Food Categories Enzyme

- 1. Complex carbohydrates + Amylase + Water $\rightarrow$ Simple sugars
- (e.g., starch, glycogen)
- 2. Proteins + Proteases + Water $\rightarrow$ Amino acids
- 3. Fats + Lipases + Water $\rightarrow$ Fatty acids and glycerol
TASTE

- The filiform papillae, found at the front of the tongue, are rough and are important in licking.
- The fungiform papillae and the circumvallate papillae, found toward the back of the tongue, all contain taste buds.
- There are four tastes: sweet, sour, salt, and bitter.

Saliva

- **Saliva** is 99.5% water, which provides a medium for dissolving foods. The remaining 0.5% consists of solutes:
  - Chlorides which activate the salivary enzyme amylase.
  - Amylase initiates the breakdown of complex carbohydrates like starch and glycogen into simple sugars.
  - Bicarbonates and phosphates, which are buffer chemicals, keep the saliva at a slightly acidic pH of 6.35 to 6.85.
  - Urea and uric acid are waste products.
  - Mucin forms mucus to lubricate food.
  - The enzyme lysozyme destroys bacteria, thus protecting the mucous membrane from infection and the teeth from possible decay.
Digestive Process

- The GI tract is a “disassembly” line
  - Nutrients become more available to the body in each step
- **There are six essential activities:**
  - Ingestion,
  - propulsion,
  - mechanical digestion
  - Chemical digestion,
  - absorption,
  - defecation

Digestion

- Processing of food
- Types
  - Mechanical (physical)
    - Chew
    - Tear
    - Grind
    - Mash
    - Mix
  - Chemical
    - Catabolic reactions
    - Enzymatic hydrolysis
      - Carbohydrate
      - Protein
      - Lipid
NEUROGENIC SECRETION:

- Three secretomotor neurotransmitters for enterocytes:
  - Substance P
  - ACh, both preganglionic and postganglionic
  - VIP, Postganglionic

- Inhibitory neurons act on the preganglionic to prevent secretomotor excitation:
  - Somatostatin
  - Sympathetics
  - Opioids: Patients on opioids can become quite constipated and get a condition called "Narcotic Bowel."

Digestion, what is it?

- Mechanical breakdown of food
- Chemical breakdown of food
- Absorption of nutrients
Regulation of Gastric Emptying

Gastrointestinal Tract Activities

- **Ingestion** – taking food into the digestive tract

- **Propulsion** – swallowing and peristalsis
  - Peristalsis – waves of contraction and relaxation of muscles in the organ walls

- **Mechanical digestion** – chewing, mixing, and churning food
The Swallowing Process

THREE STAGES:
A) ORAL STAGE - Voluntary stage
B) PHARYNGEAL STAGE - Involuntary stage
C) OESOPHAGEAL STAGE - Involuntary stage

Deglutition (swallowing)

- Sequence
  - Voluntary stage
    - Push food to back of mouth
  - Pharyngeal stage
    - Raise
      - Soft palate
      - Larynx + hyoid
      - Tongue to soft palate
  - Esophageal stage
    - Contract pharyngeal
    - Open esophagus
    - Start peristalsis
Deglutition (swallowing)

Control

- Nerves
  - Glossopharyngeal
  - Vagus
  - Accessory
- Brain stem
  - Deglutition center
    - Medulla oblongata
    - Pons
- Disorders
  - Dysphagia
  - Aphagia

SWALLOWING REFLEX
Impulses travel in V, IX, X nerves to stimulate medulla, and efferent pass through V, VII, IX, X, XII nerves to pharynx and tongue.

Swallowing Of A Bolus

Medulla oblongata and lower pons

Oral Stage (Voluntary)

Pharyngeal Stage

Oesophageal Stage (Swallowing centre)

Trachea

Bolus

Epiglottis

Oesophagus sphincter (OES)

Bolus

OES

Bolus (3 - 5 cm s⁻¹)
Gastrointestinal Tract Activities

- **Chemical digestion** – catabolic breakdown of food
- **Absorption** – movement of nutrients from the GI tract to the blood or lymph
- **Defecation** – elimination of indigestible solid wastes

Water Balance

- Digestive tract receives about 9 L of water/day
- .7 L in food, 1.6 L in drink, 6.7 L in secretions
- 8 L is absorbed by small intestine and 0.8 L by large intestine
- Water is absorbed by osmosis following the absorption of salts and organic nutrients
- Diarrhea occurs when too little water is absorbed
- Feces pass through too quickly if irritated
- Feces contains high concentrations of a solute (lactose)
Absorption and Motility

- Transit time is 12 to 24 hours
  - reabsorbs water and electrolytes
- Feces consist of water and solids (bacteria, mucus,
  - undigested fiber, fat and sloughed epithelial cells
- Haustral contractions occur every 30 minutes
  - distension of a haustrum stimulates it to contract
- Mass movements occur 1 to 3 times a day
  - triggered by gastrocolic and duodenocolic reflexes
- Filling of the stomach and duodenum stimulates motility
- Moves residue for several centimeters with each contraction

Absorption

The small intestine is the main site of absorption

Water-soluble nutrients

- Most water-soluble nutrients such as monosaccharides, small fatty acids, and many amino acids are absorbed by either active transport or facilitated diffusion.
- Once in the lining cells, they may pass freely into the numerous capillaries of the mucosa's connective tissue (the lamina propria).
- The "finishing enzymes" (brush border enzymes) in the small intestine help to break up disaccharides and small chain polypeptides that are still just a wee bit too large to absorb through the membrane.

