1. GI Pathophysiology: Review

GI Pathophysiology Review

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2007

2. Esophageal Dysfunction

Esophageal Dysfunction

- Gastroesophageal Reflux Disease (GERD)
  - Anti-reflux barrier
  - LES changes with GERD: TLESRs
- Esophagitis
  - Reflux
  - Pill-induced
  - Infectious: candida, HSV, CMV
- Barrett’s Esophagus
  - Specialized intestinal metaplasia
  - Adenocarcinoma risk
3. Pathophysiology of GERD

4. Heartburn May Indicate Severe Disease

- Age > 40 years
- Symptom duration > 3 years
- Alarming symptoms/signs
  - Dysphagia
  - Weight loss
  - Anemia

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5. Normal Esophagus/Barrett’s Esophagus

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6. Approach to the Patient with Dysphagia

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7. Achalasia

Achalasia

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8. Spastic Esophageal Motility Disorders

Syndromes
- Diffuse esophageal spasm
- Nutcracker esophagus
- Hypersensitive LES
- Nonspecific esophageal motility disorders

Symptoms
- Chest pain
- Dysphagia

Manometric Features
- Some normal peristalsis
- Simultaneous contractions
- Spontaneous contractions
- Repetitive contractions
- High-amplitude contractions
- High LES pressure

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9. Scleroderma

Scleroderma

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10. Gastric and Duodenal Disease: Parietal Cell

Gastric and Duodenal Disease
Parietal Cell

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11. Gastric and Duodenal Disease

Gastric and Duodenal Disease

- Duodenal ulcer
  - *H. pylori* associated
  - Excess acid; increased gastrin response
- Gastric ulcer
- *H. pylori*
  - Testing
    - Noninvasive: serology and UBT
    - Invasive: rapid urease test; path – special stains
- NSAID related ulcer disease
- Z-E syndrome

12. Pathophysiology of Diarrhea

Pathophysiology of Diarrhea

- Osmotic – lactose intolerance
  - High fecal osmotic gap (290-2([Na] + [K]) is >125)
- Malabsorption/Fatty
- Inflammatory
- Secretory
  - Low fecal osmotic gap (<50)
- Altered motility

I. Luminal Phase
- Reduced nutrient availability
  - Celiac disease (previous stress, gastric surgery)
  - Nutrient consumption (bacterial overgrowth)
- Impaired fat solubilization
  - Reduced bile synthesis (hepatic cell disease)
  - Impaired bile salt resorption (chronic cholestasis)
  - Bile salt inactivation (bacterial overgrowth)
  - Impaired CCK release (mucosal disease)
- Defective nutrient hydrolysis
  - Lipase insufficiency (SI disease)
  - Enzyme deficiency (pancreatic insufficiency or cancer)
  - Water mixing or rapid transit (autonomic, hypertrophic)

II. Mucosal Phase
- Extensive mucosal loss (infection, infection)
- Diffuse mucosal disease (gluten, tropical, Crohn’s, radiation, infectious, drugs, inflammasomes)
- Enterocyte defects
  - Micronutrient absorption defect
  - Brush border hydrolase deficiency
  - Transport defects (Montelukast, Rho and kinase pathways)
  - Epithelial processing (D-endorphins)

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14. Celiac Sprue

Celiac Sprue

- Gluten sensitive enteropathy
- HLA-DQ2 associated
- Tissue transglutaminase ab
- Anti-endomysial antibody
- Manifestations
  - Abdominal symptoms
  - Malnutrition
  - Low iron, low vit D, low vit K

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15. Inflammatory Bowel Disease

Inflammatory Bowel Disease

- Ulcerative Colitis
  - Bloody diarrhea
  - Rectum involved
  - Inflammation continuous
- Crohn’s Disease
  - Diarrhea, RLQ pain, fever, weight loss
  - Transmural inflammation-large ulcers, rectum spared, skip lesions
  - Fistulae
  - Strictures
- Diagnosis and Treatment

16. Complications of IBD

Complications of IBD

- Complications of UC
  - Massive hemorrhage
  - Fulminant colitis
  - Colonic stricture (rare)
  - Colon cancer
- Complications of CD
  - Bile acid malabsorption
    - Secretory diarrhea – bile acids on colon
    - Gallstones – bile more lithogenic
    - Steatorrhea – vitamin A, D, E, K malabsorption
    - Nephrolithiasis – steatorrhea causes more oxalate absorption leading to calcium oxalate stones --- NOT uric acid stones
  - Malignancy – colon cancer, small bowel cancer (lymphoma or adenocarcinoma – very rare)

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17. Colon Disorders

Colon Disorders

- Constipation
- Diverticula
- Hemorrhoids
- Anorectal fistula
- Anal fissure

18. Gallstones

Gallstones

Who Is at Risk for Gallstones?

