Conflict of Interest Disclosures

Dr. Hemstreet has no conflicts to disclose.
Learning Objectives

1. Review and apply national guideline treatment strategies for the following gastrointestinal (GI) disorders: gastroesophageal reflux disease (GERD), peptic ulcer disease (PUD), ulcerative colitis, Crohn’s disease, viral hepatitis, chronic liver disease, upper GI bleeding, constipation, diarrhea, irritable bowel syndrome (IBS), nausea, vomiting, pancreatitis, prevention of stress related mucosal disease (SRMD).

2. Recommend appropriate pharmacologic and nonpharmacologic interventions for the treatment of GERD.

3. Differentiate between clinical signs, symptoms, risk factors, and treatment of both *Helicobacter pylori* and nonsteroidal anti-inflammatory drug (NSAID)-associated PUD.
4. Discuss the role of pharmacologic intervention in the treatment of nonvariceal upper GI bleeding.

5. Review the clinical differences in signs, symptoms, and treatment of Crohn’s disease and ulcerative colitis.

6. Identify the common manifestations of chronic liver disease and their treatment.

7. Review the treatment of both acute and chronic viral hepatitis.
8. Recognize pertinent information for educating patients and prescribers regarding the appropriate use of pharmacologic agents for various GI disorders.

9. Recommend appropriate pharmacologic and nonpharmacologic interventions for diarrhea and constipation.
10. Review recommendations for the treatment and prevention of nausea and vomiting

11. Discuss the clinical and treatment differences between acute and chronic pancreatitis.

12. Discuss the role of pharmacologic intervention in the treatment of IBS.
Patient Case # 1

- **HPI:** 55 year old man with 8-month history of GERD symptoms 4-5 days/week. Currently receiving lansoprazole 15 mg once daily by mouth. No ulcers or erosions via endoscopy.

- **PMH:** Hypothyroidism, GERD

- **MEDS:** Lansoprazole 15 mg once daily, levothyroxine 100 mcg daily.
Patient Case # 1

Which treatment approach is best for this patient?

A. Add metoclopramide 10 mg 4 times/day
B. Increase lansoprazole to 15 mg twice daily.
C. Switch to omeprazole 20 mg daily
D. Add sucralfate 1000mg 4 times/day
Treatment of GERD

- Targeted nonpharmacologic/Lifestyle modifications
- Antacids
- Acid suppression (as needed or scheduled)
  - Proton Pump Inhibitors
    - Esomeprazole strontium
  - Histamine-2 Receptor Antagonists
- Promotility Agents
- Surgical intervention
### GERD Guidelines 2013 Summary

<table>
<thead>
<tr>
<th>Area</th>
<th>Recommendation (Strength/Evidence)</th>
</tr>
</thead>
</table>
| Diagnosis  | • Empiric therapy with a PPI is recommended if typical symptoms of heartburn or regurgitation (Strong/Mod)  
• Screening for *H. pylori* is NOT recommended (Strong/Low) |
| NonPharm   | • Weight loss if overweight or recent weight gain (Cond/Mod)  
• Elevate head of bed/avoid meals 2-3 hours prior to bedtime if nocturnal symptoms (Cond/Low)  
• Routine global elimination of food triggers NOT recommended (Cond/Low) |

*Am J Gastroenterol* 2013; 108:308 – 328;
## GERD Guidelines 2013 Summary

<table>
<thead>
<tr>
<th>Area</th>
<th>Recommendation (Strength/Evidence)</th>
</tr>
</thead>
</table>
| **Treatment** | - Erosive esophagitis = 8 week course of PPI; no major differences in products (Strong/High)  
- Use maintenance PPIs if return of symptoms or complications (Strong/Mod)  
- Bedtime H2RAs can be used if AM PPI and nighttime symptoms but development of tachyphylaxis occurs (Cond/Low)  
- Further testing needed prior to use of metoclopramide or baclofen (Cond/Mod)  |
| **Dosing**    | - Traditional PPIs 30-60 minutes prior to meals (Strong/Mod)  
- Newer PPIs offer dosing flexibility in relation to meals (Cond/Mod)  
- Initiate PPIs once daily prior to AM meal (Strong/Mod)  
- Twice daily PPIs if partial response to once daily and/or nighttime symptoms (Strong/low)  
- Twice daily if partial response to once daily or can switch to another PPI (Cond/Low) |
## PPI Safety Concerns

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Prevention and Management</th>
</tr>
</thead>
</table>
| Risk of Fracture (Hip, wrist, spine) | • Concern for fractures should not affect decision to use PPIs except in patients with other known risk factors for hip fracture (Cond/Mod)  
• Patients with osteoporosis can remain on PPIs  
• Limit dose and duration  
• Ensuring adequate Calcium and Vitamin D  
• BMD screening if at risk for low bone mass  
• Weight bearing Exercise                                                                 |
| Hypomagnesemia                  | • Re-evaluate need  
• Limit dose and duration  
• Consider baseline testing (diuretics, digoxin)  
• Supplementation                                                                                   |
# PPI Safety Concerns

<table>
<thead>
<tr>
<th>Adverse Effect</th>
<th>Prevention and Management</th>
</tr>
</thead>
</table>
| Hypomagnesemia                              | • Re-evaluate need  
• Limit dose and duration  
• Consider baseline testing (diuretics, digoxin)  
• Supplementation |
| *Clostridium difficile* associated diarrhea  | • Re-evaluate need  
• Limit dose and duration  
• Evaluate for *C. difficle* if patient receiving PPI has diarrhea that is not improving. Have patients report diarrhea.  
• Report cases to Medwatch |
| Community acquired Pneumonia                | • Short term use may increase risk; long term risk is not elevated (Cond/Mod) |
Other PPIs Issues

- Switching of PPIs can be considered in patients with side effects (Cond/Low)

- Interaction with clopidogrel and PPIs is not considered significant (Strong/High)

- First step in refractory GERD is optimization of PPI therapy (Strong/Low)
Patient Case # 1

Which treatment approach is best for this patient?

