Common problems in Gastroenterology for Internal medicine

Julajak Limsrivilai
Siriraj Hospital
Outline: GI tract

Upper tract
- Dyspepsia
- GERD

Pancreaticobiliary
- Gall stone and CBD stone
- Acute cholecystitis
- Ascending cholangitis
- Acute pancreatitis

Lower tract
- IBS
- Chronic diarrhea
- FOBT
- CRC screening
Outline: Liver disease

**Chronic liver disease**
- Viral hepatitis
- Alcoholic hepatitis
- NAFLD
- Autoimmune liver disease
- Metabolic liver disease

**Cirrhosis**
- Portal hypertension
- Variceal bleeding
- Ascites and complication
- Hepatorenal syndrome
- Hepatocellular carcinoma
A 40 y/o woman presents with dyspepsia for 2 months. She has no anemia or weight loss. Her brother died from CA stomach. She has not taken any medications for this symptoms.

What’s the most appropriate management next?

1. Life style modification
2. PPI
3. Urea breath test and treat H. pylori if test +ve
4. EGD with rapid urease test
Dyspepsia

- Pain or discomfort centered in the upper abdomen
  - Epigastric pain
  - Postprandial fullness
  - Early satiation
  - Belching
  - Nausea and vomiting
  - Upper abdominal bloating
Dyspepsia

- Etiology

- Guideline
Etiology

Functional dyspepsia vs Organic dyspepsia

- Normal finding
- Nonerosive gastritis
- Erosive/Hemorrhagic gastritis
- Peptic ulcer
- Polyp
- Gastric cancer
Etiology: other causes of upper abdominal pain

- Chronic pancreatitis
- Pancreatic cancer
- Gall stone
- Liver tumor
Dyspepsia

R/O symptoms from other organs
- Biliary colic
- Hepato/splenomegaly
- Cardiac cause

Symptoms from gastroduodenal lesions

Alarm features (at any age)
Alarming features: if +ve → EGD

1. GI blood loss
   - Hematemesis
   - Melena
   - IDA

2. Weight loss

3. Dysphagia

4. Persistent vomiting

Familial history of CA stomach
Dyspepsia

R/O symptoms from other organs
- Biliary colic
- Hepato/splenomegaly
- Cardiac cause

Symptoms from gastroduodenal lesions

Alarm features (at any age)

EGD/refer to GI

Yes

Normal EGD/gastritis

Manage as functional dyspepsia
- reassure
- lifestyle modification
- consider drug therapy

No

Age of onset > 55

Yes

Structural disease
- Eg. PU, cancer

Treat appropriately

Not resolved

Review medications/diet

Manage appropriately

No

Uncomplicated dyspepsia
- Dietary advice
- Lifestyle modification
- Empirical treatment for dyspepsia
- May test for H. pylori and treat

Resolved

Reassure
Who should be treated for *H. pylori*?
**H. pylori: Diagnosis**

- **Urea breath test** is the most investigated and best recommended non-invasive test in the context of a ‘test-and-treat strategy’.

- **Monoclonal Stool Ag test** can also be used.

- **Serological tests** can be used only after validation.

- In clinical practice when there is an indication for endoscopy, the **rapid urease test** is recommended as a first-line diagnostic test.

Malfertheiner P, Maastridht V, Gut 2017
<table>
<thead>
<tr>
<th>Condition</th>
<th>Level 1</th>
<th>Level 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>H. pylori: Indication for eradication</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. P. pylori-positive gastric mucosa</td>
<td>Level 1</td>
<td>Level 1</td>
</tr>
<tr>
<td>2. Atrophic gastritis</td>
<td>Level 2</td>
<td>Level 2</td>
</tr>
<tr>
<td>3. Hemorrhagic / erosive gastritis</td>
<td>Level 2</td>
<td>Level 2</td>
</tr>
<tr>
<td>4. MALToma</td>
<td>Level 1</td>
<td>Level 1</td>
</tr>
<tr>
<td>5. After gastric cancer resection</td>
<td>Level 2</td>
<td>Level 2</td>
</tr>
<tr>
<td>6. Peptic ulcer disease</td>
<td>Level 2</td>
<td>Level 2</td>
</tr>
<tr>
<td>7. Gastric cancer resection</td>
<td>Level 2</td>
<td>Level 2</td>
</tr>
<tr>
<td>8. NSAID use and gastritis</td>
<td>Level 1</td>
<td>Level 1</td>
</tr>
<tr>
<td>9. Positive serology</td>
<td>Level 2</td>
<td>Level 2</td>
</tr>
<tr>
<td>10. Hepatitis</td>
<td>Level 4</td>
<td>Level 4</td>
</tr>
</tbody>
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What’s the most appropriate management next?

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4. EGD with rapid urease test
## NSAID and Peptic ulcer

### Relative risk for GI events

<table>
<thead>
<tr>
<th>Drug</th>
<th>RR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naproxen</td>
<td>4.10 (3.22–5.23)</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>1.84 (1.54–2.00)</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>3.34 (2.79–3.99)</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>4.14 (2.91–5.90)</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>1.45 (1.17–1.81)</td>
</tr>
<tr>
<td>Rofecoxib</td>
<td>2.32 (1.89–2.86)</td>
</tr>
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</table>

### Relative risk for CV events

<table>
<thead>
<tr>
<th>Drug</th>
<th>RR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naproxen</td>
<td>1.09 (1.02–1.16)</td>
</tr>
<tr>
<td>Ibuprofen (low dose)</td>
<td>1.18 (1.11–1.25)</td>
</tr>
<tr>
<td>(high dose)</td>
<td>2.22 (1.10–4.48)</td>
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<tr>
<td>Diclofenac</td>
<td>1.40 (1.27–1.55)</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>1.30 (1.19–1.41)</td>
</tr>
<tr>
<td>Celecoxib</td>
<td>1.17 (1.08–1.27)</td>
</tr>
<tr>
<td>Etoricoxib</td>
<td>2.05 (1.45–2.88)</td>
</tr>
</tbody>
</table>

Melcarne L et al, EXPERT REVIEW OF GASTROENTEROLOGY & HEPATOLOGY, 2016
# NSAID and Peptic ulcer

<table>
<thead>
<tr>
<th>Low GI risk</th>
<th>High GI risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low CV risk</td>
<td>Non-selective NSAIDs</td>
</tr>
<tr>
<td></td>
<td>Celecoxib + PPI (several risk factors)</td>
</tr>
<tr>
<td>High CV risk</td>
<td>Naproxen; add PPI if patient is taking ASA</td>
</tr>
<tr>
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</tbody>
</table>

**GI risk**
- Age ≥ 60 years
- History of peptic ulcers
- Concomitant medication with antiplatelet agents, anticoagulants, corticosteroids, or SSRIs

**Cardiovascular risk**
- Use risk charts (e.g., Framingham risk scores or the European SCORE system)
- History of cardiovascular events or diabetes

Lanas A, Lancet 2017
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- Chronic diarrhea
- FOBT and occult GI bleeding
- CRC screening
GERD

A condition which develops when the reflux of stomach contents causes troublesome symptoms and/or complications

- **Esophageal syndromes**
  - Symptomatic syndromes
    - Typical reflux syndrome
    - Reflux chest pain syndrome
  - Syndromes with esophageal injury
    - Reflux esophagitis
    - Reflux stricture
    - Barrett’s esophagus
    - Adenocarcinoma

- **Extra-esophageal syndromes**
  - Established association
    - Reflux cough
    - Reflux laryngitis
    - Reflux asthma
    - Reflux dental erosions
  - Proposed association
    - Sinusitis
    - Pulmonary fibrosis
    - Pharyngitis
    - Recurrent otitis media
GERD

Esophageal Manifestation

EGD

NERD
50-70%

24-hr pH/impedance

NERD

Reflux esophagitis
30-40%

Barrett’s & CA
5%

Abnormal reflux
Acid reflux
Nonacid reflux

Normal reflux
Esophageal hypersensitivity/
Functional heartburn
Symptoms suggestive of GERD

Alarm

Yes

EGD/ Re-evaluation
Alarm features

Complication of GERD

Erosive esophagitis
- Odynophagia
- GI blood loss

Stricture
- Dysphagia

Cancer
- Dysphagia
- Weight loss
Alarming features

- Persistent vomiting
Symptoms suggestive of GERD

No

Typical

LSM plus Standard dose PPI 4 wk

Symptoms free

Stop

Atypical

LSM plus Double dose PPI 2 wk (consider 4-12 wks for atypical GERD)

Symptom persit

Maintain for at least 4 wks

Recurrent symptoms

On-demand/Intermittent Rx

Alarm

Yes

• Dysphagia
• Odynophagia
• Frequent vomiting
• GI bleed / anemia
• Weight loss

Symptom persist

EGD/Re-evaluation

No symptom persist

Symptom persist

*Exclude other condition

Yes
Patients failing PPI therapy

Endoscopy +/- image enhancement to assess anatomy and stratify GERD severity and exclude alternative diagnosis:
Endoscopy negative

Consider barium swallow if achalasia is a differential but manometry not available

- Optimize acid suppression
- New/alternative PPI
- Add Alginate
- Add bedtime H2RA
- Trial of pain modulator/neuromodulator

No response: Consider referral for functional testing before surgery
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- Chronic diarrhea
- FOBT
- CRC screening
Irritable bowel syndrome (IBS)

IBS ≠ IBD
Irritable bowel syndrome: Rome IV

- Recurrent abdominal pain, on average, at least 1 day/wk in the last 3 months, associated with 2 or more of the following criteria:
  - Related to defecation
  - Associated with a change in frequency of stool
  - Associated with a change in form (appearance) of stool

Symptoms must be present for the last 3 months, with onset at least 6 months before diagnosis.

