GI Review

• Disease-specific review

• Items not covered
  – Detailed anatomy
  – Embryology
  – Histology/pathology
  – Pharmacology
ESOPHAGUS
Normal Esophagus
## Lower Esophageal Sphincter

<table>
<thead>
<tr>
<th>Neurotransmitters</th>
<th>Causes of Increased Pressure</th>
<th>Causes of Decreased Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>α-adrenergic agonists</td>
<td>β-adrenergic agonists</td>
</tr>
<tr>
<td></td>
<td>Cholinergic agonists</td>
<td>α-adrenergic antagonists</td>
</tr>
<tr>
<td></td>
<td>Anticholinesterase</td>
<td>Dopamine</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anticholinergics</td>
</tr>
<tr>
<td>Hormones</td>
<td>Gastrin</td>
<td>Progesterone</td>
</tr>
<tr>
<td></td>
<td>Motilin</td>
<td>Estrogen</td>
</tr>
<tr>
<td></td>
<td>Substance P</td>
<td>Secretin</td>
</tr>
<tr>
<td></td>
<td>Bombesin</td>
<td>CCK</td>
</tr>
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<td></td>
<td></td>
<td>VIP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Somatostatin</td>
</tr>
<tr>
<td>Others</td>
<td>Protein</td>
<td>Fat</td>
</tr>
<tr>
<td></td>
<td>Metoclopramide</td>
<td>Chocolate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ethanol</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peppermint</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Smoking</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CCB, Nitrates</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diazepam</td>
</tr>
</tbody>
</table>
# Dysphagia

<table>
<thead>
<tr>
<th></th>
<th>Oropharyngeal</th>
<th>Esophageal</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Definition</strong></td>
<td><em>Initiating</em> a swallow <em>Transfer</em> of bolus to esophagus</td>
<td><em>Transport</em> of bolus down the esophagus</td>
</tr>
<tr>
<td><strong>Clinical Presentation</strong></td>
<td>Choking, coughing, regurgitation, aspiration</td>
<td>Chest fullness, chest pain</td>
</tr>
<tr>
<td><strong>Causes</strong></td>
<td><strong>Neurologic</strong>: CNS, CN controlling oropharynx, striated muscles of oropharynx</td>
<td><strong>Neuromuscular</strong>: achalasia, DES, scleroderma</td>
</tr>
<tr>
<td></td>
<td><strong>Structural</strong></td>
<td><strong>Obstruction</strong>:</td>
</tr>
<tr>
<td><strong>Differential Diagnosis</strong></td>
<td>CVA, ALS, MG, polymyositis Retropharyngeal abscess Carcinoma Thyroid enlargement Zenker’s diverticulum</td>
<td>Cancer Stricture (reflux, infection) Schatzki ring Foreign body Caustic injury Motility disorder (achalasia, DES, scleroderma)</td>
</tr>
</tbody>
</table>
Oropharyngeal Dysphagia

• Zenker’s diverticulum
  – Pharyngoesophageal false diverticulum
  – Herniation at Killian triangle
Esophageal Dysphagia
Esophageal Webs

- Can occur anywhere in the esophagus
- Cervical webs + iron deficiency anemia = Plummer Vinson syndrome
Eosinophilic Esophagitis

• Chronic inflammatory condition
• Typically young males with atopy, food allergies
• Symptoms
  – Reflux
  – Dysphagia, odynophagia (strictures, spasm)
  – Peripheral eosinophilia
• Diagnosis: > 15 eosinophils/hpf
• Treatment: steroids
EoE: Endoscopic Features
Motility Disorders

• Achalasia
  – Loss of myenteric plexus
    → high LES pressure,
    uncoordinated peristalsis

• Scleroderma
  – Smooth muscle atrophy,
    absent peristalsis
  – ↓ LES pressure
    • Acid reflux
Miscellaneous

• Mallory Weiss tear
  – Recurrent/severe emesis causing a **mucosal** tear near the GE junction
  – Alcoholics, eating disorders, etc
  – Presents with hematemesis
  – Conservative care

• Boerhaave syndrome
  – **Transmural** tear due to severe emesis
  – Pneumomediastinum
  – *Surgical emergency*
Gastroesophageal Reflux Disease

- Symptoms or mucosal damage produced by the abnormal reflux of gastric contents into the esophagus

- Erosive

- Non-erosive
  - Symptoms without esophagitis
  - Treatment similar
Pathophysiology

- Decreased esophageal clearance
  - Esophageal dysmotility
  - Hiatal hernia
  - Decreased saliva
  - Medications
- Impaired LES function
  - Medications
  - Lifestyle
- Gastric distention
  - Delayed gastric emptying
  - Large fatty meals
Gastroesophageal Reflux Disease

