



Gastroenterology and Hepatology ACP Puerto Rico Chapter Meeting

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Epidemiology of colorectal cancer

1. Incidence and mortality are higher in blacks, native Americans and Alaskan natives
2. Risk factors associated with CRC:
 - cigarette smoking
 - Obesity
 - high consumption of alcohol, red and processed meat
 - Low consumption of fruits and vegetables
 - low consumption of dietary fiber and dietary calcium
 - low physical inactivity.
 - It is estimated that over 50% of colorectal cancers in women and nearly 60% of those in man are attributable to these lifestyle factors.

Current options for colorectal cancer screening in average risk persons

1. Fecal immunochemical test (FIT)- annually
2. Highly sensitive guaiac based fecal occult blood test (Hemoccult-II Sensa)- annually
3. Multi target stool DNA (Cologuard)- every 3 years
4. Colonoscopy every 10 years
5. CT colonography every 5 years
6. Flexible sigmoidoscopy every 5 years

Colonoscopy is the only screening test for high risk persons

A 23-year-old man is evaluated in follow-up for familial adenomatous polyposis that was diagnosed 3 months ago after colonoscopy. He underwent complete colectomy and is now asymptomatic. Physical exam is normal. Laboratory studies are normal.

Which of the following surveillance procedures should be performed?

1. Abdominal ultrasound
2. Serial monitoring of liver tests
3. Upper endoscopy
4. No follow-up surveillance is required

Familial adenomatous polyposis (FAP)

Diagnosis of FAP

1. At least 100 synchronous colon or rectal adenomas
2. Autosomal dominant inheritance

People with 10 and 99 adenomas have attenuated FAP. It is also autosomally dominant

MUTYH associated polyposis is a syndrome that resembles FAP but is inherited in an autosomal recessive pattern

Surveillance for extracolonic neoplasms associated with FAP

- Gastric and small bowel adenomas- EGD starting at 25-30 yrs.
- Papillary cancer of thyroid- annual thyroid ultrasound

A 50-year-old woman is evaluated during routine examination. She is in excellent health and has no gastrointestinal symptoms. She has no history of colorectal neoplasia. Physical exam is normal. She is sent home with a high sensitivity guaiac fecal occult blood test cards and is asked to collect 2 specimens each from 3 consecutive stools. One of the 6 samples is positive.

Which of the following is the most appropriate management for this patient?

1. Colonoscopy now
2. Fecal immunochemical test in 1 year
3. Flexible sigmoidoscopy now
4. Guaiac fecal occult blood test in 1 year
4. Repeat guaiac fecal occult blood test now with

Following up on a positive non-colonoscopy screening test for colorectal cancer (CRC)

- Abnormal non colonoscopy screening tests should be followed up with a timely colonoscopy. Repeating a positive non colonoscopy test to confirm whether it is really positive is not considered an appropriate strategy
- No difference in the risk of CRC with follow-up colonoscopy performed as late as 7-9 months after a positive fecal immunochemical test. However after a delay of ≥ 10 months there was a 50% greater risk of CRC and risk of stage III or stage IV disease was double that of those who received colonoscopy sooner

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A 50-year-old woman is evaluated during routine examination. She is in excellent health and has no gastrointestinal symptoms. She has no history of colorectal neoplasia. Physical exam is normal. She is sent home with a high sensitivity guaiac fecal occult blood test cards and is asked to collect 2 specimens each from 3 consecutive stools. One of the 6 samples is positive.

Which of the following is the most appropriate management for this patient?

1. Colonoscopy now
2. Fecal immunochemical test in 1 year
3. Flexible sigmoidoscopy now
4. Guaiac fecal occult blood test in 1 year
4. Repeat guaiac fecal occult blood test now with

A 37-year-old man is evaluated during a routine exam. He has no gastrointestinal problems. He has no previous colorectal cancer screening evaluation. His mother was diagnosed with colon cancer at the age of 54 years. Other than his mother there are no additional history of familial polyps, colon cancer or other cancer diagnoses. Physical exam is normal. Which of the following is the most appropriate management?

1. Colonoscopy now
2. Colonoscopy at the age of 40 years
3. Colonoscopy at the age of 44 years
4. Fecal occult blood test at the age of 40 years

Colorectal cancer (CRC) screening in average risk individuals

- ❑ Most CRCs are diagnosed between age of 65-74 years
- ❑ Average risk for CRC is defined as someone with
 - No family history of CRC
 - No family history of known genetic disorders that predispose to CRC such as Lynch syndrome
 - Personal history of inflammatory bowel disease, or of adenomatous polyps or colorectal cancer
- ❑ The USPSTF recommend screening is average risk does 50-75 years of age for CRC starting at age 50
- ❑ Between 76 and 85 years the benefit from screening is more likely in those who have never been screened
- ❑ The benefit in adults 86 years and older is so small that screening is not recommended

Colorectal screening in persons with a family history of colorectal cancer or adenomatous polyps

- ❑ If CRC or adenomas identified in a 1st degree relative at age <60 years, or in ≥ 2 or more 1st degree relatives at any age- start screening at age 40 or 10 years before the youngest case
- ❑ If CRC or adenomas identified in a 1st-degree relative aged ≥ 60 years, or ≥ 2 second-degree relatives with colorectal cancer then start screening at age 40

A 68-year-old man evaluated during a routine examination. His mother was diagnosed with colorectal cancer at the age of 65 years. Colonoscopy discloses a 1.5 cm polyp in the ascending colon which turns out to be a villous adenoma with low-grade dysplasia and a 6 mm polyp in the sigmoid colon which turns out to be a tubular adenoma with low-grade dysplasia. The polyps are completely removed. Which of the following is the most appropriate management for this patient?

1. Colonoscopy in 2-6 months
2. Colonoscopy in 1 year
3. Colonoscopy in 3 years
4. Colonoscopy in 10 years

Surveillance colonoscopy intervals in patients with adenomas

- ❑ Small hyperplastic rectal polyps- surveillance intervals same as for average risk
- ❑ 1 or 2 small (<1 cm) tubular adenomas with low-grade dysplasia- 5-10 years after initial polypectomy
- ❑ 3-10 adenomas or one adenoma more than 1 cm or any adenoma with high-risk features that is villous features or high-grade dysplasia- 3 years after initial polypectomy provided adenomas were completely removed
- ❑ More than 10 adenomas on a single exam-less than 3 years after initial polypectomy and consider an underlying familial polyposis syndrome
- ❑ Sessile adenomas that are removed piecemeal surveillance in 2-6 months to verify complete removal

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1. Colonoscopy in 2-6 months
2. Colonoscopy in 1 year
3. Colonoscopy in 3 years
4. Colonoscopy in 10 years

A 71-year-old woman is evaluated in follow-up for ascending colon cancer that was diagnosed at recent screening colonoscopy. CT of the abdomen and pelvis showed no evidence of distant metastases. A right hemicolectomy was performed. Pathology review shows stage II cancer. No adjuvant chemotherapy is recommended. She is otherwise healthy.

Which of the following is the most appropriate management strategy for this patient?

1. Colonoscopy in 2-6 months
2. Colonoscopy in 1 year
3. Colonoscopy in 3 years
4. Colonoscopy in 5 years

CRC surveillance in patients with colorectal cancer

- ❑ 3-6 months after CRC resection if no unresectable metastasis is found during surgery
- ❑ If this is normal repeat exam at 1 year.
- ❑ If this is normal then the interval before the next colonoscopy should be 3 years
- ❑ If that is normal then the interval before the next colonoscopy should be 5 years
- ❑ If patient has undergone low anterior resection of rectal cancer, surveillance examination of the rectum by flexible sigmoidoscopy usually performed at 3-6 month intervals for the 1st 2-3 years

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Which of the following is the most appropriate management strategy for this patient?

1. Colonoscopy in 2-6 months
2. Colonoscopy in 1 year
3. Colonoscopy in 3 years
4. Colonoscopy in 5 years

A 38-year-old woman is evaluated for a 12 month history of heartburn and intermittent dysphagia. There is no weight loss. Her medical history is unremarkable. Her only medication is esomeprazole. On physical exam vital signs are normal. BMI is 23. Endoscopy reveals a short small surface stricture in the distal esophagus likely due to chronic gastroesophageal reflux, and 100s of 2-4 mm gastric polyps. Biopsies revealed fundic gland polyps with no dysplasia.

Which of the following is the most appropriate management?

1. Discontinue esomeprazole and repeat endoscopy in 3 months
2. Order APC gene testing
3. Performed colonoscopy
4. Repeat endoscopy now for extensive polypectomy

Fundic gland polyps- when to be concerned

☐ Sporadic

- Sessile polyps located in the body and fundus
- Caused by activating mutation in the beta catenin gene
- Histology- dilated glands lined by the gastric body mucosa
- Very low risk of dysplasia (<1%)

☐ Polyps associated with proton pump inhibitor use

- Common in patients who have been on PPIs for ≥ 5 years
- Withdrawal of PPI therapy leads to reduction
- Histologic characteristic is dilated oxyntic glands and parietal cell protrusions

☐ FAP associated polyposis

- Usually carpet the body of the stomach
- Incidence of dysplasia is up to 40%

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4. Repeat endoscopy now for extensive polypectomy

A 53-year-old man evaluated 1 week after his 1st screening colonoscopy. He has no history of colorectal neoplasia in 1st or second-degree relatives. The preparation was described as poor, with collections of semi-solid debris that could not be effectively cleared from several colonic segments. According to the colonoscopy report mass lesions 1 cm or more are unlikely to have been obscured by delivery. Three small hyperplastic polyps less than 3 mm were removed from the rectum.

Which of the following is the most appropriate management for this patient?

1. Repeat colonoscopy now following adequate preparation
2. Repeat colonoscopy in 3 years
3. Repeat colonoscopy in 5 years
4. Repeat colonoscopy in 10 years

When to repeat colonoscopy after poor bowel prep at baseline colonoscopy

- ❑ If the bowel prep is poor in most cases the examination should be repeated in 1 year
- ❑ If the bowel prep is fair but adequate to detect lesions >5 mm , and if small (< 10 mm) tubular adenomas are detected then follow-up at 5 years can be considered

A 34-year-old woman is evaluated for 1 day history of watery diarrhea and mild abdominal cramps. She is having 4 watery stools per day. She has not had fever or blood in her stool. She has been able to stay hydrated with oral intake. She works as a banker, and her colleagues at work have had similar gastrointestinal symptoms over recent weeks. She has no history of recent hospitalization, antibiotic use, or medication changes. She has no risk factors for HIV infection.

Vital signs are normal. The mucous membranes are moist and that is no skin tenting. Abdominal exam reveals mild abdominal tenderness with normal bowel sounds.

Which of the following is the most appropriate diagnostic test

1. Clostridium difficile polyp raised chain reaction
2. Fecal leukocyte testing
3. Flexible sigmoidoscopy with biopsies
4. General stool bacterial culture
5. No additional studies

Indications for testing in acute diarrheal illness

Majority of acute diarrhea cases resolve on their own so specific investigations are not required EXCEPT in

1. Dysentery
2. Moderate to severe disease (either forced to change their activity due to the illness or disabled because of the diarrhea)
3. Symptoms lasting for more than 7 days

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2. Fecal leukocyte testing
3. Flexible sigmoidoscopy with biopsies
4. General stool bacterial culture

5. No additional studies

A 42-year-old woman is evaluated for an 8 month history of crampy abdominal pain relieved by bowel movements and 3 loose stools daily. There are no nocturnal bowel movements, and there is no hematochezia or melena. She has not had fevers, night sweats or weight loss. She has a history of Hashimoto's disease treated with levothyroxine.

On physical examination temperature is 36.8° C, blood pressure is 128/84 mm Hg, pulse rate is 64 and respiration rate is normal. There is mild diffuse abdominal tenderness without peritoneal signs. Rectal examination is normal.

Complete blood count and TSH levels are normal.