- Constipation-predominant IBS (IBS-C)
- Diarrhea-predominant IBS (IBS-D)
- Mixed bowel pattern IBS (IBS-M)

Lacy BE, et al. Gastroenterology 2016:150;1393
Differential diagnosis

CA colon
- Age > 50 yr or have Familial Hx of CRC
- Bloody diarrhea, bowel habit change
- Anemia
- Weight loss

Chronic colitis eg. IBD, infection
- Mucous bloody diarrhea
- Fever
- Anemia
- Weight loss
Alarming features

- New onset of symptoms at 50 years or older
- Severe or progressively worsening symptoms
- Nocturnal diarrhea
- Bloody stools
- Unexplained IDA
- Unintentional weight loss
- Family history of colon cancer or IBD

Chey WD et al, JAMA 2015
Investigation

Alarming features

- Blood test: CBC, serum chemistries, TFT
- Stool test: ova, parasite

Diarrhea

Colonoscopy

Constipation

BE or colonoscopy
Investigation

Routine diagnostic testing:
- CBC
- Serum chemistries
- TFT
- Stool for ova and parasites
- FOBT
- Abdominal imaging

No alarming features

<table>
<thead>
<tr>
<th>Organic disease</th>
<th>IBS</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colitis/IBD</td>
<td>0.51-0.98</td>
<td>0.3-1.2</td>
</tr>
<tr>
<td>Colon cancer</td>
<td>0-0.51</td>
<td>0-6</td>
</tr>
<tr>
<td>Thyroid disease</td>
<td>4.2</td>
<td>5-9</td>
</tr>
<tr>
<td>Lactose maldigestion</td>
<td>38</td>
<td>26</td>
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</tbody>
</table>
### All IBS subtypes

- CBC
- Age-appropriate CRC screening

### IBS-D

- C-reactive protein or fecal calprotectin
- IgA TtG +/− quantitative IgA
- When colonoscopy performed, obtain random biopsies
- SeHCAT, fecal bile acids, or serum C4 where available

### IBS-C

- If severe or medically refractory, refer to gastroenterology specialist for physiologic testing

### IBS-M

- C-reactive protein or fecal calprotectin
- IgA TtG +/− quantitative IgA
- Stool diary
- Consider abdominal radiography to evaluate for stool accumulation

**No alarming features**
<table>
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<td>• When colonoscopy performed, obtain random biopsies</td>
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<tr>
<td>• Consider abdominal radiography to evaluate for stool accumulation</td>
</tr>
<tr>
<td>Symptom</td>
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<tr>
<td>Diarrhea</td>
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<tr>
<td>Constipation</td>
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<td>Abdominal pain</td>
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Lower tract
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Chronic diarrhea
Small bowel lesion

**Clue**

- Voluminous watery diarrhea
- Malabsorption, severe
- Hypoalbuminemia
- Mid abdominal colicky pain
- Hypokalemia
### Small Bowel Lesions

#### Infection

- Tropical sprue
- Crohn’s disease
- Eosinophilic enteritis
- Drugs: colchicine, ponstan

#### Malignancy: IPSID, lymphoma

#### Inflammation

- Tropical sprue
- Crohn’s disease
- Eosinophilic enteritis
- Drugs: colchicine, ponstan

#### Infiltrative: Amyloidosis

#### Lymphangiectasia

### Infections

<table>
<thead>
<tr>
<th>Bacteria</th>
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<tbody>
<tr>
<td>MAC</td>
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<tr>
<td>MTB</td>
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<tr>
<td>Virus</td>
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</tr>
<tr>
<td>CMV</td>
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<table>
<thead>
<tr>
<th>Protozoa</th>
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<tbody>
<tr>
<td>Cryptosporidium parvum</td>
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</tr>
<tr>
<td>Cyclospora cayetanensis</td>
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<tr>
<td>Chemoprophylaxis</td>
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</tr>
<tr>
<td>Encephalitozoon intestinalis</td>
<td></td>
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<tr>
<td>Enterocytozoon bieneusi</td>
<td></td>
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<tr>
<td>Giardia lamblia</td>
<td></td>
</tr>
<tr>
<td>Isospora belli</td>
<td></td>
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</tbody>
</table>
Suspected SB lesion

Chronic diarrhea:

Stool exam, endoscopy (Push entero, EGD) with biopsy
Colonic and Terminal Ileal lesion

**Clue**

- Chronic mucous bloody diarrhea (common in left-sided lesion)
- Tenemus (rectal involvement)
- Lower abdominal pain
- WBC in stool
Colonic and Terminal Ileal Lesion

**Infection**
- Bacteria: C. difficile, TB
- Virus: CMV, herpes simplex
- Parasite and protozoa: amebic,

**Cancer**
- Adenocarcinoma,
- Lymphoma

**Inflammation**
- IBD: UC, CD, microscopic colitis
- Eosinophilic colitis
- Autoimmune, vasculitis esp. Behcet

**Stool exam, colonoscopy with biopsy**

**Radiation**

**Drug induced**
Chronic diarrhea: Approach

Suspected SB lesion

Suspected LB lesion

Stool exam, endoscopy (Push entero, EGD) with biopsy

Stool exam, colonoscopy with biopsy
Pancreatic disease

Clue

• Frank steatorrhea
• Upper abdominal pain
• DM
• Weight loss
• Alcohol drinking
Diagnosis of CP

**Plain Film**
- Sensitivity (S): ~50%
- Specificity (Sp): 95%

**US**
- Sensitivity (S): 48-96%
- Specificity (Sp): 75-90%

**CT Scan**
- Sensitivity (S): 56-95%
- Specificity (Sp): 85-100%

**MRCP**
- Sensitivity (S): 88-91%
- Specificity (Sp): 92-98%

**ERCP**
- Sensitivity (S): 68-100%
- Specificity (Sp): 89-100%

**EUS**
- Sensitivity (S): 85-100%
- Specificity (Sp): 85-100%
Suspected SB lesion

Suspected LB lesion

Suspected pancreatic lesion

Stool exam, endoscopy (Push entero, EGD) with biopsy

Stool exam, colonoscopy with biopsy

Imaging
Small Intestinal Bacterial Overgrowth (SIBO)

Definition:
Jejunal bacteria > $10^5$ bact/ml

- **Stomach:** H. pylori
- **Prox SB:** $10^2$-$10^3$ bact/ml
- **Ileum:** $10^8$ bact/ml
- **Colon:** $10^{10}$-$10^{11}$ bact/ml

- Oral cavity: 200 species
- Colon: 400-500 species including:
  - Bacteroides
  - Eubacterium
  - Peptostreptococcus
  - Bifidobacterium
  - Ruminococcus
  - Bacillus
  - Fusobacterium
  - Clostridium
  - Lactobacillus
  - Enterococcus
  - Enterobacter
## SIBO: Etiology

### Intestinal stasis

<table>
<thead>
<tr>
<th>Anatomic:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• stricture (e.g. Crohn’s disease, radiation enteritis)</td>
</tr>
<tr>
<td>• Diverticulosis</td>
</tr>
<tr>
<td>• End-to-side enteroenteric anastomosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Motility disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Scleroderma</td>
</tr>
<tr>
<td>• Diabetic autonomic neuropathy</td>
</tr>
</tbody>
</table>

### Loss IC valve

- Fistulae
- Resection of IC valve

### Hypochlorhydria

- Chronic atrophic gastritis
- Medication

### Immunodeficiency

- Primary
- Secondary: AIDS
SIBO: Pathophysiology

- SB bacteria
- Deconjugate bile acid
- Steatorrhea
- Bact consume B12
- Megaloblastic anemia
- SB mucosal injury
- Carbo intolerance, hypoprotein
- Spare K, folate
Chronic diarrhea: Approach

- Suspected SB lesion: Stool exam, endoscopy (Push entero, EGD) with biopsy
- Suspected LB lesion: Stool exam, colonoscopy with biopsy
- Suspected pancreatic lesion: Imaging
- Suspected SIBO: Lactulose/glucose H₂ breath test
Chronic diarrhea: Approach

- Suspected SB lesion
  - Stool exam, endoscopy (Push entero, EGD) with biopsy

- Suspected LB lesion
  - Stool exam, colonoscopy with biopsy

- Suspected pancreatic lesion
  - Imaging

- Suspected SIBO
  - Lactulose/glucose H₂ breath test

- Suspected drug/endocrine
  - Stop drug, endocrine w/o
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Which of the following statements about gFOBT (guaiac test) is true?

