric phase

Mechanisms:

- **Distension of gastric fundus & body** initiating vagovagal & local plexus reflexes
- **Distension of pylorus** initiating a release of gastrin through intrinsic plexus
- **Chemical stimulation** of G cells initiating a release of gastrin

Characteristics:

- Large quantity (60%)
- High acidity & digestive power
Gastric phase
Gastric Phase

Distension of stomach (arrival of food) → Vagal/Enteric reflexes

Peptides in lumen → G cells

Gastrin/ACh → ECL cells

Gastrin → Parietal cells

ACh → Parietal cells

Histamine → Parietal cells
Intestinal phase

Mechanisms:
- Mainly humoral regulation
- Chemical & Mechanical stimulation
  initiating releases of Gastrin, Entero-
  oxyntin & Other humoral factors

Characteristics:
- Small quantity (10%)
- Lower acidity & digestive power
Intestinal phase
Regulation of Gastric Secretions occurs via 3 phases

<table>
<thead>
<tr>
<th>TABLE 15–5</th>
<th>Control of HCL Secretion during a Meal</th>
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<tbody>
<tr>
<td><strong>STIMULI</strong></td>
<td><strong>PATHWAYS</strong></td>
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<tr>
<td><strong>Cephalic phase</strong></td>
<td></td>
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<tr>
<td>Sight</td>
<td>Parasymathetic nerves to enteric nervous system</td>
</tr>
<tr>
<td>Smell</td>
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<tr>
<td>Taste</td>
<td></td>
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<tr>
<td>Chewing</td>
<td></td>
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<tr>
<td><strong>Gastric contents (gastric phase)</strong></td>
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<tr>
<td>Distension</td>
<td>Long and short neural reflexes, and direct stimulation of gastrin secretion</td>
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<tr>
<td>↑Peptides</td>
<td></td>
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<tr>
<td>↓H+ concentration</td>
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<tr>
<td><strong>Intestinal contents (intestinal phase)</strong></td>
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<tr>
<td>Distension</td>
<td>Long and short neural reflexes; secretin, CCK, and other duodenal hormones</td>
</tr>
<tr>
<td>↑H+ concentration</td>
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<tr>
<td>↑Osmolarity</td>
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<tr>
<td>↑Nutrient concentrations</td>
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Inhibitory regulation of gastric secretion

**Hydrochloric acid (HCl)**

A typical example of negative feedback

**Conditions & Mechanisms:**

- pH \( \leq 1.2 \sim 1.5 \) in the gastric antrum
  - Inhibition of G cells, Release of SST
- pH \( \leq 2.5 \) in the duodenum
  - Release of secretin, bulbogastrone

**Fat:** Initiating release of enterogastrone

**Hypertonic solution:** Entero-gastric reflex
Enterogastrones

- Hormones released from gland cells in duodenal mucosa - secretin, cholecystokinin (CCK), GIP
- Released in response to acid, hypertonic solutions, fatty acids or monoglycerides in duodenum
- Act collectively to prevent further acid build up in duodenum
- Two strategies:
  - inhibit gastric acid secretion
  - reduce gastric emptying (inhibit motility/contract pyloric sphincter)
Regulation of gastric secretion

Cephalic phase:
- Sight, smell, taste of food; chewing
  - Vagal stimulation
  - Secretion of Ach or other transmitters by nerve endings

Gastric phase:
- Distention of stomach
  - Vago-vagal and local reflexes
  - Secretion of gastrin by G-cells of stomach
    - Inhibits
    - Peptides in stomach
    - Low pH in stomach

Intestinal phase:
- Protein digestion products in duodenum
  - Hyperosmotic solution
  - Fatty acids
  - Entero-oxyntin
  - HCl
- Mechanical stimulation
- Stimulation of G-cells in intestine
  - Secretion of secretin, CCK, GIP
  - Inhibits
  - Gastric secretion (HCl and pepsin)
2. Secretion of the pancreas
Secretion of the pancreas

Endocrine - insulin & glucagon

Exocrine - enzymes and bicarbonate

essential for digestion

almost under separate hormonal control
Structure of the pancreas

Exocrine cells (secrete enzymes)

Endocrine cells of pancreas

Duct cells (secrete bicarbonate)

Pancreas

Pancreatic duct

Duodenum

Common bile duct from gallbladder

Gall bladder

Sphincter of Oddi
<table>
<thead>
<tr>
<th>Category</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proteases</td>
<td>Cleave peptide bonds</td>
</tr>
<tr>
<td>Nucleases</td>
<td>Hydrolyze DNA/RNA</td>
</tr>
<tr>
<td>Elastases</td>
<td>Collagen digestion</td>
</tr>
<tr>
<td>Phospholipases</td>
<td>Phospholipids to fatty acids</td>
</tr>
<tr>
<td>Lipases</td>
<td>Triglycerides to fatty acids + glycerol</td>
</tr>
<tr>
<td>Amylase</td>
<td>Starch to maltose + glucose</td>
</tr>
</tbody>
</table>
Activation of pancreatic proteases

**Trypsinogen**
- Trypsinogen
- Chymotrypsinogen
- Proelastase
- Procarboxypeptidase

**Trypsin**
- Trypsin
- Chymotrypsin
- Elastase
- Carboxypeptidase

**Enterokinase**

Trypsinogen → Trypsin
Regulation of pancreatic secretion

Nervous regulation

Vagus nerve: ACh, gastrin

Characteristics: $H_2O$ & $HCO_3^-$↑, enzymes↑↑

Sympathetic nerve: ACh, NA

Characteristics: weak effect

Humoral regulation

Secretin: $H_2O$ & $HCO_3^-$↑↑, enzymes↑

Cholecystokinin (CCK):

