Hepatitis, Peptic Ulcer Disease And Other Gastrointestinal Problems

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HEPATITIS

Acute vs Chronic

- Viral - Hepatitis A and B, CMV, HIV, Mono
- Toxic: mushroom, acetaminophen, other drugs
- Shock
- Alcohol

- Viral Hepatitis B / C
- Alcohol
- Medications, herbs
- NAFLD, Hemochromatosis, Wilson’s disease, A1-AT deficiency, Passive congestion
- Auto-immune

51 y.o. male with Elevated LFT’s

51 yo male seen for routine PE. No current c/o. Takes no medications

PMH: splenectomy 25 yo due to trauma. Smokes ½ ppd, works as a painting contractor. ETOH rare, denies history of drug use or known transfusions

PE normal, no stigmata of liver dz

Labs: AST 72 U/L, ALT 66 U/L, ALK PHOS 120 U/L; NORMAL CBC, BILI. Labs 3 years prior elevation of liver enzymes < 2x ULN

HEPATITIS A

- Transmission is fecal/oral
- Incubation period: 2-6 weeks
- Course of disease: Children - disease often mild, usually anicteric; Adults-more often symptomatic with jaundice
- 99% fully recover, develop lifetime immunity
- Fulminant hepatitis is rare
- No chronic hepatitis, or cirrhosis
**SEROLOGY HEPATITIS A**

- ALT
- Anti HAV
- IgM anti-HAV

**Months after exposure**

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**HEPATITIS A VACCINE**

- Pre exposure prophylaxis for travelers to high risk areas.
- Universal vaccination of infants

**ADULTS** 1.0 ml @ 0 and 6 months
**CHILDREN** (Over 1 years old) 0.5 ml @ 0, and 6 months

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**HEPATITIS B**

- 350 million persons infected globally
- 1 million deaths annually due to complications
- 1.25 million persons in the US infected (5,000 deaths annually)
- Incidence US 11.5 cases / 100,000 1985 to 1.6 cases / 100,000 in 2006
- TRANSMISSION: Blood borne- vertical, transfusion, IVDU, needle stick/splash
- Sexual contact: multiple sexual partners, homosexual men
- INCUBATION PERIOD: 45 - 160 days

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**Hepatitis B Prevalence**
Course of Disease

- 95% of adults have self limited disease
- 1/3 of those have clinical illness
- 5 -10% become chronic carriers
- Flu like prodrome, jaundice
- 10% immune complex, “serum sickness”
- Fulminant Hepatitis
- Chronic Hep B- HBsAg positive > 6 months

HBV Serology

<table>
<thead>
<tr>
<th></th>
<th>HBsAg</th>
<th>HBcAb</th>
<th>HBsAb</th>
</tr>
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<tbody>
<tr>
<td>Vaccine</td>
<td>neg</td>
<td>neg</td>
<td>pos</td>
</tr>
<tr>
<td>Immune past HBV</td>
<td>neg</td>
<td>pos</td>
<td>pos</td>
</tr>
<tr>
<td>Infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute or chronic</td>
<td>pos</td>
<td>pos</td>
<td>neg</td>
</tr>
<tr>
<td>HBV infection</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Resolved HBV infection</td>
<td>neg</td>
<td>pos</td>
<td>neg</td>
</tr>
<tr>
<td>False positive core</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low level chronic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Resolving acute infection</td>
<td></td>
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</tr>
</tbody>
</table>

Complications of Chronic Hepatitis B

- Chronic active hepatitis
- Cirrhosis and liver failure
- Transmission
- Hepatocellular Ca
**Prevention-HepB Vaccine**

- Children/adolescents
- Contacts HepBAg+
- Injection drug users
- Multiple sexual partners (>1/6mos)
- Men having sex with men
- Persons recently diagnosed with STI
- Pts with HIV
- Hemodialysis pts
- Health care/Public safety workers with blood exposure
- Clients and staff at institutions for developmentally disabled/inmates
- Travelers @ risk
- Chronic liver disease

**Treatment of Chronic Hep B**

- Goal to limit progression and prevent complications
- Alpha interferon – (PEG IFN-2a)
- Lamivudine (Epivir)
- Adefovir Dipivoxil (Hepsera)
- Entecavir
- Telbivudine
- Tenofovir
- Vaccination of family members
- Patient Education: ETOH abstinence
  - Sexual behavior
  - Toothbrushes, razors, etc.