• Classic symptoms
  – Heartburn
  – Spontaneous regurgitation of gastric contents
  – Nocturnal awakening, choking
  – Dysphagia (stricture)
  – Odynophagia (ulceration)

• Atypical symptoms
  – Pulmonary symptoms
    • Asthma
    • Aspiration
    • Wheezing
  – ENT symptoms
    • Hoarseness
    • Chronic cough
Complications of GERD

• 30-50% of patients

• Esophagitis

• Strictures

• Barrett’s esophagus

• Esophageal adenocarcinoma
Barrett’s esophagus

• Premalignant lesion
  – Risk for adenocarcinoma is 30-40 times higher
  – Diagnosed in 10-15% of patients with reflux

• Metaplastic change in the lining of the esophagus from squamous to columnar epithelium (“intestinal metaplasia”)
Barrett’s esophagus
# Esophageal Malignancy

<table>
<thead>
<tr>
<th>Squamous Cell</th>
<th>Adenocarcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Most common worldwide</td>
<td>• Most common in the US</td>
</tr>
<tr>
<td>• Upper 2/3 of the esophagus</td>
<td>• Lower 1/3</td>
</tr>
<tr>
<td>• Risk factors</td>
<td>• Risk factors</td>
</tr>
<tr>
<td>– Tobacco</td>
<td>– Barrett’s esophagus</td>
</tr>
<tr>
<td>– Alcohol</td>
<td>– Tobacco</td>
</tr>
<tr>
<td>– Caustic injury</td>
<td>– GERD</td>
</tr>
<tr>
<td>– Plummer-Vinson syndrome</td>
<td></td>
</tr>
</tbody>
</table>
STOMACH & DUODENUM
## Intestinal Hormones/Secretion

<table>
<thead>
<tr>
<th>Substance</th>
<th>Source</th>
<th>MOA</th>
<th>↑/↓</th>
<th>Disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCl</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Intrinsic Factor</td>
<td></td>
<td></td>
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<tr>
<td>Pepsinogen</td>
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<tr>
<td>Somatostatin</td>
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<tr>
<td>Histamine</td>
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</tr>
<tr>
<td>Gastrin</td>
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<tr>
<td>Cholecystokinin</td>
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<td></td>
</tr>
<tr>
<td>Substance</td>
<td>Source</td>
<td>MOA</td>
<td>↑/↓</td>
<td>Disorders</td>
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<td>---------------</td>
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</tr>
<tr>
<td>HCO3</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secretin</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Incretins (GIP, GLP)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Motilin</td>
<td></td>
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<tr>
<td>Nitric Oxide</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>VIP</td>
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</tbody>
</table>
Gastric Secretion
Parietal Cell Function

[Diagram showing the function of parietal cells with various regulatory mechanisms and pathways involving hormones and inhibitors such as H₂ blockers, somatostatin, prostaglandins, misoprostol, and proton pump inhibitors.]

Gastric parietal cell

ATPase

Proton pump inhibitors

H⁺

Gastric lumen

Carbonic anhydrase

H₂CO₃ ⇌ CO₂ + H₂O

Cl⁻

HCO₃⁻

("alkaline tide")

Gastric parietal cell

ACh

M₂ receptor

CCK₈ receptor

GRP

G cells

Vagus

No clinically useful inhibitor

Histamine

Prostaglandins/misoprostol

Somatostatin

H₂ receptor

G₁

cAMP

IP₃/Ca²⁺

H⁺ + HCO₃⁻ ⇌ H₂CO₃ ⇌ CO₂ + H₂O
Gastritis

**Acute Gastritis**
- Mucosal inflammation with acute infiltration of neutrophils
- Causes
  - *H. pylori*
  - NSAIDs (PGE2)
  - Ingestion of corrosives
  - Systemic disease (Crohn’s, sarcoid)
  - Stress gastritis
    - Severely ill
    - Changes to microcirculation

**Chronic Gastritis**
- Type A – body
  - Autoimmune disorder → chronic inflammation and mucosal atrophy
    - Ab to IF → pernicious anemia
    - Ab to parietal cells → achlorhydria
    - Normal gastrin production
- Type B – antrum
  - *H. pylori* (90%)
H. pylori

- Curved, gram negative bacillus with flagella
- Produces urease
- Can cause a chronic atrophic gastritis
- More frequently found in relation to duodenal ulcers; eradication of the bacteria reduces the relapse rate
- Increased risk of gastric adenocarcinoma, MALT lymphoma
- Diagnosis: urease breath test, stool antigen, biopsy
- Treatment: antibiotics
# Peptic Ulcer Disease