1. Avoid Fe supplement before testing
2. Lower sensitivity than immunohistochemistry FOBT for upper GI bleeding
3. More than one sample of stools can increased test sensitivity
4. Vitamin C ingestion causes false-positive result
5. is recommended for annually surveillance in HNPCC family
FOBT
<table>
<thead>
<tr>
<th></th>
<th>Guaiac</th>
<th>Heme-Porphyrin</th>
<th>iFOBT</th>
</tr>
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<tbody>
<tr>
<td><strong>False positives</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Animal Hb</td>
<td>++++</td>
<td>++++</td>
<td>0</td>
</tr>
<tr>
<td>• Dietary peroxidase</td>
<td>+++</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>False negatives</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Vitamin C</td>
<td>++</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

High false +ve and –ve
FOBT and bleeding site

Sites of Gastrointestinal Bleeding

- Upper gastrointestinal tract
  - Porphyrins, partially degraded heme, degraded globin

- Middle gastrointestinal tract
  - Porphyrins, partially degraded heme, partially degraded globin

- Lower gastrointestinal tract
  - Intact heme and intact globin

Relative Likelihood of a Positive Fecal Occult-Blood Test

- Guaiac-based
- Heme-porphyrin
- Immunochemical

Rockey DC, NEJM 1999
Fecal occult blood test: indication

Colorectal cancer screening:
Decreased mortality from CRC
Fecal occult blood test: indication

Colorectal cancer screening:
Decreased mortality from CRC

iFOBT >> gFOBT

Not indicate in symptomatic patients:
IDA, abdominal pain

Low sensitivity
Low specificity
Role of FOBT in patients with IDA

<table>
<thead>
<tr>
<th>60 cc blood ingestion</th>
<th>CA colon</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>gFOBT</strong></td>
<td><strong>iFOBT</strong></td>
</tr>
<tr>
<td>16%</td>
<td>2%</td>
</tr>
</tbody>
</table>

Rockey DC, Am J Gastroenterol 1999  
Lieberman DA. NEJM 2009

No role of FOBT in the evaluation of IDA
Iron deficiency anemia

IDA

Men, postmenopausal women
- GI tract evaluation

Premenopausal women
- GYN consultation
  - GI tract evaluation if +ve risk
+ve FOBT with Abdominal pain

183 pt met criteria IBS

15 pt

FOBT+ve

4 pt (2.2%)

lesion found

- 1 Hemorrhoids
- 2 anal fissures
- 1 Melanosis coli

Tolliver BA, Am J Gastroenterol 1994
+ve FOBT with Abdominal pain

1. กลืนลำบาก (Dysphagia)

2. มีประวัติหรือหลักฐานว่ามีเลือดออกในทางเดินอาหาร (Evidence of gastrointestinal blood loss) เช่น มีประวัติอาเจียนเป็นเลือด ซึ่งอาจเจ็บเป็น melena มีภาวะช็อคจากการขาดธาตุเหล็ก เป็นต้น

3. น้ำหนักลดโดยไม่สามารถหาเหตุผลมาอธิบายได้ (Unexplained weight loss) เช่น ไม่ได้ชั่งใจลด
   น้ำหนัก ไม่ได้เริ่มเบนเบาหวาน ไม่ได้มีภาวะต้อถูกุ้ม

4. อาเจียนต่อเนื่อง (Persistent vomiting)

No role of FOBT

Accuracy of alarm features is disappointing. Ten symptoms, such as nocturnal pain offer little discriminative value for distinguishing patients with IBS from those with organic diseases. Whereas anemia and weight loss have poor sensitivity for organic diseases, they offer very good specificity. As such, in patients who fulfill symptom-based criteria of IBS, the absence of selected alarm features, including anemia, weight loss, and a family history of colorectal cancer, inflammatory bowel disease, or celiac sprue, should reassure the clinician that the diagnosis of IBS is correct.
Which of the following statement about gFOBT (guia test) is true?

1. Avoid Fe supplement before testing
2. Lower sensitivity than immunohistochemistry FOBT for upper GI bleeding
3. More than one sample of stools can increased test sensitivity
4. Vitamin C ingestion causes false-positive result
5. is recommended for annually surveillance in HNPCC family
Outline: GI tract

**Upper tract**
- Dyspepsia
- GERD

**Pancreaticobiliary**
- Gall stone and CBD stone
- Acute cholecystitis
- Ascending cholangitis
- Acute pancreatitis

**Lower tract**
- IBS
- Chronic diarrhea
- FOBT
- CRC screening
A 57 year-old man, has recently been diagnosed advance stage colon cancer. He concerns that this malignant disease might be inherited. What would you recommend to his 30 yr-old son?

1. Colonoscopy now
2. Colonoscopy at age 40
3. Colonoscopy at age 50
4. FOBT at age 40
5. FOBT at age 50
Colon cancer screening
**Average risk : Conclusion**

Screening period: 50 to 75-85 years

<table>
<thead>
<tr>
<th>Test</th>
<th>USPSTF 2016</th>
<th>Multi-society Joint 2017</th>
<th>Asia Pacific 2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>gFOBT (3 samples)</td>
<td>1 yr</td>
<td>1 yr</td>
<td>Not recommend</td>
</tr>
<tr>
<td>iFOBT (1-2 samples)</td>
<td>1 yr</td>
<td>1 yr</td>
<td>1 yr</td>
</tr>
<tr>
<td>Sigmoidoscopy</td>
<td>5 yr</td>
<td>5 - 10 yr</td>
<td>5 yr</td>
</tr>
<tr>
<td>Colonoscopy</td>
<td>10 yr</td>
<td>10 yr</td>
<td>10 yr</td>
</tr>
<tr>
<td>CT colonography</td>
<td>5 yr</td>
<td>5 yr</td>
<td>Not recommend</td>
</tr>
</tbody>
</table>
High risk

- Familial colorectal cancer
- Hereditary colorectal cancer
- History of adenoma
- History of colorectal cancer
- Inflammatory bowel disease

Colonoscopy
Familial colorectal cancer

- No FH of CRC or adenoma: 1
- FH of adenoma: 1.99
- 1st degree relative with CRC: 2.25
- Dx CRC < age 45: 3.87
- > 1 relative with CRC: 4.25

Cumulative incidence (cases/10,000)

- Family history
- No family history

Age (yr)
### Familial colorectal cancer

<table>
<thead>
<tr>
<th>RR</th>
<th>Age to begin</th>
<th>Test</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>4x</td>
<td>40 years, or</td>
<td><strong>Colonoscopy</strong></td>
<td>Every 5 years</td>
</tr>
<tr>
<td></td>
<td>10 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>before the</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>youngest</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Either CRC or AP in
- 1st degree < 60 yr or
- 2 or more 1st degree at any age

Either CRC or AP in
- 1st degree age > 60 yr

Rex DK, Gastroenterol 2017
# Hereditary colon cancer

## Table

<table>
<thead>
<tr>
<th>Who should be screen</th>
<th>Age to begin</th>
<th>Tool for screening and age to stop</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>FAP</strong>&lt;br&gt;-mutation carrier&lt;br&gt;-family members at 50% risk if no mutation identified</td>
<td>Age 10 to 12 years</td>
<td>&lt;ul&gt;&lt;li&gt;-Annual FSIG or colonoscopy&lt;/li&gt;&lt;li&gt;until age 30 years,&lt;/li&gt;&lt;li&gt;-every 3-5 years thereafter until age 60&lt;/li&gt;&lt;/ul&gt;</td>
</tr>
<tr>
<td><strong>HNPCC</strong>&lt;br&gt;-mutation carrier&lt;br&gt;-family members at 50% risk if no mutation identified</td>
<td>Age 20 to 25 years, or 2-5 years before the youngest case</td>
<td>&lt;ul&gt;&lt;li&gt;-At least biennial colonoscopy&lt;/li&gt;&lt;li&gt;until age 40 years,&lt;/li&gt;&lt;li&gt;-annually thereafter to age 70-75 years or until co-morbidity makes it clinically inappropriate&lt;/li&gt;&lt;/ul&gt;</td>
</tr>
</tbody>
</table>
## Hereditary colon cancer

<table>
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</tr>
<tr>
<td>-mutation carrier</td>
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</tr>
<tr>
<td><strong>HNPCC</strong></td>
<td><strong>Age 20 to 25 years, or 2-5 years before the youngest case</strong></td>
<td><strong>At least biennial colonoscopy</strong>, until age 40 years, &lt;br&gt;-annually thereafter to age 70-75 years or until co-morbidity makes it clinically inappropriate</td>
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<tr>
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<td></td>
</tr>
<tr>
<td>-family members at 50% risk if no mutation identified</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**AD pattern**
<table>
<thead>
<tr>
<th>Who should be screen</th>
<th>Age to begin</th>
<th>Tool for screening and age to stop</th>
</tr>
</thead>
<tbody>
<tr>
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<tr>
<td></td>
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</tr>
<tr>
<td>HNPCC</td>
<td>Age 20 to 25 years, or 2-5 years before the youngest case</td>
<td>-At least biennial colonoscopy, until age 40 years, -annually thereafter to age 70-75 years or until co-morbidity makes it clinically inappropriate</td>
</tr>
</tbody>
</table>
FAP

Gastric
Duodenal
Ampullary

Jejunoileal

Colorectal

Congenital hypertrophy of retinal pigment epithelium (CHRPE)
Abnormal dentition
Epidermal cysts

Brain tumors
 Thyroid tumors

Epidermal cysts

Osteomas

Desmoid tumors
HNPCC

- Not polyposis

**Extracolonic cancers**

- Overall 2-20% of cases

- Most common: endometrial carcinoma (60% of female)

**Extra-colonic cancer**

- GI: stomach, small bowel (stomach to rectum)

- GU (genital): endometrium, ovary

- GU (urological): transitional cell carcinoma of the renal pelvis or ureter
### Amsterdam II criteria

- **3 or more** relatives with **HNPCC-associated cancer** (i.e. CRC, endometrial, renal pelvis, SB, ureteral cancers), one of whom is a first degree relative of the other two

- Cancer in at least 2 generations of the same family

- At least one cancer case Dx before the age of 50

- FAP should be excluded
A 57 year-old man, has recently been diagnosed advance stage colon cancer. He concerns this malignant disease might be inherited. What would you recommend to his 30 yr-old son?

