Physiology
of the
Digestive System

CM - Physiology
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Objectives

• Understand role & some pertinent physiology of GI tract
• Identify vascular supply where indicated
• Identify cellular, neural & enzymatic effectors of GI activity
• Describe digestive physiology related to key foodstuffs
Overview of GI Function

- Major function of GI tract is digestion & absorption of nutrients, lytes & water
- Waste products of digestion are combined with some metabolic waste products & eliminated
- A GI tract metaphor:
  - External, selectively permeable, muscular tube; inhabited by commensal bacteria & controlled by neuro-endocrine-immune signal systems
Overview of GI Function

• Digestion of food into minute particles
  – Mechanical
  – Biochemical
• Absorption of nutrients & water across gut lumen into bloodstream (or lymphatic syst.)
• Elimination of waste products
• Accomplished by 3 primary processes
  – Motility controlled by peristalsis: “law of the gut”
  – Cellular secretions – help to digest and absorb
  – Active & passive trans-cellular transport
The Act Of Vomiting

Higher centres:
- hypothalamus
- cerebellum
- labyrinth
- area postrema

Vomiting centre

- Soft palate
- Closure of glottis
- LES relaxation
- Respiration stop
- Abdominal pressure

Contraction of diaphragm and abdominal muscles

Stomach squeeze

Antiperistalsis

Cascade of vomit

Fig. 22-4
Important GI Tract Secretions

- Secretions of widely varying pH composition
- Produced by a variety of cell types in GI tract, pancreas & liver
- Facilitate digestion & absorption of ingested food
- All contain aqueous component, digestive enzymes, other factors important to GI function (eg – mucus cells that keep things sliding)
- Secretory activity regulated by both neural, hormonal pathways
  - Salivary
  - Gastric
  - Intestinal
  - Pancreatic & hepatic bile secretions
Intestinal Bacteria

• $\sim10^4$ bacteria live in the human gut
  – $\sim10x$ number of human cells in body

• Low concentration of aerobes in the jejunum & ileum

• Anaerobic bacteria are dominant distal to the ileocecal valve
  – SCFAs from dietary fiber…

*CFU = colony-forming units*
GI Tract

- Mouth
  - Salivary glands
  - Chewing
- Esophagus
- Stomach
- Small intestine
  - Liver, GB, Pancreas
- Large intestine
- Rectum
- Anus

Fig. 62-1
Accessory Organs of Digestion
GI Tract Anatomy

Fig. 62-2
Individual variability within this construct
Structural Anatomy of the Stomach
Small Intestine Anat & Histo

- Review intestinal functional anatomy
Functional Anatomy of the Lower GI Tract

Aortogram

Find:
- Aorta
- Celiac trunk
- Common hepatic artery
- Splenic artery
- R & L renal arteries
- R & L common iliac a.

Kidney architecture is beautifully represented in this study
Celiac Axis

Can you “visualize” the liver, pancreas & spleen?
Superior Mesenteric Artery

- Superior mesenteric a.
- Intestinal a.
- Iliocolic a.
- Right colic a.
- Middle colic a.
Inferior Mesenteric Artery

1 - Inf. mesenteric a.
2 - L colic a.
3 – Sigmoid a.
4 - Sup. Rectal a.
Hepatic Portal Circulation
Portal Vein & Main Tributaries

Hepatic portal v.

Sup. mesenteric v.

Splenic v.