Which of the following is the most appropriate next step in management

1. Breath test for bacterial overgrowth
2. Colonoscopy with random biopsies
3. Stool culture
4. Tissue transglutaminase antibody testing

Diagnostic testing in irritable bowel syndrome

Rome IV diagnostic criteria for IBS

Recurrent abdominal pain at least 1 day a week in the last 3 months associated with 2 or more of the following

1. Related to defecation
2. Change in stool frequency
3. Change in stool consistency

Diagnostic testing in irritable bowel syndrome

Limited diagnostic testing is recommended to distinguish IBS from IBD and other GI conditions with similar symptoms such as celiac disease, lactose intolerance and microscopic colitis

1. CBC- assess for anemia or leukocytosis
2. CRP and fecal calprotectin-distinguish IBS from IBD
3. Serum tissue transglutaminase antibody-screen for celiac disease in areas of high prevalence
4. Colonoscopy with random biopsies for patients who are 50 years and older
5. Breath test to rule out carbohydrate malabsorption

Diagnostic testing in irritable bowel syndrome

Features suggestive of organic pathology

1. Age ≥ 50 years
2. Blood in the stools unless from hemorrhoids or fissures
3. Unintended weight loss
4. Unexplained anemia
5. Family history of IBD, colon cancer or celiac disease
6. Abdominal mass
7. Ascites
8. Leukocytosis
9. Loss of appetite
10. Nocturnal symptoms
11. Fever
12. Recent change in symptoms

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2. Colonoscopy with random biopsies
3. Stool culture
4. Tissue transglutaminase antibody testing

A 19-year-old woman is evaluated for a 3 month history of progressively worsening diarrhea, abdominal pain and weight loss. Her brother was diagnosed with Crohn's disease at the age of 16. She is afebrile, BP 110/65 mm Hg, pulse rate is 90/min. Abdominal examination reveals tenderness in the right lower quadrant with no guarding or rebound. Perianal and rectal exam normal. Colonoscopy discloses evidence of moderate to severely active Crohn's disease involving the terminal ileum. Magnetic resonance enterography shows active inflammation involving the distal 20 cm of the ileum without other bowel inflammation or obstruction. There is no evidence of an abscess or phlegmon.

Which of the following is the most effective maintenance treatment

1. Ciprofloxacin and metronidazole
2. Infliximab
3. Mesalamine
4. Prednisone
5. Surgical resection

Management of Crohn's disease

Classify by phenotype

1. **Inflammatory**: abdominal pain, diarrhea, fatigue
2. **Fibrostenotic**: intestinal obstruction in the form of intermittent abdominal pain with nausea and vomiting
3. **Penetrating**: fistulas and abscesses

Management of Crohn's disease

Disease activity

1. Remission

- Asymptomatic
- No evidence of active disease by imaging or endoscopy

2. Mild- moderate disease

- Eating and drinking normally
- Ambulatory
- No toxic symptoms or complications
- Less than 10% weight loss
- May have diarrhea and abdominal pain
- Serum CRP may be elevated

Management of Crohn's disease

Disease activity

3. Severe

- Symptoms despite corticosteroids or biologics as outpatients
- Complications- obstruction, intra-abdominal abscesses
- Cachexia
- Often hospitalized

Management of Crohn's disease

Principles of management

Identify patients with higher risk of disease progression

1. Young age at diagnosis (< 20 years of age)
2. Ileal disease
3. Extensive bowel involvement (at diagnosis)
4. Perianal or severe rectal disease (at diagnosis)
5. Penetrating or fibrostenotic disease (at diagnosis)

Nearly 70-80% of patients will have disease progression without treatment over time

Management of Crohn's disease

Goals of treatment

1. Induce remission
2. Maintain remission
3. Prevent complications like stricture and fistula

Management of Crohn's disease

Medical therapies

1. Corticosteroids

- Useful to induce remission- short term (< 3 months)
- **No role in maintenance therapy**
- IV steroids for severe flare
- Increase risk of perforating complications (abscess or fistula)
- Should be tapered if necessary by adding steroid sparing agents

Management of Crohn's disease

2. Thiopurines (azathioprine, 6-mercaptopurine) and methotrexate

- **No role in inducing remission-** response time 8-12 weeks
- Effective as maintenance therapy usually in combination with biologics- reduces immunogenicity

Management of Crohn's disease

2. Thiopurines (azathioprine, 6-mercaptopurine) and methotrexate

- Adverse effects of Azathioprine/6MP:
 - **Pancreatitis**- idiosyncratic, STOP drug do no restart
 - **Myelosuppression**- dose dependent. Check TPMT activity
 - **Hepatotoxicity**- check liver tests
 - **Non-melanoma skin cancer**- annual skin exam
 - **Lymphoma**- higher risk in males and younger patients
 - **Hepatosplenic T-cell lymphoma**- anti-TNF + thiopurine

• Adverse effect of methotrexate

• Teratogenicity: at least 2 contraceptive methods

Management of Crohn's disease

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Management of Crohn's disease

2. Thiopurines (azathioprine, 6-mercaptopurine) and methotrexate

- Adverse effect of methotrexate
 - **Teratogenicity**- at least 2 contraceptive methods
 - **Pulmonary toxicity**
 - Others similar to thiopurines

Management of Crohn's disease

3. Biologics (anti-TNF, IL-12/23, anti-integrins)

- Effective in inducing remission and as maintenance therapy
- Anti-TNFs have rapid onset of effect (within 2 weeks)
- 1st line therapy for fistulizing Crohns
- Combination therapy with immunomodulators better than monotherapy
- Prevent post-operative recurrence

Management of Crohn's disease

3. Biologics (anti-TNF, IL-12/23, anti-integrins)

Before starting anti-TNF:

Rule out latent TB (IFN- γ release assay preferred for BCG vaccine recipients). If latent TB detected, initiate chemoprophylaxis for several weeks or months before starting anti-TNFs

Test for chronic Hepatitis B:

- If HBsAb negative: start vaccination before anti-TNF
- If HBsAg positive, initiate treatment with antivirals (entecavir or tenofovir) before and during anti-TNF therapy

Management of Crohn's disease

3. Biologics (anti-TNF, IL-12/23, anti-integrins)

Contraindications to use

Anti-TNFs

- Demyelinating diseases (optic neuritis, multiple sclerosis)
- Congestive heart failure
- Prior lymphoma or other malignancies

Natalizumab (anti- α 4 integrin)

- Associated with reactivation of JC virus leading to PML- use only if antibody to JC virus is negative

Management of Crohn's disease

3. Biologics (anti-TNF, IL-12/23, anti-integrins)

Contraindications to use

Vedolizumab (gut specific anti- $\alpha 4\beta 7$ integrin)

No risk of PML

Ustekinumab (anti-IL12/II23 antibody)

Excellent safety profile- no reported increased risk of infections or malignancies

Management of Crohn's disease

Maintenance of remission

- Biologics are first line usually in combination with immunomodulators
- Corticosteroids and 5-aminosalicylates should not be used as they are not effective in maintaining remission

A 37-year-old man is evaluated for a 1 month history of stool leakage. In the past week he has developed perianal pain and low-grade fevers. He was diagnosed 4 years ago with Crohn's disease involving the small bowel and colon. He takes 6 MP.

On physical exam temperature is 37.9° C, blood pressure is 140/90 mm Hg, and pulse rate is 88/min. Abdominal examination is normal. Perianal examination discloses a fistula orifice anterolateral to the anus with expression of white material with gentle palpation. A fluctuant, tender region is noted posterior lateral to the anus.

In addition to the examination under anesthesia, which of the following is the most appropriate management?

1. Ciprofloxacin
2. Corticosteroids
3. Infliximab
4. Metronidazole

Fistulizing Crohns

Affects 30% Crohns patients

Types of fistulas

External fistulas

- A. Simple (not involving anal sphincter)
- B. Complex (involves anal sphincter)

Internal fistula

- Rectovaginal
- Enterovesical
- Enteroenteric

Fistulizing Crohns

External fistulas

- Fistulotomy
- Seton placement
- Anti-TNF's or thiopurines or combination
- Antibiotics alone may be helpful in simple but not complex fistulae

Internal fistula

- Control inflammation with anti TNF's with/without thiopurines
- Followed by surgical excision of fistula tract

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Indications for surgery in Crohn's disease

- Small bowel obstruction stricture
- Penetrating disease
- Intractable hemorrhage
- Perforation
- Dysplasia or cancer

Risk factors for post-operative recurrence

- Tobacco smoking especially women and heavy smokers
- Penetrating disease
- Progression despite biologics and immunomodulators before surgery
- ≥ 2 prior surgeries
- < 10 years between diagnosis and surgery
- Ileocolonic disease (vs ileal alone)
- Need for corticosteroids before surgery
- Longer segment of bowel resected

Risk factors for post-operative recurrence

Patients with any risk factor for post-op recurrence should receive anti-TNFs in combination with immunomodulators after surgery to prevent recurrence

Patient without risk factors do not need post-op therapy.

A 45-year-old man is evaluated for a 1 week of nonbloody diarrhea, 10 times/day accompanied by mild abdominal cramping. He has a 5 year history of ulcerative colitis for which he takes mesalamine. On exam temperature is 37.9°C, BP normal and pulse rate is 100/min. He has hyperactive bowel sounds and mild diffuse abdominal tenderness without peritoneal signs.

Abnormal labs: WBCs 23,000/mm³, CRP 32 mg/dl, Potassium is 2.9 mEQ/L. Which of the following is the most appropriate diagnostic test to perform next

1. Abdominal CT
2. Colonoscopy
3. Right upper quadrant ultrasound
4. Stool studies for clostridium difficile

C.difficile infection and IBD

- IBD patients are at increased risk of C.difficile
- IBD patients with *C.difficile* have greater risk of hospitalization, longer inpatient stay, risk of colectomy and mortality than *C.difficile* infection in non-IBD patients
- About 40% have no prior history of antibiotic exposure

C.difficile infection and IBD

- Colonic involvement and use of immunomodulators are risk factors for *C.difficile* infection in IBD
- PCR testing for *C.difficile* toxin is recommended in all IBD patients with diarrhea

A 45-year-old man is evaluated for a 1 week of nonbloody diarrhea, 10 times/day accompanied by mild abdominal cramping. He has a 5 year history of ulcerative colitis for which he takes mesalamine. On exam temperature is 37.9°C, BP normal and pulse rate is 100/min. He has hyperactive bowel sounds and mild diffuse abdominal tenderness without peritoneal signs.

Abnormal labs: WBCs 23,000/mm³, CRP 32 mg/dl, Potassium is 2.9 mEQ/L. Which of the following is the most appropriate diagnostic test to perform next

1. Abdominal CT
2. Colonoscopy
3. Right upper quadrant ultrasound
4. Stool studies for clostridium difficile

A 24-year-old woman is evaluated during a routine examination in November. She has ulcerative colitis, which was diagnosed 10 years ago. She currently takes 6 mercaptopurine.