1. Colonoscopy now
2. Colonoscopy at age 40
3. Colonoscopy at age 50
4. FOBT at age 40
5. FOBT at age 50
Outline: GI tract

Upper tract
- Dyspepsia
- GERD

Lower tract
- IBS
- Chronic diarrhea
- FOBT
- CRC screening

Pancreaticobiliary
- Gall stone and CBD stone
- Acute cholecystitis
- Ascending cholangitis
- Acute pancreatitis

Dyspepsia
GERD
Acute cholecystitis
Ascending cholangitis
Acute pancreatitis
A 40 year-old woman presents with acute epigastric pain for 4 hr. LFTs: TB 0.6, DB 0.4, AST 350, ALT 320, ALP 120, A/G 4.4/2.6. U/S reveals gall stone, no biliary duct dilatation.

What’s the most appropriate next management?

1. check for HAV, HBV, and HEV infection
2. LC
3. ERCP
4. Endoscopic ultrasonography
Gall stone and complications
Asymptomatic GS
60-80%
Biliary pain 20%
Acute cholecystitis 10%
Biliary pain (with ↑ AST/ALT)

Obstructive jaundice

Cholangitis

5%
GS pancreatitis <5%
Gall stone and CBD stone
<table>
<thead>
<tr>
<th>References</th>
<th>Characteristic</th>
<th>No. of cases</th>
<th>Average follow-up period (years)</th>
<th>No. of acute cholecystitis cases (%)</th>
<th>Only those with remarkable jaundice cases (%)</th>
<th>Cholangitis</th>
<th>Cholecystitis</th>
<th>Gallbladder cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comfort et al.</td>
<td>Asymptomatic</td>
<td>112</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Lund</td>
<td>Asymptomatic</td>
<td>95</td>
<td>13</td>
<td>?</td>
<td>?</td>
<td>1(?)</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Gracie et al.</td>
<td>Asymptomatic</td>
<td>123</td>
<td>11</td>
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<td>0</td>
<td>1</td>
<td>0</td>
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<tr>
<td>McSherry et al.</td>
<td>Asymptomatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Friedman et al.</td>
<td>Asymptomatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Thistle et al.</td>
<td>Asymptomatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Wenckert et al.</td>
<td>Mild symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3</td>
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<tr>
<td>Ralston et al.</td>
<td>Mild symptoms</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
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<tr>
<td>Friedman et al.</td>
<td>Mildly symptomatic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Newman et al.</td>
<td>Symptomatic</td>
<td>332</td>
<td>10</td>
<td>38 (11.4)</td>
<td>?</td>
<td>?</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>McSherry et al.</td>
<td>Symptomatic</td>
<td>556</td>
<td>7</td>
<td>47 (8.5)</td>
<td>?</td>
<td>?</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

*Do only in symptomatic cases*
<table>
<thead>
<tr>
<th>Special subgroups</th>
<th>Comments</th>
<th>recommend</th>
</tr>
</thead>
</table>
| Chronic hemolytic syndromes (eg. sickle cell) | - Onset in younger age  
- ↑ life-time risk of complication | Yes       |
| Transplantation                               | - Some drugs (cyc, tacro) – prolithogenic  
- Imm suppress agents mask S&S ⟷  
Delayed Dx ⟷ ↑ morbid & mortal  
- Recent studies : not support hypothesis | No        |
| DM                                            | - Autonomic neuropathy & poor imm ⟷  
delayed Dx and ↑ severity  
- Recent studies : not support hypothesis | No        |
| Cirrhosis of liver                            | - Most are asymptomatic and Sx is rarely required                       | No        |
| GB cancer                                     | - Porcelain GB                                                          | Yes       |

Behari A, Indian J Surg 2012
CBD stone

- up to 50% developing complication
- Difficult to diagnose

<table>
<thead>
<tr>
<th>Test</th>
<th>Sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transabdominal U/S</td>
<td>75% dilated ducts, 50% non-dilated</td>
</tr>
<tr>
<td>CT scan</td>
<td>70-75%</td>
</tr>
<tr>
<td>MRCP</td>
<td>88-92% all comers, 90-95% dilated ducts</td>
</tr>
<tr>
<td>EUS</td>
<td>90-97%</td>
</tr>
</tbody>
</table>
CBD stone: clinical predictors in who have GS

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Presence of any very strong</th>
<th>High</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBD stone on US</td>
<td></td>
<td></td>
</tr>
<tr>
<td>clinical ascending cholangitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bilirubin &gt; 4 mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strong</td>
<td></td>
<td></td>
</tr>
<tr>
<td>dilated CBD on US (&gt;6 mm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bilirubin 1.8-4 mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>abnormal LFT other than bilirubin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>age &gt; 55 yr</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GS pancreatitis</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ASGE guideline 2010
CBD stone

**Predictor**

<table>
<thead>
<tr>
<th>Very strong</th>
<th>Intermediate patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>CBD stone on US</td>
<td></td>
</tr>
<tr>
<td>clinical ascending cholangitis</td>
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<td>bilirubin &gt; 4 mg/dL</td>
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<table>
<thead>
<tr>
<th>Strong</th>
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<td>dilated CBD on US (&gt;6 mm)</td>
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<tr>
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<td>age &gt; 55 yr</td>
<td></td>
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<tr>
<td>GS pancreatitis</td>
<td></td>
</tr>
</tbody>
</table>

| Presence of any very strong      | High                  |
| Presence of both strong          | High                  |
| No predictors present            | Low                   |
| All other patients               | Intermediate          |

**ASGE guideline 2010**

Low: LC

Intermediate: LC with IOC or Preop EUS/MRCP

High: ERCP
A 40 year-old woman presents with acute epigastric pain for 4 hr. LFTs: TB 0.6, DB 0.4, AST 350, ALT 320, ALP 120, A/G 4.4/2.6. U/S reveals gall stone, no biliary duct dilatation.

What’s the most appropriate next management after controlling her abdominal pain?

1. check for HAV, HBV, and HEV infection
2. LC
3. ERCP
4. Endoscopic ultrasonography
Acute cholecystitis
# Acute cholecystitis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>RUQ pain, RUQ tenderness</td>
<td>90%</td>
</tr>
<tr>
<td>Fever</td>
<td>50%</td>
</tr>
<tr>
<td>Prior history of biliary colic</td>
<td>75%</td>
</tr>
<tr>
<td>Murphy’s sign</td>
<td>Sens 65%</td>
</tr>
<tr>
<td></td>
<td>Spec 87%</td>
</tr>
<tr>
<td>Jaundice</td>
<td>20%</td>
</tr>
<tr>
<td>• Sepsis</td>
<td></td>
</tr>
<tr>
<td>• CBD stone</td>
<td></td>
</tr>
<tr>
<td>• Mirizzi’s syndrome</td>
<td></td>
</tr>
</tbody>
</table>
Cholecystitis: Diagnosis

US
Sens 88%, Spec 80%
US Murphy sign
Sens 63%, Spec 94%

Distention (41%),
wall thickening (59%),
fat strand (52%),
pericholecystic fluid (31%)

Tc-HIDA scan
Sensitivity 80-90%
False positive 10-20%
# Cholecystitis: Diagnosis

<table>
<thead>
<tr>
<th>Item</th>
<th>Signs</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Local signs of inflammation</td>
<td>Murphy’s sign</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RUQ mass/pain/tenderness</td>
</tr>
<tr>
<td>B</td>
<td>Systemic sign of inflammation</td>
<td>Fever</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Elevated CRP (&gt; 3 mg/dl)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Elevated WBC (&gt; 10,000 mm$^3$/dl)</td>
</tr>
<tr>
<td>C</td>
<td>Imaging findings</td>
<td>Characteristic of acute cholecystitis</td>
</tr>
</tbody>
</table>

**Suspected diagnosis:** A + B

**Definitied diagnosis:** A + B + C

*Sens 91.2%, Spec 96.9%*
Cholecystitis: Treatment

- IV ATB and supportive care
- Specific Rx
  - Cholecystectomy
  - Cholecystostomy
Acute cholecystitis: management

Grade I: not II and III
ATB and general support care

Grade II: 1/4 of
Duration > 72 hr,
palpable tender mass,
WBC > 18,000/mm³,
Mark local inflam by image
ATB and general support care