**HEPATITIS C**

- Approximately 3 million persons in US
- Most are not yet identified
- Of those diagnosed, most have not been treated
- Transmission: Blood borne
  - Sexual contact
- Incubation period: 2 - 22 weeks

**Risk Factors for Hepatitis C**

- Injection drug users, tatoos, cocaine
- People with multiple sexual partners
- Babies born to infected mothers
- Hemodialysis patients
- People who received blood products before 1992
- Sexual contacts of infected person
- ONE TIME UNIVERSAL SCREENING those born 1945 – 1965??
Course of Disease Hep C

- Acute: Majority are asymptomatic
  One third develop jaundice
  Not associated with fulminant disease
- Chronic: 85% develop chronic hepatitis
  Approximately 20% will develop cirrhosis

Serology of Hepatitis C

- EIA Antibody test
- Quantitative PCR RNA viral load
- Genotyping: subtypes 1, 2, 3..

Treatment of Hepatitis C

- Pegalated interferon + ribavirin + telaprevir or boceprevir
- Patient Education: ETOH abstinence
  Sexual behavior
  Toothbrush, razors, etc.
  Hepatitis A, B vaccines

HEPATITIS D

- Transmission: blood borne (IVDU)
- Serology: RIA - HDV antibody
- Course of disease: "tag along hepatitis"
  Acute: co-infection with HBV required
  Fulminant: co-infection or carrier
  Chronic: infection in chronic HBV may result in CAH
HEPATITIS E

- Transmission: fecal/oral
- Epidemiology: Indian subcontinent, South central Asia, Middle East, Mexico
- Course of Disease:
  - Acute: moderate to severe disease
  - 1 - 2% mortality
  - No chronic or carrier state
- Vaccine is being field tested

51 y.o Male Initial Lab Results

- Results:
  - HBAg negative
  - HCAb positive
  - Normal Iron and transferrin

Recommendations

A. Vaccinate against HepB, HepA
B. Test spouse
C. Advise alcohol abstinence
D. Obtain quantitative HCV RNA, genotype
E. Refer to GI / obtain liver biopsy

ALCOHOLIC HEPATITIS

- Can be acute or chronic ingestion
- Clinical: jaundice, tender hepatomegaly, leukocytosis, fever, vomiting
- Laboratory: AST/ALT ratio 2:1
  - Transaminase elevation < 300
  - Alkaline phosphatase < 400
  - Bilirubin elevated
- Elevated MCV
- Treatment: abstinence, nutrition, high index of suspicion for SBP (ANC > 250)
**TOXIC HEPATITIS**
- Industrial: Carbon tetrachloride
- Ingestion: Aminita mushrooms
- Medications: many

**Medications**
- Acetaminophen
- Antibiotics
  - Ciprofloxin, Sulfamethoxazole, Nitrofurantoin, Amoxicillin-clavulanic acid
  - Isoniazid
  - Ketoconazole, Fluconazole, Terbinafine
- Anticonvulsants
  - Phenytoin, Carbamazepine
- Statins
  - Simvastatin, Lovastatin, atorvastatin, Pravastatin, Rosuvastatin
- NSAID
- Anti-dysrhythmics
  - Amiodarone

**Medications and Herbs**
- Sulfonylureas
  - Glypizide, Glyburide
- Glitazones
  - Pioglitazone, Rosiglitazone
- Antiretrovirals
  - Protease inhibitors
  - Nucleoside analogues
- Niacin
- Herbs
  - Chaparral leaf
  - Germander
  - Alchemilla
  - Senna
  - Shark Cartilage
  - Ma huang
  - Ji bu huan
  - Mistletoe
  - Kava

**METABOLIC HEPATITIS**
- Fatty Liver: Steatohepatitis
- Hemochromatosis
  - Iron deposition in liver and other organs
- Wilson’s Disease
  - Copper deposition in liver, brain
- Alpha 1-AT deficiency
- Ischemic hepatitis, passive congestion
**FATTY LIVER**

- Diagnosis: imaging studies, liver biopsy
- NAFLD: Non Alcoholic Fatty Liver Dz
- NASH: Non Alcoholic Steatohepatitis
- Natural History: 30% progress, 60% no change, 10% improvement
- Treatment: Weight loss, “many tried, none have reached consensus” Gemfibrozil, Metformin, Thioglitazones, Rimonabant

**Risk factors in pts with NAFLD**

- Obesity (BMI>30 kg/m2) 30-100%
- Diabetes Mellitus type 2 10-75%
- Hyperlipidemia (esp TRIG) 20-92%
- FHx steatohepatitis and cryptogenic cirrhosis
- Insulin resistance underlies most cases
Hemochromatosis

- Most common genetic disorder in adults
- Autosomal recessive
- Prevalence: 1 in 400 in US
- Inappropriate iron absorption leads to cirrhosis, HCC, diabetes, heart disease
- HFE detects mutation C282Y, H63D
- Variable penetrance