Which of the following vaccinations is contraindicated for this patient

1. Hepatitis B
2. Human papilloma virus
3. Pneumococcal polysaccharide vaccine
4. Tri valent inactivated influenza
5. Varicella

Preventive care in IBD patients

Live vaccines should be avoided in patients receiving immunomodulators or biologics

- Measles-mumps-rubella
- Chicken pox
- Yellow fever
- Live attenuated influenza vaccine
- Varicella
- Oral polio
- BCG

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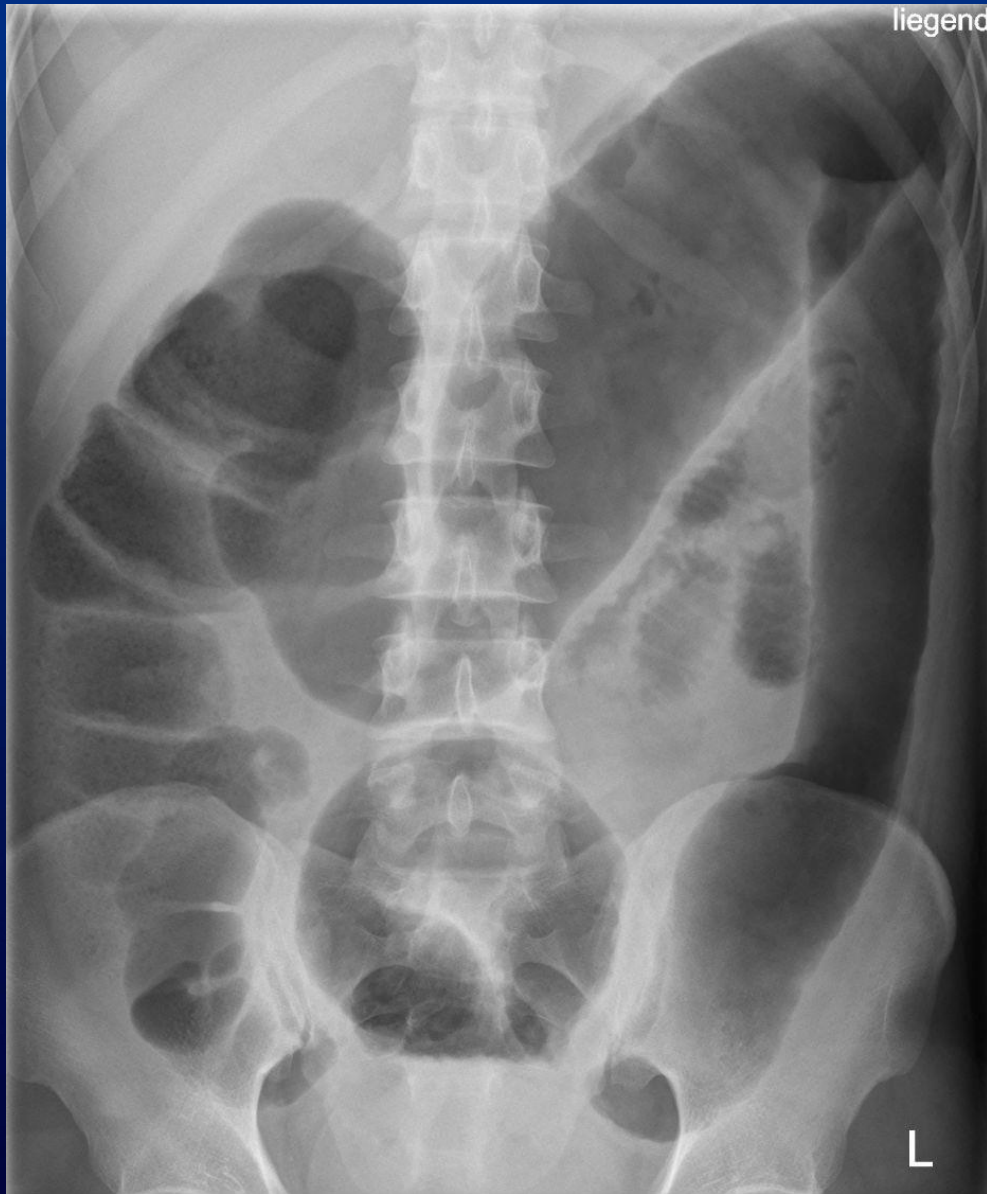
Which of the following vaccinations is contraindicated for this patient

1. Hepatitis B
2. Human papilloma virus
3. Pneumococcal polysaccharide vaccine
4. Trivalent inactivated influenza
5. Varicella

A 37-year-old woman is evaluated in the emergency department for the acute onset of pain after 2 weeks of bloody diarrhea. She has ulcerative colitis diagnosed 2 years ago. She currently takes azathioprine

On physical exam she appears ill. Following aggressive fluid resuscitation temperature is 38.9° C, blood pressure 70/40 mm Hg, pulse rate is 148/min, and respiration rate is 35. Abdominal exam discloses absent bowel sounds, distention and diffuse marked tenderness with mild palpation.

Laboratory studies revealed a leukocyte count of 16,800. Abdominal x-ray is shown



Which of the following is the most appropriate management

1. CT scan
2. Immediate surgical consult
3. Start infliximab
4. Start IV hydrocortisone

Identifying and managing toxic megacolon

Diagnosis

≥3 of the following

- Temperature > 38.6 °C
- Heart rate > 120/min
- WBC count > 10,500
- Anemia

Plus ≥1 of the following

- Dehydration
- Altered mental status
- Electrolyte disturbance
- Hypotension

Other clinical features

- Abdominal distension and tenderness
- Decreased or absent bowel sounds
- Dilated colon on x-ray

Identifying and managing toxic megacolon

Predisposing factors

- *C.difficile* infection
- Narcotics
- Anticholinergics (diphenoxylate, hyoscyamine)
- Narcotic antidiarrheals (loperamide)
- Barium enema



Which of the following is the most appropriate management

1. CT scan
2. Immediate surgical consult
3. Start infliximab
4. Start IV hydrocortisone

Identifying and managing toxic megacolon

Management

- Early surgical consult for consideration of colectomy
- NPO, IV fluids, broad spectrum antibiotics
- Ask patient to roll in bed from side to side or lie in knee elbow position every 30 minutes
- Treat underlying ulcerative colitis or *C.difficile* infection

A 52-year-old woman is evaluated for a 9 year history of intermittent rectal bleeding with associated mucus. Over the past several weeks, she has noticed fecal urgency, tenesmus, rectal bleeding. There is no family history of IBD or colorectal cancer.

Colonoscopy discloses normal endoscopic appearance of the entire colon. Random biopsies showed no evidence of inflammation and no dysplasia. The rectal mucosa shows loss of vascular markings, erythema and friability. Biopsies showed chronic inflammatory changes including crypt distortion and crypt atrophy consistent with ulcerative proctitis. No dysplasia is noted

Which of the following is the most appropriate approach to colorectal cancer surveillance for this patient

Which of the following is the most appropriate approach to colorectal cancer surveillance for this patient

1. Colonoscopy in 1 year
2. Colonoscopy in 3 years
3. Colonoscopy in 5 years
4. Colonoscopy in 10 years

Understanding screening and surveillance of dysplasia in IBD

Risk factors for colorectal cancer in IBD

- Ulcerative colitis (UC) like symptoms for at least 8 years
- Primary sclerosing cholangitis (PSC)
- Family history of colorectal cancer
- Severe inflammation

Recommendations for screening

- UC-like symptoms for at least 8 years
- At time of diagnosis of PSC

When to repeat surveillance

If no dysplasia on initial colonoscopy

- Every 1-2 years: If inflammation extends proximal to the sigmoid colon
- Annually in Primary sclerosing cholangitis

If inflammation limited to rectum (proctitis) or rectosigmoid (proctosigmoiditis)

- no greater risk of colorectal cancer than non-IBD – same screening guidelines as for average risk

40-year-old woman is evaluated for a 1 year history of reflux symptoms. She has heartburn and regurgitation several times a week. Lifestyle modifications and trial of once daily proton pump inhibitor 12 weeks ago produced minimal relief of symptoms. For the past 6 weeks she has taken the PPI twice daily without relief of symptoms. She has intermittent solid food dysphagia. Which of the following is the most appropriate next step in management?

1. Add H2 blocker at night
2. Ambulatory esophageal pH study
3. Endoscopy
4. Fundoplication

Diagnosis and management of GERD

A clinical diagnosis of GERD only requires typical symptoms like heartburn and regurgitation.

An empiric trial of PPIs is recommended unless patient has following indications for EGD:

- Alarm symptoms such as dysphagia or weight loss
- Has risk factors for Barrett's
- Elderly
- Unresponsiveness to PPI trial warrants an EGD
-

Diagnosis and management of GERD

Ambulatory pH monitoring is recommended

- Pre operatively for patients with nonerosive GERD
- In patients with refractory GERD symptoms
- When the diagnosis of GERD is in question.

40-year-old woman is evaluated for a 1 year history of reflux symptoms. She has heartburn and regurgitation several times a week. Lifestyle modifications and trial of once daily proton pump inhibitor 12 weeks ago produced minimal relief of symptoms. For the past 6 weeks she has taken the PPI twice daily without relief of symptoms. She has intermittent solid food dysphagia. Which of the following is the most appropriate next step in management?

1. Add H2 blocker at night
2. Ambulatory esophageal pH study
3. Endoscopy
4. Fundoplication

A 50-year-old man is evaluated for persistent heartburn and regurgitation despite taking a high dose proton pump inhibitor twice daily for 6 months. His symptoms have improved, but he continues to have symptoms many times a week. No dysphagia, chest pain or weight loss. BMI of 31. Endoscopy reveals persistent esophagitis and a moderately large hiatal hernia.

Which of the following is the most appropriate next step in management?

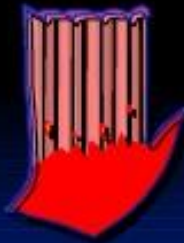
1. Add twice daily sucralfate
2. Fundoplication
3. Increase the dose of esomeprazole
4. Radiofrequency ablation

Los Angeles (LA) Grade Classification of Erosive Esophagitis

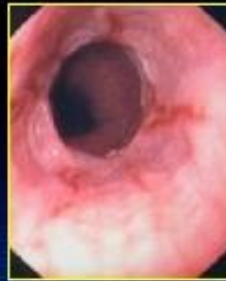
LA Grade A



One or more mucosal breaks no longer than 5mm, not bridging the tops of mucosal folds



LA Grade B



One or more mucosal breaks longer than 5mm, not bridging the tops of mucosal folds



LA Grade C



One or more mucosal breaks bridging the tops of mucosal folds involving <75% of the circumference



LA Grade D



One or more mucosal breaks bridging the tops of mucosal folds involving >75% of the circumference



Lundell et al. Gut. 1999;45:172-180.

Management of erosive esophagitis

- An 8-12 week course of once daily PPI is the treatment of choice for erosive esophagitis
- In patients with partial symptom improvement increasing the dose to twice daily or switching to a different PPI may help

Management of erosive esophagitis

- Indications for maintenance PPI therapy
- Recurrence of symptoms after discontinuing PPIs
- Grade C and D esophagitis
- Barrett's esophagus
- Complications- peptic stricture or Schatzki's ring

- There is no role for sucralfate in the non pregnant GERD patient
- PPIs are safe in pregnant patients if clinically indicated

Management of refractory GERD

1. EGD to rule out other causes such as EoE
2. If endoscopy negative then ambulatory pH monitoring is recommended preferably off therapy
3. Abnormal pH study and significant association between symptoms and episodes of acid reflux-consider surgery vs. medications like baclofen
4. Esophageal manometry recommended before surgery to rule out major her motility disorders like achalasia and scleroderma

Surgery for GERD

Indications

- Patient's desire to discontinue medical therapy
- Noncompliance with medical therapy
- Side effects with medical therapy
- Large hiatal hernia
- Esophagitis refractory to medical therapy
- persistent symptoms documented to be caused by GERD

Surgery for GERD

Surgical options

- Fundoplication
- Bariatric surgery in those with obesity

Predictors of good response to surgery

- Typical symptoms of heartburn or regurgitation that responded well to PPI therapy
- Abnormal pH testing with significant symptom to reflux association

A 50-year-old man is evaluated for persistent heartburn and regurgitation despite taking a high dose proton pump inhibitor twice daily for 6 months. His symptoms have improved, but he continues to have symptoms many times a week. No dysphagia, chest pain or weight loss. BMI of 31. Endoscopy reveals persistent esophagitis and a moderately large hiatal hernia.

Which of the following is the most appropriate next step in management?

1. Add twice daily sucralfate
2. Fundoplication
3. Increase the dose of esomeprazole
4. Radiofrequency ablation

A 30-year-old man is evaluated for 5 years of progressively worsening solid food dysphagia. He has occasional heartburn. He went to the emergency department 2 weeks ago for an episode of food impaction and underwent disimpaction of food bolus. He takes no medications. Endoscopy reveals a rings in the esophagus and mid esophageal biopsies showed 30 eosinophils per high-power field. Which of the following is the most appropriate next step in management?