Fat-soluble nutrients

- Cannot be absorbed so simply, and must be processed by the lining cells.
- After packaging lipids into little bubbles of membrane they are exuded from the cell and pass into lymphatic capillaries called lacteals in the villus.
- Like most nutrients, these will find themselves headed for the liver for processing.
GI Tract

- External environment for the digestive process

- **Regulation of digestion involves:**
  - Mechanical and chemical stimuli — stretch receptors, osmolarity, and presence of substrate in the lumen
  - Extrinsic control by CNS centers
  - Intrinsic control by local centers

Receptors of the GI Tract

- **Mechano- and chemoreceptors respond to:**
  - Stretch, osmolarity, and pH
  - Presence of substrate, and end products of digestion

- They initiate reflexes that:
  - Activate or inhibit digestive glands
  - Mix lumen contents and move them along
Nervous Control of the GI Tract

- **Intrinsic controls**
  - Nerve plexuses near the GI tract initiate short reflexes
  - Short reflexes are mediated by local enteric plexuses (gut brain)

- **Extrinsic controls**
  - Long reflexes arising within or outside the GI tract
  - CNS centers and extrinsic autonomic nerves
TYPES OF MOTILITY:

- **PERISTALSIS**: Propulsion of material in the *aboral* (away from mouth) direction.
  - Rate of peristalsis varies in region, but peristaltic generally gets slower as we move down the tract.
  - Peristalsis occurs by segmental hyperpolarization followed by depolarization of muscle.
  - Mechanism: Bolus of food in a particular location stimulates mechanoreceptors and chemoreceptors in the GI lumen, ultimately resulting in peristalsis:
    - Relaxation of the muscle occurs distal to the bolus, so that the food can go forward. This is mediated by VIP / NO.
    - Contraction of Longitudinal Muscle layer also occurs distal to bolus, because longitudinal contraction causes widening of the GI lumen.
    - Contraction of the muscle occurs proximal to the bolus, in order to propel the bolus forward.
    - There is a basal level of VIP inhibition in the muscle, and a bolus of food turns off this inhibition: distensio of lumen by a bolus will cause inhibition of release of VIP / NO ----> contraction of proximal region.

- **RHYTHMIC SEGMENTATION**: Mixing and churning of materials without propelling them forward in the tract.
  - Only involved the circular muscle --- not longitudinal
  - Common in small and large intestine

- **TONIC CONTRACTION**: Blocking of the passage of material, as in sphincters.
  - Tonic Contraction is myogenic -- it doesn’t depend on innervation.

Digestive Enzymes
Digestive Enzymes

- Are secreted by:
  - salivary glands
  - tongue
  - stomach
  - pancreas

- Break molecular bonds in large organic molecules:
  - carbohydrates, proteins, lipids, and nucleic acids
  - in a process called hydrolysis
- Are divided into classes by targets:
  - **carbohydrases:**
    - break bonds between simple sugars
  - **proteases:**
    - break bonds between amino acids
  - **lipases:**
    - separate fatty acids from glycerides
Functions of the digestive system

- Ingestion
- Mechanical processing
- Digestion
- Secretion
- Absorption
- Excretion

Movement of digestive materials

- Visceral smooth muscle shows rhythmic cycles of activity
  - Pacemaker cells
- Peristalsis
  - Waves that move a bolus
- Segmentation
  - Churn and fragment a bolus
Esophagus

- Function – food passageway
- Location – from pharynx → stomach
  - 1. passes thru mediastinum
  - 2. behind the trachea
  - 3. moves through diaphragm
- Esophageal sphincter – distal end of esophagus prevents regurgitation of food

Esophageal Peristalsis

- 1° Peristalsis:
  - Initiated by swallowing (not after vagotomy)
- 2° Peristalsis:
  - Caused by residual food in esophagus
  - Vagal nuclei run the show (ambiguus, DMN)
  - SM Peristalsis persists after vagotomy (enteric NS takes over)
Peristalsis

**STEP 1:**
Contraction of circular muscles behind food mass

**STEP 2:**
Contraction of longitudinal muscles ahead of food mass

**STEP 3:**
Contraction of circular muscle layer forces food mass forward

---

**Diseases of the Esophagus**

- **Achalasia:**
  - Stenosis of LES, dilation of body of esophagus
    - “bird-beak” appearance on barium study

- **Hiatal Hernia**
  - LES protrudes into thoracic cavity
    - LES tends to be patent due to negative pressure in thoracic cavity

- **LES Tone:**
  - Increased by Ach, Gastrin
  - Decreased by Sympathetics, PGE$_1$
Control of the digestive system

- Movement of materials along the digestive tract is controlled by:
  - Neural mechanisms
    - Parasympathetic and local reflexes
  - Hormonal mechanisms
    - Enhance or inhibit smooth muscle contraction
  - Local mechanisms
    - Coordinate response to changes in pH or chemical stimuli

The Regulation of Digestive Activities

Figure 24.5
## Functions of Saliva

Moistens ingested food and helps turn it into a semisolid bolus that is more easily swallowed.
- Moistens and cleanses the oral cavity structures.
- First step in chemical digestion occurs when amylase in saliva begins to break down carbohydrates.
- Contains antibodies and an antibacterial element called lysozyme that help inhibit bacterial growth in the oral cavity.
- Watery medium into which food molecules are dissolved so taste receptors can be stimulated.

## Salivary glands – what is their function?

- Two main purposes:
  - 1. secrete saliva – chemical digestion
  - 2. solvent – dissolves food – so can taste cleanses mouth and teeth
Taste physiology

Cells in taste bud
- **Supporting cells** - contain microvilli, appear to secrete substances into lumen of taste bud.
- **Sensory receptor cell** - has peg-like extensions projecting into lumen. These contain the sites of sensory transduction.
- **Basal cells** - these differentiate into new receptor cells. They are derived from surrounding epithelium. The cells are continuously renewed every 10 days or so.
The sense of taste is equivalent to excitation of taste receptors, and receptors for a large number of specific chemicals have been identified that contribute to the reception of taste. Despite this complexity, five types of tastes are commonly recognized by humans:

- **Sweet** - usually indicates energy rich nutrients
- **Umami** - the taste of amino acids (e.g. meat broth or aged cheese)
- **Salty** - allows modulating diet for electrolyte balance
- **Sour** - typically the taste of acids
- **Bitter** - allows sensing of diverse natural toxins
### Examples of some human thresholds

<table>
<thead>
<tr>
<th>Taste</th>
<th>Substance</th>
<th>Threshold for tasting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Salty</td>
<td>NaCl</td>
<td>0.01 M</td>
</tr>
<tr>
<td>Sour</td>
<td>HCl</td>
<td>0.0009 M</td>
</tr>
<tr>
<td>Sweet</td>
<td>Sucrose</td>
<td>0.01 M</td>
</tr>
<tr>
<td>Bitter</td>
<td>Quinine</td>
<td>0.000008 M</td>
</tr>
<tr>
<td>Umami</td>
<td>Glutamate</td>
<td>0.0007 M</td>
</tr>
</tbody>
</table>

