Hepatitis, Peptic Ulcer Disease
And Other Gastrointestinal Problems

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HEPATITIS

- INFECTIOUS: Viral, bacterial, mycobacterial, fungal
- TOXIC: Alcohol, acetaminophen, mushroom poisoning, other drugs
- METABOLIC: Shock, passive congestion, hemochromatosis, Wilson’s disease, fatty liver
- IMMUNOLOGIC: Auto-immune hepatitis

HEPATITIS Acute vs Chronic

- Acute
  - Viral- Hep A and B, CMV, HIV, Mono
  - Toxic: mushroom, acetaminophen, other drugs
  - Shock
  - Alcohol
- Chronic
  - Viral B and C
  - Alcohol
  - Medications, herbs
  - Passive congestion, hemochromatosis, Wilson’s disease, NAFLD, A1-AT deficiency
  - Auto-immune

HEPATITIS A

- Transmission: fecal / oral
- Household contacts
- Daycare facilities
- Common source epidemics from food/water
- Parenteral transmission via transfusion, rare but reported
HEPATITIS A

- 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

0 1 2 3 4 5 6 7 8 9 10 11 12 13 14

Months after exposure

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 year old) 0.5 ml @ 0, and 6 months

HEPATITIS B

- TRANSMISSION:
  Blood borne - vertical, transfusion, IVDU, needle stick/splash
  Sexual contact - multiple sexual partners, homosexual men
- INCUBATION PERIOD:
  45 - 160 days
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

Complications of Chronic Hepatitis B

- Chronic active hepatitis
- 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

• Alpha interferon – (PEG IFN-2a)
• Lamivudine (Epivir)
• Adefovir Dipivoxil (Hepsera)
• Entecavir
• Telbivudine
• 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, tattoos, 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
**Course of Disease Hep C**

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

**Serology of Hepatitis C**

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

**Treatment of Hepatitis C**

- Pegalated interferon plus Ribavirin
- Patient Education: ETOH abstinence
  - Sexual behavior
  - Toothbrush, razors, etc.
- Hepatitis A, B vaccines

**Treatment Response Rates**

- Treatment Response by Genotype and Duration of Therapy
  - Geno 1 - 12 months
  - Geno 2,3 - 6 months
  - Treatment Response Rates:
PEG IF + Ribavirin

- Length of therapy: Genotype 1 – 48 weeks
  Genotype 2 – 24 weeks
- 3 month quantitative viral PCR
  2 log decrease
- 6 month post therapy viral PCR
- Treatment of anemia with Erythropoietin and GCSF for ANC<500

HEPATITIS D

- Transmission: blood borne (IVDU)
- Serology: RIA - HDV antibody
- Course of disease:
  Acute: coinfection with HBV required
  Fulminant: coinfection 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

ALCOHOLIC HEPATITIS

- Clinical: jaundice, tender hepatomegaly, leukocytosis, fever, vomiting
- Laboratory: AST/ALT ratio 2:1
  Transaminase elevation < 300
  Alkaline phosphatase < 400
  Bilirubin elevated
- Treatment: abstinence, nutrition, high index of suspicion for SBP (ANC > 250)
### TOXIC HEPATITIS

- **Industrial:** Carbon tetrachloride
- **Ingestion:** Aminita mushrooms
- **Medications:** many

**Drugs and Other Substances That May Cause Abnormal Liver Function Test Results**

<table>
<thead>
<tr>
<th>Substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
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<tr>
<td>Antituberculosis agents</td>
</tr>
<tr>
<td>Metabolism</td>
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<tr>
<td>Carcinoid</td>
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<tr>
<td>Hypertension inhibitors</td>
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<tr>
<td>Glyburide (Diabeta, Glynase)</td>
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<tr>
<td>Metformine (Glucophage)</td>
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<tr>
<td>Cimetidine (Tagamet)</td>
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<tr>
<td>Ranitidine (Zantac)</td>
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<tr>
<td>Histamine blockers</td>
</tr>
<tr>
<td>Anticonvulsants</td>
</tr>
<tr>
<td>Antiepileptics agents</td>
</tr>
<tr>
<td>Significant</td>
</tr>
<tr>
<td>Alkaloid</td>
</tr>
<tr>
<td>Tetrahydroxycarbamide</td>
</tr>
<tr>
<td>Sulfonylureas</td>
</tr>
<tr>
<td>Glomerular</td>
</tr>
<tr>
<td>Antihistamines</td>
</tr>
<tr>
<td>Glyburide</td>
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<tr>
<td>Antithyroid agents</td>
</tr>
<tr>
<td>Anticoagulants</td>
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<tr>
<td>Oral hypoglycemic agents</td>
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<td>Oral contraceptives</td>
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<td>Sulfonylureas</td>
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</tr>
<tr>
<td>Oral contraceptives</td>
</tr>
</tbody>
</table>