A. Add metoclopramide 10 mg 4 times/day

B. Increase lansoprazole to 15 mg twice daily.

C. Switch to omeprazole 20 mg daily

D. Add sucralfate 1000mg 4 times/day
Patient Case # 2

- **HPI**: 68 year old female with heme positive, stools anemia, and abdominal pain. Use of OTC ketoprofen for 2 months.

- **PMH**: Type 2 DM, Peripheral neuropathy, Hypertension

- **MEDS**: metformin, aspirin, gabapentin, lisinopril

- **Diagnostics**: endoscopy reveals 1 cm gastric ulcer with an intact clot, *H. pylori* negative via CLO Test
Patient Case # 2

Which one of the following treatments is best for this patient’s ulcer?

A. Ranitidine 150 mg 2 times/day for 4 weeks
B. Lansoprazole 30 mg 2 times/day plus amoxicillin 1000 mg 2 times/day plus clarithromycin 500 mg 2 times/day for 10 days.
C. Lansoprazole 30 mg/day for 8 weeks
D. Misoprostol 200 mcg 2 times/day for 8 weeks.
Peptic Ulcer Disease (PUD)

- **Classification**
  - Duodenal ulcer
  - Gastric ulcer

- **Etiologies**
  - *Helicobacter pylori* (carcinogen)
  - NSAIDs

- **Symptoms**
  - Epigastric pain, nausea, anorexia, belching
  - May be temporally related to food intake
NSAID Associated PUD

- **NSAIDs have topical and systemic adverse GI effects**
  - COX-2 vs. COX-1 effects

- **Risk Factors**
  - Age >60, History of PUD +/- complications
  - Corticosteroids, anticoagulants, low dose aspirin

- **Contributing factors**
  - *H. pylori*, Smoking, CVD, RA, SSRIs
Management of NSAID-Associated PUD

- Remove and reevaluate need for NSAID and/or aspirin
  - Test for *H. pylori* and treat if positive

- Acid suppression
  - PPI for 8-12 weeks

- Misoprostol

- COX-2 Inhibitors
  - Cardiovascular risks
  - Use with aspirin
Patient Case # 2

Which one of the following treatments is best for this patient’s ulcer?

A. Ranitidine 150 mg 2 times/day for 4 weeks

B. Lansoprazole 30 mg 2 times/day plus amoxicillin 1000 mg 2 times/day plus clarithromycin 500 mg 2 times/day for 10 days.

C. Lansoprazole 30 mg/day for 8 weeks

D. Misoprostol 200 mcg 2 times/day for 8 weeks.
Patient Case #3

- **HPI**: 42 year old male with sharp epigastric pain for 6 weeks. Pain is worse with eating and is present approximately 5 days per week. Some relief with OTC antacids.

- **MEDS**: antacids as needed

- **Allergies**: Sulfa (rash)

- **UBT for *H. pylori*** is positive
Patient Case #3

Which one of the following treatments for *H. pylori* is best?

A. Amoxicillin, clarithromycin, omeprazole for 10 days
B. Cephalexin, clarithromycin, omeprazole for 10 days
C. Bismuth, tetracycline, metronidazole, omeprazole for 14 days
D. Levofloxacin, metronidazole, omeprazole for 10 days
Diagnosis of *H. pylori*

- **Invasive testing (endoscopic)**
  - Histology
  - Rapid urease (affected by antisecretory agents)
  - Culture

- **Non-invasive testing**
  - Serologic (IgG)
  - Urea breath test (affected by antisecretory agents)
  - Fecal antigen (affected by antisecretory agents)
Treatment of *H. pylori*

- **Triple therapy**
  - PPI + amoxicillin or metronidazole + clarithromycin
  - 10-14 days of treatment (14 preferred)
  - Efficacy affected by previous macrolide exposure

- **Quadruple Therapy**
  - PPI + Bismuth + Metronidazole + Tetracycline
  - 1st line, PCN allergy, previous macrolide exposure, failure of triple therapy
  - 10-14 days of treatment (14 preferred)
Patient Case #3

Which one of the following treatments for *H. pylori* is best?

- Amoxicillin, clarithromycin, omeprazole for 10 days
- Cephalexin, clarithromycin, omeprazole for 10 days
- Bismuth, tetracycline, metronidazole, omeprazole for 14 days
- Levofloxacin, metronidazole, omeprazole for 10 days

Handout Page 96; Answer Page 155
Patient Case #4

- **HPI:** 35 year old male with mild-moderately active ulcerative colitis confined to descending colon and rectum.

- **PMH:** UC, seasonal allergies

- **Meds:** Loratidine 10 mg/day
Patient Case #4

Which drug regimen is best at this time?

A. Balsalazide 750 mg twice daily
B. Methotrexate 25 mg IM weekly
C. Infliximab 5 mg/kg IV
D. Mesalamine enema 1000 mg daily
<table>
<thead>
<tr>
<th>Clinical Findings</th>
<th>Ulcerative Colitis</th>
<th>Crohn’s Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel Involvement</td>
<td>Rectum/Colon</td>
<td>Mouth to Anus</td>
</tr>
<tr>
<td>Perianal Involvement</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Depth</td>
<td>Superficial</td>
<td>Submucosa/deeper</td>
</tr>
<tr>
<td>Pattern of inflammation</td>
<td>Continuous</td>
<td>Patchy</td>
</tr>
<tr>
<td>Histology</td>
<td>Crypt abscesses</td>
<td>Granulomas</td>
</tr>
<tr>
<td>Fistula, perforation, or</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Strictures</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Toxic megacolon</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Colorectal cancer</td>
<td>Yes</td>
<td>Uncommon</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Rare</td>
<td>Yes</td>
</tr>
<tr>
<td>Pseudopolyps</td>
<td>Common</td>
<td>Fairly Common</td>
</tr>
</tbody>
</table>
Drug Treatment Options