1. Endoscopic dilation
2. Food allergy testing
3. Initiate omeprazole
4. Initiate swallowed aerosolized fluticasone

Management of eosinophilic esophagitis

Diagnosis

1. Symptoms of esophageal dysfunction- dysphagia, non-exertional chest pain
2. More than 15 eosinophils per high-power field on esophageal biopsy
3. Rule out other conditions that can potentially cause esophageal eosinophilia

Management of eosinophilic esophagitis

Supporting criteria

1. Atopic conditions (rhinitis, asthma and eczema) are present in up to 60% of EoE patients
2. Endoscopic findings are suggestive but not entirely reliable
3. Eosinophilic infiltration should be isolated only to the esophagus

Testing for food allergies by skin prick or patch testing is not recommended

Causes of esophageal eosinophilia

1. Eosinophilic esophagitis
2. Eosinophilic gastritis gastroenteritis or colitis with esophageal involvement
3. GERD
4. Achalasia and other disorders of esophageal motility
5. Hypereosinophilic syndrome
6. Crohn's disease with esophageal involvement
7. Fungal and viral infections
8. Connective tissue disorders
9. Autoimmune disorders and vasculitis
10. Dermatologic conditions with esophageal involvement like pemphigus
11. Drug hypersensitivity reactions
12. Pill esophagitis
13. Graft-versus-host disease
14. Mendelian disorders like Marfan's syndrome type 2, hyper IgE syndrome, PTEN hamartoma tumor syndrome

Management of eosinophilic esophagitis

Untreated EOE leads to esophageal remodeling, fibrosis and ultimately stricture formation (likelihood of stricture nearly 90% if diagnosis delayed by 20 years)

Treatment

1. PPIs – 1st line

- Usually at a dose of 20-40 mg twice daily
- Induces clinical and histologic remission in about 30 to 40% of patients after 8 weeks
- In these patients PPIs should be continued At the lowest effective dose to maintain remission

Management of eosinophilic esophagitis

Treatment

2. Topical steroids (oral viscous budesonide or inhaled fluticasone) induces histological remission in nearly 70% of patients. However its effect on improving symptoms is less clear.

3. In patients will respond to topical steroids, long-term therapy is effective in maintaining remission in about 40% of patients

4. Systemic steroids (e.g. prednisone) are not recommended in EOE

Elimination diet

Six food elimination diet (SFED) avoiding milk, wheat, egg, soy, peanut/tree nuts, fish and seafood

- induced histologic remission in ~ 70%
- Most patients have 1 or 2 food intolerances.
- Four food elimination diet avoiding cow's milk, wheat, egg, soy and legumes achieves histologic remission in 54% patients
- The most common trigger is cow's milk. A 2 food elimination diet excluding cow's milk and wheat is effective in up to 40% of patients.
- Used if PPIs and topical steroids fail to improve symptoms/histology

Endoscopic dilation

- Improves dysphagia in nearly 75% of adult eoe patient's but has no effect on the underlying inflammation.
- Perforation rate less than 1%

Therapy should be individualized based on discussion with the patient. The efficacy of the chosen therapy should be checked by EGD after 6-12 weeks.

A 30-year-old man is evaluated for 5 years of progressively worsening solid food dysphagia. He has occasional heartburn. He went to the emergency department 2 weeks ago for an episode of food impaction and underwent disimpaction of food bolus. He takes no medications. Endoscopy reveals a rings in the esophagus and mid esophageal biopsies showed 30 eosinophils per high-power field. Which of the following is the most appropriate next step in management?

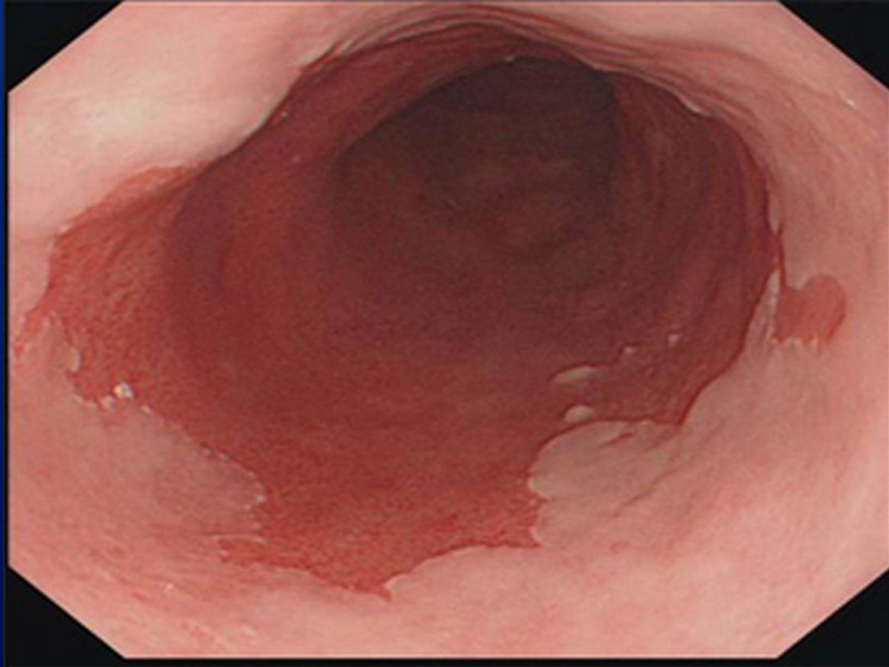
1. Endoscopic dilation
2. Food allergy testing
3. Initiate omeprazole
4. Initiate swallowed aerosolized fluticasone

A 55-year-old man is evaluated for 6 years history of typical GERD symptoms treated on an as-needed basis with PPIs. However, the frequency of his reflux symptoms as recently increased and his episodes do not respond to treatment as completely as in the past. An upper endoscopy revealed a for 4 cm segment of salmon colored mucosa in the distal esophagus. Biopsy from this segment reveals intestinal metaplasia and goblet cells with no dysplasia.

In addition to starting a daily PPI, which of the following is the most appropriate management?

1. Daily cyclooxygenase-2 inhibitor therapy
2. Endoscopic ablation
3. Fundoplication
4. Repeat endoscopy in 3 year

Barrett's esophagus



- Extension of salmon colored mucosa into the tubular esophagus >1 cm proximal to the GE junction
- Histologically- intestinal metaplasia with goblet cells (\pm dysplasia)

Am J Gastroenterol 2016; 111:30–50

Risk factors for Barrett's esophagus (BE)

- GERD symptoms for > 5 years
- Males
- Age > 50 years
- Central obesity
- Tobacco smoking- ever
- Caucasian race

Annual risk of esophageal adenocarcinoma in BE

- Non dysplastic BE 0.2-0.5%
- Low grade dysplasia 0.7%
- High grade dysplasia 7%

Screening for Barrett's esophagus (BE)

Symptoms of GERD for more than 5 years or at least once a week *Plus* at least 2 risk factors

1. Age >50 years
2. Male
3. Caucasian race
4. Central obesity (waist circumference >102 cm or waist to hip ratio more than 0.9)
5. Current or past history of smoking
6. Confirmed family history of BE or esophageal adenocarcinoma in a 1st degree relative

Screening and surveillance in BE

1. Initial EGD no BE- repeat endoscopy to search for BE not recommended
2. Initial EGD esophagitis- repeat EGD after 8-12 weeks treatment with PPIs
3. Dysplasia of any grade should be reviewed by 2 pathologist's at least 1 of whom is a GI pathologist
4. BE without dysplasia- surveillance EGD every 3-5 years
5. Indefinite for dysplasia- repeat EGD in 3-6 months after PPI therapy

Treatment of dysplasia in BE

1. Confirmed low-grade dysplasia without life-threatening comorbidities-endoscopic therapy (EMR, ESD, RFA) or repeat EGD in 12 months
2. BE with high-grade dysplasia-managed with endoscopic therapy unless they have life limiting comorbidities

A 55-year-old man with 4 cm non dysplastic Barrett's esophagus.

In addition to starting a daily PPI, which of the following is the most appropriate management?

1. Daily cyclooxygenase-2 inhibitor therapy
2. Endoscopic ablation
3. Fundoplication
4. Repeat endoscopy in 3 year

A 45-year-old woman is evaluated for a 2 year history of dysphagia to solids and liquids, intermittent nonexertional chest pain and regurgitation. Her weight has been stable. She lives in a remote rural area. Barium swallow is shown.



Which of the following is most appropriate management?

1. Botulinum toxin injection into the lower esophageal sphincter
2. Pneumatic balloon dilation
3. Laparoscopic myotomy
4. Sublingual nifedipine

Achalasia

It is a disorder characterized by impaired relaxation of the lower esophageal sphincter due to irreversible destruction of nitric oxide releasing neurons in the myenteric plexus.

When to suspect:

1. Dysphagia to solids and liquids
2. Regurgitation unresponsive to a trial of B.I.D. PPI
3. Upper endoscopy reveals retained saliva, liquid or food in the esophagus without mechanical obstruction from a stricture or mass.

Achalasia

Diagnosis

1. Esophageal manometry is the definitive test
2. Upper endoscopy and barium esophagram may suggest the diagnosis but are not as sensitive and specific as manometry

Management of achalasia

Available treatments

- ☐ Laparoscopic myotomy with partial fundoplication
- ☐ Per oral endoscopic myotomy
 - Surgical myotomy usually combined with partial fundoplication to reduce GERD
 - Comparable efficacy of pneumatic dilation (92%) and laparoscopic myotomy (83%) at 2 years
 - POEM available only in few select centers
- ☐ Pneumatic dilation
- ☐ Botulinum toxin
- ☐ Pharmacotherapy

Management of achalasia

Pneumatic dilation

- Disrupts LES by distending a balloon
- Perforation rate is about 2%- therefore must be near a center with expertise to manage perforation including esophagectomy if necessary
- Predictors of favorable response:
 - Older age (> 45 years)
 - Women
 - Narrow esophagus before dilation
- Advantage: Can be repeated

Management of achalasia

Botulinum toxin

- Inhibits release of acetylcholine from nerve endings causing short-term paralysis of the esophageal sphincter
- While initial response is high the effect eventually wears off and repeat injections are required
- Generally used in patients who cannot undergo pneumatic dilation or myotomy because of patient related risk factors.

Management of achalasia

Pharmacotherapy

- Calcium channel blockers and long acting nitrates
- Short duration of action
- Side effects- hypotension, headache, pedal edema
- Reserved for patients who refuse definitive therapies and have failed Botox injection

Which of the following is most appropriate management of a 45 year old woman with achalasia who lives in a remote rural area?

1. Botulinum toxin injection into the lower esophageal sphincter
2. Pneumatic balloon dilation
- 3. Laparoscopic myotomy**
4. Sublingual nifedipine

A 50-year-old man is evaluated for a 6 month history of worsening dysphagia to both solids and liquids. He has lost 4.5 kg.

Barium esophagram is shown.

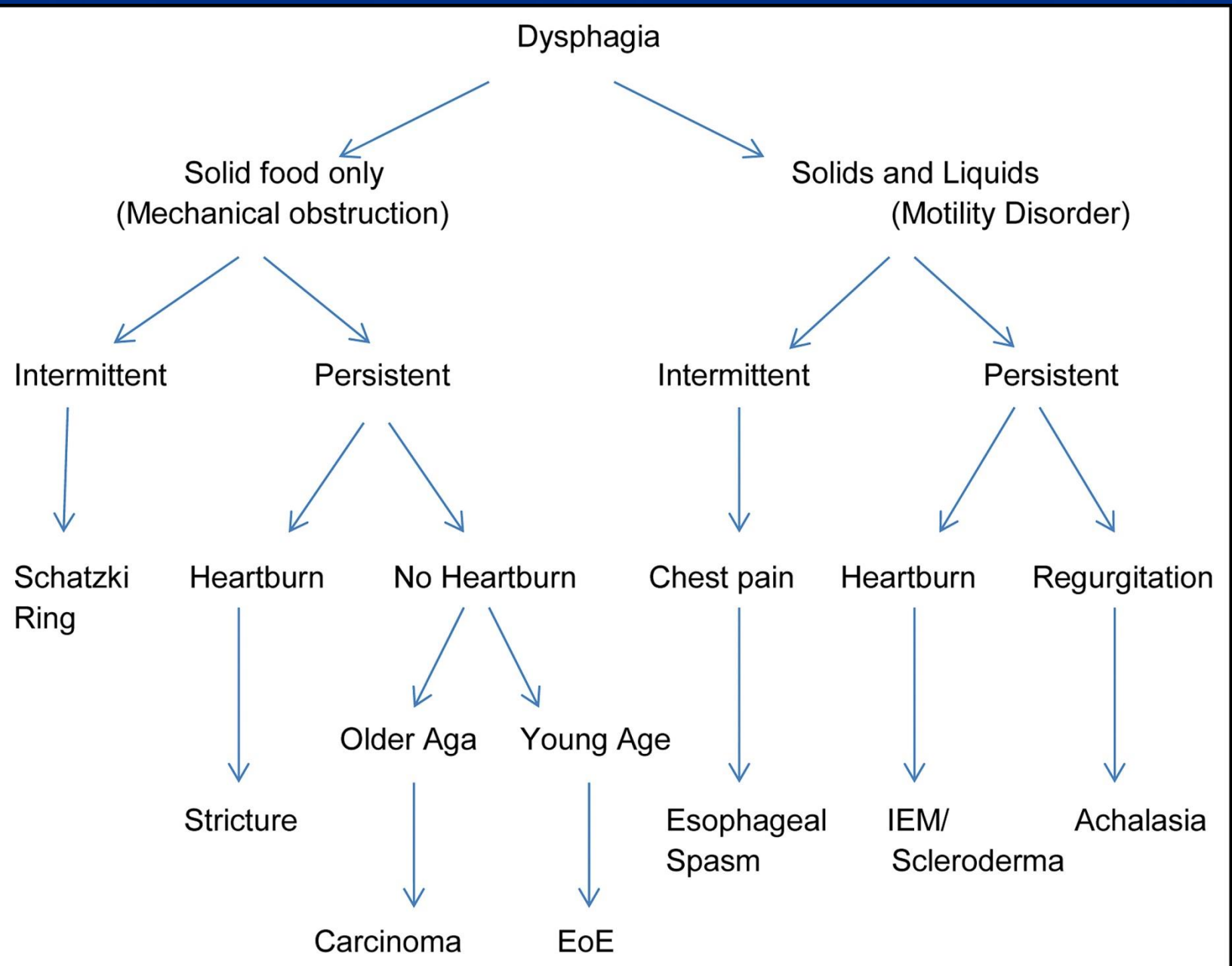
Esophageal manometry shows no peristalsis. Which of the following is the most appropriate management