Hemochromatosis

- Diagnosis: Serum transferrin saturation greater than 50% (often elevated ferritin)
- Genetic markers: HFE Gene C282Y, H63D mutation
- Treatment: phlebotomy to maintain ferritin < 50ug/L

Autoimmune Hepatitis

- Often a diagnosis of exclusion, biopsy
- Consider in young women with other autoimmune disorder - thyroditis, ulcerative colitis, or Sjogren’s syndrome.
- Elevated IgG; ANA positive in 80%; smooth muscle antibodies in 70%;
- Treatment with prednisone and azathioprine improves survival rates in patients with severe disease
Clinical Case

– 53 y/o male with 15 year history of intermittent heartburn, presents with daily symptoms for the past 6 months. Denies dysphagia, bleeding or weight loss.

GERD

• Diagnosis reliably made by typical symptoms and response to therapy. Diagnostic testing not typically indicated
• Remember very poor correlation between endoscopic findings and symptoms
• Testing (EGD) usually reserved for concern for stricture, Barrett’s metaplasia, adenocarcinoma, and to evaluate treatment failures.

GERD TREATMENT

• PPI’s now recommended first line
• PPI’s should be given 30-60 min ac (except dexilant)
• Reducing fat, chocolate, coffee, alcohol, and peppermint intake
• Avoiding irritants : onions, citrus,tomato-based foods
• Smoking cessation, weight loss
• Avoid late meals (within 3 hours of bedtime), elevate head of bed

Should one screen for Barrett’s?
Controversy Exists

ACG recommends screening for Barrett’s
10%-15% of patients with GERD will have Barrett’s
The risk of esophageal adenocarcinoma is 30-40x higher in patients with Barrett’s
Over 50 years old with GERD for more than 5 years.
Surveillance every 2-3 years if no dysplasia detected on initial biopsies (likely to be extended with recent large studies on incidence of progression to cancer)

• CGA, AGAI do not recommend screening for Barrett’s
• Insufficient evidence that screening reduces the death rate from adenocarcinoma of the esophagus
• 0.12%-0.13% of pts with Barrett’s will develop cancer per year.
• Many or most patients diagnosed with adenocarcinoma of the esophagus or stomach cardia don’t have Barrett’s

Surgical Indications - GERD

• Laproscopic Nissen Fundoplication
• Failed medical management
• Patient preference despite successful medical therapy
• Large hiatal hernia

GERD Endoscopic Treatments

• Stretta Procedure – radiofrequency heating of gastroesophageal junction
• Endocinch Procedure – endoscopic suture ligation GE junction

Dyspepsia

• Exclude by history:
  • GERD
  • Irritable bowel syndrome
  • Biliary pain
  • Medication induced dyspepsia

• Risk factors for serious disease:
  • Age > 55 years
  • Dysphagia
  • Odynophagia
  • Protracted vomiting
  • Anorexia/weight loss
  • Melena or anemia
  • Palpable mass

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### TABLE 1
**Differential Diagnosis of Dyspepsia**

<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>Approximate prevalence*</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Functional” dyspepsia</td>
<td>Up to 60 percent</td>
</tr>
<tr>
<td>Peptic ulcer disease</td>
<td>15 to 25 percent</td>
</tr>
<tr>
<td>Reflux esophagitis</td>
<td>5 to 15 percent</td>
</tr>
<tr>
<td>Gastric or esophageal cancer</td>
<td>&lt; 2 percent</td>
</tr>
<tr>
<td>Biliary tract disease</td>
<td>Rare</td>
</tr>
<tr>
<td>Gastritis</td>
<td>Rare</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>Rare</td>
</tr>
<tr>
<td>Carbohydrate malabsorption (lactose, sorbitol, fructose, mannitol)</td>
<td>Rare</td>
</tr>
<tr>
<td>Medications (see Table 4)</td>
<td>Rare</td>
</tr>
<tr>
<td>Infiltrative diseases of the stomach (Crohn’s disease, sarcoidosis)</td>
<td>Rare</td>
</tr>
<tr>
<td>Metabolic disturbances (hypercalcemia, hyperkalemia)</td>
<td>Rare</td>
</tr>
<tr>
<td>Hepatoma</td>
<td>Rare</td>
</tr>
<tr>
<td>Ischemic bowel disease</td>
<td>Rare</td>
</tr>
<tr>
<td>Systemic disorders (diabetes mellitus, thyroid and parathyroid disorders, connective tissue disease)</td>
<td>Rare</td>
</tr>
<tr>
<td>Intestinal parasites (Giardia, Strongyloides)</td>
<td>Rare</td>
</tr>
<tr>
<td>Abdominal cancer, especially pancreatic cancer</td>
<td>Rare</td>
</tr>
</tbody>
</table>