Inf. mesenteric v.
Enteric Nervous System & ANS

• Motility of GI tract is controlled by ANS via neural circuits & hormones
  – Exceptions: chewing, swallowing, defecation
• Stimulate or inhibit the following:
  – Muscular contractions that propel ingested material
  – Timely secretion of substances that aid digestion
• Neuroanatomy of the GI tract is complex
Enteric Nervous System & ANS

- Digestive system is innervated via both sympathetics & parasympathetics
  - Provide extrinsic neural control
- Sensory nerve afferents inform the CNS about the condition of the gut
  - Nuclei in ENS, spinal cord & brain stem
- Influenced by input from higher centers in CNS
  - Cortical & olfactory centers influence brain stem motor centers (parasympathetic outflow)
Enteric Nervous System & ANS

- Parasympathetic system is dominant
  - Stimulates digestive activity (secretion & motility)
  - Via intrinsic ENS located in the gut wall

- Two divisions
  - Cranial (vagus) to proximal 1/2 of large intestine
    - Esp. esophagus, stomach & pancreas
  - Sacral (2-4th segs) distal portions
    - Defecation reflexes

- Sympathetic (T5-L2) is inhibitory
  - Via celiac & other ganglia to interneurons & muscle
  - “Fight or flight”
Nominal innervation of GI tract is inherent within the enteric wall.
Enteric Nervous System (ENS)

• GI function proceeds in absence of extrinsic innervation as long as ENS is intact

• “The little brain”
  – Locally mediates brain’s influence on digestive functions

• Consists of two sets of nerve plexi
  – Submucosal (Meissner’s) plexus
  – Myenteric (Auerbach’s) plexus

• Both plexi contain sensory neurons, motor neurons & interneurons

• [Some texts note subserosal plexus also]
  – Lymphatics associated w/ this tissue layer
ENS Neurophysiology

- Afferent sensory neurons in submucosal plexus
  - Chemoreceptors detect different chemicals in gut lumen
  - Stretch receptors respond to tension in gut wall
- Short-loop effector neurons increase digestive gland secretion
- Interneurons between plexi
- Neurons in myenteric plexus control smooth muscle via acetylcholine & substance P
  - Increased “tone”
  - Increased strength & rate of contractions
  - Increased linear conduction velocity
- Inhibitory neurons relax smooth muscle via vasoactive intestinal peptide (VIP) and nitric oxide (NO)
  - ie, relaxation wave preceding bolus
Neurophysiology of GI Muscle Potentials & Contractions

- Persistent slow waves
- Spikes activate contractions
- Parasympathetic & sympathetic signals affect mV
Peristalsis

- Distinctive pattern of smooth muscle contractions
- Propels foodstuffs distally through GI tract
- Mediated by ENS
  - Ex: peristalsis is not affected to any significant degree by vagotomy or sympathectomy

www.sci-health.org/RRTC/presentations/PPT/Bowel_Neuroanatomy_and_Physiology.ppt
Peristalsis

- **Excitatory motor neurons** above the bolus activated
  - Contraction of smooth muscle above bolus
    - Ach, substance P
- **Inhibitory motor neurons**
  - Relaxation of smooth muscle below the bolus
    - Via nitric oxide, vasoactive intestinal peptide

[Image of a diagram showing peristalsis with labeled parts such as Mucosal effects, Contraction, and Relaxation.]
Another Map of the ENS

- Sympathetic ANS input is excluded from this map
- Demonstrates importance of Parasympathetic & hormonal control

http://ethesis.helsinki.fi/julkaisut/laa/biola/vk/peuhkuri/chap2.html
**Myenteric Plexus** (Auerbach's)

- Nerve cell bodies between GI muscle layers
  - Extensive interneuronal connections
- Throughout GI tract
  - From esophagus to rectum
- ENS Afferents reach this plexus from deep ENS interneurons
- Efferent fibers activate muscles to affect gut motility & secretory cells within the mucosa
  - Some extrinsic connections to CNS motor & sensory divisions
Submucosal Plexus (Meissner’s)

- Found only in intestines
- Regulates endocrine output, vascular tone & secretions of digestive glands
- Cell bodies of mucosal mechano- & chemoreceptors within this plexus
- Afferent & efferent nerves relay ANS information between this plexus & cells of the GI tract
  - Primarily through interneuronal connections via myenteric plexus
  - Some direct sympathetic & parasympathetic ANS connections
GI Tract
“Stem-to-stern”
Mouth