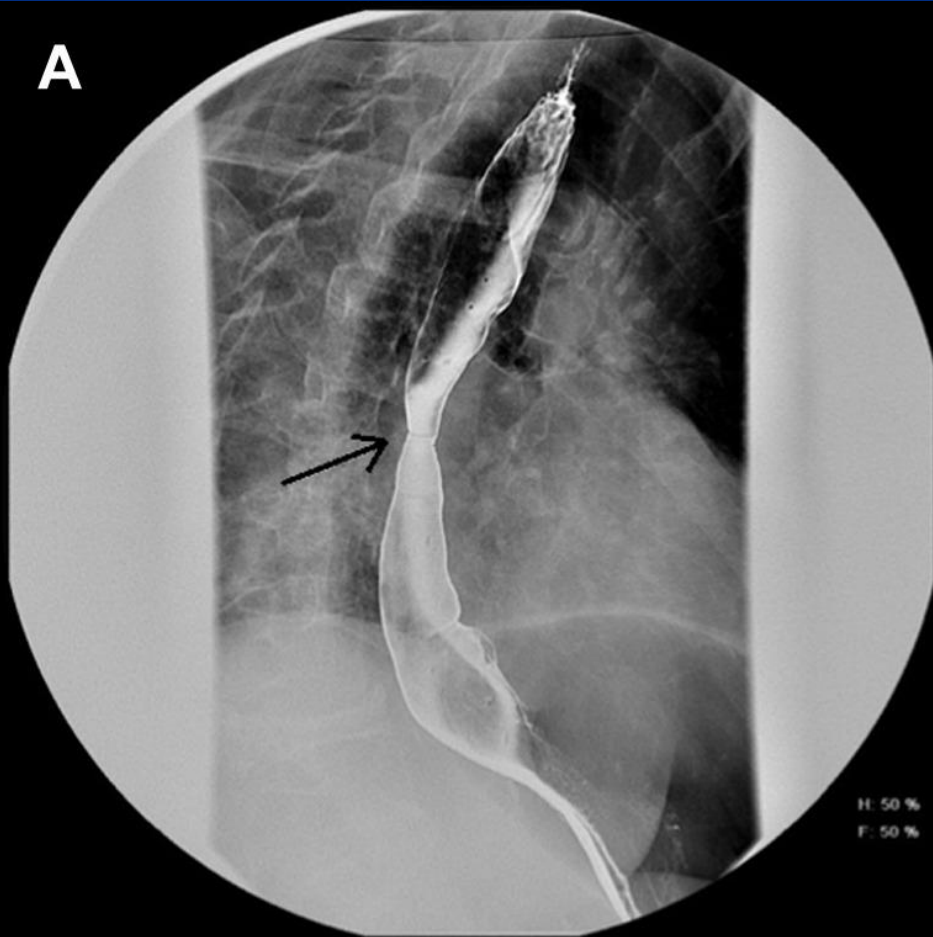
1. CT of the chest and abdomen
2. Endoscopy
3. Myotomy
4. Trial of aerosolized corticosteroids



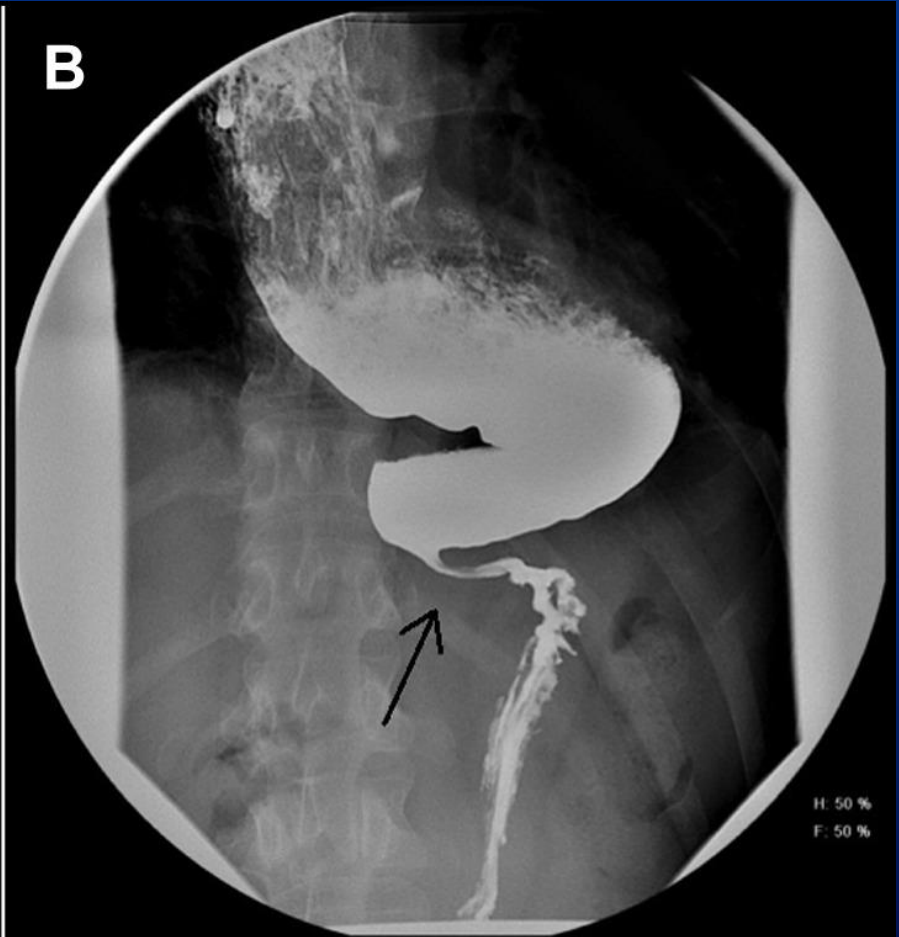
Evaluation of new onset dysphagia with alarm symptoms

Endoscopic assessment of the gastroesophageal junction and cardia is recommended in **all** patients with dysphagia to rule out pseudo achalasia due to tumors infiltrating the gastric cardia (gastroesophageal junction cancer, pancreatic, breast, lung or hepatocellular cancer)





Stricture



Bird beak-
achalasia

A 65-year-old woman with amyotrophic lateral sclerosis is evaluated for a 1 month history of difficulty swallowing. She experiences choking and coughing while attempting to swallow solids or liquids and has intermittent nasal regurgitation of liquids. Two weeks ago she was treated for pneumonia. Which of the following is the most appropriate initial diagnostic test to evaluate this patient's swallowing disorder?

1. Endoscopy
2. Esophageal manometry
3. Upper GI series
4. video fluoroscopy

Evaluation of oropharyngeal dysphagia

- Systemic neuromuscular diseases like scleroderma usually cause dysphagia of the lower esophagus while amyotrophic lateral sclerosis or myasthenia gravis usually effect oropharyngeal function
- Patient with oropharyngeal dysphagia may note nasal regurgitation, coughing during swallowing, drooling and voice changes.
- A video swallow study is the preferred 1st investigation for oropharyngeal dysphagia to assess for presence of aspiration

A 42 year old asymptomatic man is evaluated in follow-up for elevated liver tests. He has a 6 year history of type-2 diabetes mellitus, hyperlipidemia, and hypertension. His current medications are metformin, simvastatin and lisinopril. He does not drink alcohol. BMI is 32. Abdominal exam discloses mid hepatomegaly.

Laboratory studies

Alkaline phosphatase	90 U/L
ALT	120 U/L
AST	85 U/L
Total bilirubin	1.1 mg/dl
Hep B sAb	Positive
Hep C virus antibody	Negative

Abdominal ultrasound reveals increased hepatic echotexture consistent with hepatic steatosis. Hepatic configuration is otherwise normal

In addition to weight loss, which of the following is the most appropriate management?

- A. Discontinue simvastatin
- B. Initiate entecavir
- C. Phlebotomy
- D. Serial monitoring of aminotransferases

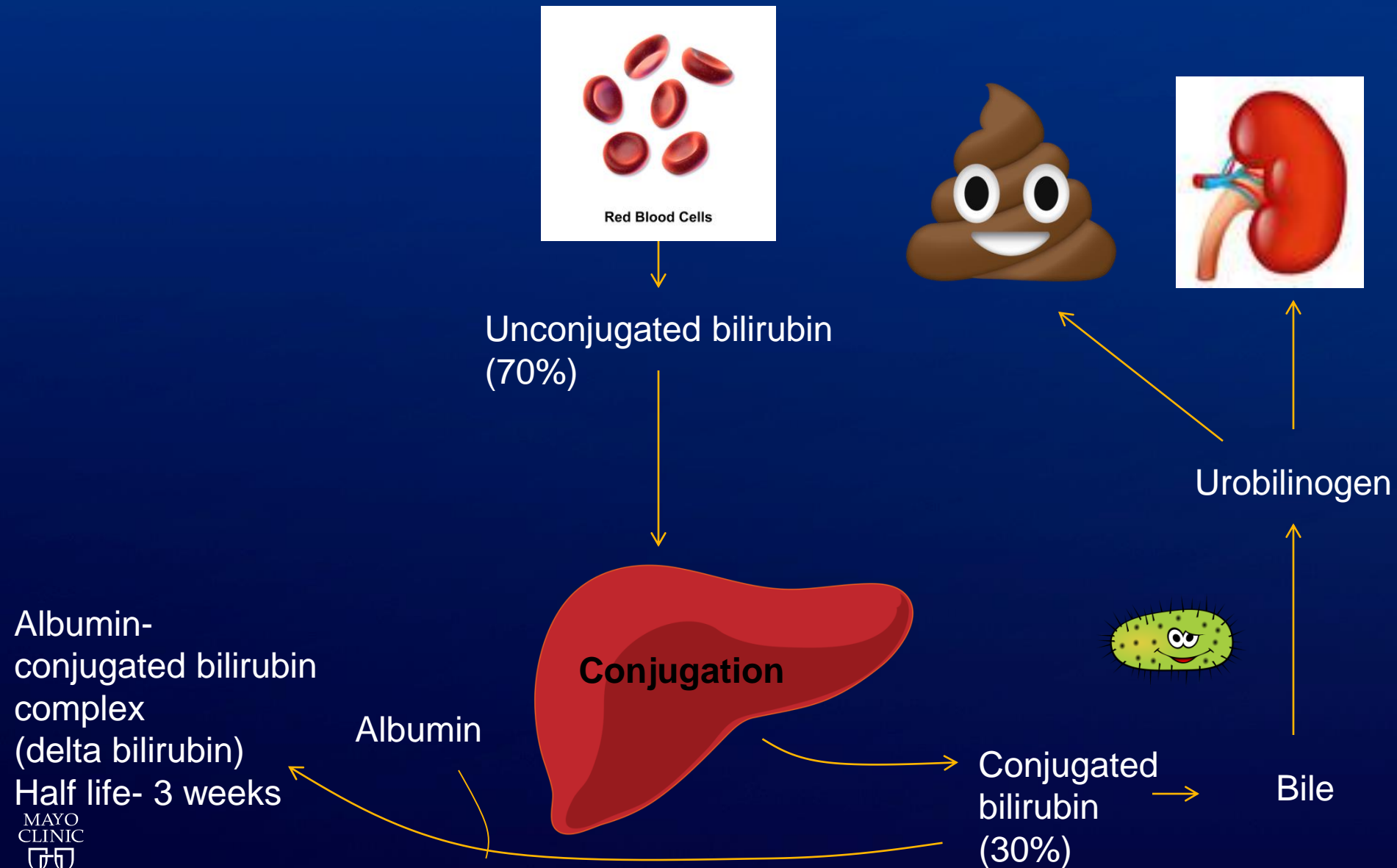
Liver function tests?