- **5-Aminosalicylates**
  - Sulfasalazine
  - Mesalamine
  - Olsalazine
  - Balsalazide

- **Antibiotics**
  - Metronidazole
  - Ciprofloxacin

- **Corticosteroids**
  - Prednisone
  - Budesonide

- **Immunomodulators**
  - Azathioprine
  - 6-Mercaptopurine
  - Methotrexate
  - Cyclosporine
  - Tacrolimus

- **Antibiotics**

- **Biologics**
  - Infliximab
  - Adalimumab
  - Certolizumab
  - Golimumab
  - Natalizumab
  - Vedolizumab

- **Anti-TNFα**
- **Anti α-integrin**
Approach to the Treatment of IBD

1. **Indentify disease:** UC vs. CD

2. **Severity:** Active (mild to fulminant) or remission

3. **Determine extent and location of disease**
   - Extensive vs. left-sided vs. rectal

4. **Pick drug(s) based on**
   - Onset of action
   - Formulation (Oral, Topical, Parenteral)
   - Effectiveness
   - Potential adverse effects or contraindications
## IBD Treatment Guidelines

<table>
<thead>
<tr>
<th>Severity</th>
<th>UC</th>
<th>Crohn’s</th>
</tr>
</thead>
</table>
| Mild-Moderate | Extensive: Aminosalicylate or Budesonide +/- topical  
Left sided: Enema  
Rectal: suppository | Aminosalicylate or Budesonide (ileal) +/- topical  
Left sided: Enema  
Rectal: suppository |
| Moderate to Severe | TNF-α inhibitor +/- Azathioprine/6-MP +/- Corticosteroid (short-term)  
Vedolizumab (last line) | TNF-α inhibitor  
Azathioprine/6-MP or methotrexate +/- Corticosteroid (short-term)  
Natalizumab or Vedolizumab (last line) |
# Key Safety Concerns in IBD

<table>
<thead>
<tr>
<th>Drug(s)</th>
<th>Adverse Effects</th>
</tr>
</thead>
</table>
| TNF-alpha antagonists       | • Risk of infection (screen for TB and Viral hepatitis)  
                                  • Risk of Heart Failure and/or exacerbation  
                                  • Hepatosplenic T-cell lymphoma when used with azathioprine or 6-MP in young male patients  
                                  • Antibody formation and infusion reactions (infliximab) |
Patient Case #4

Which drug regimen is best at this time?

A. Balsalazide 750 mg twice daily
B. Methotrexate 25 mg IM weekly
C. Infliximab 5 mg/kg IV
D. Mesalamine enema 1000 mg daily
Patient Case #5

- **HPI:** 25 year old woman with Crohn’s disease affecting the colon and terminal ileum. Presents with a 12 week history of crampy abdominal pain, fever, fatigue, and 3-4 bloody stools per day.

- **MEDS:** None

- **PMH:** Crohn’s Disease (new onset)

- **Vitals:** Ht 65 inches, Wt 120 lb, Temp 98°F, HR 100 bpm, BP 118/68 mmHg, RR 18 bpm

- **Allergies:** Penicillin (rash)
Patient Case #5

Which of the following therapeutic choices is best?

A. Pentasa 4 grams/day

B. Infliximab 275 mg IV + azathioprine 110 mg

C. Entocort 9 mg once daily

D. Adalimumab 40 mg SC
Patient Case #6

- **HPI:** 47 year old woman with nausea, abdominal pain, fever. Abdominal distention with tenderness and shifting dullness.

- **PMH:** Cirrhosis (Class C)

- **MEDS:** Furosemide, spironolactone

- **Diagnostics:** Paracentesis (albumin 0.9 g/dl, WBC 1000/mm$^3$ (45% PMNs), Scr 1.2 mg/dl, BUN 37 mg/dl, AST IU/ml, ALT 20 IU/ml, Albumin 2.5 g/dl, T bili 3.2 mg/dl
Patient Case #6

Which recommendation is best at this time for treatment?

A. Intravenous albumin and await culture results
B. Intravenous vancomycin plus tobramycin
C. Intravenous cefotaxime plus albumin
D. Oral trimethoprim/sulfamethoxazole DS daily
Complications of Cirrhosis

- Variceal bleeding
- Ascites
- Infection
- Hepatorenal Syndrome
- Hepatopulmonary Syndrome
- Encephalopathy
Spontaneous Bacterial Peritonitis

**Definition:** Primary infection of the ascitic fluid

**Pathogens**
- Enteric gram negatives
- Streptococci

**Clinical features**
- Fever, abdominal pain, AMS, vomiting
- High risk of hepatorenal syndrome, increased mortality
- Ascitic fluid PMN > 250 mm$^3$
SBP Treatment and Prevention

- **Treatment:** 3rd gen Cephalosporin + albumin

- **Primary Prevention**
  - During setting of an acute GI bleed
  - Ascitic fluid protein $< 1.5$ g/dl + Scr $> 1.2$ mg/dl or BUN $> 25$ mg/dl or Na $< 130$ mEq/L, or CP $> 9$ with bilirubin $> 3$ mg/dl

- **Secondary Prevention:** any patient with prior episode

- **Hospital:** Ceftriaxone/Cefotaxime, Fluoroquinolone

- **Outpatient:** TMP/SMX, Norfloxacin/ciprofloxacin
Patient Case #6

Which recommendation is best at this time for treatment of this patient’s SBP?