- Mechanical & biochemical processes
- Forms a bolus in preparation for swallowing
- Food is reduced to small particles (mechanical)
  - MTPP via V.3*
- Mixed with saliva (immuno-enzymatic)
  - Water with mucus, enzymes, Na\(^+\), HCO\(_3\)\(^-\), Cl\(^-\), K\(^+\)
    - Enzymes (amylase & lingual lipase) initiate digestion
    - Immune surveillance: IgAs
    - Antibiotic: thiocyanate
Muscles of Mastication

- Innervation by CN V.3 n.
- Four muscles (MTPP): masseter, temporal, med. & lat. pterygoids
Anatomy of Salivary Apparatus

- http://academic.kellogg.cc.mi.us/herbrandsonc/bio201_McKinley/f26-4a_salivary_glands_c.jpg
Salivary Glands

• Three pairs
  – Submandibular
  – Sublingual
  – Parotid

  – Controlled by sympathetic & parasympathetic fibers
Salivary Glands

- Composition of saliva depends on secretions of these glands
- Secrete ≥1 L/d (pH 6-7)
  - 0.1 ml/min at rest
  - 4 ml/min during active stimulation
- Submandibular glands produce 70% of the daily secretion of saliva
  - Mucous & serous cells
- Parotids produce ~ 25% of saliva from serous cells
- Sublingual glands only 5%
  - Mostly mucous cells
Swallowing Reflex

• Complex neuromotor pattern (3 stages)
  – Voluntary
    • Oropharyngeal or buccal- chewed up and vol put to back of throat
  – Involuntary
    • Pharyngeal (V, IX, X, XII n.)
    • Esophageal – get into smooth muscle action

• Coordination of 25 sets of muscles
  – Both respiratory & swallowing centers involved in neuromotor loop
Etiology of Dysphagias

• Stroke most common in older population
  – Above or below brainstem
• Other locations – other pathologies
  – Peripheral nerves, muscles & neuromotor junction
• Others causes:
  – Trauma, Parkinson’s, dementias, CP, MS, epilepsy, tumors, meds (sedatives, anti-dopa, anticholinergics)
  – Herpes z., Guillen-Barré s., Eaton-Lambert s.
Esophagus

• Muscular tube posterior to the trachea
  – Upper 1/3 skeletal m.; middle 1/3 mixed; lower 1/3 smooth m.

• Esophageal peristalsis is involuntarily
  – Primary & secondary waves

• Mechanoreceptors initiate feedback loop for transit of bolus
  – Closely coordinated with contraction/relaxation of upper & lower esophageal sphincters
    • Upper contracted during respirations, relaxed during swallowing
    • Lower relaxes to allow passage of bolus, contracts to inhibit reflux
Eosophageal Peristaltic Wave
Some GI Peptide Hormones

• Secreted in response to stimuli associated with food ingestion
• They act to regulate motility & exocrine secretory activity of the intestine, pancreas, liver, gallbladder
• Gastrin (pylorus, early duodenum)
  – Stimulates gastric acid secretion
  – Relaxes the fundus of the stomach
• Cholecystokinin/CCK (small intestine)
  – Stimulates pancreatic enzyme secretion, gall bladder contraction
  – Inhibits gastric motility & emptying
• Secretin (small intestine)
  – Stimulates pancreatic & hepatic secretion
  – Inhibits gastrin release & sensitivity of parietal cells to gastrin
Stomach

1 - lesser curvature
2 - greater curvature
3 - cardia
4 - fundus
5 - body
6 - pylorus
7 - pyloric sphincter
8 - rugae
9 - gastric air bubble
10 - esophagus
Stomach

- Hollow, muscular organ
  - Empty internal volume ~50cc
- Stores food, secretes digestive juices, mixes to create chyme
- Blood supply: celiac artery branches
- Venous drainage by gastric & splenic v.
  - Enters hepatic portal circulation
- ANS central control
  - Sympathetic: celiac plexus
  - Parasympathetic: vagus nerve
Stomach