Tests of liver injury	Tests of liver function
AST	Prothrombin time
ALT	Albumin
Alkaline phosphatase	Bilirubin
Bilirubin	

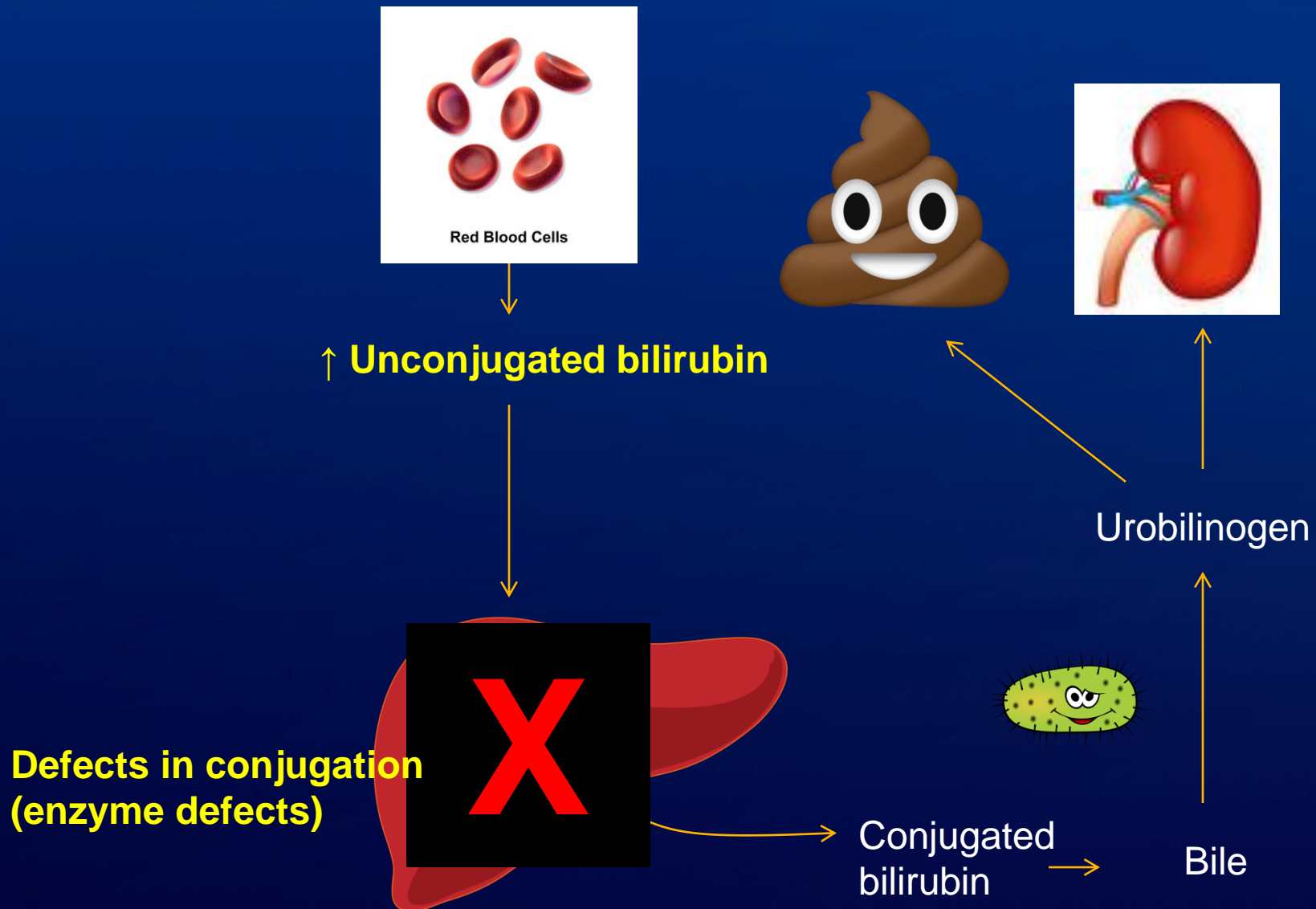
Extrahepatic sources of enzymes released during liver injury

Enzyme	Extra-hepatic source
AST	Muscle- cardiac and skeletal
	Kidney
	Brain
Alkaline phosphatase	Bone
	Placenta
	Intestine
	Kidney

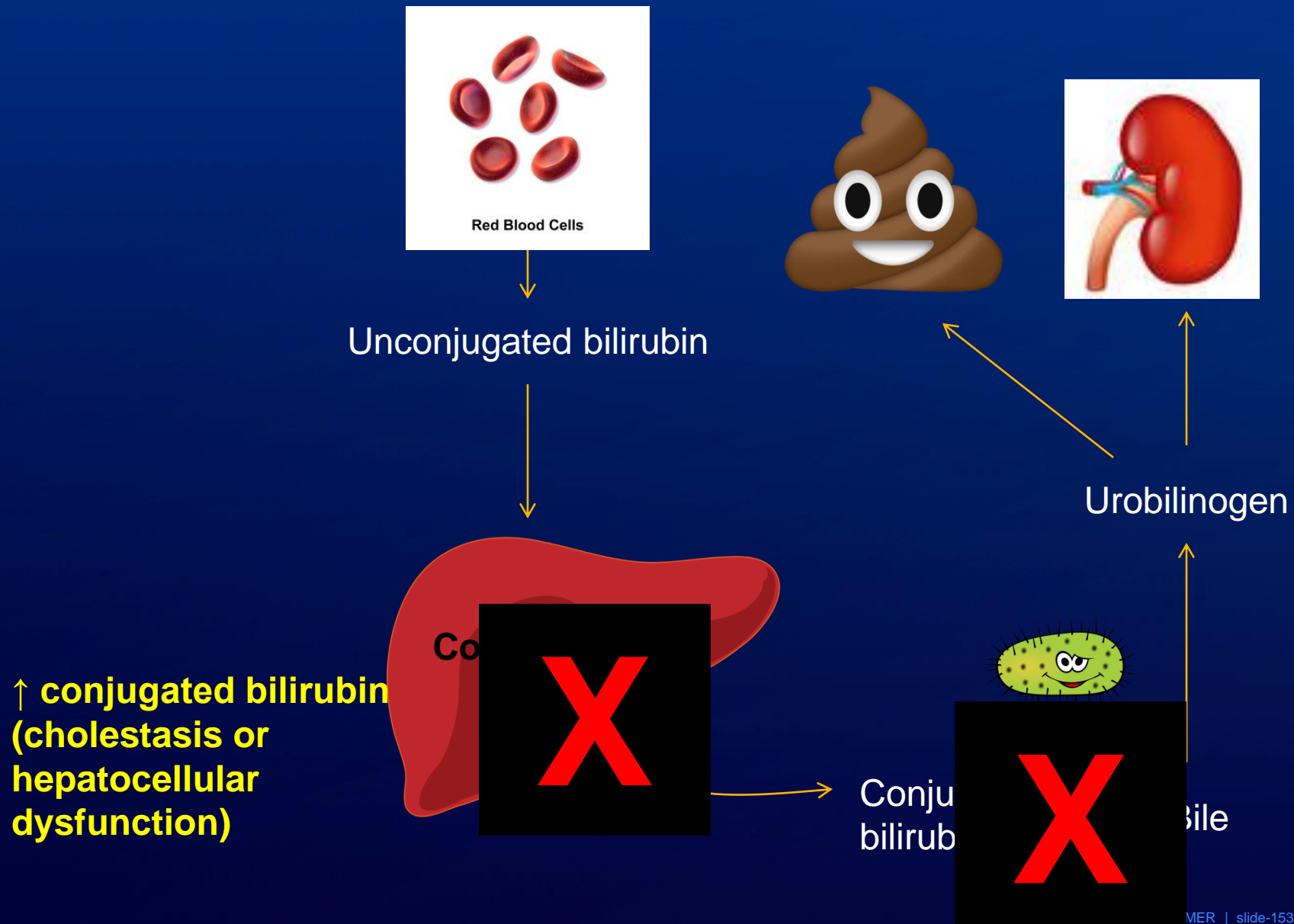
Bilirubin- Normal



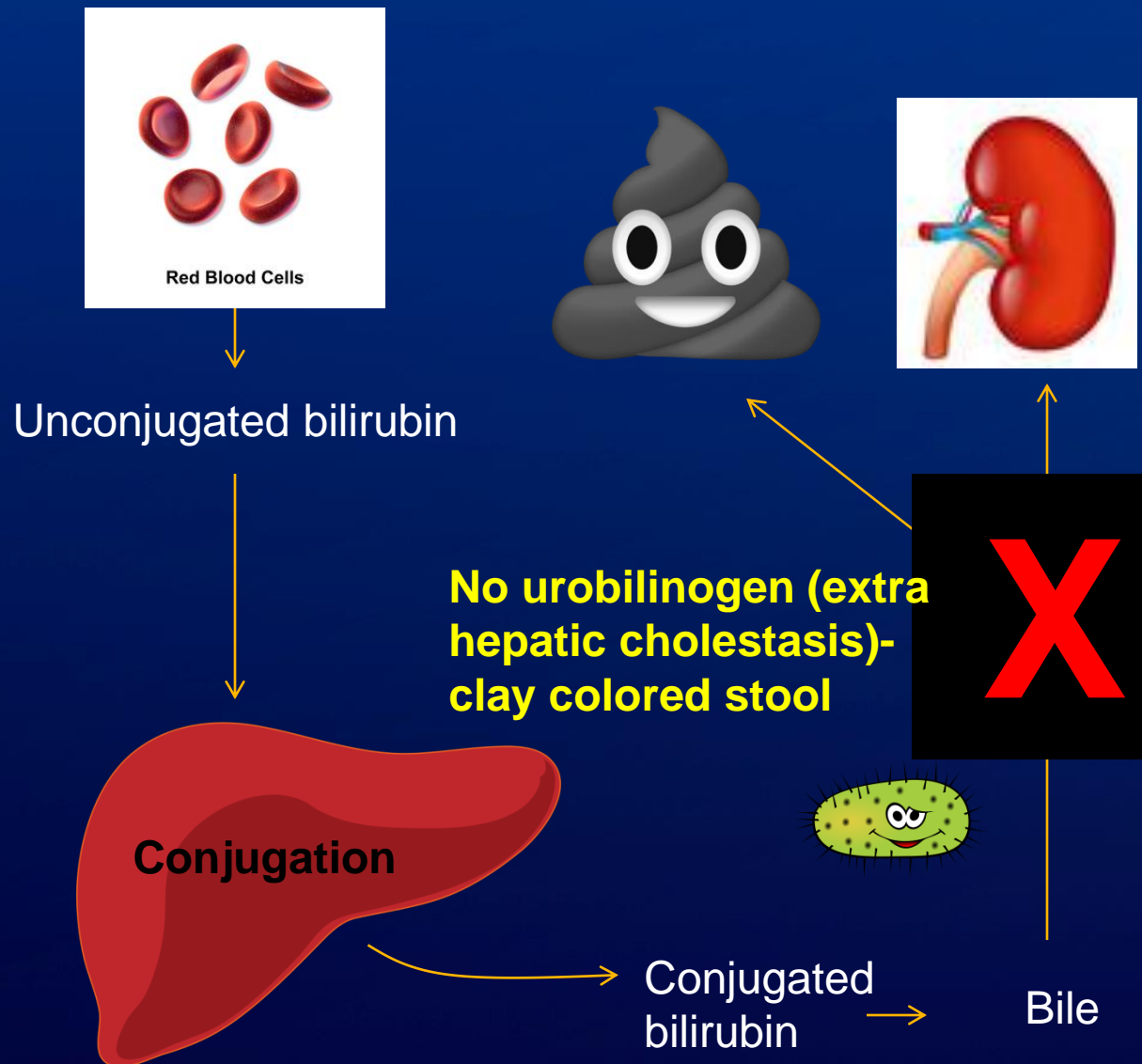
Bilirubin- Pathology



Bilirubin- Pathology



Bilirubin- Pathology



Albumin

- Exclusively synthesized by liver
- Half life 3 weeks

Take home point 1

- Low albumin (<3.5 g/dl) indicates liver disease of at least 3 weeks duration
- Any acute illness can decrease albumin levels due to effect of cytokines

Prothrombin time

- Normal level requires level of factors 1,2,5,7,9, 10
- Factors 2,7,9 and 10 require Vitamin K- therefore in cholestasis, where vitamin K is not absorbed PT is prolonged
- Hepatocellular dysfunction also increases PT due to clotting factor deficiency
- Vitamin K deficiency in absence of chronic liver disease indicates steatorrhea

Prothrombin time

Take home point 1

- Clotting factor levels need to fall below 10% before PT is prolonged
- Causes of prolonged PT- warfarin, heparin bolus, DIC and hypothermia

Approach to abnormal liver tests for boards



Is this a real elevation?