<table>
<thead>
<tr>
<th></th>
<th>Gastric</th>
<th>Duodenal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Incisura</td>
<td>bulb</td>
</tr>
<tr>
<td>MCC</td>
<td>NSAIDs</td>
<td>H. Pylori</td>
</tr>
<tr>
<td>MOA</td>
<td>Decreased mucosal protection</td>
<td>Increased acid secretion</td>
</tr>
<tr>
<td>Relation to meals</td>
<td>No relation</td>
<td>Better after meal</td>
</tr>
<tr>
<td>Cancer risk</td>
<td>+++</td>
<td>unlikely</td>
</tr>
</tbody>
</table>
Complications of PUD

- Gastric outlet obstruction
- Bleeding
- Perforation
- Malignancy
Zollinger-Ellison Syndrome

- Gastrinoma
  - Sporadic
  - Hereditary (MEN I)
- Exogenous gastrin $\rightarrow$ uninhibited HCl production $\rightarrow$ PUD
  - Fasting gastrin $> 1,000$ pg/mL
- Diagnosis
  - Fasting gastrin, secretin stimulation test
- Treatment
  - Surgical resection (risk of malignancy)
Gastric Malignancy

- Symptoms late in course: weight loss, gastric outlet obstruction, anemia
- Poor prognosis due to aggressive local spread
- Morphology
  - Intestinal
    - *H. pylori*, nitrosamines, tobacco, achlorhydria, chronic gastritis
  - Gastric
  - Diffuse
    - Signet ring cells
SMALL INTESTINE
Absorption

• Brush border of enterocytes with large surface area
• 9 L of fluid/day, of which 90% is absorbed
• Duodenum: Fe, folic acid
• Jejunum: dietary nutrients – carbs, protein, fat
• Ileum: B12, bile salts

• Disorders of the small intestine result in diarrhea, steatorrhea, vitamin and mineral deficiency
Diarrhea

• Infection

• Inflammation
  – Inflammatory bowel disease
  – Mesenteric ischemia
  – Diverticulosis

• Fat malabsorption
  – Pancreatic insufficiency
  – Small bowel disease: celiac
Malabsorption

• Carbohydrate: usually dietary
• Protein: rare
• Fat
  – Luminal/mucosal
    • Zollinger-Ellison: decreased duodenal pH
    • Bacterial overgrowth: deconjugation of bile salts
    • Celiac, Crohn’s: diminished surface area
  – Enzymatic
    • Pancreatic insufficiency: decreased lipase
Celiac Disease: Gluten-sensitive Enteropathy

- Incidence: 1/250 persons
- Genetically inherited, HLA-DQ2/8 on chromosome 6
- Immune disorder triggered by gluten in genetically predisposed individuals (wheat, barley, rye)
- Classic features
  - Villous atrophy
  - Malabsorption
  - Resolution with withdrawal of gluten-containing foods
- Clinical presentation
  - Diarrhea
  - Nutritional deficiencies
  - Anemia: Fe, folate, B12 malabsorption
  - Vitamin deficiency
  - Dermatitis herpetiformis
Celiac Disease

• Diagnosis: anti-endomysial Ab, antibody to tissue transglutaminase, duodenal biopsies
• Treatment: gluten free diet
• Complications
  – Refractory sprue
  – T-cell lymphoma
B12 Absorption

• Adequate absorption
  – Dietary intake
  – Acid-pepsin in stomach $\leftarrow$ achlorhydria
  – Pancreatic proteases $\leftarrow$ pancreatic insufficiency, bacterial overgrowth
  – Intrinsic factor (parietal cells) $\leftarrow$ H. pylori, atrophic gastritis
  – Intact ileum $\leftarrow$ surgery, IBD

• Deficiency: neuropsychiatric problems, megaloblastic anemia
COLON
Normal Function

• Absorption of water, sodium, chloride
• Secretion of potassium, bicarbonate

• An intact colon is not necessary to sustain life
## IBD: Crohn’s

<table>
<thead>
<tr>
<th>Location</th>
<th>Any portion of the GI tract, non-contiguous (&quot;skip&quot; lesions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
<td>Transmural inflammation</td>
</tr>
<tr>
<td>Microscopic Findings</td>
<td>Non-caseating granulomas, Lymphoid aggregates</td>
</tr>
<tr>
<td>Clinical Presentation</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Extraintestinal manifestations</td>
<td>Erythema nodosum*, Ankylosing spondylitis, Migratory polyarthritis (large joints), Pyoderma gangrenosum*, Aphthous ulcers, Uveitis, Primary Sclerosing cholangitis (5%)</td>
</tr>
<tr>
<td>Complications</td>
<td>Strictures, fistulae, colorectal cancer, gallstones</td>
</tr>
<tr>
<td>Treatment</td>
<td>CS, immunomodulators, anti-TNF</td>
</tr>
</tbody>
</table>
**IBD: Ulcerative Colitis**