#### Medications

- **Acetaminophen**
- **Antibiotics**
  - Ciprofloxin, Sulf, Nitrofurantoin, Amoxicillin-clavulanic
  - Isoniazid
  - Ketoconazole, Fluconazole, Terbinafine
- **Anticonvulsants**
  - Phenytoin, Carbamazepine
- **Statins**
  - Simvastatin, Lovastatin, Atorvastatin, Pravastatin, Rosuvastatin
- **NSAID**
- **Anti-dysrhythmics**
  - Amiodarone
- **Sulfonylureas**
  - Glypizide, Glyburide
- **Glitazones**
  - Pioglitazone, Rosiglitazone
- **Antiretrovirals**
  - Protease inhibitors
  - Nucleoside analogues
- **Niacin**
Herbs
- Chaparral leaf
- Germander
- Alchemilla
- Germander
- Senna

Drugs/Others
- Anabolic steroids
- Cocaine
- MDMA, ecstasy
- Angel dust (Phencyclidine)
- Glues/solvents
  - Toluene, chloroform, trichloroethylene

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

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

**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, 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

**Metabolic Syndrome**
- Insulin resistance
- NAFLD
- Obesity
- Hyperlipidemia (inc Trig, LDL; low HDL)
- Hypertension
Diffuse Steatosis on Non-Contrast CT

Fatty Liver on Ultrasound

AUTOIMMUNE HEPATITIS

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

External Factors | Aggressive Factors | Defensive Factors | External Factors
---|---|---|---
Zollinger Ellison Syndrome | ACID | Mucus Secretion | Helicobacter pylori
Peptic ulcer disease | PEPCIN | Bicarbonate production | NSAID use

Dyspepsia

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

- Risk factors for serious disease:
  - Age > 50 years
  - Dysphagia
  - Protracted vomiting
  - Anorexia/weight loss
  - Melena or anemia
  - Palpable mass

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>Dyspepsia caused by structural or biochemical disease</td>
<td></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>Gastroparesis</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>Mediations (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>
GERD TREATMENT

• PPI’s now recommended first line
• PPI’s must be given 30-60 min ac
• Reducing fat, chocolate, coffee, alcohol, and peppermint intake
• Avoiding onions, citrus, tomato-based foods
• Smoking cessation, weight loss
• Avoid late meals, elevate head of bed

Endoscopic Screening for Barrett's

• Recommended in patients over 50 y/o or with more than 5 years of symptoms
• Replacement of squamous epithelium in the distal esophagus with metaplastic intestinal columnar epithelium
• 10-20% Adults in US have GERD
• ~10% of pts with GERD have Barrett’s
• 5-10% of pts with Barrett’s will develop cancer

Surgical Indications - GERD

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

GERD Surgical Candidates

• Endoscopic esophagitis
• Normal esophageal motility
• Normal gastric emptying
• At least partial response to acid suppression therapy
GERD Surgical Consequences

- 10-20% patients have solid food dysphagia, belching or diarrhea
- 50-60% of patients require antireflux medications 3-5 years post procedure

GERD Endoscopic Treatments

- Stretta Procedure – radiofrequency heating of gastroesophageal junction
- Endocinch Procedure – endoscopic suture ligation GE junction
**H. Pylori**

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

**H. Pylori - Testing**

- CLO test – invasive, requires endoscopy
- Urea Breath Test – sensitive, office based testing may be inconsistent. Allow 4 weeks post treatment.
- Serology – not reliable for post treatment

**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>Amoxicillin 1gm 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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</table>
**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
IBD - Pathogenesis

- Bacteria
- Antigen presenting cell
- Type I helper T cell
- Macrophage
- Macroage migration inhibitor factor
- TNF, IL-1, IL-6
- IL-12, IL-18

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.