### STOMACH PHYSIOLOGY
3 Main cells:

1. **Mucous cells** – mucous
2. **Chief** – digestive enzymes
   a. Pepsin – digests protein
   b. Alkaline substance – protects lining
   c. Intrinsic factor – absorbs Vitamin B12
3. **Parietal cells** → hydrochloric acid
Gastric Secretion
• Stomach secretes water, electrolytes (H+, K+, Na+, Cl−, HCO3−),
• enzymes with activity at acid pH (pepsin, lipase) and glycoproteins (intrinsic factor, mucins)
Stomach

- J shaped
- Can hold about a liter

Functions:
- 1. receives food
- 2. mixes food with gastric juice
- 3. moves food to small intestine

Mixing in the Stomach

- **Chyme** – semifluid made by mixing food with digestive juices.
  - 1. pushed toward small intestine
  - 2. water moves right through
  - 3. Movement thru fastest to slowest:
    - carbs → proteins → fats (4-6hrs for fats)

Microscopic Anatomy

- Parietal cells
  - Location- neck of gastric pit
  - Stimulated by Ach, Histamine and Gastrin
  - Secretes HCl + Intrinsic Factor
- Chief Cells
  - Location- base of gastric pit
  - Stimulus- Vagal
  - Secretes Pepsinogen (eventually leads to pepsin-digestive enzyme)
Microscopic Anatomy

Antral Glands
- **Gastrin cells**
  - Location: mucosa of distal stomach
  - Stimulus: amino acids
  - Secretion: Gastrin (stimulates HCl production by way of parietal cells)
- **Somatostatin**
  - Location: mucosa of distal stomach + Duodenum
  - Stimulus: HCl or low pH in duodenum
  - Actions: Inhibits gastric emptying, Pancreatic secretions, and gallbladder contraction

### TABLE 15.4

<table>
<thead>
<tr>
<th>HORMONE</th>
<th>SOURCE</th>
<th>FUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrin</td>
<td>Gastric cells, in response to food</td>
<td>Causes gastric glands to increase their secretory activity</td>
</tr>
<tr>
<td>Cholecystokinin</td>
<td>Intestinal wall cells, in response to proteins and</td>
<td>Causes gastric glands to decrease their secretory activity and inhibits</td>
</tr>
<tr>
<td></td>
<td>fats in the small intestine</td>
<td>gastric motility; stimulates pancreas to secrete fluid with a high digestive enzyme concentration; stimulates gallbladder to contract and release bile</td>
</tr>
<tr>
<td>Secretin</td>
<td>Cells in the duodenal wall, in response to acidic</td>
<td>Stimulates pancreas to secrete fluid with a high bicarbonate ion concentration</td>
</tr>
</tbody>
</table>
• Cardia – mucus, endocrine and undifferentiated cells
• Fundus & body – oxyntic glands
  – Parietal, chief, endocrine, mucus neck, undifferentiated cells
• Antrum & pylorus – pyloric glands
  – Endocrine, mucus neck, G-cells

• Endocrine cells
  – G cells – secrete gastrin
• Paracrine cells
  – D cells – secrete somatostatin
  – Enterochromaffin-like (ECL) cells – secrete histamine
Parietal Cell

- Stimulated by histamine, gastrin, acetylcholine
- Inhibited by somatosatin, prostaglandins

Somatostatin

- Secreted by D cells
- Stimulated by CCK
- Effects $H^+$ secretion via inhibitory effects on oxyntic ECL cells and pyloric G cells
- D cell in pylorus stimulated by acid
CCK

- Produced by duodenal endocrine cells in response to dietary fatty acids and amino acids
- In vitro stimulates parietal cells
- In vivo inhibits acid production through D cells

Secretin

- Produced by duodenal S cells in response to H^+
- Inhibits gastric acid secretion, stimulates pancreatic HCO_3^- production
Pepsinogens

- Pepsins cleave peptide bonds formed by phenylalanine and tyrosine
- PG secretion stimulated by acetylcholine analogs, histamine, gastrin, secretin
- Inhibited by somatostatin

Intrinsic Factor

- Secreted by parietal cells
- Binds cobalamin (B₁₂) to facilitate absorption
- 2 cobalamin binding proteins – IF/R
- Initially binds to cobalamin R in acidic stomach then is cleaved in duodenum and binds to IF
- Attaches to ileal mucosa
- B₁₂ malabsorption may result from IF deficiency, achlorhydria or hypochlorhydria, bacterial overgrowth, pancreatic insufficiency, ileal receptor defect, ileal disease, ileal resection
Physiology

- **Gastrin**
  - Most important stimulus is a meal
    - Amino acids that result from proteolysis
    - Fat and carbohydrates are not stimuli for gastrin secretion
    - Gastric distention that occurs from a meal will stimulate cholinergic neurons thereby releasing gastrin
    - Gastrin will then prompt parietal cell to secrete HCl
  - Once gastric distention diminishes, VIP-containing neurons are activated causing stimulation of somatostatin, thus attenuating gastrin secretion
  - Overall, a lumen pH >3.0 will potentiate gastrin release, whereas a pH <3.0 will inhibit its release

---

**Hormonal regulation:**

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Stimulus</th>
<th>Site of Action</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>gastrin</td>
<td>distention of stomach, vagus</td>
<td>stomach wall</td>
<td>release gastric secretions</td>
</tr>
<tr>
<td>secretin</td>
<td>acid in duodenum</td>
<td>duodenum</td>
<td>release pancreatic chyme</td>
</tr>
<tr>
<td>cholecystokinin</td>
<td>fatty acids in duodenum</td>
<td>duodenum</td>
<td>1) slow peristalsis, 2) contract gall bladder, 3) suppress appetite</td>
</tr>
</tbody>
</table>
**Physiology**

- **Somatostatin**
  - Like Gastrin, plays an integral role in gastric physiology
  - Also, used for important therapeutic applications in treatment of digestive diseases
    - Main stimulus is a low or acidic (<3.0) luminal pH
    - Many peptides have shown to release somatostatin
      - Ex. Secretin, Cholecystokinin and gastrin
    - In contrast, stimulation of Vagal nerves along with cholinergic neurons inhibit somatostatin
  - Overall, the most important gastric function of somatostatin is to regulate acid secretion and gastrin release

---

**Phases of Gastric Acid Secretion**

- **Cephalic**
  - Sight
  - Smell
  - Taste
  - Thought

- **Gastric**
  - Antral distention
  - Protein content
  - pH (>4)