- Intravenous albumin
- Intravenous vancomycin plus tobramycin
- Intravenous cefotaxime plus albumin
- Oral trimethoprim/sulfamethoxazole DS daily

Handout Page 119; Answer Page 156
Patient Case #7

- **HPI**: A 56-year-old man is admitted with a 2-day history of confusion, disorientation, somnolence, and reduced oral intake. On examination he is afebrile, with abdominal tenderness, reduced reflexes, dry mucous membranes, and asterixis.

- **PMH**: Cirrhosis, alcohol abuse

- **Meds**: Propranolol 40 mg 3 times/day

- **Diagnostics**: Paracentesis is negative for infection
Patient Case #7

Which treatment is best for this patient?

A. Rifaximin 550mg orally twice daily
B. Lactulose 30 ml orally every 2 hours
C. PEG 3350 17g orally twice daily
D. Ceftriaxone 1 g IV once daily
Hepatic Encephalopathy

- **Subtypes according to underlying disease**
  - Type A: Due to acute liver failure
  - Type B: Due to portosystemic bypass or shunting
  - Type C: Due to cirrhosis

- **Duration**
  - Episodic
  - Recurrent (occurs within a time frame of 6 months or less)
  - Persistent: Denotes a pattern of behavioral alteration that is always present and interspersed with relapses of overt HE.

- **Presence or absence of precipitating factors**
  - Precipitated
  - Nonprecipitated
# Hepatic Encephalopathy

<table>
<thead>
<tr>
<th>West Haven Criteria</th>
<th>ISHEN*</th>
<th>Clinical Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Unimpaired</strong></td>
<td></td>
<td>No current or history of encephalopathy</td>
</tr>
<tr>
<td><strong>Minimal</strong></td>
<td>Covert</td>
<td>Psychometric or neuropsychological alterations of tests exploring psychomotor speed/executive functions or neurophysiological alterations without clinical evidence of mental change</td>
</tr>
</tbody>
</table>
| **Grade I**         |        | Trivial lack of awareness  
|                     |        | Euphoria or anxiety  
|                     |        | Shortened attention span  
|                     |        | Impairment of addition or subtraction  
|                     |        | Altered sleep rhythm |
| **Grade II**        | Overt  | Lethargy or apathy  
|                     |        | Disorientation for time  
|                     |        | Obvious personality change  
|                     |        | Inappropriate behavior  
|                     |        | Dyspraxia  
|                     |        | Asterixis |
| **Grade III**       |        | Somnolence to semistupor  
|                     |        | Responsive to stimuli  
|                     |        | Confused  
|                     |        | Gross disorientation  
|                     |        | Bizarre behavior |
| **Grade IV**        |        | Coma |

Hepatology 2014;715-35
Episodic Overt Hepatic encephalopathy

- Remove/treat precipitating factors
  - Infection, drugs, electrolyte disturbances, constipation, bleeding

- Lactulose
  - Titrate to 2-4 loose BMs/day
  - Acute and maintenance

- Rifaximin 550mg twice daily
  - Similar efficacy to lactulose
  - Approved for add on prevention after > 1 episode

- Neomycin, metronidazole
  - Renal insufficiency (neomycin)
Patient Case #7

Which treatment is best for this patient?

A. Rifaximin 550mg orally twice daily
B. Lactulose 30 ml orally every 2 hours
C. PEG 3350 17g orally twice daily
D. Ceftriaxone 1 g IV once daily

Handout Page 119; Answer Page 156
Patient Case #8

- **HPI:** 45-year old woman with history of IVDA. Diagnosed 8 months ago with HBV. Treatment naive. No ascites or encephalopathy.

- **Labs**
  - Scr 0.9 mg/dl, INR 1.3, Albumin 3.9 g/dl
  - AST 650 IU/ml, ALT 850 IU/ml
  - HBSAg (+), HBeAg (+), YMDD mutation
  - HBV DNA 107,000 IU/ml

- **Liver biopsy:** severe necroinflammation and bridging fibrosis.
Patient Case #8

What is the most appropriate course of action at this time?

A. No treatment; Recheck HBV DNA in 6 months
B. Initiate PEG-IFN + ribavirin
C. Initiate lamivudine 100 mg/day
D. Initiate tenofovir 300 mg/day
Hepatitis B

- DNA Virus, Genotypes A-H

- Transmission
  - Parenteral, bodily fluids, sexual contact, perinatal

- Detect via serologies, symptoms, LFTs
  - Patients with active disease will be HBsAg (+)

- Treat patients with chronic disease (> 6 months)
  - > 2 x ALT, HBV DNA > 20,000 IU/ml
Chronic Hepatitis B Treatment

• Need to distinguish if HBV:
  • is HBeAg positive or negative
  • Harbors the “YMDD mutation” of the DNA polymerase

• Difficult patient populations
  • Decompensated liver disease
  • Co-infection
  • Treatment experienced
<table>
<thead>
<tr>
<th>HBV Population</th>
<th>Preferred Treatment Options</th>
<th>Duration</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBeAg positive</td>
<td>Entecavir and tenofovir are preferred oral agents Use of the other oral reverse transcriptase inhibitors is possible but not preferred</td>
<td>Minimum of 1 year</td>
<td>Preferred if contraindications or nonresponse to INFα</td>
</tr>
<tr>
<td></td>
<td>INFα PEG-INFα</td>
<td>16 weeks 48 weeks</td>
<td>If contraindication or no response, use entecavir and tenofovir</td>
</tr>
<tr>
<td>HBeAg negative</td>
<td>Entecavir and tenofovir are preferred oral agents Use of the other oral reverse transcriptase inhibitors is possible but not preferred</td>
<td>&gt; 1 year</td>
<td>Preferred if contraindications or no response to INFα</td>
</tr>
<tr>
<td></td>
<td>INFα PEG-INFα</td>
<td>≥ 1 year</td>
<td>If contraindication or nonresponse, use entecavir and tenofovir</td>
</tr>
</tbody>
</table>
Nucleoside Analog Adverse Effects

- **Class effects**
  - Rebound hepatitis upon discontinuation
  - GI Effects (N/V/D/Abdominal pain)
  - HIV resistance
  - Lactic Acidosis (rare)
  - Reductions in bone mineral density

- **Nephrotoxicity (adefovir)**

- **Telbivudine**
  - Elevations in CK
  - Peripheral neuropathy

- **Renally dose adjust all medications**
Patient Case #8

- What is the most appropriate course of action at this time?