Grade III: organ failure
ATB and general support care

In pt with Sx risk
Observation

Early LC
Emergency Sx

Advanced laparoscopic technique available
Successful Rx
Delayed/elective LC

Failure Rx

Urgent/early GB drainage
Percutaneous cholecystostomy

Yokoe M, J Hepatobiliary Pancreas Sci 2013
Ascending cholangitis
### Ascending cholangitis

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Fever</td>
<td>95%</td>
</tr>
<tr>
<td>2. RUQ tenderness</td>
<td>90%</td>
</tr>
<tr>
<td>3. Jaundice</td>
<td>80%</td>
</tr>
<tr>
<td>4. Confusion</td>
<td>15%</td>
</tr>
<tr>
<td>5. Hypotension</td>
<td>15%</td>
</tr>
</tbody>
</table>

1+2+3 = Charcot’s triad (20-70% of patients)

1+2+3+4+5 = Reynolds’ pentad
### Ascending cholangitis: Diagnosis

<table>
<thead>
<tr>
<th>Item</th>
<th>Signs</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Systemic inflammation</td>
<td>Fever (&gt; 38 °C) and/or shaking chills</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Laboratory data evidence of inflammation</td>
</tr>
<tr>
<td>B</td>
<td>Cholestasis</td>
<td>Jaundice (&gt; 2 mg/dL)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Laboratory data: abnormal LFTs (&gt; 1.5x STD)</td>
</tr>
<tr>
<td>C</td>
<td>Imaging findings</td>
<td>Biliary dilatation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Evidence of the etiology on imaging (stricture, stone, stent, etc.)</td>
</tr>
</tbody>
</table>

**Suspected diagnosis:** A + (B or C)

**Definitied diagnosis:** A + B + C

Sens 91.8%, Spec 77.7%
Cholangitis: Treatment

IV ATB and supportive care + Specific Rx

- ERCP
- PTBD
- Surgery
Ascending cholangitis: Treatment

Grade I: not II and III
- ATB and general support care

Grade II: 2/5 of
- Age ≥ 75 yr, T ≥ 39°C, TB ≥ 5mg/dl, Alb ≤ 2.5g/dl
- WBC < 4,000 or > 12,000
- Early biliary drainage
  - ATB and general support care

Grade III: organ failure
- Urgent biliary drainage
  - Organ support, ATB

Biliary drainage
- Finish course of ATB
- Organ support, ATB
- ERCP, PTBD, Sx

Treatment for etiology if still needed
- (endoscopic Rx, percutaneous Rx, or surgery)

Yokoe M, J Hepatobiliary Pancreas Sci 2013
Acute pancreatitis
Acute Pancreatitis

- ALT ≥ 3x ULN or GS detected by US
  - + GS pancreatitis
  - TG ≥ 1000 mg/dl or elevated Ca
    - + Hyper TG or Hypercalcemia
    - Definite drugs or other causes
      - Alcohol ≥ 80 g/day ≥ 5 years
        - + Alcoholic pancreatitis
        - CT scan if age ≥ 40
          - + Identified cause
          - EUS
            - + Identified cause
            - Idiopathic AP
Local complication of pancreatitis

- Pancreatic necrosis
- Peripancreatic fluid collection
- Wall-off necrosis
- Pseudocyst
Dx of AP

Dx of etiology esp. GS

Assess severity

Mild

Supportive Rx

Severe

Enteral Nutrition

CT at 3-7 d

No necrosis

Improved

Necrosis

Conservative Rx ± ATB 5-7 d

Not improved

CT/US-guided FNA

Infected

Surgery

ABP + cholangitis

ERCP within 72 hr

Gas

Sterile
Outline: Liver disease

Chronic liver disease
- Viral hepatitis
- Alcoholic hepatitis
- NAFLD
- Autoimmune liver disease
- Metabolic liver disease

Cirrhosis
- Portal hypertension
- Variceal bleeding
- Ascites and complications
- Hepatorenal syndrome
- Hepatocellular carcinoma
Outline: Liver disease

Chronic liver disease
- Viral hepatitis
- Alcoholic hepatitis
- NAFLD
- Autoimmune liver disease
- Metabolic liver disease

Cirrhosis
- Portal hypertension
- Variceal bleeding
- Ascites and complications
- Hepatorenal syndrome
- Pulmonary complications
- Hepatocellular carcinoma
Who should be started anti-HBV treatment?

1. 30 year-old man with HBsAg and HBeAg +ve, HBV VL > 170,000,000 IU/L, ALT 30, US – normal liver

2. 30 year-old man with HBsAg and HBeAg +ve, HBV VL 500,000 IU/L, ALT 50, US – normal liver

3. 50 year-old man with HBsAg +ve, HBeAg –ve, HBV VL 1,500 IU/L, ALT 30, US – cirrhotic liver

4. 50 year-old man with HBsAg +ve, HBeAg –ve, HBV VL 1,000 IU/L, ALT 80, US – fatty liver
### Viral hepatitis B

#### Treatment

**Immune tolerant**
- HBsAg
- Log IU/mL
- Anti-HBs
- HBeAg PELU/mL
- Anti-HBe
- HBV DNA IU/mL

**Immune active**
- Serum ALT U/L
- Liver histology

**Immune control**

**Immune escape**

**Occult**

---

### Cirrhosis

- 30-40 years

Modified from Dandri M, Locarnini. Gut 2012
Viral hepatitis B

HBeAg +ve

ALT < 1 x ULN
- Q 6 mo ALT
- Q 6-12 mo HBeAg
- Bx if age > 40, Rx as needed

ALT 1-2 x ULN
- Q 3-6 mo ALT, HBeAg
- Fibrosis assessment
- Consider Rx if
  - Significant fibrosis
  - Family Hx of HCC

ALT > 2 x ULN,
VL > 20,000 IU/ml
- Q 3 mo ALT, HBeAg
- Treat if persist 3-6 mo
- Bx optional
- Immediate Rx if Jx or decompensated

Immune tolerance

Immu ne active

Lok AS, AASLD guidelines; Chronic hepatitis B 2009
Terranult NA, AASLD guidelines; Chronic hepatitis B 2015
Viral hepatitis B

HBeAg-ve

ALT < 1x ULN
VL < 2,000 IU/mL

Q 6-12 mo ALT, HBV VL
Look for other causes of hepatitis if ALT is elevated

ALT < 2x ULN
VL < 2,000 IU/mL

Q 3-6 mo ALT, VL
Fibrosis assessment
Consider Rx if
• Significant fibrosis
• Family Hx of HCC

ALT > 2x ULN
VL > 2,000 IU/mL

ALT next 3 months
Treat if persistent ↑,
Liver biopsy optional

Inactive

Reactivation

Lok AS, AASLD guidelines; Chronic hepatitis B 2009
Terranult NA, AASLD guidelines; Chronic hepatitis B 2015
Viral hepatitis B

Cirrhosis/HCC

Treat if HBV VL detectable regardless of ALT level

Thailand Practice Guideline for management of chronic hepatitis B and C 2012
Who should be started anti-HBV treatment?

1. 30 year-old man with HBsAg and HBeAg +ve, HBV VL > 170,000,000 IU/L, ALT 30, US – normal liver

2. 30 year-old man with HBsAg and HBeAg +ve, HBV VL 500,000 IU/L, ALT 50, US – normal liver

3. 50 year-old man with HBsAg +ve, HBeAg –ve, HBV VL 1,500 IU/L, ALT 30, US – cirrhotic liver

4. 50 year-old man with HBsAg +ve, HBeAg –ve, HBV VL 1,000 IU/L, ALT 80, US – fatty liver
A 27 year-old man consults you because he missed the 3rd dose of hepatitis B vaccine. He received second dose at 12 months ago.

What would you recommend?

1. Restart full course of hepatitis B vaccine
2. Continue 3rd dose as soon as possible
3. Check anti-HBs, and restart full course of hepatitis B vaccine if result is negative
4. Check anti-HBs, and continue 3rd dose as soon as possible if result is negative
Viral hepatitis B: vaccine

Different manufacturer between doses?  OK

Interruption

Not need to be restarted

Interrupt at 1\textsuperscript{st} dose:
- 2\textsuperscript{nd} dose as soon as possible,
- 3\textsuperscript{rd} dose at 8 wk interval from 2\textsuperscript{nd}

Interrupt at 2\textsuperscript{nd} dose:
- 3\textsuperscript{rd} dose as soon as possible

http://www.cdc.gov
A 27 year-old man consults you because he forgets to receive the 3rd dose of hepatitis B vaccine. He received second dose at 12 months ago.

What would you recommend?

1. Restart full course of hepatitis B vaccine
2. Continue 3rd dose as soon as possible
3. Check anti-HBs, and restart full course of hepatitis B vaccine if result is negative
4. Check anti-HBs, and continue 3rd dose as soon as possible if result is negative
Viral hepatitis C

Thailand Practice Guideline for management of chronic hepatitis B and C 2012

Age > 18 years with HCV RNA +ve

Genotype 1, 4, 6

Significant fibrosis
- F2 on Metavir
- Fibroscan > 7 kPa

50%

Consider Rx with PegIFN + RBV 12 mo

Genotype 2, 3

Consider Rx with PegIFN + RBV 6 mo

90%

Advise and F/U
Viral hepatitis C

Direct-acting antiviral agents (DAAs)

Adapted from the US Food and Drug Administration, Antiviral Drugs Advisory Committee Meeting, April 27-28, 2011, Silver Spring, MD.
Viral hepatitis C

Treatment is recommended for all patients with chronic HCV infection.