<table>
<thead>
<tr>
<th>Location</th>
<th>Rectum spreading proximally in a continuous manner</th>
</tr>
</thead>
</table>

| Clinical Presentation | Bloody diarrhea, tenesmus |

| Extraintestinal manifestations | Pyoderma gangrenosum, Erythema nodosum, PSC, Ankylosing spondylitis |

| Complications        | Toxic megacolon, Colon cancer |

| Treatment            | 5-ASA, immunomodulators, anti-TNF, surgery |
Diverticular Disease

- Diverticulae = herniation of mucosa and submucosa through the muscularis propria
- Predominantly elderly, Western society, sigmoid location
- Complications
  - Bleeding (5%)
  - Diverticulitis
Acute Mesenteric Ischemia

- Irreversible decrease in intestinal blood flow → bowel necrosis
  - Primary: arterial emboli, arterial/venous thrombi, sudden and prolonged low flow state, vasculitis
  - Secondary: extrinsic vascular compression, trauma
- Most commonly affected: SMA
- Risk Factors
  - Age > 50
  - Comorbidities
- Clinical presentation
  - Severe abdominal pain out of proportion exam
  - Bloody diarrhea
  - Nonspecific complaints: fever, nausea, vomiting, etc
Acute Mesenteric Ischemia

• Diagnosis: AXR, CT, angiography
• Treatment: IV fluids, treat underlying cause, surgery if necrosis or perforation
Ischemic colitis

• Temporary decrease in blood flow to \textbf{colon} \rightarrow ischemia in \textit{watershed areas}
  – Atherosclerotic disease, non-occlusive low-flow states (marathon runners, medications/drugs, heart disease)

• Clinical presentation
  – Acute abdominal pain, diarrhea (+/- blood), fever, etc

• Diagnosis:
  – AXR, CT scan, colonoscopy

• Treatment
  – Underlying cause, fluid resuscitation, surgery
Irritable Bowel Syndrome

• Diagnosis of exclusion; not explained by identifiable structural or biochemical abnormalities

• Presentation
  – Women: men 3:1
  – Constipation or diarrhea predominant
  – lower abdominal discomfort/pain
  – Altered bowel function
  – Bloating

• Treatment: symptom control
Colon Polyps
Colon Cancer

- Adenocarcinoma (98%), lymphoma, carcinoid, leiomyosarcoma, metastatic disease
- Clinical presentation
  - Abdominal pain
  - Bleeding, anemia
  - Weight loss
  - Change in bowel habits
  - Obstruction
Colon Cancer

• Risk Factors
  – Age > 50
  – Family history of CRC
  – IBD
  – Lifestyle: tobacco, red meat, low fiber

• Diagnosis
  – Colonoscopy vs. flexible sigmoidoscopy vs. stool cards
Adenoma-Carcinoma Sequence

Normal colon $\rightarrow$ mucosa at risk $\rightarrow$ adenoma $\rightarrow$ CRC

- Mutations in “gatekeeper” gene = APC
  - Mutated in 85% of cancers
- Mutations in “caretaker” genes = MSH, MLH
  - Microsatellite instability
- Activation of oncogenes
  - K-ras: 50% of large adenomas, adenocarcinomas
  - p53
# Familial Adenomatous Polyposis

<table>
<thead>
<tr>
<th><strong>Gene involved</strong></th>
<th>APC (AD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prevalence</strong></td>
<td>1/5,000-1/7,500</td>
</tr>
<tr>
<td><strong>Colon findings</strong></td>
<td>100-1000 polyps throughout the colon</td>
</tr>
<tr>
<td><strong>Extracolonic findings</strong></td>
<td>Duodenal adenomas, gastric polyps, mandibular osteomas, supernumerary teeth</td>
</tr>
<tr>
<td><strong>Cancer risk</strong></td>
<td>~ age 40</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Prophylactic colectomy, surveillance EGDs</td>
</tr>
<tr>
<td><strong>Variants</strong></td>
<td>Attenuated FAP, Gardner’s syndrome, Turcot’s syndrome</td>
</tr>
</tbody>
</table>
# Hereditary Non-Polyposis Colorectal Cancer (Lynch)