  - No treatment; Recheck HBV DNA in 6 months
  - Initiate PEG-IFN + ribavirin
  - Initiate lamivudine 100 mg/day
  - Initiate tenofovir 300 mg/day

Handout Page 135; Answer Page 156
Hepatitis B Vaccine Recommendations

- All HCP should receive 3 dose HBV series
  - Additional doses for incompletely vaccinated

- Testing for HCP at risk for HBV infection
  - HBsAg + anti-Hbc or Anti-HBs if no postvaccination testing
  - Test for Anti-HBs 1-2 months after last dose for recently vaccinated

- Immune = documented 3 dose series + anti-HBs ≥ 10 mIU/ml

- If completely vaccinated and anti-HBs < 10 mIU/ml administered one additional dose and retest at 1-2 months.
  - Administered 2 additional doses if needed

*MMWR 2013;62:1-19*
## Post-exposure Management

<table>
<thead>
<tr>
<th>HBV Status of HCP</th>
<th>Postexposure Testing</th>
<th>Postexposure Prophylaxis</th>
<th>Postvaccination Serologic Testing&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source Patient (HBsAg)</td>
<td>HCP Testing (anti-HBs)</td>
<td>HBIG</td>
<td>Vaccination</td>
</tr>
<tr>
<td>Documented responder&lt;sup&gt;b&lt;/sup&gt;</td>
<td>No action needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Documented nonresponder after six doses&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Positive /unknown</td>
<td>HBIG x 2 separated by 1 month</td>
<td>—</td>
</tr>
<tr>
<td>Negative</td>
<td>No action needed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Response unknown after three doses&lt;sup&gt;d&lt;/sup&gt;</td>
<td>Positive /unknown</td>
<td>HBIG x 1</td>
<td>Initiate revaccination</td>
</tr>
<tr>
<td>Negative</td>
<td>&lt; 10 mIU/mL&lt;sup&gt;d&lt;/sup&gt;</td>
<td>None</td>
<td></td>
</tr>
<tr>
<td>Any result</td>
<td>≥ 10 mIU</td>
<td>No action needed</td>
<td></td>
</tr>
<tr>
<td>Unvaccinated or incompletely vaccinated or vaccine refusers</td>
<td>Positive /unknown</td>
<td>HBIG x 1</td>
<td>Complete vaccination</td>
</tr>
<tr>
<td>Negative</td>
<td>—</td>
<td>None</td>
<td>Complete vaccination</td>
</tr>
</tbody>
</table>

<sup>a</sup>1–2 months after last dose of HBV vaccine series.<br><sup>b</sup>Anti-Hbs > 10 mIU/mL after > 3 doses of HBV vaccine.<br><sup>c</sup>Anti-Hbs < 10 mIU/mL after > 6 doses of HBV vaccine.<br><sup>d</sup>HCPs who have anti-HBs < 10 mIU/mL, or who are unvaccinated or incompletely vaccinated, and sustain an exposure to a source patient who is HBsAg positive or has unknown HBsAg status, should undergo baseline testing for HBV infection as soon as possible after exposure, and follow-up testing about 6 months later.<br>HBIG = hepatitis B immune globulin; HBV = hepatitis B virus; HCP = health care provider.

*MMWR 2013;62:1-19*
Patient Case #9

- **HPI:** 38 year old male with chronic hepatitis C (genotype 1a) compensated disease.

- **MEDS:** none

- **NKDA**

- **LABS:**
  - AST 350 IU/ml, ALT 420 IU/ml
  - HCV RNA 950,000 IU/ml
  - SCr 1 mg/dl, Hb 12 g/dl, WBC 12 x 10^3
  - NS3 80 QK polymorphism.

- **Liver Biopsy:** Metavir F3/A2
Patient Case #9

What is the most appropriate course of action at this time?

A. Reassess in 12 months
B. Initiate sofosbuvir and simeprevir
C. Initiate sofosbuvir and ledipasvir
D. Initiate ribavirin and sofosbuvir
Hepatitis C

RNA Virus
- Genotypes 1-7 (1-3 most common is US)
  - Several subtypes
- Genotype 1 most resistant to drug treatment
- Transfusion, IV drug abuse, transplant

Major cause of chronic liver disease
- > 3 million infected in the US
- 60-80% progression following acute infection
- #1 reason for transplant
Hepatitis C Testing

Test if:

- Adults born between 1945-1965
- Suspected exposure
- HIV Infection
- IV Drug Abuse
- Clotting factors before 1987 or blood before 1992
- Hemodialysis
- Abnormal ALT
- Organ transplant prior to 1992
Hepatitis C Testing

Recommended Testing Sequence for Identifying Current Hepatitis C Virus (HCV) Infection

HCV antibody

Nonreactive

No HCV antibody detected

STOP*

Reactive

Not Detected

No current HCV infection

Additional testing as appropriate†

Detected

Current HCV infection

Link to care

* For persons who might have been exposed to HCV within the past 6 months, testing for HCV RNA or follow-up testing for HCV antibody is recommended. For persons who are immunocompromised, testing for HCV RNA can be considered.