- Women
- People over age 60
- Native Americans
- Mexican Americans
- Overweight men and women
- People who fast or lose a lot of weight quickly
- Pregnant women, women on hormone therapy, and women who use birth control pills
19. Gallstones

Gallstones

- Cholesterol stones – 90% of stones in US
  - Hypersecretion of cholesterol into bile
    - Obesity, OCPS, estrogen, rapid weight loss
  - Hyposcretion of bile acids
    - Impaired synthesis, intestinal loss (i.e., resection), progesterone
  - Impaired gallbladder function – stasis
    - Progesterone, pregnancy, TPN

- Pigment stones
  - Black pigment – cirrhosis, hemolytic anemia
    (hemoglobinopathy, red cell disorders)
  - Brown pigment – Asian patients (infection)

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20. Gallstones

Gallstones

- Cholesterol – hydrophobic – precipitates unless held in solution by bile salts
- Bile salts form micelles – contain cholesterol in center
- Mixed micelles – bile salts with phospholipid (lecithin) – cholesterol in center

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21. Gallstones

22. Gallstones
23. Gallstones

- “Biliary” pain
- Cholecystitis
- Choledocholithiasis

- Dx: ultrasound
- Treatment
  - Laparoscopic cholecystectomy

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25. Pancreatitis: Etiology

Pancreatitis: Etiology

- Alcohol
- Gallstones
- Idiopathic
- Other
- Drugs
  - Infectious agents
  - Hyperlipidemia
  - Hypercalcemia
  - Ductal obstruction
- Trauma
- Hypotension
- Post-operative
- Miscellaneous

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26. Pancreatitis: Local Effects of Enzymes

Pancreatitis: Local Effects of Enzymes

- Inflammation
- Third space losses
- Fat necrosis
- Pancreatic and peripancreatic necrosis

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27. Pancreatitis: Clinical Features

Pancreatitis: Clinical Features

<table>
<thead>
<tr>
<th>Signs &amp; Symptoms</th>
<th>Lab Tests</th>
<th>Differential Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>↑ WBC</td>
<td>Cholelithiasis</td>
</tr>
<tr>
<td>Abdominal tenderness</td>
<td>↑ Serum amylase</td>
<td>Perforated ulcer</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>↑ Serum lipase</td>
<td>Mesenteric ischemia</td>
</tr>
<tr>
<td>Fever</td>
<td></td>
<td>Intestinal obstruction</td>
</tr>
<tr>
<td>Tachycardia</td>
<td></td>
<td>Salpingitis</td>
</tr>
</tbody>
</table>

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28. Chronic Pancreatitis: Etiology

Chronic Pancreatitis: Etiology

- Calcific pancreatitis of the tropics
- Hereditary pancreatitis
- Hyperparathyroidism
- Cystic fibrosis
- Pancreas divisum
- Miscellaneous
- Alcohol
- Idiopathic
- Other

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29. Liver Function Tests

Liver Function Tests

- Aminotransferase elevations
- Elevated alkaline phosphatase
- Elevated total bilirubin
  - Direct
  - Indirect
- Liver synthetic function
  - Albumin
  - Prothrombin time

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30. Liver Tests: Acute Liver Disease

Liver Tests: Acute Liver Disease

- Hepatocellular injury
  - Marked increase in the ALT and AST
  - Lesser increase in alkaline phosphatase
- Cholestatic injury
  - Marked increase in the alkaline phosphatase
  - Lesser increase in the ALT and AST
- The bilirubin can be elevated in both

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31. Liver Blood Tests: Transaminases > 1000

Liver Blood Tests
Transaminases > 1000

• A – Acute Hepatitis A, Autoimmune hepatitis
• B – Acute Hepatitis B
• C – Acute Hepatitis C (rare)
• D – Drug induced (acetaminophen most common), Hepatitis D
• E – Acute Hepatitis E
• F – Flow = ischemia
• G – Rarely gallstones

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32. Viral Hepatitis

Viral Hepatitis

• Hepatitis A
  – Not chronic
  – Fecal-oral
  – Vaccine available

• Hepatitis B
  – Acute and chronic
  – Blood-blood transmission
  – Increased risk of hepatocellular cancer in chronic state
  – Most infectious – i.e., easiest to transmit
  – Vaccine available

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33. Viral Hepatitis, cont.