F0–F1
F2
F3
F4
Decompensated cirrhosis

Treatment should be considered for all patients (treatment-naïve and -experienced) with compensated disease\textsuperscript{1,2}

EASL Recommendations on Treatment of Hepatitis C. 2016
AASLD and IDSA. Recommendations for Testing Managing and Treating Hepatitis C. 2016
Alcoholic liver disease:

(Acute) Alcoholic steatohepatitis

Suspect ASH

- Rapid deterioration of liver function
- New-onset of clinical decompenation

Prognostic assessment

- Maddrey’s DF $\geq 32$
- MELD $> 18$
- ABIC (age, bilirubin, INR, Cr) $> 9$
- Glasgow score $> 8$

EASL guideline 2012
### Alcoholic liver disease:

**(Acute) Alcoholic steatohepatitis**

<table>
<thead>
<tr>
<th></th>
<th>Bilirubin</th>
<th>PT/INR</th>
<th>Cr/urea</th>
<th>WBC</th>
<th>Age</th>
<th>Albumin</th>
<th>Change in bilirubin from D0 to D7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maddrey</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MELD</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GAHS</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>ABIC</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Lille</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
<td>+</td>
<td></td>
</tr>
</tbody>
</table>

EASL guideline 2012
**Alcoholic liver disease:**

**(Acute) Alcoholic steatohepatitis**

**Suspect ASH**
- Rapid deterioration of liver function
- New-onset of clinical decompensation

**Prognostic assessment**
- Maddrey’s DF $\geq 32$
- MELD $> 18$
- ABIC (age, bilirubin, INR, Cr) $> 9$
- Glasgow score $> 8$

**High risk**

**Low risk**

EASL guideline 2012
Low risk

Nutrition assessment

+ Treatment of complications in cirrhotic patients

EASL guideline 2012
High risk

- Screening for HBV, HCV, and HIV
- Abdominal US to exclude other causes of jaundice
- Systemic bacterial infection screening and blood, ascites, and urine culture
- Screen of renal failure and early treatment of HRS
- Proper control hyperglycemia

Sepsis
Renal failure
Poor glycemic control

Pentoxifylline
(400 mg tid for 4 wk)

Prednisolone
(40 mg QD for q wk)

Continue treatment 3 more weeks

Lille model
7 days

< 0.45
≥ 0.45

Stop prednisolone
Consider early OLT in highly selected patients
Non alcoholic fatty liver disease (NAFLD)

Metabolic syndrome

Fatty liver  NASH

rare  20-25%

Cirrhosis

40%

Liver-related death

Hepatocellular carcinoma

20-25%
<table>
<thead>
<tr>
<th>Score</th>
<th>age</th>
<th>BMI</th>
<th>FBS</th>
<th>TG</th>
<th>AST</th>
<th>ALT</th>
<th>PLT</th>
<th>ALB</th>
</tr>
</thead>
<tbody>
<tr>
<td>FIB-4</td>
<td>O</td>
<td></td>
<td></td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>NAFLD fibrosis score</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
<tr>
<td>BARD</td>
<td></td>
<td>O</td>
<td>O</td>
<td></td>
<td>O</td>
<td>O</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BAAT</td>
<td>O</td>
<td></td>
<td></td>
<td></td>
<td>O</td>
<td>O</td>
<td>O</td>
<td>O</td>
</tr>
</tbody>
</table>
NAFLD: Noninvasive Diagnosis of Liver Fibrosis in NAFLD

- Transient elastography (fibroscan)
- MR elastography
## NAFLD: Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Recommendation</th>
<th>Comment</th>
</tr>
</thead>
</table>
| Weight reduction   | Yes            | • 3-5 %: improve steatosis  
|                    |                | • 10%: improve necroinflammation                                        |
| Metformin          | No             | 6-12 mo of MF did not improve aminotransferases or liver histology      |
| Pioglitazone       | Yes            | Improve histology in biopsy-proven NASH, in both with and without DM    |
| Vitamin E          | Yes            | Dose 800 IU/d improves histology in non-diabetic adults with biopsy-proven NASH |
| UDCA               | No             | No histological effect                                                  |
| Omega-3 fatty acid | N/A            | May be 1\textsuperscript{st} line agent to Rx hyperTg in NAFLD          |
| Statin             |                | Can be used to Rx dyslipidemia in NAFLD                                |
Autoimmune liver disease

Liver parenchyma:
- AIH

Small duct:
- PBC

Large duct:
- PSC
AIH: Clinical Clues

Clinical presentation

- Acute hepatitis on top chronic hepatitis 40-50%
- Chronic hepatitis 40-50%
- Acute hepatitis 10%

<table>
<thead>
<tr>
<th>Type 1</th>
<th>Type 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>Infants to elderly</td>
</tr>
<tr>
<td>Female</td>
<td>78%</td>
</tr>
<tr>
<td>Concurrent immune diseases</td>
<td>38%</td>
</tr>
<tr>
<td>Typical concurrent autoimmune diseases</td>
<td>Autoimmune thyroiditis</td>
</tr>
<tr>
<td></td>
<td>Graves’ disease</td>
</tr>
<tr>
<td></td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Organ-specific antibodies</td>
<td>4%</td>
</tr>
<tr>
<td>Serum gamma globulin elevation</td>
<td>+++</td>
</tr>
</tbody>
</table>
### AIH: Investigation

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Type</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>ANA</td>
<td>1</td>
<td>60-80%</td>
</tr>
<tr>
<td>SMA</td>
<td>1</td>
<td>60-80%</td>
</tr>
<tr>
<td>LKM-1</td>
<td>2</td>
<td>4%</td>
</tr>
</tbody>
</table>

- Plasma cell infiltration
- Interface hepatitis
- Hepatocyte rosette formation
### AIH: diagnosis

**Table 3. Revised Original Scoring System of the International Autoimmune Hepatitis Group**

<table>
<thead>
<tr>
<th>Sex</th>
<th>Female</th>
<th>+2</th>
</tr>
</thead>
<tbody>
<tr>
<td>AP:AST (or ALT) ratio</td>
<td>&gt;3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>&lt;1.5</td>
<td>+2</td>
</tr>
<tr>
<td>γ globulin or IgG level above normal</td>
<td>&gt;2.0</td>
<td>+3</td>
</tr>
<tr>
<td></td>
<td>1.5-2.0</td>
<td>+2</td>
</tr>
<tr>
<td></td>
<td>1.0-1.5</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td>&lt;1.0</td>
<td>0</td>
</tr>
<tr>
<td>ANA, SMA, or anti LKM1 titers</td>
<td>&gt;1:80</td>
<td>+3</td>
</tr>
<tr>
<td></td>
<td>1:80</td>
<td>+2</td>
</tr>
<tr>
<td></td>
<td>1:40</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td>&lt;1:40</td>
<td>0</td>
</tr>
<tr>
<td>AMA</td>
<td>Positive</td>
<td>4</td>
</tr>
<tr>
<td>Viral markers</td>
<td>Positive</td>
<td>3</td>
</tr>
<tr>
<td>Drugs</td>
<td>Yes</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>+1</td>
</tr>
<tr>
<td>Alcohol</td>
<td>&lt;25 g/day</td>
<td>+2</td>
</tr>
<tr>
<td></td>
<td>&gt;60 g/day</td>
<td>2</td>
</tr>
<tr>
<td>HLA</td>
<td>DR3 or DR4</td>
<td>+1</td>
</tr>
<tr>
<td>Immune Disease</td>
<td>Thyroiditis, colitis, others</td>
<td>+2</td>
</tr>
<tr>
<td>Other markers</td>
<td>Anti SLA, anti actin, anti LC1, pANCA</td>
<td>+2</td>
</tr>
<tr>
<td>Histological features</td>
<td>Interface hepatitis</td>
<td>+3</td>
</tr>
<tr>
<td></td>
<td>Plasmacytic</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td>Rosettes</td>
<td>+1</td>
</tr>
<tr>
<td></td>
<td>None of above</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Biliary changes</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Other features</td>
<td>3</td>
</tr>
<tr>
<td>Treatment response</td>
<td>Complete</td>
<td>+2</td>
</tr>
<tr>
<td></td>
<td>Relapse</td>
<td>+3</td>
</tr>
</tbody>
</table>