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**PEPTIC ULCER DISEASE**

<table>
<thead>
<tr>
<th>External Factors</th>
<th>Aggressive Factors</th>
<th>Defensive Factors</th>
<th>External Factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zollinger Ellison Syndrome</td>
<td>ACID</td>
<td>Mucus Secretion</td>
<td>Helicobacter pylori</td>
</tr>
<tr>
<td>PEPCIN</td>
<td>Bicarbonate production</td>
<td>NSAID use</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mucosal blood flow</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cell mediators</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Prostaglandins</td>
<td></td>
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</tr>
</tbody>
</table>
**H. Pylori**

- Test and treat strategy validated
- Strongly associated with duodenal ulcer
- Eradication decreases PUD recurrence
- Eradication not convincing in relieving symptoms in “non ulcer dyspepsia”
- Associated with development of gastric cancer
- Associated with “MALT Lymphoma”

**H. Pylori - Testing**

- **Non Endoscopic**
  - **Serologic test**: inexpensive, not specific for current infection, not recommended for confirmation of eradication.
  - **Urea Breath Test**: High sensitivity and specificity, useful for confirmation, at least 4 weeks post treatment, avoid PPI’s x 2 weeks
  - **Fecal antigen test**: High sensitivity and specificity, useful for confirmation 4-6 weeks post treatment, avoid PPI’s x 2 weeks
- **Endoscopic**
  - **Urea based CLO test**: rapid, inexpensive. Same caution regarding PPI’s and antibiotics
  - **Histology**: good sensitivity and specificity
  - **Culture**: cumbersome, not widely available and relatively insensitive

**H. Pylori - Treatment**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Days</th>
<th>% Eradication</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole 20mg BID</td>
<td>14 days</td>
<td>80-85</td>
</tr>
<tr>
<td>Amoxicillin 1gm BID</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Clarithromycin 500mg BID</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Lansoprazole 30mg BID</td>
<td>10-14 days</td>
<td>86</td>
</tr>
<tr>
<td>Metronidazole 500mg BID</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Clarithromycin 500mg BID</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Bismuth Subsalicylate 525mg QID</td>
<td>14 days</td>
<td>80</td>
</tr>
<tr>
<td>Metronidazole 250mg QID</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Tetracycline 500mg QID</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>Ranitidine 300mg BID</td>
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</tbody>
</table>
Clinical Case

- A healthy 27 y/o male presents with 4 days of acute watery diarrhea, with blood, fever to 102, cramping and nausea, without vomiting.

Initial Assessment

- Dehydration (BP, P, skin turgor, mucus membranes, urination, oral intake)
- Duration and severity of illness
- Evidence of inflammation (fever, tenesmus, bleeding)

Diarrhea

**ACUTE**

- Viral
- Bacterial - food borne, person to person, antibiotic use, travel,
- Food poisoning
- Associated with other serious illness

**CHRONIC**

- Infectious
- Inflammatory Bowel
- Ischemic Bowel
- Irritable Bowel
- Microscopic colitis
- Collagenous colitis
- Celiac disease

Identify Clinical Clues

- Clinical
  - Bloody diarrhea
  - Abdominal pain
  - Weight loss
  - Fecal WBC
- Epidemiologic
  - Food borne,
  - Recent antibiotics
  - Travel
  - Common source
  - Seasonal factors
Infectious Pathogens

Viral
- Norovirus
- Rotavirus
- Others “flu like”

Bacterial
- Salmonella
- Campylobacter
- Shigella
- E.Coli (O157:H7)
- C. Difficile
- Vibrio, Yersinia, Listeria

Parasites
- Giardia
- E. Histolytica
- Cryptosporidium
- Isospora,cyclospora,

Common Epidemiologic Factors

- Norovirus – winter outbreaks in families, nursing homes, schools, cruise ships, ingestion undercooked shell fish
- Salmonella – foodborne outbreaks, community acquired
- Campylobacter – community acquired, uncooked poultry
- Shigella – community acquired, person to person
- Shiga toxin producing E. coli – foodborne, especially undercooked hamburger or raw sprouts
- C.difcile – Nosocomial spread , antibiotic use
- Yersinia – community acquired, foodborne
- Giardia – Day care, waterborne transmission, travel
- Cryptosporidium – waterborne, travel, immunocompromised
- E.coli (enteropathic, etc) – travel

Empirical Antibiotic Therapy

- Moderate to severe traveler’s diarrhea
- Febrile, community – acquired if invasive disease suspected
- Severe nosocomial diarrhea, pending results of C.difficile toxin assay
- Suspected Giardia

- 1-5 days Cipro, norfloxacin , or levaquin
- 1-5 days cipro, norfloxacin, or levaquin
- Stop offending antibiotics, metronidazole 500mg TID, vancomycin 125mg QID
- Metronidazole 500mg TID 10 days

33 yo with bloody diarrhea

33 yo male presents with 4 weeks of loose stools with blood. 1-3 stools daily. Denies abdominal pain, fever, weight loss, recent travel or prior history of bleeding.