Volume can reach ~ 1-1.5 L

Muscle layers become thicker toward the pylorus
Gastric Motility

• Gastrin & vagal input increase gastric motility
  – Also secretion of stomach acids
• Secretin & sympathetic activity inhibit motility
  – Epi may increase acid production
• Cholecystokinin inhibits gastric motility & emptying
  – Secreted when products of fat digestion are in small intestine
Stomach Histology (100x)

- **Mucosa**
  - Rugae
  - Gastric epithelium (simple columnar epithelium)
  - Gastric pits & glands, lamina propria
- **Muscularis mucosa**
- **Submucosa**
- **Muscularis externa**
  - Oblique: thin & incomplete
  - Circular: most prominent
  - Longitudinal/outer
Gastric Juice

• Fluid secreted into the stomach is called gastric juice (~1.5L/d)
  – A mixture of secretions from gastric glands & epithelial cells
  – High secretory rates favor higher [H\(^+\)] and [Cl\(^-\)]
  – K\(^+\) is always higher in gastric juice than in plasma
    • Vomiting can lead to hypokalemia

• High [HCl] (<pH 3)
  – Converts pepsinogen to pepsin
  – Kills bacteria & cleaves proteins
Effect of Eating on Gastric [H+]
Gastric Mucosal Layer

- ~ 20,000 gastric pits/cm²
- Each pit comprises glandular cells & mucus cells
- Chief cells are located near the base of pits
  - Secrete pepsinogen (inactive precursor of pepsin)
- Parietal cells are widely distributed
  - Secrete HCl & intrinsic factor
  - Small intestine needs intrinsic factor to absorb vitamin B12
  - Antrum lacks parietal cells
- G cells of the lower part of the stomach secrete gastrin
- Surface mucosa cells secrete a thick, alkaline-rich mucus
  - Gastric mucosal barrier protects stomach & duodenum from acid conditions
  - Can be damaged by bacteria, viruses, drugs e.g. aspirin
Gastric Pits & Gastric Glands

Cell Types | Substance Secreted
---|---
Mucous neck cell | Mucus (protects lining)
Bicarbonate
Parietal cells | Gastric acid (HCl)
Intrinsic factor (absorption)
Enterochromaffin-like cell | Histamine (stimulates acid)
Chief cells | Pepsinogen
Gastric lipase
D cells | Somatostatin (inhibits acid)
G cells | Gastrin (stimulates acid)
Gastric (+) Cells

- Mucus neck cells esp. prominent in pylorus
  - Bicarbonate & mucus
- Parietal cells
  - Hydrochloric acid & intrinsic factor
- Enterochromaffin-like (ECL) cells
  - Histamine
- Chief cells
  - Pepsinogen
  - Gastric lipase
- D cells in stomach, intestine, pancreas
  - Somatostatin
- G cells in pylorus & early intestine
  - Gastrin
Secretion of HCl from ____ Cells

- H+ are pumped vs. a concentration gradient up to 1,000,000:1
- H+ secretion leads to alkalinity of cells
- This is dissipated via HCO$_3^-$ /Cl$^-$ exchange
- Results in alkalinization of plasma
Control of Gastric Acid Secretion

- Ach, histamine, & gastrin, effect receptors on parietal cells to stimulate HCl release
  - Via cAMP or Ca++ as second messenger

- Inhibitors of HCl secretion:
- Endogenous:
  - Somatostatin, secretin

- Exogenous
  - Atropine: Ach antagonist
  - Cimetidine: a histamine antagonist
  - Omeprazole: H+ pump inhibitor
3 Phases of Gastric Secretion

• Cephalic phase elicited before food arrives in stomach
  – Thought, smell, sight, taste of food signals limbic system
  – Reflex secretion modulated by hunger