† To differentiate past, resolved HCV infection from biologic false positivity for HCV antibody, testing with another HCV antibody assay can be considered. Repeat HCV RNA testing if the person tested is suspected to have had HCV exposure within the past 6 months or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.

HCV Treatment Goals

- Clinical cure

- Sustained Virologic Response (SVR)
  - Undetectable HCV RNA (IU/ml) 12 weeks post treatment
  - Correlated with treatment cure in 99% of patients

- Avoidance of interferon and ribavirin

- Prevention of transmission and complications
  - End stage liver disease and hepatocellular carcinoma


Journal of Hepatology 2014 vol. 60 j 392–420
## Prioritization for Treatment

<table>
<thead>
<tr>
<th>Highest Priority</th>
<th>Next Highest Due to High Risk for Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Advanced fibrosis (Metavir F3) or compensated cirrhosis (Metavir F4)</td>
<td>• Fibrosis (Metavir F2)</td>
</tr>
<tr>
<td>• Organ transplant</td>
<td>• HIV-1 Co-infection</td>
</tr>
<tr>
<td>• Type 2 or 3 mixed cryoglobulinemia with end organ manifestations such as vasculitis.</td>
<td>• Hepatitis B Virus Co-infection</td>
</tr>
<tr>
<td>• Proteinuria, nephrotic syndrome, or membranoproliferative glomerulonephritis</td>
<td>• Other coexistent liver disease such as NASH</td>
</tr>
<tr>
<td></td>
<td>• Debilitating fatigue</td>
</tr>
<tr>
<td></td>
<td>• Type 2 Diabetes (insulin resistant)</td>
</tr>
<tr>
<td></td>
<td>• Porphyria cutanea tarda</td>
</tr>
</tbody>
</table>

# Pros and Cons of Current HCV Therapies

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Interferon</td>
<td>• Effective</td>
<td>• Injectable</td>
</tr>
<tr>
<td></td>
<td>• Durable response</td>
<td>• Significant adverse effect profile</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Use in decompensated liver disease</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Differing effects based on genotype</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Required duration with ribavirin</td>
</tr>
<tr>
<td>Ribavirin</td>
<td>• Effective in combination with interferon and</td>
<td>• Adverse effect profile</td>
</tr>
<tr>
<td></td>
<td>protease inhibitors and NS5B inhibitors</td>
<td>• Kinetics (renal disease)</td>
</tr>
<tr>
<td></td>
<td>• Oral</td>
<td>• Cannot use as monotherapy</td>
</tr>
<tr>
<td></td>
<td>• Inexpensive</td>
<td>• No fixed dosing</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Required duration with interferon</td>
</tr>
<tr>
<td>Telaprevir/Boceprevir</td>
<td>• Oral</td>
<td>• Multiple day dosing</td>
</tr>
<tr>
<td></td>
<td>• Synergistic with interferon/ribavirin</td>
<td>• Kinetics (absorption)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Adverse effect profile (rash, anemia)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Expense</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Resistance</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Drug interactions</td>
</tr>
</tbody>
</table>
Simeprevir (Olysio®)

- **Mechanism**
  - NS3/4A protease inhibitor (Macrocyclic)

- **Approved indication**
  - Treatment of chronic hepatitis C infection as a component of a combination antiviral treatment regimen (PEG-INF and Ribavirin)
  - Genotype 1 in patients with compensated disease

- **Dose**
  - 150 mg capsule once daily with food x 12 weeks
  - CrCl > 30 ml/min
Simeprevir (Olysio®)

- **Efficacy**
  - SVR rates = ~80-90%

- **Considerations**
  - NS3 Q80K Polymorphism Genotype 1a
  - Patients of East Asian Ancestry
  - Moderate/Severe liver disease
  - Drug Interactions with CYP 3A Inducers/Inhibitors

- **Adverse Effects**
  - Rash, photosensitivity, fatigue, anemia

*www.hcvguidelines.org/full-report-view*
Sofosbuvir (Sovaldi®)

- Mechanism
  - Nucleotide NS5B polymerase inhibitor
  - Prodrug

- Approved indication
  - Treatment of chronic hepatitis C infection as a component of a combination antiviral treatment regimen (Ribavirin +/- PEGINF)
  - Genotypes 1-4 (5/6), including those with HCC or HIV Co-infection

- Dose
  - 400 mg tablet once daily with or without food x 12-24 weeks
  - RBV dosing: 1000 mg/day for < 75 kg and 1200 mg/day for > 75 kg
  - CrCl > 30 ml/min
Sofosbuvir (Sovaldi®)

- **Efficacy**
  - SVR rates
    - ~89-97% (Genotypes 1, 2, 4)
    - ~60-71% Genotype 3

- **Considerations**
  - Adjustment of ribavirin dose for Hb & cardiac disease
  - Use of potent P-glycoprotein inducers; anticonvulsants
  - Presence of cirrhosis or prior treatment

- **Adverse Effects**
  - Fatigue, headache, nausea

*www.hcvguidelines.org/full-report-view*
Sofosbuvir/Ledipasvir (Harvoni®)

- **Ledipasvir Mechanism**
  - Nucleotide NS5A inhibitor

- **Approved indications**
  - Treatment of chronic hepatitis C genotype 1 infection
  - Treatment experienced or naïve, with or without cirrhosis: 12 weeks
  - Possibly 8 weeks if pretreatment HCV RNA < 6 million IU/L
  - Treatment experienced with cirrhosis: 24 weeks

- **Dose**
  - 1 tablet (90mg Ledipasvir/400mg sofosbuvir) once daily with or without food
  - CrCl > 30 ml/min
Viekira Pak® ("3D" or AOD)