Viral Hepatitis, cont.

- Hepatitis C
  - Acute and Chronic
  - IVDA, blood transfusion
  - No vaccine available
- Hepatitis D
  - Requires hep B coinfection
- Hepatitis E
  - Fecal-oral → pregnant women Southeast Asia

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34. Hepatitis A

Hepatitis A

- Hep A IgM antibody – acute
- Hep A IgG antibody – prior infection

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35. Hepatitis B: Clinical Outcomes of Acute HBV Infections

36. Hepatitis B Serology

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37. Portal Hypertension

Portal Hypertension

Portal hypertension is the result of increases in both resistance to portal flow and in portal venous inflow. Backward and Forward Theories Apply.

- Intra-hepatic resistance >> normal
- Collateral resistance > normal intra-hepatic resistance

\[ \Delta P = Q \times R \]

38. Hepatic Venous Pressure Gradient (HVPG)

Hepatic Venous Pressure Gradient (HVPG)

The Hepatic Venous Pressure Gradient (HVPG) is the difference between the Wedged (WHVP) and the Free (FVHP) Venous Pressures.

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39. Portal Hypertension: HVPG (WHVP-FHVP) >12mmHg

Portal Hypertension
HVPG (WHVP-FHVP) >12mmHg

- **Pre-hepatic** → Normal HVPG
  - Portal or splenic vein thrombosis
  - AV fistulas in the splanchnic bed or spleen

- **Intra-hepatic**
  - Pre-sinusoidal → Normal HVPG
    - Sarcoid, Schistosomiasis
  - Sinusoidal → High HVPG (WHVP>FHVP)
    - Cirrhosis – any cause
  - Post-sinusoidal → Budd Chiari – can’t get into hepatic veins (clot in veins)

- **Post-hepatic** → Normal HVPG (High WHVP and FHVP)
  - Webs in IVC
  - Cardiac disease → constrictive pericarditis, right heart failure

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40. Hyperdynamic Circulatory State

Hyperdynamic Circulatory State

Present in Patients with Cirrhosis and Portal Hypertension

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41. Possible Mechanisms

Possible mechanisms for the hyperdynamic splanchnic and systemic circulations in portal hypertension:
- Increased production of vasodilators
- Decreased clearance of vasodilators
- Receptor mechanisms
- Increased levels of humoral vasodilators
- Decreased reactivity to humoral vasoconstrictors
- Plasma volume expansion
- Vasodilation
- Hyperdynamic circulation

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42. Cirrhosis Complications

Cirrhosis Complications

- Varices
- Ascites
- Hepatic encephalopathy
- Hepatorenal syndrome

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43. Portal Hypertension

Portal Hypertension

• Leads to the Formation of Portal Systemic Collaterals

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44. Conditions Other Than Hepatorenal Syndrome

Cirrhosis

• There are many conditions other than Hepatorenal syndrome that can lead to renal failure in patients with Cirrhosis

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45. Example Questions

Example Questions

46. Question 1

Question 1

A 50 year old (yo) man complains of heartburn. He has a history of hypertension and takes nifedipine. You advise him to raise the head of his bed.

Which of the following will most likely reduce his GERD symptoms?

A. Eating fatty food  
B. Cigarette smoking  
C. Peppermint gum  
D. Switching anti-hypertensive medication  
E. Three large meals daily
Question 2

A 60 yo woman has several years of dysphagia to solids and liquids. It has become progressively worse lately and she has lost some weight. She denies significant coughing at night. She complains of heartburn, joint discomfort, and tight skin on the face and hands.

An esophageal motility study would most likely have which of the following findings?

A. Low LES pressure, absent peristaltic activity in the esophageal body, normal relaxation of the LES with swallowing
B. Low LES pressure, normal peristaltic activity in the esophageal body, normal relaxation of the LES with swallowing
C. Normal LES pressure, high amplitude peristaltic contractions in the esophageal body, failure of the LES to relax with swallowing
D. High LES pressure, absent peristaltic activity in the esophageal body, failure of the LES to relax with swallowing
E. High LES pressure, high amplitude non-peristaltic contractions in the esophageal body, failure of the LES to relax with swallowing

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Question 3

A 33 yo man has chronic heartburn. He has tried numerous over the counter remedies.

Which of the following medications works by altering the function of the gastric parietal cell?