- **Intestinal**
  - Intestinal gastrin
  - Absorbed amino acids

**Increased circulating gastrin**

**Decreased intragastric pH**

**Increased H+ secretion**

Histamine

From enterochromafin-like cells (ECL cells) in the gastric mucosa

- produce, store, & release histamine
- activated by ACh, gastrin, & secretagogues
Inhibition of Gastric Secretion

- Important for protection of duodenum
- **Gastric pH < 3 ---> gastric D cells release somatostatin which inhibits gastrin release**
- Acid in duodenum ---> secretin & CCK--> inhibits gastric secretion and motility
- Acid, fats, hyper-osmotic solutions in the duodenum ---> release of enterogastrones ---> inhibit gastric motility and secretion
- *Gastric Inhibitory Peptide (GIP) from duodenum ---> inhibits parietal cell function*

**Inhibitors of Gastric Secretion**

- GIP
- CCK
- Secretin

---

Gastric Acid Secretion

- Basolateral membrane of the parietal cell contains specific receptors for the three major stimulants of acid production
  - Histamine
  - Gastrin
  - Acetylcholine
- Each stimulant has its own 2nd messenger system which allows for stimulation of the parietal cell
**Gastric Acid Secretion**

- Humans normally secrete 2 to 5 mEq/h of HCl in the fasting state, constituting basal acid secretion
  - Both Vagal tone and ambient Histamine secretion are presumed to regulate basal acid secretion
  - Gastrin is not thought to play a role in basal acid secretion
  - Therefore, a Vagotomy or use of H2 blockers (ex. Cimetidine) will decrease basal acid production

**Gastric Acid Secretion**

- Stimulated acid secretion begins with
  - Cephalic phase
    - Thought, sight or smell of food stimulates acid secretion
    - Mediated by Vagal stimulation
  - Vagal discharge
    - Directs the cholinergic mechanism for stimulation
      - Can be inhibited by Atropine (anticholinergic)
    - Inhibits release of somatostatin
      - Vagal effects inhibit tonic inhibition that is provided by somatostatin
Gastric Acid Secretion

- **Gastric Phase**
  - Begins when food enters the stomach
  - The following are responsible for stimulation of acid secretion
    - Presence of partially hydrolyzed food constituents
    - Gastric distention
    - Gastrin is the most important mediator of this phase
  - Ends when Antral mucosa is exposed to acid
    - When luminal pH is <2.0 in the antrum, gastrin release stops
    - Somatostatin release is increased
  - Entry of digestive products into the intestine begins the intestinal-phase inhibition of gastric acid secretion

- **Intestinal Phase**
  - Also, releases HCl by way of Gastrin
  - Releases secretin to inhibit Gastrin which ultimately decreases Acid production
Other Factors

- Pepsin
  - Secreted from gastric chief cells
  - Contributes to the overall coordination of the digestive process
  - Main function is to initiate protein digestion, usually is incomplete
    - Partially hydrolyzed protein by pepsin are important signals for release of
      - Gastrin
      - Cholecystokinin

Other Factors

- Intrinsic Factor (IF)
  - Located in the parietal cells (oxyntic gland)
  - Main function is to absorb cobalamin (Vitamin B12) form ileal mucosa and then transported to the liver
  - Secretion of IF is similar to acid secretion
    - stimulated
      - Ach
      - Histamine
      - Gastrin

Other Factors

- **Bicarbonate**
  - Secreted from the gastric mucosa
  - Theory is that bicarbonate is secreted to maintain a neutral pH at the mucosal surface, even if acidic in lumen
  - Cholinergic agonist, vagal nerve stimulation have been shown to increase gastric bicarbonate production

Acid Regulation in the Stomach

- Cephalic Phase of Gastric Acid Secretion
- Stretch
- Gastric Phase of Gastric Acid Secretion

- Vagus
- ACh (neurocrine)
- Protein and amino acids
- gastrin (endocrine)
Gastric Emptying

- Contraction in the stomach
  - Orad <<<< Caudad (3/minute)
  - Primarily peristaltic
- Solid food is usually forced back into stomach for mixing
- Duodenum contracts much more often but is phasic (pseudosphincter)
Main Functions of Small Intestine

**Digestion** - various enzymes:
- 1. **peptidases** – protein digestion
- 2. **sucrase**, maltase and lactase – sugar digestion
- 3. **lipase** – fat digestion

**Absorption** – performed by villi (small fingerlike projections)

Release of waste to large intestine

Functions of Large Intestine

- Absorbs water and electrolytes
- Contain intestinal flora (bacteria) – break down some of the molecules not broken down in the small intestine
  - Bacteria use the materials for energy they make certain vitamins like K, thiamine, riboflavin and B12 – absorbed through intestine wall
Defecation

- Presence of food in the stomach:
  - Activates the gastrocolic reflex
  - Initiates peristalsis that forces contents toward the rectum

- Distension of rectal walls caused by feces:
  - Stimulates contraction of the rectal walls
  - Relaxes the internal anal sphincter

- Voluntary signals stimulate relaxation of the external anal sphincter and defecation occurs

---

**RECTAL DISTENTION**

- External anal sphincter (EAS) and Puborecalsis (PR) muscles CONTRACT
- Internal anal sphincter (IAS) RELAXES

**DEFECATION URGE**

- If appropriate EAS and PR relax
  - Stool passage
- Not appropriate EAS and PR remain contracted
  - IAS recovers tone
  - Defecation urge passes
Defecation cycle,

- is normally a combination of both voluntary and involuntary processes.
- The defecation cycle is the interval of time between the completion of one bowel movement, and the completion of the following bowel movement.
- At the start of the cycle, the rectum ampulla (anatomically also: ampulla recti) acts as a temporary storage facility for the unneeded material.
- As additional fecal material enters the rectum, the rectal walls expand.
- A sufficient increase in fecal material in the rectum causes stretch receptors from the nervous system located in the rectal walls to trigger the contraction of rectal muscles, relaxation of the internal anal sphincter and an initial contraction of the skeletal muscle of the external sphincter.
- The relaxation of the internal anal sphincter causes a signal to be sent to the brain indicating an urge to defecate.

If this urge is not acted upon, the material in the rectum is often returned to the colon by reverse peristalsis where more water is absorbed, thus temporarily reducing pressure and stretching within the rectum.

The additional fecal material is stored in the colon until the next mass 'peristaltic' movement of the transverse and descending colon.

If defecation is delayed for a prolonged period the fecal matter may harden, resulting in constipation.

Once the voluntary signal to defecate is sent back from the brain, the final phase of the cycle begins.