- **Approved December 2014**

- **Indication:** Genotype 1 infection with or without compensated cirrhosis

- **Components**
  - Paritaprevir (ABT-450): (NS3/4A PI) 75 mg
  - Ombitasvir (NS5A inhibitor) 12.5 mg
  - Ritonavir 50 mg (booster)
  - Dasabuvir (NS5B inhibitor) 250 mg
### Dose
- 2 Paritaprevir/Ombitasvir/Ritonavir tablets once daily (AM) +
- 1 Dasabuvir tablet twice daily
- With or without food

<table>
<thead>
<tr>
<th>Patient Population</th>
<th>Treatment</th>
<th>Duration* (Weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Genotype 1a (no cirrhosis)</td>
<td>Viekira Pak + Ribavirin</td>
<td>12</td>
</tr>
<tr>
<td>Genotype 1a (cirrhosis)</td>
<td>Viekira Pak+ Ribavirin</td>
<td>24</td>
</tr>
<tr>
<td>Genotype 1b (no cirrhosis)</td>
<td>Viekira Pak</td>
<td>12</td>
</tr>
<tr>
<td>Genotype 1b (cirrhosis)</td>
<td>Viekira Pak+ Ribavirin</td>
<td>12</td>
</tr>
</tbody>
</table>

*Recommended duration for transplant patients is 24 weeks*
### Adverse Effects
- Fatigue, nausea, pruritus
- Ribavirin related
- Avoid in CP Class C liver disease
- Pregnancy category B

### Major Drug Interactions
- CYP 3A4 substrates and inducers
- CYP 2C8 substrates and inhibitors (dasabuvir)

### Contraindicated with ethinyl estradiol
- Discontinue prior to use and check ALT in first 4 weeks
## Treatment of Chronic HCV

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Recommended Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>1a</td>
<td>LDV (90mg)/SOF (400mg) x 12 weeks</td>
</tr>
<tr>
<td></td>
<td>SOF (400mg) + SMV (150mg)(^c) ± RBV(^a) × 12 weeks(^d)</td>
</tr>
<tr>
<td></td>
<td>PVR/RITON/OMBI/ DAS + RBV(^a) × 12 weeks(^d)</td>
</tr>
<tr>
<td>1b</td>
<td>LDV (90mg)/SOF (400mg) x 12 weeks</td>
</tr>
<tr>
<td></td>
<td>SOF (400mg) + SMV (150mg)(^c) × 12 weeks(^d)</td>
</tr>
<tr>
<td></td>
<td>PVR/RITON/OMBI/ DAS (+/- RBV)(^e) × 12 weeks(^d)</td>
</tr>
<tr>
<td>2</td>
<td>SOF + RBV × 12 weeks; extend to 16 weeks if cirrhosis</td>
</tr>
<tr>
<td>3</td>
<td>SOF + RBV × 24 weeks</td>
</tr>
</tbody>
</table>
## Treatment of Chronic HCV

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Recommended Therapies</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>LDV (90mg)/SOF (400mg) x 12 weeks</td>
</tr>
<tr>
<td></td>
<td>SOF (400mg)+ RBV&lt;sup&gt;a&lt;/sup&gt; × 24 weeks</td>
</tr>
<tr>
<td></td>
<td>PVR/RITON/OMBI/ DAS + RBV&lt;sup&gt;a&lt;/sup&gt; × 12 weeks&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>SOF + RBV + PEG × 12 weeks</td>
</tr>
<tr>
<td>6</td>
<td>LDV (90mg)/SOF (400mg) x 12 weeks</td>
</tr>
</tbody>
</table>
Choosing New Therapies

- Genotype
- Pill burden
- Organ function
- Potential for drug interactions
- Cost
Patient Case #9

What is the most appropriate course of action at this time?

- Reassess in 12 months
- Initiate sofosbuvir and simeprevir
- Initiate sofosbuvir and ledipasvir
- Initiate ribavirin and sofosbuvir

Handout Page 135; Answer Page 156
Patient Case #10

- **HPI**: 55 year old man with chronic alcohol abuse and chronic pancreatitis. Steatorrhea and weight loss (now 135 lb)

- **LABS**: Albumin 2.1 g/dl, Fecal fat 20g/day

- **Medications**: morphine CR, oxycodone IR as needed
Patient Case #10

What is the best course of action for this patient?

A. Increase morphine CR to 60 mg twice daily
B. Initiate dronabinol to improve appetite
C. Initiate pancrelipase 30,000 units/meal
D. Add a multivitamin to his regimen
Overview

Pancreatitis

Acute
- Mild-Severe Inflammation
- Generally reversible exocrine and/or endocrine function
- Rarely progresses to chronic
- Pain, N/V, sepsis, organ dysfunction

Chronic
- Longstanding pancreatic injury
- Fibrosis/destruction of tissue
- Irreversible exocrine and/or endocrine function
- Pain, steatorrhea, malnutrition, diabetes
Acute Pancreatitis

- Largely supportive Care
- Pain management
- Antiemetics
- Nutritional support
  - Enteral
  - Hyperglycemia
- Antibiotics
  - Infection, abscess, or necrosis
<table>
<thead>
<tr>
<th>Complication</th>
<th>Targeted Therapies</th>
<th>Comments</th>
</tr>
</thead>
</table>
| Pain                               | Narcotic +/- non-narcotic therapies | • Acetaminophen and/or NSAIDs  
• Long acting narcotic preparations + IR breakthrough  
• Caution with acetaminophen and narcotics if alcohol use is continued |
|                                    | Pancreatic enzymes          |                                                                          |
| Maldigestion and Malabsorption     | Pancreatic enzymes          | • Start around 30,000-40,000 lipase units per meal; ½ dose for snacks  
• Do not crush or chew  
• Max 2500 u/kg/dose; 10,000 u/kg/day  
• Titrate to steatorrhea + weight gain  
• Porcine based so avoid if pork allergy  
• ADEK                                                                 |
|                                    | Fat soluble vitamins        |                                                                          |
| Diabetes                           | Insulin                     | • Long acting + short acting  
• Oral intake may be variable                                          |
Patient Case #10

What is the best course of action for this patient?