• Gastric phase
  – Begins when food enters stomach
  – Stimulates stretch receptors & peptide sensitive chemoreceptors
  – Initiates central reflex loops & local, enteric reflexes
  – Most daily gastric secretion results from gastric phase

• Intestinal phase
  – Chyme in the duodenum causes neuro-endocrine response
  – First stimulates, later inhibits acid secretion
  – Cells in the duodenum & jejunum respond to peptides, fatty acids & pH
  – Various hormones are released into the blood & feedback to stomach
Cephalic Phase of Gastric Secretion

- CN X activated by sight, smell & taste of food
- ACh secretion mediated by vagal efferents & enteric plexi
- Stimulates HCl secretion
  - Directly stimulates parietal cells
  - Via G cells in antrum: stimulates gastrin secretion
- Vagotomy will abolish this response
Gastric Phase of Gastric Secretion

- Enteric & vagovagal pathways initiated by food in stomach
- Stimuli: distention & presence of amino acids/peptides
- 2/3 gastric acid secretion is associated with gastric phase
- ACh mediates parietal acid secretion via 4 mechanisms
  - Directly or via endocrine/paracrine signaling
- Vagotomy will not fully eliminate this phase
Intestinal Phase of Gastric Secretion

• Acidity of gastric chyme in duodenum leads to neural & endocrine responses

• Initially parietal cells stimulated to secrete gastric acid
  – Chyme pH >3 (early gastric emptying)
  – Peptides & amino acids in duodenum cause G cells in the duodenum & upper jejunum to release gastrin

• When buffering capacity is exhausted (pH <2), duodenum releases secretin
Intestinal Phase of Gastric Secretion

- Secretin inhibits gastrin release & reduces sensitivity of parietal cells to gastrin
- Products of triglyceride digestion in duodenum & jejunum stimulates release of CCK & gastric inhibitory peptide
  - CCK stimulates gallbladder contraction
  - Both inhibit parietal cell secretion & gastric emptying
- This limits amount of chyme entering duodenum
- Ensures optimal processing of duodenal chyme
Intestines
Intestinal Transport of Selected Substances

**Small Intestine**

- **Proximal**
  - Sugars
  - Amino Acids
  - Most Vitamins, Cl-, Ca++, Na+, B12, Bile Acids

- **Middle**
  - Long-chain FAs

- **Distal**
  - K+
  - Short-chain FAs via bacteria

**Large Intestine**

- Secreted substances
Intestinal Cells

- Absorptive cells more prominent in SI
  - Apical surface area of each is greatly increased by an array of microvilli (brush border)
  - In the small intestine, brush border enzymes contribute to digestive breakdown
    - These enzymes are lacking in the colon

- Goblet cells more prominent in LI
  - Proportion increases along length of the bowel
  - Relatively few in duodenum, many in the colon
  - Secrete mucus
Small Intestine

• Functionally divided into three segments
• Duodenum (20-30 cm) runs from the pyloric sphinctor to the ligament of Treitz
• Jejunum (~120 cm) doesn’t have a specific end point
  – Dense & deep circular folds (plicae)
• Ilium (~150 cm) terminates at the iliocecal valve
  – Has few, short circular folds (plicae)
• Muscle layers
  – Outer longitudinal layer
  – Inner circular layer
  – Submucosal muscle layer (muscularis mucosae) with both circular & longitudinal fibres that moves the mucosal villi
• Arterial supply varies over the course of the intestines
Small Intestine

- Digestive enzymes reduce large, complex molecules to simpler forms
- Small molecular products are transported across the intestinal epithelium
- Enzymes act on 3 major classes of foods
- Carbohydrates & proteins transported by enterocyte membrane transporters
- Fats are emulsified then re-
- Carbohydrates are absorbed as monosaccharides
- Reduced to fructose, glucose, & galactose
• Proteins reduced to short peptides or aa fragments prior to absorption
Fat absorption requires emulsification
- Glycerol & FAs absorbed by portal blood stream
- Chylomicrons & VLDLs absorbed by lymphatics
Ingestion of $H_2O$ & ‘lytes