The rectum now contracts and shortens in peristaltic waves, thus forcing fecal material out of the rectum and out through the anal canal.

The internal and external anal sphincters along with the puborectalis muscle allow the feces to be passed by pulling the anus up over the exiting feces in shortening and contracting actions.
Defecation is normally assisted by taking a deep breath and trying to expel this air against a closed glottis (Valsalva maneuver). This contraction of expiratory chest muscles, diaphragm, abdominal wall muscles, and pelvic diaphragm exert pressure on the digestive tract. Ventilation at this point temporarily ceases as the lungs push the chest diaphragm down in order to exert the pressure.

**Cardiovascular aspects**

During defecation, the thoracic blood pressure rises, and as a reflex response the amount of blood pumped by the heart decreases. Death has been known to occur in cases where defecation causes the blood pressure to rise enough to cause the **rupture of an aneurysm** or to dislodge blood clots. Also, in release of the Valsalva maneuver blood pressure falls, this coupled often with standing up quickly to leave the toilet results in a common incidence of blackouts in this situation.

**Neurological aspects**

• When defecating, the external sphincter muscles relax.
• The anal and urethral sphincter muscles are closely linked, and experiments by Dr. Harrison Weed at the Ohio State University Medical Center have shown that they can only be contracted together, not individually, and that they both show relaxation during urination. This explains why defecation is frequently accompanied by urination, and why urination is frequently accompanied by flatulence.
• Defecation may be involuntary or under voluntary control.
• Young children learn voluntary control through the process of toilet training.
• Once trained, loss of control causing fecal incontinence may be caused by physical injury (such as damage to the anal sphincter that may result from an episiotomy), intense fright, excessive pressure placed upon the abdomen, inflammatory bowel disease, impaired water absorption in the colon and psychological or neurological factors.
• The loss of voluntary control of defecation is experienced frequently by those undergoing a terminal illness.
Feces

- Makeup: water, undigested food, electrolytes, mucous, shed intestinal cells, and bacteria
- 75% water
- Odor – usually a result of bacterial action

LIVER PHYSIOLOGY
The functions of the liver are so numerous and important that we cannot live without it.

- It produces heparin, prothrombin, and thrombin.
- Its Kupffer’s cells phagocytose bacteria and worn-out blood cells.
- It stores excess carbohydrates as glycogen. It stores copper, iron, and vitamins A, D, E, and K.
- It stores or transforms poisons into less harmful substances.
- It produces bile salts that emulsify or break down fats.

**Liver Functions:**

- Helps in the break down of carbohydrates
- Maintains blood sugar level
- Breaks down fatty acids – lipoproteins, cholesterol and phospholipids
- Breaks down amino acids
- Stores glycogen, iron and Vitamins A, D, B12
- Breaks down old and damaged RBC
- Removes toxins
- Secretes bile

**Hepatocytes’ functions include:**

- Production of bile
- Processing bloodborne nutrients
- Storage of fat-soluble vitamins
- Detoxification
- Secreted bile flows between hepatocytes toward bile ducts in portal triads
Metabolic function

- Carbohydrate metabolism
  - Gluconeogenesis
  - Glycogenolysis and glycogenesis
- Hormone metabolism
- Lipid Metabolism
  - Synthesis of fatty acids, cholesterol, lipoproteins
  - Ketogenesis
- Drug Metabolism
- Protein Metabolism
  - Synthesis of plasma proteins
  - Urea synthesis

Storage function
- Glycogen
- All fat-soluble vitamins (A, D, E, K) and some
  - Water soluble vitamins (B12)
  - Iron

Protection

Detoxification — converts noxious or insoluble compounds into less toxic or more water soluble forms

Kupffer cells ingest bacteria or other foreign material from blood

Liver Tests:

- Aminotransferases (AST/ALT)
- Alkaline Phosphatase
- Gammaglutamly Transpeptidase (GGTP)
- Bilirubin
- Total Protein/Albumin/Globulin
- Prothrombin Time (INR)
Aminotransferases
- enzymes that leak when liver cells damaged
- AST = aspartate aminotransferase
- ALT = alanine aminotransferase
- AST:ALT ratio: >2:1 alcoholic liver disease
- pyridoxine (B6) = coenzyme in synthesis
- B6 deficiency: inhibits ALT>AST
- Alcohol causes mitochondrial injury
- AST: cytosol & mitochondria

Alkaline Phosphatase (ALP)
- enzyme found in many body tissues
- >80% in liver and bone
- component of cells lining bile ducts
- ↑ ALP synthesis by liver in cholestasis
- ALP >3-5X: cholestatic disease
- doesn't differentiate intra/extrahepatic
- t½ = 7d :↑ after several days

Transaminases
- Located in hepatocytes
  - Released after hepatocellular injury
- 2 Forms
  - AST
    - Non-specific to liver: heart, skeletal muscle, blood
  - ALT
    - More specific: elevated in myopathies
Transaminases

- May not be elevated in chronic liver disease
  - HCV- apoptosis
  - Cirrhosis
- Minimal ALT elevations (<1.5 X normal)
  - Race/Gender
  - Obesity
  - Muscle injury

Transaminases

- Mild elevations – more to come
- Marked elevations
  - Acute toxic injury- ie tylenol, ischemia
  - Acute viral disease
  - Alcoholic hepatitis
Transaminases

- **AST:ALT ratio**
  - Elevated in alcoholic disease
  - 2:1
  - If AST > 500 consider other cause
  - No alcohol use suggests cirrhosis

Extravascular Pathway for RBC Destruction

(Liver, Bone marrow, & Spleen)

- Phagocytosis & Lysis
- Hemoglobin
  - Globin
    - Amino acids
  - Amino acid pool
- Heme
  - Fe^{2+}
  - Bilirubin
    - Excreted
NORMAL BILIRUBIN METABOLISM

- Uptake of bilirubin by the liver is mediated by a carrier protein (receptor)
- Uptake may be competitively inhibited by other organic anions
- On the smooth ER, bilirubin is conjugated with glucoronic acid, xylose, or ribose
- Glucoronic acid is the major conjugate - catalyzed by UDP glucuronyl transferase
- "Conjugated" bilirubin is water soluble and is secreted by the hepatocytes into the biliary canaliculi
- Converted to stercobilinogen (urobilinogen) (colorless) by bacteria in the gut
- Oxidized to stercobilin which is colored
- Excreted in feces
- Some stercobilin may be re-adsorbed by the gut and re-excreted by either the liver or kidney
The causes of jaundice