**Pre** treatment aggregate score:
- Definite Dx > 15
- Probable Dx 10-15

**Post** treatment aggregate score:
- Definite Dx > 17
- Probable Dx 12-17


AMA, antimitochondrial antibody; anti LC1, antibody to liver cytosol type 1; anti liver antigen; ANA, antinuclear antibody; AP:AST (or ALT) ratio, ratio of alkaline phosphatase to AST (ALT) ratio; IgG, immunoglobulin G; pANCA, perinuclear anti neutrophil cytoplasmic antibody.
<table>
<thead>
<tr>
<th>Absolute</th>
<th>Relative</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum AST ≥ 10-fold ULN</td>
<td>Symptoms (fatigue, arthralgia, jaundice)</td>
<td>Asymptomatic with normal or near normal serum AST and γ-globulin levels</td>
</tr>
<tr>
<td>Serum AST ≥ 5-fold ULN and γ-globulin level ≥ 2-fold ULN</td>
<td>Serum AST and/or γ-globulin less than absolute criteria</td>
<td>Inactive cirrhosis or mild portal inflammation (portal hepatitis)</td>
</tr>
<tr>
<td>Bridging necrosis or multinodular necrosis on histological examination</td>
<td>Interface hepatitis</td>
<td>Severe cytopenia (white blood cell counts &lt;2.5 × 10⁹/L or platelet counts &lt;50 × 10⁹/L) or known complete deficiency of TPMT activity precludes treatment with azathioprine</td>
</tr>
<tr>
<td>Incapacitating symptoms</td>
<td>Osteopenia, emotional instability, hypertension, diabetes, or cytopenia (white blood cell counts ≤2.5 × 10⁹/L or platelet counts ≤50 × 10⁹/L)</td>
<td>Vertebral compression, psychosis, brittle diabetes, uncontrolled hypertension, known intolerances to prednisone or azathioprine</td>
</tr>
</tbody>
</table>

*Manns et al, AASLD Practice Guideline, Hepatology 2010;51:2193*
# AIH treatment

<table>
<thead>
<tr>
<th>Reasons for Preference</th>
<th>Monotherapy</th>
<th>Combination Therapy</th>
<th>Azathioprine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Prednisone only* (mg/day)</td>
<td>Prednisone* (mg/day)</td>
<td>USA (mg/day)</td>
</tr>
<tr>
<td>Week 1</td>
<td>60</td>
<td>30</td>
<td>50</td>
</tr>
<tr>
<td>Week 2</td>
<td>40</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Week 3</td>
<td>30</td>
<td>15</td>
<td>50</td>
</tr>
<tr>
<td>Week 4</td>
<td>30</td>
<td>15</td>
<td>50</td>
</tr>
<tr>
<td>Maintenance until endpoint</td>
<td>20 and below</td>
<td>10</td>
<td>50</td>
</tr>
</tbody>
</table>

- **Prednisone only**: Prednisone can be used in place of prednisone in equivalent doses.
- **Cytopenias**: Cytopenias may occur with azathioprine as a dose-related toxicity.
- **Thiopurine methyltransferase deficiency**: Thiopurine methyltransferase deficiency may affect the metabolism of azathioprine.
- **Postmenopausal state**: Postmenopausal state may increase the risk of osteoporosis.
- **Osteoporosis**: Azathioprine may cause osteoporosis.
- **Brittle diabetes**: Azathioprine may cause brittle diabetes.
- **Obesity**: Azathioprine may cause obesity.
- **Acne**: Azathioprine may cause acne.
- **Emotional lability**: Azathioprine may cause emotional lability.
- **Hypertension**: Azathioprine may cause hypertension.
- **Pregnancy**: Azathioprine may cause hypertension.
Primary biliary cirrhosis (PBC)

Small duct (interlobular bile ducts) destruction by autoimmune inflammatory process.
## PBC: Clinical

<table>
<thead>
<tr>
<th>Finding</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>21-85</td>
</tr>
<tr>
<td>Pruritus</td>
<td>19-55</td>
</tr>
<tr>
<td>Jaundice</td>
<td>3-10</td>
</tr>
<tr>
<td>Right upper quadrant pain</td>
<td>8</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>25</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>25</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>15</td>
</tr>
<tr>
<td>Xanthelasma</td>
<td>10</td>
</tr>
<tr>
<td>None (ALP elevation)</td>
<td>25-61</td>
</tr>
</tbody>
</table>
PBC: Diagnosis

- AMA +ve
- ALP > 1.5x
- AST < 5x

Ductopenia
Granuloma

PPV > 98%
PBC: Treatment

UDCA
13-15 mg/kg/d

Cirrhosis complication

Cholestatic complication

• Pruritus: Cholestyramine, rifacimarin, opioid antagonist
• Steatorrhea: MCT
• Bone disease: Vit D + Ca
• Coagulopathy: Vit K

Inadequate response

Add 2nd line:
• obeticholic acid 5 mg
• fibrate
Primary sclerosing cholangitis

Large duct destruction by autoimmune inflammatory process
PSC: Clinical features

Intermittent biliary obstruction

Secondary biliary cirrhosis

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>65-75</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>24-72</td>
</tr>
<tr>
<td>Pruritus</td>
<td>15-69</td>
</tr>
<tr>
<td>Fever/night sweats</td>
<td>13-45</td>
</tr>
<tr>
<td>Asymptomatic</td>
<td>15-44</td>
</tr>
<tr>
<td>Weight loss</td>
<td>10-34</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Signs</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Jaundice</td>
<td>30-73</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>34-62</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>32-34</td>
</tr>
<tr>
<td>Hyperpigmentation</td>
<td>14-25</td>
</tr>
<tr>
<td>Ascites</td>
<td>4-7</td>
</tr>
</tbody>
</table>
PSC: Treatment

- UDCA
- Immunosuppressive and other agents
- ERCP and endoscopic therapy
- Liver transplantation

Less benefit
Outline: Liver disease

Chronic liver disease
- Viral hepatitis
- Alcoholic hepatitis
- NAFLD
- Autoimmune liver disease
- Metabolic liver disease

Cirrhosis
- Portal hypertension
- Variceal bleeding
- Ascites and complications
- Hepatorenal syndrome
- Hepatocellular carcinoma
Question

Which condition can cause varix only at fundus of stomach?

1. Primary biliary cirrhosis
2. Essential thrombocytosis with portal vein thrombosis
3. Chronic pancreatitis
4. Budd-Chiari syndrome
5. Schistosomiasis
Portal hypertension

Left sided portal HT:
- Isolated fundal varices

Caput medusa:
- Cirrhosis

Left sided portal HT:
- Isolated fundal varices
Portal hypertension: Etiologies

**Prehepatic**
- Portal V thrombosis
- Splenic V thrombosis

**Posthepatic**
- Budd-Chiari syndrome
- Constrictive pericarditis
- Rt-sided HF

**Intrahepatic**
- Presinusoidal: Schistosomiasis
- Sinusoidal: cirrhosis
- Postsinusoidal: VOD

**Variceal bleeding**
- Ascites (high prot)
- hepatomegaly

**Variceal bleeding**
- Ascites (low prot)

**Variceal bleeding**
- Portal V thrombosis
- Splenic V thrombosis
Question

Which condition can cause varix only at fundus of stomach?

1. Primary biliary cirrhosis
2. Essential thrombocytosis with portal vein thrombosis
3. Chronic pancreatitis
4. Budd-Chiari syndrome
5. Schistosomiasis
Variceal bleeding
No varices
8% per year
Small varices
No hemorrhage
8% per year
Med/Large varices
No hemorrhage
5-15% per year
Variceal hemorrhage
60%
Recurrent hemorrhage
Variceal growth → rupture

\[ T = tp \times \frac{r}{w} \]

\[ V = I \times R \]

OLT
cirrhosis

TIPS, Shunt
↑ Resistance to portal flow

↑ Portal pressure

Somatostatin, telipressin, Non-select BB

Splanchnic vasodilatation
↑ Portal blood flow
### Variceal Bleeding

**No varices**
- 8% per year

**Small varices**
- No hemorrhage
  - 8% per year

**Med/Large varices**
- No hemorrhage
  - 5-15% per year

**Variceal hemorrhage**
- 60%

**Recurrent hemorrhage**

---

**EGD in all cirrhosis except in who**
- with LS < 20 kPa and Plt > 150,000

- **Prevent variceal formation:** no benefit
- **Prevent variceal progression:** BB
  - CTP-C or presence of red wale sign
- **Repeat EGD:**
  - No varices: 2 y (active), 3 y (quiescent)
  - Small varices: 1 y (active), 2 y (quiescent)

- **Prevent variceal rupture**
  - BB or EVL

- **Stop variceal bleeding**
  - Somatostatin/telipressin + EVL,
    - if fail → TIPS or OLT

- **Prevent rebleeding**
  - BB & EVL, if fail → TIPS or OLT
Ascites
Ascites: What’s SAAG

Exudate VS Transudate

- Exudate: High protein
- Transudate: Low protein

Right-sided CHF: High protein
SBP: Low protein
Ascites: What’s SAAG

\[ S_H - S_O = PC_H - PC_O \]

\[ S_H = S_O + PC_H - PC_O \]

Portal pressure = Serum Alb – Ascites Alb
Ascites


1.1

2.5

97% accuracy

Serum – ascites albumin gradient (g/dL)

Ascitic fluid total protein (g/dL)

Cirrhotic ascites
Cardiac ascites
Peritoneal malignancy

Ascites

High gradient > 1.1 g/dl
- Sinusoid
  - Cirrhosis
  - Alcoholic hepatitis
  - Mixed ascites
- Post sinusoid
  - Veno-occlusive disease Budd-Chiari syndrome
  - Cardiac ascites
- Myxedema

Low gradient ≤ 1.1 gm/dl
- Peritoneal disease
  - Peritoneal carcinomatosis
  - TB peritonitis
  - Pancreatic ascites
  - Bowel obstruction /infarction
  - Biliary ascites
  - Postop lymphatic leak
  - Serositis in CNT diseases
- Nephrotic syndrome