- Increase morphine CR to 60 mg twice daily
- Initiate dronabinol to improve appetite
- Initiate pancrelipase 30,000 units/meal
- Add a multivitamin to his regimen
Patient Case #11

- **HPI:** 32-year-old woman with crampy abdominal pain, bloating and constipation for 6 months. Not food related. Diagnosed with IBS-C.

- **LABS:** within normal limits

- **Medications and allergies:** none
Patient Case #11

A. Which of the following therapeutic interventions is best for this patient?

A. Amitriptyline 50 mg/day
B. VSL #3 three capsules daily
C. Tegaserod 6 mg twice daily
D. Lubiprostone 8 mcg twice daily
Irritable bowel syndrome

- **Categories**
  - Diarrhea Predominant (IBS-D)
  - Constipation Predominant (IBS-C)
  - Mixed Pattern (IBS-M)

- **Features**
  - Change in frequency and/or stool appearance
  - Pain, bloating, Relief with defecation

- **Target main symptoms and comorbidities**
<table>
<thead>
<tr>
<th>Therapies</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyoscyamine, dicyclomine</td>
<td>• Target pain due to spasm and also treat diarrhea</td>
</tr>
<tr>
<td></td>
<td>• Initial or adjunctive therapy for IBS-D or IBS-M</td>
</tr>
<tr>
<td>Tricyclic antidepressants</td>
<td>• Target pain and diarrhea</td>
</tr>
<tr>
<td></td>
<td>• Generally reserved for IBS-D</td>
</tr>
<tr>
<td></td>
<td>• Low doses</td>
</tr>
<tr>
<td>SSRIs, SNRIs</td>
<td>• Target pain and often have promotility action in IBS-D</td>
</tr>
<tr>
<td></td>
<td>• Can also treat comorbid depression and anxiety</td>
</tr>
<tr>
<td>Lubiprostone</td>
<td>• Indicated for IBS-C in women &gt; 18 years</td>
</tr>
<tr>
<td></td>
<td>• Main adverse effect is nausea, more expensive option</td>
</tr>
<tr>
<td>Loperamide</td>
<td>• Adjunctive for IBS-D, but does not treat pain</td>
</tr>
<tr>
<td>Probiotics</td>
<td>• Some potential improvement in global symptoms and pain</td>
</tr>
<tr>
<td>Alosetron</td>
<td>• Indicted for IBS-D in women &gt; 18 years failing other therapies</td>
</tr>
<tr>
<td></td>
<td>• Must be enrolled in prescribing program</td>
</tr>
<tr>
<td></td>
<td>• Risk of ischemic colitis</td>
</tr>
<tr>
<td>Tegaserod</td>
<td>• Indication: IBS-C; available on emergency use only due to CV risk</td>
</tr>
<tr>
<td>Rifaximin</td>
<td>• Some data to support improvement in bloating</td>
</tr>
</tbody>
</table>
Patient Case #11

Which of the following therapeutic interventions is best for this patient?

- Amitriptyline 50 mg/day
- VSL #3 three capsules daily
- Tegaserod 6 mg twice daily
- Lubiprostone 8 mcg twice daily
Patient Case #12

- **HPI:** 30-year-old pregnant woman (14 weeks) with myalgias, watery diarrhea (4-5), vomiting x 1.

- **LABS:** influenza (-), WBC 8000 x 10^3

- **Medications:** prenatal vitamin

- **Allergies:** none
Patient Case #12

What is the most appropriate course of action at this time for this patient's diarrhea?

A. Loperamide
B. Bismuth subsalicylate
C. Lactase
D. Pyridoxine
Management of Diarrhea

- Remove correct underlying cause
  - Identify drug-induced causes

- Rehydration
  - ORS
  - Parenteral

- Dietary modification
## Antidiarrheal Preparations

<table>
<thead>
<tr>
<th>Therapies</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loperamide</td>
<td>• OTC and prescription products, tablet and liquid</td>
</tr>
<tr>
<td></td>
<td>• OTC indicated in age &gt; 6</td>
</tr>
<tr>
<td></td>
<td>• Pregnancy category B</td>
</tr>
<tr>
<td>Opioids (diphenoxylate, tincture of opium)</td>
<td>• Generally reserved for more severe cases</td>
</tr>
<tr>
<td></td>
<td>• Increased risk of CNS adverse effects</td>
</tr>
<tr>
<td>Bismuth subsalicylate</td>
<td>• OTC tablet and liquid preparations</td>
</tr>
<tr>
<td></td>
<td>• Avoid:</td>
</tr>
<tr>
<td></td>
<td>• Patients &lt; 12 years of age</td>
</tr>
<tr>
<td></td>
<td>• Pregnancy</td>
</tr>
<tr>
<td></td>
<td>• Salicylate allergy</td>
</tr>
<tr>
<td></td>
<td>• Signs/symptoms of bleeding or mucous</td>
</tr>
<tr>
<td></td>
<td>• Stool and tongue discoloration</td>
</tr>
<tr>
<td></td>
<td>• Chelation interactions</td>
</tr>
<tr>
<td>Lactase</td>
<td>• Suspected or diagnosed lactose intolerance</td>
</tr>
<tr>
<td>Probiotics</td>
<td>• Data in AAD, IBD, IBS, radiation induced</td>
</tr>
<tr>
<td>Teduglutide (Gattex)</td>
<td>• Short bowel syndrome for patients on TPN</td>
</tr>
</tbody>
</table>
Patient Case #12

What is the most appropriate course of action at this time for this patient’s diarrhea?

- Loperamide
- Bismuth subsalicylate
- Lactase
- Pyridoxine
THE END