<table>
<thead>
<tr>
<th>Type</th>
<th>Cause</th>
<th>Clinical example</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prehepatic</td>
<td>hemolysis</td>
<td>autoimmune abnormal hemoglobin</td>
<td>uncommon depends on region</td>
</tr>
<tr>
<td>intrahepatic</td>
<td>infection</td>
<td>hepatitis A, B, C</td>
<td>common/very common</td>
</tr>
<tr>
<td></td>
<td>chemical/drug</td>
<td>acetaminophen alcohol</td>
<td>common</td>
</tr>
<tr>
<td></td>
<td>genetic errors: bilirubin metabolism</td>
<td>Gilbert’s syndrome</td>
<td>1 in 20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Crigler–Najjar syndrome</td>
<td>very rare</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dubin–Johnson syndrome</td>
<td>very rare</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rotor’s syndrome</td>
<td>very rare</td>
</tr>
<tr>
<td>genetic errors:</td>
<td>Wilson’s disease</td>
<td></td>
<td>1 in 200 000</td>
</tr>
<tr>
<td>specific proteins</td>
<td>α1 antitrypsin</td>
<td></td>
<td>1 in 1000 with genotype</td>
</tr>
<tr>
<td>autoimmune</td>
<td>chronic active hepatitis</td>
<td></td>
<td>uncommon/rare</td>
</tr>
<tr>
<td>neonatal</td>
<td>physiologic</td>
<td></td>
<td>very common</td>
</tr>
<tr>
<td>Posthepatic</td>
<td>intrahepatic bile ducts</td>
<td>drugs primary biliary cirrhosis</td>
<td>common/uncommon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cholangitis</td>
<td>common/uncommon</td>
</tr>
<tr>
<td></td>
<td>extrahepatic bile ducts</td>
<td>gall stones</td>
<td>very common/ uncommon</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pancreatic tumor</td>
<td>rare</td>
</tr>
</tbody>
</table>
Bile

- Yellowish green liquid
- Make up: bile salts, bile pigments, cholesterol and electrolytes.
- Bile salts – breaks down fat into smaller molecules.
Components of Bile

- **50% Bile Acids** *(Cholic, chenodeoxycholic, deoxycholic, and lithocholic acid)*
  - Product of Cholesterol + 7a-Hydroxylase, most is recycled from distal ileum
  - Form micelles - amphipathic
  - pK≈ approx. 7 if unconjugated
  - conjugated to taurine or glycine - pK goes down, allows them to be soluble in the intestine

- **Phospholipids (lecithin)**
  - solubilized by bile salts

- **Cholesterol**

- **Bile pigments**
  - bilirubin glucuronide

- **Composition of Bile** A yellow-green, alkaline solution containing bile salts, bile pigments, cholesterol, neutral fats, phospholipids, and electrolytes

- Bile salts are cholesterol derivatives that:
  - Emulsify fat
  - Facilitate fat and cholesterol absorption
  - Help solubilize cholesterol

- Enterohepatic circulation recycles bile salts

- The chief bile pigment is bilirubin, a waste product of heme

- **Regulation of Bile Release** Acidic, fatty chyme causes the duodenum to release:
  - Cholecystokinin(CCK) and secretin into the bloodstream

- Bile salts and secretin transported in blood stimulate the liver to produce bile

- Vagal stimulation causes weak contractions of the gallbladder

- **Cholecystokinin causes:**
  - The gallbladder to contract
  - The hepatopancreatic sphincter to relax

- As a result, bile enters the duodenum
Regulation of Bile Release

Vagal stimulation causes weak contractions of gallbladder
- Cholecystokinin (via bloodstream) causes gallbladder to contract and hepatopancreatic sphincter to relax; bile enters duodenum
- Acidic, fatty chyme entering duodenum causes release of cholecystokinin and secretin from duodenal wall enteroendocrine cells
- Cholecystokinin and secretin enter the bloodstream
- Bile salts and secretin transported via bloodstream stimulate liver to produce bile more rapidly
- Bile salts reabsorbed into blood

Figure 23.25

COMPONENTS:
- **BILE SALTS**, (formed in the liver from cholesterol) are the most essential part of bile.
- **BILE PIGMENTS**—The pigment bilirubin (red) and biliverdin (green), derived from hemoglobin, give bile its greenish color because it secretes bile into ducts.
- **CHOLESTEROL**
- **PHOSPHOLIPIDS**
FUNCTIONS OF BILE

1. It breaks down the fats that you eat so that your body can utilize them.
2. Bile is a very powerful antioxidant which helps to remove toxins from the liver.

hepatic artery and hepatic portal vein
  drain through the
  leaky liver sinusoids
  ↓
  The sinusoids drain into the central vein
  ↓
  Bile flows back through the bile canaliculi into the bile duct
  ↓
  stored in the gallbladder
  ↓
  Cholecystokinin (CCK) is releases bile
Pancreatic juice is composed of two secretory products critical to proper digestion: digestive enzymes and bicarbonate. The enzymes are synthesized and secreted from the exocrine acinar cells, whereas bicarbonate is secreted from the epithelial cells lining small pancreatic ducts.
The endocrine cells are the islets of Langerhans:

- Alpha cells – Glucagon
- Beta cells – Insulin
- Both of above regulated by serum blood sugar.
- Delta cells – Gastrin and other polypeptide hormones
Functions

Most (> 80%) of the cells in the pancreas are involved in the exocrine activity of the organ:

- The production and export of inactive precursors, known collectively as the zymogens, for twenty major digestive enzymes including proteases, lipases, nucleases, and amylase. The pancreas produces more protein per gram of tissue than any other organ.

- The secretion of a bicarbonate-rich alkaline fluid (1200 ml/day in humans) which functions to neutralize the acidic chyme produced in the stomach. The alkalinization is necessary for digestive enzyme activity.

The remainder of the cells are responsible for the production of hormones (predominantly insulin and glucagon) that are released into the blood stream (endocrine function). They are organized in the islets of Langerhans.