- Water, electrolytes also absorbed primarily in the small intestine
- Relatively small amount of water, electrolytes absorbed in the colon
- Water moves along osmotic gradients generated by solute absorption
  - Can travel in either direction
  - Typically 85-90% absorbed into body in small intestine
  - Some transport occurs in large intestine also
Lower GI tract

• Four parts of large intestine/colon
  – Ascending
  – Transverse
  – Descending
  – Sigmoid

• Rectum stores feces

• Anus controls defecation
Large Intestine

- Cecum receives chyme from jejunum
  - 500-700 cc/d
- Tinea coli: 3 linear muscle bands
  - Merge in recto-sigmoid into longitudinal layer
- Semi-lunar folds separate colon into hausta
- Rugae & Crypts of Lieberkuhn, but no villi
- Some fluid & electrolytes are absorbed by epithelial cells
- Bacteria digest some products
- Goblet cells secrete mucus: lubricate fecal mass
Large Intestine Physiology

- Segmental movements occur during fasting
- Transit times: 4~9h to cecum; LI: 6,9,12h; 3-7 d.
- Gastrocolic reflex
  - Bolus of chyme results in increased motor activity throughout colon
  - Gastrin & CCK stimulate, epinephrine inhibits this reflex
- Aldosterone influences sodium/H$_2$O absorption
Distal Tract Physiology

• Defecation: complex, neurally controlled
  – Includes voluntary & involuntary elements
• Internal anal sphinctor usually maintained in state of contraction by sympathetic ANS
• Defecation reflex
  – As feces distends rectum, int. sphinctor relaxes
  – Afferents signal urge to defecate
  – Can be over-ridden
• Rectum can distend or contract in retrograde direction
• Squatting facilitates alignment of ano-rectal angle
• Valsalva increases intra-abdominal pressure
Accessory Organs of Digestion
Blood Supply of Liver

- Hepatic portal vein is primary blood conduit
  - Drains stomach, intestine, pancreas & spleen
  - Carries nutrients & contaminants (drugs, toxins from food, bacteria, byproducts of blood-cell recycling) absorbed through intestinal mucosa or produced in spleen

- Hepatic a. carries oxygenated blood to liver
  - Branch of Celiac a.
  - Branches: cystic a. (supplies GB), Gastroduodenal a.
  - Anastomosis w/ Sup. Mesenteric a.

- Blood from both mixes together in the hepatic sinusoids

- Passes out of liver via central, hepatic veins to IVC
Liver Lobules
Hepatocyte

- The main cell type in liver
- Constitutes ~60% of all liver cells
  - It is the most versatile cell type in the human body
  - Carries out all the main liver functions
- During a single passage through the lobule 60-100% of most metabolites are removed
- Produce ~100 g/day of proteins
- Continuously synthesizes bile acids
  - A metabolite of cholesterol
Hepatic Circulation

Perilobular Region

Centrolobular Region

Blood Flow

Disse's space

Perilobular cells

Centrolobular cells

Oxygen

Extrahepatic Hormones

Key Glycolysis Enzymes

Key Glucose-Liberating Enzymes

Key Fatty-Acid-Oxidation Enzymes

Key Fatty-Acid-Synthesizing Enzymes
Hepatic Vessel Architecture
Cellular Anatomy

- Center of lobule is the central vein (upper right)
- At the periphery of the lobule are portal triads (lower left)
  - Artery, vein, bile duct
- Can be divided into 3 zones, based upon oxygen supply
  - Zone 1 encircles the portal triads - O₂ rich blood enters via hepatic arteries
  - Zone 3 located around central veins - oxygenation is poor
  - Zone 2 is located in between
Functional Anatomy of Liver