PMH: no chronic medical conditions, no previous surgery

Medications: none

FHX: Mother and Father alive, no chronic medical problems

2 siblings healthy

Physical exam: Healthy male, VS wnl

HEENT: WNL

GI: Non tender, NABS, no organomegaly

Anoscopy: no hemorrhoids, erythematous mucosa
Inflammatory Bowel Disease

- Chronic relapsing inflammatory disorder of the gastrointestinal tract
- Ulcerative Colitis - primarily involves mucosal and submucosal layers of colon - involves rectum and extends proximally to involving all or part of colon
- Crohn’s - characterized by transmural inflammation, often discontinuous, may involve alimentary tract from mouth to anus

Epidemiology

- Reported in all regions of the world
- More common in developed countries - United States and Western Europe
- In US
  - Prevalence: ~ 1.3 million persons
  - Gender distribution:
    - Crohn’s – slight female predominance
    - UC – slight male predominance
  - Age distribution - bimodal

IBD – Family History

- 10-25% IBD patients have 1st degree relative with IBD
- Relatives of patients with UC/ Crohn’s tend to get UC/ Crohn’s
- 10% lifetime risk for siblings and offspring of patients with IBD

IBD - Pathogenesis

- Exact etiology is unknown
- Proposed mechanism:
  - Intestinal epithelial barrier is breached by genetic variation, ineffective response to injury, or external agents (NSAID)
  - Chronic intestinal inflammation stimulated by luminal bacteria
  - Activation of cell-mediated immune response with immune dysregulation
Clinical Presentation

- Ulcerative Colitis: abdominal pain, bloody diarrhea, occasional fever, weight loss, increased incidence of cancer, especially with pancolitis
- Crohn’s: abdominal pain (often RLQ), diarrhea (with or without blood) fever, weight loss, fistulae
  Small bowel involvement: malabsorption of Vit B12, iron, folic acid, electrolytes, etc.

IBD - Lab Evaluation

- CBC, metabolic panel
- Elevated ESR, CRP
- Liver enzymes, albumin
- Stool – WBC’s, RBC’S
- Stool Cultures ova and parasites, bacterial, Clostridium Difficile
Crohn’s – Strictures, Fistulae

Extraintestinal Manifestations

• Arthropathy
• Dermatologic
• Liver

• Peripheral migratory
  Ankylosing spondylitis
• Erythema nodosum
  Pyoderma
  Gangrenosum
• Hepatic steatosis
  Primary Sclerosing
  Cholangitis

Treatment of IBD

• 5 – Aminosalicylates (oral / rectal)
• Corticosteroids/Budesonide
• Immunomodulators (azathioprine, 6-
  mercaptopurine)
• Antibiotics
• Biologics (anti-TNF agents)
• Probiotics
• Nutritional therapy
Factors Influencing Choice of Therapy

- Diagnosis - Crohn’s vs. UC
- Extent of disease
  - UC: proctitis vs left-sided colitis vs pancolitis
  - Crohn’s: colitis vs ileal vs small bowel
- Clinical Goal
  - Induction of remission vs maintenance
- Severity/ complications
  - Mild vs severe with or without complications
- Refractoriness

33 y.o. male Lab and Sigmoidoscopy results

CBC: WBC 7.2 normal differential, Hbg 14.2 mg/dl
ESR: 13
Stool culture: Negative bacterial pathogens, Ova and Parasites, and C. Difficile toxins

Sigmoidoscopy results: moderate inflamed friable mucosa to 20 cm, remaining mucosa to 65 cm appeared normal. Biopsies at 10 cm and 20 cm: mild active chronic proctitis. 30 cm: normal mucosa.

RX Hydrocortisone Enema for 2 weeks with remission

Cancer Surveillance Recommendations

- Not recommended for distal proctitis
- Begin after 8-10 years for pancolitis
- Begin at 12-15 years for left-sided colitis
- Immediate in those with sclerosing cholangitis
- Surveillance interval q 1-3 years
- Biopsies taken every 10 cm and “suspicious areas”