- **Exocrine function** - Secretes pancreatic juice which breaks down all categories of foodstuff. Water solution of enzymes and electrolytes (primarily HCO₃⁻)
  - Neutralizes acid chyme
  - Provides optimal environment for pancreatic enzymes

- **Enzymes are released in inactive form and activated in the duodenum**
  - Examples include
    - Trypsinogen is activated to trypsin
    - Procarboxypeptidase is activated to carboxypeptidase

- **Active enzymes secreted**
  - Amylase, lipases, and nucleases
  - These enzymes require ions or bile for optimal activity

- **The pancreas also has an endocrine function - release of insulin and glucagon**
  - Regulation of Pancreatic Secretion: Secretin and CCK are released when fatty or acidic chyme enters the duodenum
  - CCK and secretin enter the bloodstream
  - Upon reaching the pancreas:
    - CCK induces the secretion of enzyme-rich pancreatic juice
    - Secretin causes secretion of bicarbonate-rich pancreatic juice
  - Vagal stimulation also causes release of pancreatic juice
Pancreatic Secretions:

- **Hydrelatic**
  - HCO₃⁻ rich aqueous fluid
  - neutralizes stomach HCl
  - dilutes the chyme

- **Ecbolic**
  - enzyme rich secretion
  - Proteases - endopeptidases
  - Trypsinogen → trypsin
  - Chymotrypsinogen → chymotrypsin
  - Proelastase → elastase
  - Proteases - exopeptidases
  - Procarboxypeptidase → carboxypeptidase
  - Proaminopeptidase → aminopeptidase

**Protease Activation**
- Pancreatic secretion contains trypsinogen and trypsin inhibitor
- Enterokinase in intestine activates trypsin
- Trypsin inhibitor is diluted by chyme

**Hormonal Regulation of Pancreatic Secretion**
- Secretin
  - peptide hormone
  - pancreatic secretion rich in HCO₃⁻
- Cholecystokinin (CCK)
  - peptide hormone (33 amino acids)
  - pancreatic secretion rich in enzyme

Pancreatic Secretion:

- **Cephalic Phase**
  - Sight, taste, smell of food
  - Release of ACh & gastrin in response to vagal stimulation
  - Increased pancreatic flow, especially ecbolic

- **Gastric Phase**
  - Protein in chyme → gastrin
  - Gastric distention → ACh from vagus
  - Increased pancreatic secretion, esp. ecbolic

- **Intestinal Phase**
  - Acid in chyme → secretin
  - hydrelatic secretion
  - Long chain fatty acids & amino acids and peptides in chyme
  - CCK & vagovagal reflex
  - ecbolic secretion

- **Bile from the Liver**

**Bile Acids**
- Primary from cholesterol by addition of OH and COOH
- Secondary formed in intestine by resident bacteria
- conjugated to taurine or glycine

**Bile Flow**
- Released as CCK causes contraction of gall bladder and relaxation of Sphincter of Oddi
- CCK (33 amino acid hormone) released in response to fatty acids and lipids in chyme
Pancreatic and Bile Secretions

- Acid in Duodenum activates Secretion of **Secretin** to initiate $\text{HCO}_3^-$ secretion
- AA, Lipids stimulate **Gastrin** (quick response) and **CCK** (prolonged response) to initiate pancreatic enzyme secretion.
- **CCK** also causes GB contraction, Sphincter of Oddi relaxation, and increased Bile Salt excretion by the liver.

Physiology – Exocrine Pancreas

- Secretion of water and electrolytes originates in the centroacinar and intercalated duct cells
- Pancreatic enzymes originate in the acinar cells
- Final product is a colorless, odorless, and isomotic **alkaline** fluid that contains digestive enzymes (amylase, lipase, and trypsinogen)
Physiology – Exocrine Pancreas

- 500 to 800 ml pancreatic fluid secreted per day
- Alkaline pH results from secreted bicarbonate which serves to neutralize gastric acid and regulate the pH of the intestine
- Enzymes digest carbohydrates, proteins, and fats

Bicarbonate Secretion

- Centroacinar cells and ductular epithelium secrete 20 mmol of bicarbonate per liter in the basal state
- Fluid (pH from 7.6 to 9.0) acts as a vehicle to carry inactive proteolytic enzymes to the duodenal lumen
- Sodium and potassium concentrations are constant and equal those of plasma
- Chloride secretion varies inversely with bicarbonate secretion
**Bicarbonate Secretion**

- Bicarbonate is formed from carbonic acid by the enzyme carbonic anhydrase
- **Major stimulants**
  - Secretin, Cholecystokinin, Gastrin, Acetylcholine
- **Major inhibitors**
  - Atropine, Somatostatin, Pancreatic polypeptide and Glucagon
- **Secretin** - released from the duodenal mucosa in response to a duodenal luminal pH < 3

**Enzyme Secretion**

- Acinar cells secrete isozymes
  - amylases, lipases, and proteases
- **Major stimulants**
  - Cholecystokinin, Acetylcholine, Secretin, VIP
- Synthesized in the endoplasmic reticulum of the acinar cells and are packaged in the zymogen granules
- Released from the acinar cells into the lumen of the acinus and then transported into the duodenal lumen, where the enzymes are activated.
Enzymes

- **Amylase**
  - only digestive enzyme secreted by the pancreas in an active form
  - functions optimally at a pH of 7
  - hydrolyzes starch and glycogen to glucose, maltose, maltotriose, and dextrins

- **Lipase**
  - function optimally at a pH of 7 to 9
  - emulsify and hydrolyze fat in the presence of bile salts

Enzymes of Pancreas

- **Proteases**
  - essential for protein digestion
  - secreted as proenzymes and require activation for proteolytic activity
  - duodenal enzyme, enterokinase, converts trypsinogen to trypsin
  - Trypsin, in turn, activates chymotrypsin, elastase, carboxypeptidase, and phospholipase

- Within the pancreas, enzyme activation is prevented by an antiproteolytic enzyme secreted by the acinar cells
Insulin

- Synthesized in the B cells of the islets of Langerhans
- 80% of the islet cell mass must be surgically removed before diabetes becomes clinically apparent
- Proinsulin, is transported from the endoplasmic reticulum to the Golgi complex where it is packaged into granules and cleaved into insulin and a residual connecting peptide, or C peptide

Insulin

- **Major stimulants**
  - Glucose, amino acids, glucagon, GIP, CCK, sulfonylurea compounds, β-Sympathetic fibers
- **Major inhibitors**
  - somatostatin, amylin, pancreastatin, α-sympathetic fibers
Glucagon

- Secreted by the A cells of the islet
- Glucagon elevates blood glucose levels through the stimulation of glycogenolysis and gluconeogenesis
- Major stimulants
  - Aminoacids, Cholinergic fibers, β-Sympathetic fibers
- Major inhibitors
  - Glucose, insulin, somatostatin, α-sympathetic fibers