Characteristics: $H_2O$ & $HCO_3^-$↑, enzymes↑↑

Feedback: CCK-releasing peptide
3. Biliary secretion
• Bile secretion & gallbladder emptying
  * Nature, Compositions & functions
    Hepatic bile: pH 7.4, golden yellow
    Bladder bile: pH 6.8, color become darker
    Compositions: H$_2$O, ions, bile acid, bile pigment, fatty acid, cholesterol, lecithin, mucoprotein, etc., but no enzyme
    Functions of bile (mainly by bile salt):
      Fat emulsification; lipid absorption;
      Promote the absorption of fat-soluble Vits
Control of bile secretion & gallbladder emptying

Nervous regulation

Vagus nerve: ACh, gastrin

Hepatic bile secretion↑ (small amounts)
Gallbladder contraction↑ (slightly)

Humoral regulation

Gastrin: direct to hepatic cells & gallbladder;
indirect to stomach→HCl→secretin

Secretin: act to bile duct & not to hepatic cells,
so: H₂O & HCO₃⁻↑, bile salt (−)

Cholecystokinin (CCK): gallbladder
contraction & Oddi’s sphincter dilatation

Bile salt: enterohpetic circulation of bile salt
Sites of absorption

The short bowel syndrome resulting in dehydration and malabsorption occurs as a result of massive intestinal resection, especially of the ileum with or without the colon. Resection of up to 100 cm of ileum causes diarrhea, because there are progressively greater degrees of bile salt malabsorption. Malabsorbed bile salts enter the colon where they cause water secretion by activating cyclic adenosine monophosphate. When the resection exceeds 100 cm, there is progressively more fatty acid loss in the colon, which also adds to water secretion and diarrhea. There is also malabsorption of vitamin B₁₂. In addition, there is loss of energy in the form of increased fat loss. Moreover, as the length of the resection increases, there is malabsorption of all micronutrients, namely, fat, carbohydrate and protein. The malabsorbed carbohydrate entering the colon is fermented to produce flatulence and diarrhea. In addition, there is malabsorption of vitamins and trace elements such as zinc.
Digestion in the intestine

- Pancreatic juice & its secretion
  * Nature, Compositions & functions
  pH 7.8~8.4, colorless & odourless, 1~2 L/day
  Bicarbonate ($\text{HCO}_3^-$)
  Neutralize HCl & provide a weak basic medium favoring digestive enzyme action
  
  Pancreatic enzymes: amylase, lipase, colipase, trypsinogen & chymtrypsinogen, etc.
  Turn trypsinogen into trypsin by entero-kinase, turn chymtrypsinogen into chym-trypsin by trypsin
  Trypsin inhibitor: a polypeptide
§ 6. Absorption in the small intestine

- **Sites of absorption**
  - Oral cavity & Stomach: *little*
  - Duodenum & Upper jejunum: *most nutrients*
  - Ileum: *bile salts & Vit. B<sub>12</sub>*
  - Colon: *water & electrolytes*

- **Proofs as the main absorptive region**
  - Huge absorptive surface (200 m<sup>2</sup>)
  - Plenty of capillaries & lymph capillaries
  - Large quantity of digestive fluid (6~8 L/day)
  - Food has almost completely been digested
Enlargement of the surface area of the intestine
• Absorption of main nutrients

* Water
  8 L/day, passive & iso-osmotic absorbed
  Different absorbability in different parts

* Inorganic slats
  Sodium: 95%~99%, jejunum>ileum>colon
    active transport
  Ferrum: 1/10, mainly in duodenum & jejunum,
    transferrin dependent, active transport
  Calcium: promote by Vit. D, active transport
  Anions: mainly Cl⁻ & HCO₃⁻, passive transport
* Carbohydrate
  Absorptive form: monosaccharide
  Mechanism: secondary active transport

* Protein
  Absorptive form: amino acid
  Mechanism: secondary active transport

* Fats
  Absorptive form: glycerol, monoglyceride, fatty acid, cholesterol
  Mechanism: passive diffusion
  Pathway: blood & lymph
Digestion & absorption of fats in the intestine
Digestive Homeostasis Disorders

- ULCERS – erosion of the surface of the alimentary canal generally associated with some kind of irritant
Digestive Homeostasis Disorders

• **CONSTIPATION** – a condition in which the large intestine is emptied with difficulty.
• Too much water is reabsorbed
• and the solid waste hardens
Digestive Homeostasis Disorders

• DIARRHEA – a gastrointestinal disturbance characterized by decreased water absorption and increased peristaltic activity of the large intestine.
• This results in increased, multiple, watery feces.
• This condition may result in severe dehydration, especially in infants
Digestive Homeostasis Disorders

- APPENDICITIS – an inflammation of the appendix due to infection
- Common treatment is removal of the appendix via surgery
Digestive Homeostasis Disorders

• GALLSTONES – an accumulation of hardened cholesterol and/or calcium deposits in the gallbladder
• Can either be “passed” (OUCH!!) or surgically removed
Digestive Homeostasis Disorders

• HEART BURN – ACID from the stomach backs up into the esophagus.