A. Ranitidine
B. Calcium carbonate
C. Metoclopramide
D. Sucralfate
E. Misoprostol

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49. Question 4

A 55 yo woman has a very stressful job. She comes in complaining of terrible epigastric pain. This is associated with some nausea but no vomiting. She is found to have a duodenal ulcer.

Which of the following most likely explains the pathogenesis of duodenal ulcers?

A. Low acid production in response to a meal
B. Excess gastric acid production
C. Effect of NSAID’s
D. Alcohol use
E. Stress

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50. Question 5

A 27 yo woman complains of severe RUQ abdominal pain about 1 hour after eating a meatball sub. She is with her 1 month old baby girl who she takes to the ER with her. An abdominal ultrasound in the ER shows numerous shadowing gallstones in the gallbladder and a thickened gallbladder wall. Her bile duct is minimally dilated. Her ALT is 327 and AST 345. Her alkaline phosphatase is 185 and total bilirubin is 2.3.

Which of the following would you most likely find in this patient?

A. The majority of the gallbladder stones are brown pigment stones
B. The majority of the gallbladder stones are black pigment stones.
C. Normal serum cholesterol.
D. Diabetes mellitus
E. Inflamed terminal ileum

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Question 6

A 25 yo second year medical student was vaccinated for hepatitis B prior to starting medical school. She had an episode of jaundice 3 years ago after a trip to Mexico. This illness resolved spontaneously without specific treatment. Testing at the time was consistent with acute hepatitis A.

Which of the following hepatitis serologies is most likely in this patient?

<table>
<thead>
<tr>
<th>Hep B Ag</th>
<th>Hep B Ab</th>
<th>Hep B core IgM</th>
<th>Hep B s Ag</th>
<th>Hep A IgG</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>B</td>
<td>Negative</td>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
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<tr>
<td>C</td>
<td>Negative</td>
<td>Negative</td>
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<td>Positive</td>
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<tr>
<td>D</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>E</td>
<td>Negative</td>
<td>Positive</td>
<td>Negative</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Question 7

A 48 yo man with a history of alcohol abuse and hepatitis C has new onset of jaundice. He has also noticed that his pants don’t fit as well and he has had to loosen his belt. On examination, he has scleral icterus, gynecomastia, and a protuberant abdomen with shifting dullness. His albumin is 2.8, Total bilirubin is 4.5, ALT is 49, AST is 95, Alkaline phosphatase is 155.

Which of the following would you most likely find in this patient?

A. Normal hepatic vein pressure gradient
B. Low splanchnic blood flow
C. Elevated wedged hepatic vein pressure
D. High peripheral vascular resistance
E. Normal cardiac output
53. Question 8

A 38 yo woman has a persistent (lasting more than 2 months), non-bloody diarrhea. She has associated abdominal cramps. She has not lost any weight. She has a history of Crohn’s disease and had 30 cm of ileum removed 10 years ago.

Which of the following is the most likely explanation for the diarrhea?

A. Bacterial overgrowth syndrome
B. Diarrhea-predominant irritable bowel syndrome
C. Colon cancer
D. Giardia infection
E. Lactose intolerance

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54. Question 9

A 24 yo man presents with a 3 month history of diarrhea. He is diagnosed with Ulcerative Colitis. He also complains of a painful left knee and a Rheumatologist feels he has arthritis.

Which of the following extraintestinal manifestations of ulcerative colitis will most likely parallel the intestinal disease course and seem to improve with the intestinal symptoms?

A. Primary sclerosing cholangitis
B. Pyoderma gangrenosum
C. Ankylosing spondylitis
D. Peripheral arthritis
E. Uveitis

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Question 10

A 32 yo woman complains of severe acute peri-umbilical abdominal pain 2 hours after eating a cheeseburger. She has glass of wine with dinner on weekends. On physical exam she does not have a fever but is tender to palpation in the peri-umbilical area. Her lab tests are as follows:

- ALT 254 U/l
- AST 104 U/l
- Total bilirubin 3.6 mg/dl
- Alkaline phosphatase 225 U/l
- White blood cell count 11,500
- Amylase 955 U/l
- Lipase 1254 U/l

The most likely explanation for these findings is:

A. Acute alcoholic hepatitis
B. Acute peptic ulcer disease
C. Acute cholecystitis
D. Acute pancreatitis
E. Acute hepatitis A

Answers to Example Questions

1. D 6. E
2. A 7. C
3. A 8. A
5. C 10. D