• “Classic” lobule: a six-sided prism 2 mm long x 1 mm in diameter
  – Central veins
  – In corners are portal triads
  – Delimited by interlobular connective tissue

• Acini are arbitrary zones based on O₂ supply
  – Relate structural units to arterial branches of the portal triad

• Portal lobules emphasize the bile drainage by the vessels of the portal triads
Functional Anatomy of Liver

• “Classic" liver lobule
  – Interconnecting hepatocytes
  – A radial pattern from central vein to perimeter
  – 6 sided polyhedral prism
  – Portal triads (hepatic artery, portal vein, and bile duct) at each corner
  – Sinusoids receive mixed portal and arterial blood
  – Long axis transversed by central vein
    • Receives blood from the sinusoids
Functional Anatomy of Liver

• Liver acinus
  – Describes vascular perfusion of hepatic cells
  – One axis defined by 2 portal triads along border between two "classic" lobules
  – Each central vein forms end point of 6 acini

• Allows interpretation of patterns of degeneration, regeneration, toxic effects in liver parenchyma
Functional Anatomy of Liver

• The portal lobule
  – Morphologic center is bile duct
  – 1/3 of portal triad of "classic" lobule
  – Outer margins are imaginary lines drawn between 3 central veins closest to bile duct

• The portal lobule identifies bile secretion function of the liver
Functions of the Liver

• Major functions: metabolize, detoxify, inactivate, store
  – Return to circulation or excrete into bile
  – Liver enzymes alter some toxins for easier urine excretion
• Emulcifies fats to facilitate their digestion
• Stores glycogen, lipids, minerals, vitamins (A, D, K, B12)
• Metabolizes & synthesizes proteins
• Remove worn out red blood cells from the blood
• Metabolizes cholesterol, fat, ammonia
• Synthesizes albumin, other plasma proteins, coagulation factors, urea
• Processes steroid hormones & vitamin D
• Phagocytosis of debris & bacteria
Functions of the Liver

• Synthesizes & stores products of digestion
  – Portal circulation
  – Maintains glucose levels during fasting
    • Gluconeogenesis (amino acids & lactate)
    • Glycogenolysis
  – Energy storage & conversion
    • Glycogen synthesis
    • Lipogenesis
    • Ketone bodies
  – Synthesizes other essential substances
    • Albumin & other plasma proteins
Functions of the Liver

• Synthesizes, secretes & recycles bile acids
  – Micelles & membranes
  – Lipid absorption & intravascular transport
  – Enterohepatic circulation

• Take up organic molecules from blood
  – Anions (bilirubin), cations (anesthetics, antibiotics), neutral

• Transport, secrete organic molecules
  – Bile (see Table 54-3)
Functions of the Liver

• Biotransforms & detoxifies organic compounds

  – Phase 1 reactions
    • Ox-redox reaction via Cytochrome P-450 enzymes
    • Hydroxylation creates a terminal hydroxyl group
    • can activate or inactivate (eg vitamins, drugs)

  – Phase 2 reactions
    • Conjugation into hydrophilic compounds
    • Readily secreted into blood or bile for elimination
Few Other Functions of the Liver

- Blood storage
- Synthesizes clotting factors
- Absorb & stores fat-soluble vitamins
- Metabolism of fats
- Metabolism of bilirubin
- Secretion of bile
Gallbladder

- A saclike organ that lies on the inferior surface of the liver
- Store & concentrates bile between meals
- GB can concentrate hepatic bile by 5x
- Can hold ~90 mL
- CCK reaches GB wall via blood
- Causes contractions of GB & relaxation of sphincter of Oddi
- Gastrin has small CCK-effect
- VIP/acetylcholine inhibits GB contractions
Normal Gallbladder Ultrasound
Pancreas

- Two separate functional units: digestion, glucose metabolism
- Exocrine pancreas consists of acinar and duct cells
- Endocrine pancreas: 4 specialized cell types
- Secretes hormones into the bloodstream
Exocrine Pancreas