Take home point 1

- If it's a new elevation always confirm by repeating liver tests
- If alkaline phosphatase is elevated check a GGT or fractionate alkaline phosphatase to assess if the elevation is coming from the liver

Approach to abnormal liver tests for boards



Hepatocellular
(\uparrow AST/ALT) or
cholestatic (\uparrow ALP)?

Take home point 1

- R-ratio: (ALT/ ULN for ALT) >5 = hepatocellular
----- <2 = cholestatic
(Alk Phos/ ULN for Alk Phos) 2-5= mixed

Predominantly elevated AST/ALT

Approach to abnormal liver tests for boards



Could this be Hep C?

Risk factors

- intravenous or intranasal drug use
- Tattoos or body piercings
- Needle stick exposure
- Blood transfusion before 1992
- Birth date between 1945-1965

Hepatitis C testing

Anti-HCV antibody

- Becomes positive 6-8 weeks after acute infection
- 92-97% sensitive
- False positive rate upto 5%
- Upto 30% people with no risk factors can be falsely positive if tested ,so always confirm a positive test with Hepatitis C RNA PCR
- Screening: Everyone born between 1945 and 1965

Hepatitis C testing

Take home point 1

- Anti-HCV Ab may be negative in acute Hep C. Always check HCV RNA if suspecting acute Hep C
- Acute Hep C may be asymptomatic

Approach to abnormal liver tests for boards



Could this be Hep B?

Risk factors

- Born in endemic area
- Any IV drug use
- Men who have sex with men
- Dialysis patients
- HIV infected
- Pregnant
- Family members, sexual partners and household contacts of Hep B infected

Approach to abnormal liver tests for boards



Could this be Hep B?

Take home point 1

- HbsAg and HbC IgM are positive in acute Hep B.

Hepatitis B testing

Test	What does a positive test mean
Hepatitis B surface antigen	Infection
Hepatitis B core antibody, IgM	Acute infection
Hepatitis B core antibody, IgG	Past infection
Hepatitis B surface antibody	Immunity either from infection or vaccine

Chronic Hepatitis B infection	Acute Hepatitis B infection
Hepatitis B surface antigen or Hepatitis B DNA positive	Hepatitis B surface antigen and Hepatitis B core antibody, IgM subtype positive

Approach to abnormal liver tests for boards



Could this be Hep A?

History

- Acute hepatitis
- Feco-oral exposure

Take home point 1

- Hep A IgM positive in acute Hep A

Approach to abnormal liver tests for boards



Could this be Hep E?

History

- Acute hepatitis
- Feco-oral exposure
- Tests for Hep A, B and C negative
- Visit to endemic area (Central America or Asia)

Take home point 1

- Hep E IgM positive in acute Hep A

Approach to abnormal liver tests for boards



Could this be Alcoholic hepatitis?

History

- Alcohol use: > 140 g/week women (10 standard drinks) or 210 g/week men (15 standard drinks)
- AST > ALT, usually < 300 IU/L
- AST/ALT at least 2:1. Ratio 3:1 or more makes it highly likely

Approach to abnormal liver tests for boards



Could this be Alcoholic
hepatitis?

Take home point 1

- Estimate alcohol use in patients with liver disease

Non Alcoholic Fatty Liver Disease

- No specific serologic test
- No specific pattern of liver test abnormalities
- ALT generally more than AST but usually < 300 IU/L
- NASH- requires liver biopsy to diagnose (inflammation and fibrosis)
- NASH more likely if steatosis accompanied by elevated transaminases
- Elastography (ultrasound or MRI) can identify advanced fibrosis non-invasively

What Is a Standard Drink?

**12 fl oz of
regular beer**



**8–9 fl oz of
malt liquor**
(shown in a
12 oz glass)



**5 fl oz of
table wine**



**1.5 fl oz shot of
distilled spirits**
(gin, rum, tequila,
vodka, whiskey, etc.)



about 5%
alcohol



about 7%
alcohol



about 12%
alcohol



about 40%
alcohol

Each beverage portrayed above represents one standard drink (or one alcoholic drink equivalent), defined in the United States as any beverage containing .6 fl oz or 14 grams of pure alcohol. The percentage of pure alcohol, expressed here as alcohol by volume (alc/vol), varies within and across beverage types. Although the standard drink amounts are helpful for following health guidelines, they may not reflect customary serving sizes.

Approach to abnormal liver tests for boards



Could this be Hereditary hemochromatosis?

- All other tests negative
- Screening test: transferrin saturation and ferritin . If saturation $\geq 45\%$ or ferritin elevated test for HFE gene mutation

Approach to abnormal liver tests for boards



Could this be Hereditary
hemochromatosis?

Take home point 1

- Screen for HFE with ferritin and transferrin saturation
- HFE gene mutation testing to diagnose hemochromatosis

Approach to abnormal liver tests for boards



Could this be Autoimmune hepatitis?

- ANA > 1:160 especially homogenous pattern
- Anti-smooth muscle antibody
- Histology required for confirmation

Approach to abnormal liver tests for boards



Could this be Autoimmune hepatitis?

Take home point 1

- Test for autoimmune hepatitis with anti nuclear, anti smooth muscle antibodies and serum IgG level

Approach to abnormal liver tests for boards



Could this be Wilsons disease?

History

- Age < 55
- Screening: low serum copper, ceruoplasmin and uric acid
- Confirm: elevated 24 hr urinary copper or KF rings on slit lamp examination

Approach to abnormal liver tests for boards



Could this be alpha-1
antitrypsin deficiency?

Screening: serum alpha-1 antitrypsin,
phenotype (PiZZ= “Zero” antitrypsin. PiMM=
“Many” antitrypsin, PiMZ= can cause liver
damage if fatty liver or viral hepatitis present

Take home point 1

- Test for alpha-1 antitrypsin phenotype

Approach to abnormal liver tests for boards



Could this be drug induced
liver injury?

History

- use of OTC, complementary, herbals and supplements

Predominantly
elevated Alkaline
phosphatase

Approach to abnormal liver tests for boards



Could this be PBC?

- Fatigue, pruritus
- Elevated alkaline phosphatase (\pm elevated bilirubin)
- 95% have anti-mitochondrial antibodies

Take home point 1

- PBC= anti-mitochondrial antibodies
- Confirmation is by histology

Approach to abnormal liver tests for boards



Could this be PSC?

- History of inflammatory bowel disease- particularly UC
- Buzz words:
 - “string of beads” appearance of bile ducts on MRCP/ERCP
 - “Onion skin” appearance due to concentric fibrosis on histology
- Risk of hepatocellular carcinoma and cholangiocarcinoma

Approach to abnormal liver tests for boards



Could this be PSC?

- History of inflammatory bowel disease- particularly UC
- Buzz words:
 - “string of beads” appearance of bile ducts on MRCP/ERCP
 - “Onion skin” appearance due to concentric fibrosis on histology
- Risk of hepatocellular carcinoma and cholangiocarcinoma

Take home point 1

- PSC- strongly associated with ulcerative colitis

Approach to abnormal liver tests for boards



Other causes of elevated alkaline phosphatase

- Bile duct obstruction
- Medications
- Sepsis
- Total parenteral nutrition
- Infiltrative disorders-Sarcoidosis, lymphoma
- Celiac disease

Approach to abnormal liver tests for boards

Take home point 1

All patients with elevated alkaline phosphatase should be tested for

- Primary biliary cirrhosis with anti-mitochondrial antibodies
- Primary sclerosing cholangitis with MRI-MRCP plus serum IgG4

Approach to abnormal AST/ALT

Fold increase	Differential
< 5	<ul style="list-style-type: none">➤ viral hepatitis B/C➤ Alcohol/NAFLD➤ Hereditary hemochromatosis➤ Autoimmune hepatitis➤ Wilsons➤ alpha-1 antitrypsin def.➤ Drugs/supplements
> 5 but less than 15	<ul style="list-style-type: none">➤ Acute hepatitis A/B/C➤ Same as above
>15 or >10,000 U/L	<ul style="list-style-type: none">➤ Tylenol toxicity➤ Ischemia, mushroom poisoning

Board buzzwords

Buzzword	Condition	Tbili	Unique
Isolated unconjugated hyperbilirubinaemia	Gilbert's (UDP glucuronyltransferase deficiency)	Tbili usually < 3 mg/dl. Never > 6 mg/dl	Worse with fasting or illness. Resolves with eating or phenobarbital
Low haptoglobin, increased reticulocyte count	Hemolysis	Tbili usually < 5 mg/dl	

Board buzzwords

Buzzword	Condition	Tbili	Unique
conjugated hyperbilirubine mia	Dubin-Johnson and Rotor syndrome	Tbili usually < 3 mg/dl. Never > 6 mg/dl	Worse with fasting or illness. Resolves with eating or phenobarbital
Total bilirubin > 30 mg/dl	Cirrhosis with sepsis or renal failure Alcoholic hepatitis		

45 year old cirrhotic is admitted with 2 days of fever and abdominal pain. Known esophageal varices, ascites and minimal hepatic encephalopathy. Medications are furosemide, spironalactone, nadolol, lactulose, zinc, vitamin A and vitamin D. Abdominal exam discloses distension consistent with ascites. Abdomen is non tender to palpation.

Labs

Hgb 10 g/dl, WBC 3500/ μ L, Platelet count 70,000/ μ L, INR 1.5, Albumin 2.5 g/dl, Alkaline phosphatase 220 U/L, AST 40 U/L, ALT 30 U/L
Total bilirubin 4 mg/dl, Creatinine 1.8 mg/dl
Urine analysis normal

Abdominal ultrasound shows a cirrhotic liver, splenomegaly, ascites, patent portal and hepatic veins and no hydronephrosis. Diagnostic paracentesis yields a cell count of 2000 / μ L with 20% neutrophils, total protein level of 1 g/dl, albumin level of 0.7 g/dl.

Which of the following is the most appropriate treatment?

- A. Cefotaxime
- B. Cefotaxime and albumin
- C. Furosemide and spironolactone
- D. Large volume paracentesis

Ascites for the Boards

- Diagnostic paracentesis should be performed in ALL patients with NEW onset ascites
- Initial tests in all ascites fluid samples:
 - Cell count with differential
 - Total protein
 - Albumin
- If infection is suspected ascites fluid should be inoculated into aerobic and anerobic culture bottles at the bedside- increased yield of positive cultures

Ascites for the Boards

Diagnostic paracentesis should be performed in

- ☐ ALL patients with NEW onset ascites
- ☐ ALL inpatients with cirrhosis and ascites upon admission
- ☐ ALL outpatients with cirrhosis and ascites who develop signs of infection (fever, abdominal pain, leucocytosis, encephalopathy, new renal failure or metabolic acidosis)

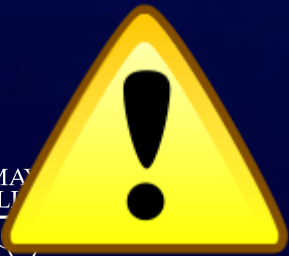


Ascites for the Boards

- ❑ Spontaneous bacterial peritonitis:
 - ❑ Polymorphonuclear cells ≥ 250 / μ l
 - ❑ Positive culture

Treatment

- ❑ If no recent beta lactam exposure- 3rd generation cephalosporine (Cefotaxime 2 g Q 8hrs)
- ❑ If recent beta lactam exposure or nosocomial infection- treat based on local data on bacterial susceptibility in cirrhotics



SBP for the Boards

- ☐ When can oral quinolones be used to treat SBP?
 - ☐ No prior exposure to quinolones
 - ☐ Not in shock
 - ☐ Not vomiting
 - ☐ None or Grade I encephalopathy
 - ☐ Serum creatinine < 3 mg/dl



45 year old man with cirrhosis and ascites is admitted with 2 days of fever.
Ascites fluid analysis shows PMN count of $100/\mu\text{l}$

What is the next best step?