<table>
<thead>
<tr>
<th>Gene involved</th>
<th>MMR genes (AD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>“3-2-1 rule”: 3 relatives with HNPCC-related malignancies across 2 generations, 1 of whom was diagnosed before age 50</td>
</tr>
<tr>
<td>Colon findings</td>
<td>Proximal colon polyps, 80% progress to CRC</td>
</tr>
<tr>
<td>Extracolonic findings</td>
<td>Skin, uterine, ovarian, gastric, urinary, small bowel, biliary tumors</td>
</tr>
<tr>
<td>Cancer risk</td>
<td>~ age 46</td>
</tr>
<tr>
<td>Treatment</td>
<td>Surveillance colonoscopy, polypectomy</td>
</tr>
<tr>
<td>Variants</td>
<td>Muir-Torre</td>
</tr>
</tbody>
</table>
# Peutz-Jeghers Syndrome

<table>
<thead>
<tr>
<th>Gene involved</th>
<th>LKB1/STK11 (AD)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosis</strong></td>
<td>Two or more confirmed PJS polyps; any PJ polyps with family history of PJS; mucocutaneous pigmentation with FHx of PJS or characteristic polyps</td>
</tr>
<tr>
<td><strong>Colon findings</strong></td>
<td>Hamartomas throughout the GI tract</td>
</tr>
<tr>
<td><strong>Extracolonic findings</strong></td>
<td>Melanin deposition around lips, buccal mucosa, face, genitalia, hands, feet; other GI cancers (small bowel, pancreas, bile ducts, gallbladder), ovarian sex cord tumors, Sertoli cell tumors, breast cancer</td>
</tr>
</tbody>
</table>
| **Cancer risk** | ~ 40 years = 20%  
Colorectal > stomach > small bowel |
| **Treatment** | Surveillance colonoscopy, polypectomy |
## Juvenile Polyposis Syndrome

<table>
<thead>
<tr>
<th>Gene involved</th>
<th>PTEN, SMAD4 (AD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon findings</td>
<td>Hamartomatous polyps throughout the colon; children &lt; 5 years</td>
</tr>
<tr>
<td>Extracolonic findings</td>
<td>Skin, uterine, ovarian, gastric, urinary, small bowel, biliary tumors</td>
</tr>
<tr>
<td>Cancer risk</td>
<td>20% risk</td>
</tr>
<tr>
<td>Treatment</td>
<td>Surveillance colonoscopy, polypectomy</td>
</tr>
</tbody>
</table>

***Hamartomatous polyps: juvenile polyposis syndrome, Peutz-Jeghers syndrome***
• **Cholestatic**
  – Genetic
  – Without obstruction:
    • Primary biliary cirrhosis
    • Primary sclerosis cholangitis
    • Drug-induced cholestasis
  – With obstruction:
    • Choledocholithiasis

• **Hepatocellular**
  – Alcoholic

• **Viral**

• **Metabolic**
  – Hemochromatosis
  – Wilson’s disease
  – Alpha1-antitrypsin disease

• **Vascular**
  – Budd-Chiari

• **Autoimmune hepatitis**

• **Infiltrative**
Functions of the Liver

• Production of bile salts
  – Cholesterol metabolism
  – Bilirubin metabolism

• Toxin filtration

• Clotting cascade
  – Albumin, prothrombin, fibrinogen
  – Factors V, VII, IX, X, XI, XII
## Liver Function Tests

<table>
<thead>
<tr>
<th>Test</th>
<th>Hepatocellular</th>
<th>Cholestatic</th>
<th>Infiltrative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aminotransferase</td>
<td>++/+++</td>
<td>0/+</td>
<td>0/+</td>
</tr>
<tr>
<td>Alkaline Phosphatase</td>
<td>0/+</td>
<td>+++/+</td>
<td>++/+++</td>
</tr>
<tr>
<td>Bilirubin</td>
<td>0/+</td>
<td>0/+</td>
<td>0/+</td>
</tr>
<tr>
<td>Prothrombin Time</td>
<td>Nml or prolonged</td>
<td>Nml or prolonged</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>*responds to vit K</td>
<td></td>
</tr>
<tr>
<td>Albumin</td>
<td>Decreased (chronic disorders)</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Examples</td>
<td>Alc hepatitis, Viral hepatitis</td>
<td>Biliary obstruction HCC</td>
<td>Sarcoidosis Lymphoma</td>
</tr>
</tbody>
</table>
Bile Synthesis

- Heme $\rightarrow$ biliverdin $\rightarrow$ unconjugated bilirubin $\rightarrow$ conjugation with glucuronide to form conjugated bilirubin $\rightarrow$ excretion
  - Cholesterol is insoluble without bile acids

- Adult liver secretes 1500 mL/day
- Driving factor: bile acid secretion
- Recycled 5-15 times/day, net loss of 20-30%
- Reabsorption in the ileum
  - > 100 cm of ileum resected $\rightarrow$ bile acid loss
Kidney