False low SAAG

- Different in time
- Hypoalbuminemia < 1.1 mg/dl
- Hyperglobulinemia: glob contribute to serum oncotic P
- Hypotension: decrease portal pressure

False high SAAG

- Chylous ascites: lipid interfere with albumin measurement
<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Only detectable by US</td>
<td>No treatment</td>
</tr>
<tr>
<td>2</td>
<td>Moderate symmetrical distension of abdomen</td>
<td>Restriction of salts and diuretic</td>
</tr>
<tr>
<td>3</td>
<td>Large or gross ascites with marked abdominal distention</td>
<td>LVP</td>
</tr>
</tbody>
</table>
Grade 2 ascites

Low-sodium diet (70-90 mEq/day)

Diuretics

No peripheral edema

- Spironolactone
- or Amiloride

Goal:
Weight loss 0.5 kg/day

Peripheral edema

- Spironolactone + furosemide

Goal:
Weight loss 1 kg/day

Maintenance therapy

Grade 3 ascites

Large-volume Paracentesis/TIPS

< 5 L

- Synthetic plasma expanders

> 5 L

- Albumin (6-8 g/L of ascites tapped)

Low sodium diet (70-90 mEq/day)

Diuretics

↓ Post paracentesis circulatory dysfunction

# Ascites infection

<table>
<thead>
<tr>
<th>Type of infection</th>
<th>PMN (/mm3)</th>
<th>Culture result</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spontaneous bacterial peritonitis</td>
<td>≥ 250</td>
<td>Positive (usually 1 Organism)</td>
<td>ATB + alb</td>
</tr>
<tr>
<td>Culture-negative neutrocytic ascites</td>
<td>≥ 250</td>
<td>Negative</td>
<td>ATB + alb</td>
</tr>
<tr>
<td>Monomicrobial nonneutrocytic bacterascites</td>
<td>&lt; 250</td>
<td>Positive (1 Organism)</td>
<td>Symp : as SBP</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Asymp : repeat</td>
</tr>
<tr>
<td>Secondary bacterial peritonitis</td>
<td>≥ 250</td>
<td>Positive (polymicrobial)</td>
<td>Surgery</td>
</tr>
</tbody>
</table>
SBP : Albumin infusion

- 1.5 g/kg within 6 hr and 1 g/kg on day 3
- ↓ type I HRS (30%->10%) and MR (29%->10%)
- Indicated in
  1. Cr >1mg/dL
  2. BUN >30 mg/dL
  3. TB > 4mg/dL
## Ascites infection

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<td>≥ 250</td>
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<td>Surgery</td>
</tr>
</tbody>
</table>
Ascites infection

PMN > 250?

Culture Positive?

TREATMENT NOT INDICATED

Repeat Paracentesis

PMN > 250?

Culture Positive?
# Ascites infection

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<td>Surgery</td>
</tr>
</tbody>
</table>
## Primary VS Secondary peritonitis

### Ascitic profiles

<table>
<thead>
<tr>
<th>Ascitic profiles</th>
<th>Sensitivity*</th>
<th>Specificity*</th>
</tr>
</thead>
<tbody>
<tr>
<td>2/3 of</td>
<td>100</td>
<td>45</td>
</tr>
<tr>
<td>• Total protein &gt; 1g/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• LDH &gt; ULN of serum LDH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Glucose &lt; 50 mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• CEA &gt; 5 ng/mL or ALP &gt; 240 units/L</td>
<td>92</td>
<td>88</td>
</tr>
</tbody>
</table>

*Only for free perforation*  

Akriviadis EA, Runyon BA. Gastroenterology 1990  
Wu SS et al. J Hepatol 2001
Hepatorenal syndrome

Functional renal failure in cirrhosis

- Decompenated cirrhosis
  - NO, CO, endogenous canabinoids
  - Splanchnic vasodilatation
  - ↓ effective circulatory volume
  - RAAS → Renal vasoconstriction
  - Renal failure

- Type 1
  - Liver function
  - Infection:
    - SBP, UTI

- Type 2
Hepatorenal syndrome: Diagnosis

1. Cirrhosis with ascites
2. Serum creatinine > 1.5 mg/dL
3. No improvement after at least 2 days with diuretic withdrawal and volume expansion with albumin (1g/kg/d, max 100 g/d)
4. Absence of other causes
   1. shock
   2. recent treatment with nephrotoxic drugs
   3. parenchymal renal disease (proteinuria > 0.5 g/d, rbc > 50/HF, abnormal U/S)

Type 1
Rapidly progressive (Cr >2.5 mg/dL or Ccr <20 ml/min in 2 wk)

Type 2
Slow (months)
Refractory ascites
# Hepatorenal syndrome: Treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Type I</th>
<th>Type II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Correct precipitating factor</td>
<td>+++</td>
<td></td>
</tr>
<tr>
<td>Vasoactive drugs plus albumin</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Renal replacement therapy</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>TIPS</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Liver dialysis</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>Liver transplantation</td>
<td>+++</td>
<td>+++</td>
</tr>
</tbody>
</table>

**Vasoactive agents:** Terlipressin, Norepinephrine, Midodrine
A 56 year-old man with HBV cirrhosis is detected a 6 cm arterial enhancing mass with portovenous wash out in left lobe liver by 3-phase liver CT scan. PV is patent.

Lab : Hb 12 g/dL, Platelet 150,000, TB 1.5 g/dL, DB 1.2 g/DL, AST 50 IU/L, ALT 40 IU/L, ALP 110 IU/L, Alb 3.5 g/dL, Glob 4.0 g/dL.

What is the most appropriate management next?

1. Request serum Alpha fetoprotein to confirm diagnosis of HCC
2. Mass biopsy to confirm diagnosis of HCC
3. Hepatectomy with mass resection
4. Liver transplantation
5. Transarterial chemoembolization
Hepatocellular carcinoma

**Screening**

- **US + AFP**
- q 6 months

**Cirrhosis CTP-A,B**
- Cirrhosis CTP-C if on transplantation waiting list
- Chronic HBV infection
  - Asian male > 40 yr
  - Asian female > 50 yr
  - Family history of HCC

Bruix J, AASLD practice guideline 2010
Heimbach JK, AASLD practice guideline 2018
Diagnosis

Cirrhosis/CH-B with liver nodule

< 1cm

Repeat US q 3 mo

Growing

Ix according to size

Stable for 2 yr

Routine surveillance

> 1cm

4-phase MDCT/dynamic CE MRI

Typical lesion

Bruix J, AASLD practice guideline 2010
Typical HCC on 3-phase CT

A. hypervascular

V. or delayed phase wash out

A phase 30 sec

V phase 80 sec
Diagnosis

Cirrhosis/CH-B with liver nodule

- < 1 cm
  - Repeat US q 3 mo
    - Growing
      - Ix according to size
    - Stable for 2 yr
      - Routine surveillance

- > 1 cm
  - 4-phase MDCT/dynamic CE MRI
    - Typical lesion
      - HCC
        - Other CE study
          - Y: N
          - N: Bx

Bruix J, AASLD practice guideline 2010
## Hepatocellular carcinoma staging

**TNM-7 Classification for Hepatocellular Carcinoma 2010**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
<th>T</th>
<th>N</th>
<th>M</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Single, no vascular invasion</td>
<td>0</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>T2</td>
<td>Single with vascular invasion, or Multiple tumors non&gt; 5cm</td>
<td>0</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>T3a</td>
<td>Multiple tumor with any &gt; 5cm</td>
<td>0</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>T3b</td>
<td>Any T with major portal vein or hepatic vein</td>
<td>0</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>T3c</td>
<td>T4 adjacent organ, No GB, No perforation of visceral peritoneum</td>
<td>0</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>IVa</td>
<td>Any T</td>
<td></td>
<td>N1</td>
<td>0</td>
</tr>
<tr>
<td>IVb</td>
<td>Any T</td>
<td></td>
<td></td>
<td>Any N</td>
</tr>
</tbody>
</table>
Treatment

HCC

- Stage 0
  - PST 0, Child-Pugh A
  - Very early stage (0)
    - Single < 5 cm
      - Single
      - Portal pressure/bilirubin
        - Increased
          - Associated diseases
            - Normal
            - Yes
            - No

- Stage A-C
  - PST 0-2, Child-Pugh A-B
  - Early stage (A)
    - Single or 3 nodules ≤3 cm, PS 0
      - Single
      - Increased

  - Intermediate stage (B)
    - Multinodular, PS 0

  - Advanced stage (C)
    - Portal invasion, N1, M1, PS 1-2

- Stage D
  - PST >2, Child-Pugh C*

EASL guideline 2012
AASLD guideline 2018

Bridging LRT in T2

- Resection
- Liver transplantation (CLT/LDLT)
- RF/PEI
- TACE
- Sorafenib
- Best supportive care

Curative treatment (30-40%)
Median OS >60 mo; 5-yr survival: 40-70%

Target: 20%
OS: 20 mo (45-14)

Target: 40%
OS: 11 mo (6-14)

Target: 10%
OS: <3 mo
A 56 year-old man with HBV cirrhosis is detected a 6 cm arterial enhancing mass with portovenous wash out in left lobe liver by 3-phase liver CT scan. PV is patent.

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Thank you for your attentions