Somatostatin

- Secreted by the D cells of the islet
- Inhibits the release of growth hormone
- Inhibits the release of almost all peptide hormones
- Inhibits gastric, pancreatic, and biliary secretion
- Used to treat both endocrine and exocrine disorders
To resume

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Hormone Family</th>
<th>Site of Secretion</th>
<th>Stimuli for Secretion</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrin</td>
<td>Gastrin-CCK</td>
<td>G cells of the stomach</td>
<td>Small peptides and amino acids Distention of the stomach Vagal stimulation (GRP)</td>
<td>↑ Gastric H⁺ secretion Stimulates growth of gastric mucosa</td>
</tr>
<tr>
<td>Cholecystokinin (CCK)</td>
<td>Gastrin-CCK</td>
<td>I cells of the duodenum and jejunum</td>
<td>Small peptides and amino acids Fatty acids</td>
<td>↑ Pancreatic enzyme secretion ↑ Pancreatic HCO₃⁻ secretion Stimulates contraction of the gallbladder and relaxation of the sphincter of Oddi Stimulates growth of the exocrine pancreas and gallbladder Inhibits gastric emptying</td>
</tr>
<tr>
<td>Secretin</td>
<td>Secretin-glucacon</td>
<td>S cells of the duodenum</td>
<td>H⁺ in the duodenum Fatty acids in the duodenum</td>
<td>↑ Pancreatic HCO₃⁻ secretion ↑ Tertiary H⁺ secretion ↓ Gastric H⁺ secretion Inhibits trophic effect of gastrin on gastric mucosa</td>
</tr>
<tr>
<td>Gastric inhibitory peptide (GIP)</td>
<td>Secretin-glucacon</td>
<td>Duodenum and jejunum</td>
<td>Fatty acids Amino acids Oral glucose</td>
<td>↑ Insulin secretion from pancreatic β cells ↓ Gastric H⁺ secretion</td>
</tr>
</tbody>
</table>

Dr. Alzoghaibi presentation
### Regulation of Gastric Activity

1. **Cephalic Phase**
   - a) Begins with smelling, thinking, taste about food
   - b) Stimulates the production of gastric juices
   - c) This is a short lived phase

2. **Gastric Phase**

3. **Intestinal Phase**

---

<table>
<thead>
<tr>
<th>Substance</th>
<th>Source</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetylcholine (ACh)</td>
<td>Cholinergic neurons</td>
<td>Contraction of smooth muscle in wall</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Relaxation of sphincters</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ Salivary secretion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ Gastric secretion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ Pancreatic secretion</td>
</tr>
<tr>
<td>Norepinephrine (NE)</td>
<td>Adrenergic neurons</td>
<td>Relaxation of smooth muscle in wall</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Contraction of sphincters</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ Salivary secretion</td>
</tr>
<tr>
<td>Vasoactive intestinal peptide (VIP)</td>
<td>Neurons of mucosa and smooth muscle</td>
<td>Relaxation of smooth muscle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ Intestinal secretion</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ Pancreatic secretion</td>
</tr>
<tr>
<td>Gastrin-releasing peptide (GRP) or bombesin</td>
<td>Neurons of gastric mucosa</td>
<td>↑ Gastrin secretion</td>
</tr>
<tr>
<td>Enkephalins (opiates)</td>
<td>Neurons of mucosa and smooth muscle</td>
<td>Contraction of smooth muscle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↓ Intestinal secretion</td>
</tr>
<tr>
<td>Neuropeptide Y</td>
<td>Neurons of mucosa and smooth muscle</td>
<td>Relaxation of smooth muscle</td>
</tr>
<tr>
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<td>↓ Intestinal secretion</td>
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<tr>
<td>Substance P</td>
<td>Cosecreted with ACh</td>
<td>Contraction of smooth muscle</td>
</tr>
<tr>
<td></td>
<td></td>
<td>↑ Salivary secretion</td>
</tr>
</tbody>
</table>
2. Gastric Phase
   a) Begins with arrival of food
   b) Stimuli include
      (1) Distension of the stomach
      (2) Increase in pH of stomach contents
      (3) Presence of undigested materials
   c) Lasts about 3-4 hours
   d) Main action is to release more products from chief cells and parietal cells
      (1) Also increased muscle contractions to mix chyme
   e) Neural response – stimulation by chemo and stretch receptors coordinate short reflexes and chief and parietal cell releases
   f) Hormonal response – gastrin enters the capillaries at the stomach and stimulate chief and parietal cells

3. Intestinal Phase
   a) Starts when chyme enters the small intestine
   b) Small amounts of liquidy material is squirted into the small intestines
   c) Lasts a long time
   d) Primary action is to inhibit gastric acid and pepsinogen production, reduction of gastric mixing
   e) Hormonal response - stimulation of CCK (cholecystokinin) and gastric inhibitory peptide (GIP)
   f) Release of buffers in the small intestine to bring the pH back up
Enzymes of the Small Intestine
(1) Enterokinase - activates proenzymes secreted by the pancreas
(2) Gastrin, cholecystokinin and secretin

Intestinal Hormones

1. Enterocrinin - hormone stimulates the Submucosal glands

2. Secretin - cause an increase in the secretion of bile and buffers
   a) Secondly reduces gastric motility and secretory rates (to duodenum)

3. Cholecystokinin - accelerates the secretion of all digestive enzymes
   a) Increase pancreatic enzymes
   b) Push pancreatic secretions and bile into duodenum

4. Gastric Inhibitory Peptide
   a) Inhibit gastric activity [Glucose dependent]
   b) Activates the Submucosal glands
   c) Works to make glucose go into the blood and target the fat cells

5. Gastrin - facilitates large amounts of protein enzymes to be released
Small Intestine

- **Mucosa**
  - Absorptive cells
  - Goblet cells -- mucous
  - Enteroendocrine cells -- cholecystokinin (CCK), secretin
  - GIP - glucose dependent insulinotropic peptide
  - Somatostatin
  - Intestinal crypts (Crypts of Lieberkühn)

- **Submucosa**
  - Brunner’s glands in duodenum - alkaline secretion
  - Peyer’s patches in ileum.
  - 5. Surface area increasing structures - plicae circulares, villi, microvilli
  - 6. Segmentation and Peristalsis