- Pancreas is classical mixed gland
  - Both endocrine, exocrine elements
- The exocrine pancreas is an abdominal “salivary gland”
- Secretes enzymes & alkaline fluids to assist in digestion
- Is composed of acini & networks of ducts
  - Acinar cells produce digestive enzymes
  - Constitute ~ 90% pancreatic tissue
  - Organized into grape-like clusters
- Pancreatic duct (Wirsung duct)
  - Adds mucous & bicarbonate
- Ampulla of Vater
Exocrine Pancreas

- Acinar cells producing a primary secretion (see next slide)
- Zymogen inactive precursor of digestive enzymes
- Ionic composition similar to that of plasma
- Organic components: major enzymes necessary for digestion of dietary nutrients
- Duct cells form secondary secretion by modification of the primary secretion
- Secretions collect in acinar duct
- Travel through a network of converging ducts into the common bile duct
- Enter duodenum at duodenal papilla (Vater)
Pancreatic Acinus

The Pancreatic Acinus

- Interacellular Duct
- Zymogen Granules
- Centracinar Cells

Pancreas in situ

- Pancreas
- Stomach
- Large intestine
- Small intestine

- Acinar cells
- Capillary network
- Alpha cell
- Beta cell
- Delta cell
- Central duct

Flow of digestive enzymes to duodenum

Interlobular ducts

Hepatopancreatic ampulla (ampulla of Vater)

Pancreatic duct (duct of Wirsung)

Body of pancreas

Tail of pancreas

Duodenum

Plicae circulares

Duodenal papilla (papilla of Vater)

Bile

Common bile duct

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Exocrine Pancreas

• Secretions
  – Potassium, sodium, \textit{bicarbonate}, magnesium, calcium, chloride

• Enzymes
  – Trypsinogen, chymotrypsinogen, and procarboxypeptidase
  – Trypsin inhibitor
  – Pancreatic alpha-amylase
  – Pancreatic lipase
Three Phases of Pancreatic Secretion

- **Cephalic phase** - elicited before food reaches stomach
  - Olfactory signals (via the limbic system) + visual & tactile signals (via thalamic relay) processed in brain
  - Vagal signals reach antral mucosa
  - Gastrin (from G-cells) induces secretion of low volume of pancreatic juice with high enzyme content
- **Gastric phase** - elicited by food in stomach
  - Gastric distension & peptides in antrum trigger release of more gastrin
  - Induces secretion of small volume of pancreatic juice rich in enzymes
- **The intestinal phase** is elicited by duodenal and jejunal mechanisms
  - Both secretin & CCK released
  - Secretin promotes copious secretion of HCO3- rich fluid
  - CCK increases acinar production of pro-enzymes (>vagal or gastrin)
Secretin & CCK

- Secretin (S-cells in mucosa of upper small intestine) when acid chyme arrives
  - Stimulates secretion of $\text{HCO}_3^-$ & $\text{H}_2\text{O}$ by pancreatic duct cells
  - Secretin inhibits gastrin release & gastrin’s effect on stomach parietal cells
- CCK (duodenal I-cells) stimulates GB contraction & pancreatic acinar secretion
  - Bile enters duodenum, fat is emulsified
- Most important stimulus for CCK release: chyme (amino acids, peptides, long chain fatty acids) in duodenum
- CCK also acts as an enterogastrone (intestinal hormone that inhibits emptying and motility)
  - An intestinal hormone that inhibits gastric activity & emptying
References

• Textbook in Medical Physiology And Pathophysiology, Essentials and clinical problems
  – Poul-Erik Paulev, M.D., D.Sci
• Accessible at [http://www.mfi.ku.dk/ppaulev/chapter22/kap%2022.htm](http://www.mfi.ku.dk/ppaulev/chapter22/kap%2022.htm)
• Barrett, etal. (2010). *Ganong’s Review of Medical Physiology*