DDx Chronic Diarrhea

- Infectious Colitis - sudden onset pathogens in stool
- IBS - meets Rome II criteria, no alarm signs
- Ischemic Colitis - older age, sudden onset, often painful
- Clostridium difficile colitis - recent antibiotic use, C. difficile toxin in stool
- Microscopic colitis
- Adrenal insufficiency

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
Ulcerative Colitis

- Continuous mucosal friability with easy bleeding
- Not transmural, no small bowel involvement
- Fissures and fistulae are uncommon
- Complications include malignancy and toxic megacolon

Crohn’s Disease

- Characterized by “skip areas”, cobblestone inflammation, submucosal granulomas
- Transmural inflammation
- Fissures, fistulae, and small bowel involvement common
- Extra intestinal involvement: arthritis, erythema nodosum, aphthous ulcers, nutritional deficiencies
Crohn’s – Strictures, Fistulae

Extraintestinal Manifestations

- Arthropathy
  - Peripheral migratory
  - Ankylosing spondylitis
- Dermatologic
  - Erythema nodosum
  - Pyoderma Gangrenosum
- Liver
  - Hepatic steatosis
  - Primary Sclerosing Cholangitis
Treatment of IBD

- Aminosalicylates
- Corticosteroids/Budesonide
- Immunmodulators
- Antibiotics
- Anti-metabolites
- Biologic Modifiers
- 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

Aminosalicylates

- Sulfasalazine (Azulfadine) – 5 ASA with AZO bond to sulfapyridine
- Mesalamine
  - (Asacol) coated tablets
  - (Pentasa) capsule granules
- Olsalazine (Dipentum)
- Balsalzide (Colazal) – 5 ASA with 4 amino benzoyl beta alanine
**Corticosteroids**

- **Efficacy:**
  - 90% response rate
- **Oral dose:**
  - Prednisone 40-60mg/day, taper over 8-12 weeks
- **IV dose:**
  - Hydrocortisone 300mg/day, solumedrol 60-80 mg/day
- **Indications:**
  - Induction of remission in moderate to severe UC or CD
  - Not indicated for maintenance

**Budesonide**

- Extensive first pass metabolism, results in little systemic absorption, mostly active topically distal ilium and colon
- Indicated for remission induction mild to moderate UC or CD
- Dose: 9mg daily x 8 weeks

**Immunomodulators**

**Azathioprine and 6 MP**

- Purine analogs – inhibit ribonucleotide synthesis
- **Efficacy:** 50-80%
- **Dosing:** Azathioprine 1.5-2.5 mg/kg/day
  6MP 1-1.5 mg/kg/day
- **Indications:** steroid dependent UC or CD
  maintenance or remission after steroids, cyclosporin or infliximab

**Cyclosporin**

- Indications: severe steroid refractory active UC, refractory Crohn’s – related fistulae

**Methotrexate**

- Indication: induction or maintenance of remission in steroid dependent Crohn’s; those who fail 6 MP/ AZA or infliximab
- Response ~30%
- **Dosing:** Induction : 25mg IM/SQ weekly
  Maintenance: 15 mg IM/SQ weekly

**Immunomodulators**

- Indications: steroid dependent UC or CD
**Antibiotics**  
*Metronidazole and Ciprofloxin*

- Have been used for monotherapy in mild UC or CD
- Primarily used as adjunctive therapy for induction of remission
- May be most useful in CD pts with fistula

**Infliximab (Remicade)**

- Mechanism of action:  
  - Inhibits TNF alpha
- Indications:  
  - Induction of remission in moderate-severe CD  
  - 1st line therapy for fistulizing CD  
  - Should be avoided in bowel obstruction
- Response: 60-80 %
- Dosing: 5mg/kg IV over 2 hrs, interval variable

**Probiotics**

- Mechanism is tolerance restitution  
  - Decreased TH-1, increased TH-2  
  - Increase T suppressor cells
- Mesalamine 800mg tid vs *E.Coli* (O6:D5:H1) 2 caps BID
- Gentamycin pre-treatment
- Remission: *E.Coli* 65%, mesalamine 75%
- Realpse: *E.Coli* 76%, mesalamine 73%
  * Rembaker Lancet, 1999

**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”