- Urinary Excretion (~0.5 mg/d)
- Mesenteric & arterial blood flow to hepatocyte

Portal venus return to hepatocytes (95% of biliary secretion)

Biliary Secretion: 3 g in pool x 4-12 cycles/d

Spillover into Systemic Circulation

- Synthesis (0.2 to 0.6 g/d)
- Active biliary excretion
- Cholangio-hepatic shunt
- Postprandial secretion into intestine
- Storage in gallbladder
- Passive absorption

Ileal active transport

Colonic passive transport

Fecal Excretion (0.2 to 0.6 g/d)
Gallstones

• Risk Factors:
  – Female > Male (20% women, 10% men in US)
    • Up to 100% in Native Am women (Pima, Chippewa)
  – Overweight (BMI > 30 = 6x risk)
  – Age
  – Drug therapy (progesterone, estrogen, OCPs, etc)
Gallstone Formation

• Cholesterol supersaturation
  – Cholesterol hypersecretion: obesity, hormones, genetic disorders, rapid weight loss
  – Bile acid hyposcretion: congenital, cholestatic liver disease

• Cholesterol nucleation (crystallization)
  – Mucin, calcium

• Gallbladder hypomotility
Gallstones

• Cholesterol stones (80%)
• Pigment stones: black/brown
  – Bilirubin and calcium salts (rather than cholesterol)
  – Unconjugated bilirubin: chronic hemolysis, cirrhosis
  – Infections
Gallstone complications

- 70-80% of patients never have symptoms
- Up to 30% may have only one attack
- 20% have complications
- Once symptoms occur, recurrence is likely and treatment is indicated

Diagnosis: ultrasound

Treatment: surgery if cholecystitis; ERCP if stone retained in bile duct
# Primary Biliary Cirrhosis

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Females (90%), 50s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Lab abnormalities</td>
<td>↑ alkaline phosphatase&lt;br&gt;Antimitochondrial antibodies (AMA)</td>
</tr>
<tr>
<td>Treatment</td>
<td>Ursodiol&lt;br&gt;Transplant</td>
</tr>
<tr>
<td>Associated conditions</td>
<td>Sjogren syndrome&lt;br&gt;RA, CREST&lt;br&gt;Celiac disease</td>
</tr>
</tbody>
</table>
# Primary Sclerosing Cholangitis

<table>
<thead>
<tr>
<th>Patient population</th>
<th>Males, 40s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presentation</td>
<td>Pruritus, jaundice, fevers, RUQ pain</td>
</tr>
<tr>
<td>Lab abnormalities</td>
<td>p-ANCA</td>
</tr>
</tbody>
</table>
| Treatment                    | ERCP (strictures, cholangitis)  
                              | Transplant            |
| Associated conditions        | IBD (70%)             
                              | **can lead to cholangiocarcinoma** |
Complications of Cholestasis

• Malabsorption of fat-soluble vitamins
  – A,E,D,K replacement
• Hypercholesterolemia
• Pruritis
  – Ursodiol for PBC
• Osteoporosis
  – Loss of bone at 2x rate of normal population
  – Calcium, vitamin D
Alcoholic Liver Disease

Oxidative metabolism

Ethanol $\xrightarrow{\text{Alcohol dehydrogenase}}$ Acetaldehyde $\xrightarrow{\text{Acetaldehyde dehydrogenase}}$ Acetate

NAD$^+$ NADH NAD$^+$ NADH

Microsomal enzyme oxidation system

Ethanol $\xrightarrow{\text{Cytochrome P4502E1}}$ Acetaldehyde

NADPH NADP$^+$
Fatty Liver Disease

• Fatty liver/ Hepatic steatosis
  – Short periods of alcohol abuse
  – Can be reversible
Alcoholic Hepatitis

• Asymptomatic or non-specific symptoms
  – Tender hepatomegaly, fever, tachycardia, jaundice, splenomegaly, etc
• > 60-80 g EtOH/day for several years (lower for women)
• AST>ALT, increased bilirubin, increased PT
• Treatment
  – Abstinence
  – Nutrition, vitamins
  – Decrease oxidative stress: corticosteroids, pentoxifylline
Alcoholic Cirrhosis

• 20% of patients with prolonged heavy alcohol use

• Increased PT/bilirubin, decreased albumin

• Liver biopsy: micronodular cirrhosis, fibrosis

• Treatment: abstinence, try to keep disease compensated (nutrition, diuretics, HCC surveillance, etc)
Non-alcoholic Fatty Liver Disease

• Hepatic steatosis
• Can progress to cirrhosis, increased risk of HCC
  – Older age
  – Diabetes
  – Elevated aminotransferases
  – BMI > 28 kg/m2
  – Fibrosis on biopsy
# Viral Hepatitis

<table>
<thead>
<tr>
<th></th>
<th>HAV</th>
<th>HBV</th>
<th>HCV</th>
<th>HDV</th>
<th>HEV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incubation (d)</td>
<td>15-50</td>
<td>30-160</td>
<td>14-160</td>
<td>Unknown</td>
<td>15-60</td>
</tr>
<tr>
<td>Transmission</td>
<td>Fecal-oral</td>
<td>Parenteral</td>
<td>Parenteral</td>
<td>Parenteral</td>
<td>Fecal-oral</td>
</tr>
<tr>
<td>Course</td>
<td>Acute</td>
<td>Acute or chronic</td>
<td>Acute or chronic</td>
<td>Acute or chronic</td>
<td>Acute; Rare chronic</td>
</tr>
<tr>
<td>Jaundice</td>
<td>Common</td>
<td>30%</td>
<td>Uncommon</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td>Test for diagnosis</td>
<td>Anti-HAV IgM</td>
<td>HBsAg</td>
<td>HCV RNA</td>
<td>Anti-HDV</td>
<td>Anti-HEV IgM</td>
</tr>
<tr>
<td>Other</td>
<td>Pregnancy</td>
<td></td>
<td>IVDU, tattoos &amp; transfusions</td>
<td>Co-infection with HBV</td>
<td>Pregnancy</td>
</tr>
</tbody>
</table>
Hepatitis B

- **Surface Antigen, HBsAg**: current infection
- **e Antigen, HBeAg**: active infection, highly infectious
- **Surface Antibody, HBsAb**: recovery or immunity
- **e Antibody, HBeAb**: inactive virus
- **Core Antibody, HBcAb**: present or past infection
- **HBV DNA**: virus activity
Alpha-1-Antitrypsin Disease

• AD, AAT gene, chromosome 14
  – Inability to protect tissues from proteases
  – Mutated AAT builds up in the endoplasmic reticulum

• Phenotypes
  – Pi*MM: 95% of the population, normal levels AAT
  – Pi*ZZ: severe deficiency, clinically relevant
  – Pi*MZ: indeterminate deficiency
A1AT Deficiency

• Clinical Manifestations
  – Lung: premature emphysema due to uninhibited elastases and proteases
  – Liver: hepatitis, cirrhosis, HCC

• Diagnosis
  – AAT phenotyping
  – Serum levels can be falsely high with inflammation, malignancy, pregnancy, etc
  – Liver biopsy: PAS+ diastase resistant globules in the ER
A1AT Deficiency

• Treatment
  – AAT infusions helpful for lung disease only
  – OLT definitive treatment
    • Recipient assumes the phenotype of the donor
    • Must be performed before advanced lung disease develops
Hemochromatosis

• AR, chromosome 6 \textit{HFE} gene –C282Y, H63D
  – Increased intestinal Fe absorption
  – Increased Fe deposition
  • Liver $\rightarrow$ cirrhosis, \textit{HCC}
  • Heart $\rightarrow$ cardiomyopathy
  • Pancreas $\rightarrow$ diabetes
  • Endocrine organs
    – Hypothyroidism
    – Hypogonadism, impotence
  • Joints $\rightarrow$ arthropathy
  • Skin $\rightarrow$ bronzing
Hemochromatosis

• Diagnosis
  – Increased transferrin saturation > 45%
  – Increased serum ferritin
  – \( HFE \) gene testing
  – Liver biopsy
Hemochromatosis

• Treatment
  – Therapeutic phlebotomy
  – Transplantation (accounts for < 1% of OLTx)
Wilson’s Disease

• AR, chromosome 13 \textit{ATP7B}, > 100 mutations
  – Codes for a copper transporter
  – Majority of cases are compound heterozygotes
• Normal intestinal absorption but decreased biliary excretion $\rightarrow$ failure to enter circulation as ceruloplasmin
  – Copper deposition in liver, brain, cornea, kidney $\rightarrow$ generation of free radicals
  – Decrease in serum ceruloplasmin
Wilson’s disease

• Clinical Presentation (*age 20-50*)
  – Hepatic (42%)
  – Neurologic (34%)
  – Psychiatric (10%)
  – Hematologic (12%)
Wilson’s disease

• Diagnosis:
  – Ceruloplasmin
  – Kayser-Fleisher rings
  – Neurologic symptoms
  – Liver copper concentration > 250 ug/g

• Treatment
  – Metal chelators (penicillamine, trientine), zinc
  – Transplantation if fulminant liver failure
Cirrhosis

- Fibrosis and nodular regeneration
  - Disrupts normal architecture, flow within liver
Hepatic Encephalopathy

• Increased NH3 production/absorption: dietary protein, GI bleed, infection
• Decreased NH3 removal: renal failure, diuretics, portosystemic shunts
• Clinical Features
  – Asterixis
  – Somnolence, coma
• Treatment
  – Lactulose
  – Rifaximin
GI Bleeding

Pathologic blood flow in portal HTN
Flow through TIPS, re-establishing normal flow direction
Normal venous drainage

1. Esophageal varices
2. Caput medusae
3. Rectal varices
4. TIPS

To the azygos vein

Esophageal veins
IVC

Portal vein
Splenic vein
Left gastric vein (coronary vein)

Paraumbilical vein

Superior mesenteric vein
Inferior mesenteric vein

Colon

Superior rectal vein (superior hemorrhoidal vein)

Middle and inferior rectal veins

Anus
Ascites

- Decrease in splanchnic pressure → stimulation of renin-angiotensin-aldosterone pathway → fluid retention
- Treatment:
  - Diuretics
  - Paracentesis
  - Transplant
- SBP
Cirrhosis Complications: HCC

• Increased risk with all cirrhotic diseases
  – Exception: HBV with or without cirrhosis
• Clinical presentation
  – Decompensation of cirrhosis
• Diagnosis
  – Alpha fetoprotein
  – Abdominal ultrasound vs. triple phase CT scan

• Screening for all patients with cirrhosis, all HBV patients: AFP + U/S every 6 months
PANCREAS
Pancreatic Function

• Exocrine
  – Proenzymes that are activated in the duodenum
    • Breaks down carbohydrates, proteins, lipids
    • Trypsinogen, chymotripsinogen, proelastase, prophospholipase
  – Active enzymes: amylase, lipase
  – Bicarbonate, water
  – Stimulus: CCK, ACh, VIP, secretin

• Endocrine
  – Alpha cell: glucagon
  – Beta cell: insulin
  – Delta cell: somatostatin (inhibits a/b cells)
  – PP cell: pancreatic polypeptide
Embryogenesis

Congenital Disorders

A. Normal
- Common bile duct
- Lesser duct (duct of Santorini)
- Major duct (duct of Wirsung)
- Ventral Wirsung

B. Pancreas divisum
- Common bile duct
- Major duct (duct of Wirsung)

Gay, SB. "Radiology Recall" Lippincott Williams & Wilkins 2000, p394.

Acute Pancreatitis

1. Abdominal pain characteristic of acute pancreatitis
   - Periumbilical pain, can radiate to the back or shoulder
2. Serum amylase and/or lipase ≥ 3 times the upper limit of normal
3. Characteristic findings of acute pancreatitis on CT scan
Acute Pancreatitis

• Idiopathic
• Gallstones
• Ethanol
• Trauma
• Steroids
• Mumps (and other infections)
• Autoimmune & Hereditary
• Scorpion sting
• Hyperlipidemia (TG > 1000)/Hypercalcemia
• ERCP
• Drugs
Acute Pancreatitis

- Mortality rate of 4-8%
- Majority of patients have a mild course, but 15-20% can progress
- Important to recognize severe disease early
  - Multisystem organ failure: mortality 50%
  - Patients typically progress within the first 48 hours
  - Need for close monitoring
Pancreatitis Complications

• Pseudocysts
  – Duodenal obstruction
  – CBD obstruction
• Biliary strictures
• Pseudoaneurysms
• Pancreatic necrosis
• Splenic vein thrombosis
  – Gastric varices
Chronic Pancreatitis

• Progressive inflammatory disease leading to irreversible destruction of the pancreas
  – Pain
  – Maldigestion (exocrine)
  – Diabetes (endocrine)
Chronic Pancreatitis Treatment

• Pancreatic enzymes for steatorrhea
• Nutritional support
  – Decreased fat intake
  – Replacement of fat soluble vitamins, Calcium, Cyanocobalamin
• Abdominal pain
  – ERCP for treatment of pancreatic stones or strictures
  – Surgery: lateral pancreaticoduodenectomy
• Risk of pancreatic cancer
  – 3-15% increase
  – Abdominal pain, weight loss
Pancreatic Cancer

• 5% survival rate
• Risk factors
  – Hereditary pancreatitis (trypsinogen mutations)
  – Chronic pancreatitis
  – Cystic lesions of the pancreas (IPMN, MCN)
  – Genetic factors (BRCA, PJS)
• Presentation
  – Head of pancreas: biliary obstruction
  – Body/tail: non-specific symptoms
Questions

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