- 1) IV Albumin
- 2) Midodrine
- 3) IV Albumin plus cefotaxime
- 4) IV fluids

SBP for the Boards

- ❑ Patients with cirrhosis and ascites but PMN count $< 250/\mu\text{l}$ should receive empiric antibiotics



Child-Pugh Classification of Cirrhosis

Factor	Units	1	2	3
Serum bilirubin	mol/L	<34	34-51	>51
	mg/dL	<2.0	2.0-3.0	>3.0
Serum albumin	g/L	>35	30-35	<30
	g/dL	>3.5	3.0-3.5	<3.0
Prothrombin time	seconds	0-4	4-6	>6
	prolonged INR	<1.7	1.7-2.3	>2.3
Ascites		None	Easily controlled	Poorly controlled
Hepatic encephalopathy		None	Minimal	Advanced

The Child-Pugh score is calculated by adding the scores of the five factors and can range from 5 to 15. Child-Pugh class can be A (a score of 5-6), B (7-9), or C (10 or above). Decompensation indicates cirrhosis with a Child-Pugh score of >7 (class B). This level has been the accepted criterion for listing liver transplantation.

Ascites in Cirrhosis for the Boards

- Initial treatment: sodium restriction (2000 mg/d) PLUS diuretics (furosemide + spironalactone)
- Refer patients with cirrhosis and ascites for liver transplantation
- Administer IV albumin (6-8 g/liter of ascites fluid removed) if ≥ 4 liters removed in one sitting

Refractory ascites in Cirrhosis

- Unresponsive to sodium restriction/ diuretics
- Intolerable side effects to sodium restriction/diuretics

Avoid these pitfalls while managing patients with cirrhosis and ascites



Cirrhosis with ascites- **DON'T** **DO'S**

- Order CA125 on ascites fluid- not helpful
- Fluid restrict in the absence of hyponatremia (<125 mEQ/L)
- Choose vaptans (e.g. tolvaptan) as an option for treatment – not recommended due to expense, lack of effect on clinical outcomes in cirrhosis with ascites



Cirrhosis with ascites- **DON'T** **DO'S**

- Use ACE inhibitors or ARBs- can be harmful
- Use NSAIDs
- Use non selective beta blockers- increased mortality due to hypotension



A 32 year old woman is evaluated for a 10 day history of malaise, right upper quadrant discomfort and progressive jaundice. No recent travel outside of the US, does not drink alcohol and no recent ingestion of drugs including acetaminophen or herbal remedies. Up until now, she has been healthy. She has a history of type 1 diabetes for which she takes insulin. She has no other medical problems. On exam, temperature is 37.5 C, BP is 106/68, pulse rate is 90/min and respiratory rate is 18/min. BMI is 24. Mental status is normal. Jaundice and scleral icterus are noted. Abdominal exam reveals tender hepatomegaly.

Labs

INR 0.9

Albumin 3.8 g/dl

Alkaline phosphatase 220 U/L

AST 850 U/L

ALT 920 U/L

Total bilirubin 14.4 mg/dl

Direct bilirubin 10.6 mg/dl

Abdominal ultrasound shows hepatomegaly with edema surrounding the gallbladder. There is no biliary dilation. The portal vein and spleen are normal.

Which of the following is the most likely diagnosis?

A. Acute viral hepatitis

B. Fulminant liver failure

C. Hemochromatosis

D. Primary biliary cirrhosis

A 50 year old man with alcoholic cirrhosis, 3 month history of hepatic encephalopathy characterized by forgetfulness and personality changes that is well controlled with lactulose is seen. He has not consumed alcohol in the last 2 years. One year ago he developed ascites that required diuretics. At that time a screening upper endoscopy revealed no varices. His current medications are lactulose, spironalactone and furosemide. On physical examination he is alert, oriented but has mild psychomotor slowing. Vital signs are normal. Scleral icterus, temporal muscle wasting, and spider angiomas are noted. Neurologic examination reveals mild asterixis.

Labs: Hematocrit 33%, Platelet count 75,000 / μ l
INR 1.4, Albumin 2.9 g/dl, ALT 32 U/L, AST 45 U/L
Total bilirubin 4 mg/dl, Creatinine 1.3 mg/dl,
Electrolytes normal

What is the most appropriate management?

- A. Add nadolol
- B. Begin a low protein diet
- C. Continue medical treatment without any changes
- D. Refer for liver transplant

Mechanism of portal hypertension

1. Fibrosis of the liver
2. Intrahepatic vaso constriction due to decreased endogenous production of nitric oxide

Management of complications of portal hypertension

Reasons for persistence of portal hypertension in spite of development of collaterals

1. Increase in portal venous inflow due to splanchnic arteriolar vaso dilatation
2. Insufficient portal decompression through collaterals as these have a higher resistance than the normal liver

Evaluation of portal hypertension

- Measured by hepatic vein pressure gradient (HVPG) = wedged hepatic venous pressure (WHVP) – free hepatic vein pressure (FHVP)
- It is a measure of intrahepatic portal hypertension so it will be elevated in parenchymal fibrosis but will be normal in pre hepatic portal hypertension such as due to portal vein thrombosis
- Normal hepatic main pressure gradient is 3-5 mm of mercury

Natural history of varices

- Gastroesophageal varices are clinically the most relevant portosystemic collaterals because their rupture results in variceal bleeding
- Patients with cirrhosis and gastroesophageal varices have a HVPG of at least 10-12 mm of Hg
- Presence of gastroesophageal varices correlates with severity
- Patients without varices develop them at a rate of 8% per year

Natural history of varices

- Strongest predictor for development of varices in cirrhotic is HVPG > 10 mm Hg
- Patient's with small varices developed large varices at the rate of 8% per year
- Decompensated cirrhosis, alcoholic cirrhosis and presence of red wale marks at the time of baseline endoscopy predict progression from small to large varices

Natural history of varices

- Variceal hemorrhage occurs at the rate of 5-15% per year
- Varices bleed when HVPG is > 20 mm Hg
- Bleeding stops when the HVPG decreases to <12 mm Hg

Gastric varices

- present in 5-30% of patients
- Type 1 : extend along the lesser curvature of the stomach. Considered extensions of esophageal varices
- Type 2: extend along the fundus
- Isolated gastric varices: occur in the absence of esophageal varices. Those in the fundus are called type 1 and those located in the body, antrum or pylorus are called type 2
- Presence of type 1 isolated gastric varices requires excluding the presence of splenic vein thrombosis

Surveillance endoscopy for varices that have not bled

1. Compensated cirrhotics who have no varices on screening endoscopy: repeat endoscopy in 2-3 years
2. Compensated cirrhotics who have small varices on endoscopy- repeat endoscopy in 1-2 years
3. Decompensated cirrhotic- The EGD should be performed when decompensation is 1st identified and annually thereafter

Management of esophageal varices that have not bled

Large varices

- Non selective beta blockers like propranolol and nadolol decreasing cardiac output (β_1) thereby decreasing portal pressure and cause splanchnic vasoconstriction (β_2) thereby reducing portal blood flow
- Their dose is adjusted to the maximum tolerated dose
- Propranolol usually started at 20 mg twice daily and nadolol at 40 mg once daily

Management of esophageal varices that have not bled

Large varices

- β blockers should be continued indefinitely unless the patient decompensates
- Other contraindications for β -blockers are asthma, insulin-dependent diabetes (cause hypoglycemia) and peripheral vascular disease
- Common side effects-lightheadedness fatigue and shortness of breath. Nadolol has a lower reported incidence of side effects

Management of esophageal varices that have not bled

Large varices

- 2nd option is endoscopic band ligation. Should be considered in patients who have contraindications to β -blockers, are intolerant to β -blockers or concern for compliance
- patients on prophylactic β blockers do not need surveillance EGD for varices

Management of acute variceal bleeding

- Stabilize the patient by managing airway, large-bore peripheral IV access and resuscitation promptly
- Transfuse cautiously with the goal of maintaining hemodynamics stability and hemoglobin of approximately 8 grams/dl.
- Overzealous transfusion or crystalloid infusion should be avoided as it increases portal pressures increasing risk of rebleeding

Management of acute variceal bleeding

- Due to risk of aspiration intubation may be required prior to endoscopy particularly in patients with hepatic encephalopathy
- Cirrhotic with upper GI bleed have a high risk of developing severe bacterial infections associated with early recurrence of variceal hemorrhage and mortality. Use of short duration prophylactic antibiotics in cirrhotics with GI hemorrhage with or without ascites not only decreases rate of bacterial infections but also increase survival

Management of acute variceal bleeding

- Norfloxacin given orally at 400 mg twice daily for 7 days is recommended antibiotic
-
- Rationale- as it is a poorly absorbed quinolone it will selectively eradicate gram-negative bacteria in the gut
- In patients with Child B or C cirrhosis and GI hemorrhage ceftriaxone 1 g per day was more effective than oral norfloxacin

Specific measures to control acute hemorrhage

- Somatostatin analogs octreotide causes splanchnic vasoconstriction thereby helps to control acute variceal bleeding
- An advantage of octreotide is that it can be given safely for up to 5 days
- EGD should be performed within 12 hr of admission
- TIPS is an option for patients who fail endoscopic and pharmacotherapy

Specific measures to control acute hemorrhage

- Type 1 gastric varices are an extension of esophageal varices and managed similarly
- Isolated fundic varices which are secondary to splenic vein thrombosis are treated by splenectomy
- Acutely bleeding fundic varices are treated by cyanoacrylate glue injection or by TIPS

Management of patients who have recovered from acute variceal hemorrhage

- Patient's were have no bleeding for at least 24 hr can be started on a non selective β -blocker
- Endoscopic band ligation is repeated every 1-2 weeks until the varices are completely obliterated
- Thereafter EGD is after 1-3 months. If no recurrence is seen, then its repeated every 6-12 months

Role of shunt surgery in variceal bleeding

- TIPS is very effective but markedly increases the risk of hepatic encephalopathy. It has no effect on survival
- Patient's should be referred to the liver transplant center for evaluation

A 25 year old woman is evaluated for intractable pruritus that keeps her awake at night. She is 25 weeks pregnant. Her only medications are prenatal vitamin and folic acid.

Exam is normal. Mental status is normal. Scleral icterus is noted and there are scattered excoriations on the arms, chest and legs.

Labs: Hematocrit 36%, Leucocyte count 4500/ μ L, Platelet count 350,000/ μ L, INR 1.1, Albumin 3.4 g/dl, Alkaline phosphatase 160 U/L, ALT 32 U/L, AST 32 U/L, Total bilirubin 2.2 mg/dl

Abdominal ultrasound is normal with a 25 week gravid uterus. No free abdominal fluid and no organomegaly.

Which of the following is the most likely diagnosis?

A.Acute fatty liver of pregnancy

B.HELLP (Hemolysis, elevated liver tests, low platelet count)

C.Hyperemesis gravidarum

D.Intrahepatic cholestasis of pregnancy

Liver diseases during pregnancy

- Majority of liver tests are normal in pregnancy except those produced by the placenta (alkaline phosphatase and alpha-fetoprotein) or those impacted by hemodilution (albumin and hemoglobin)
- Any abnormality in transaminases or bilirubin in a pregnant woman needs further evaluation

Liver diseases during pregnancy

Imaging in pregnancy

- Ultrasound is the preferred imaging modality to assist abnormal liver tests
- MRI without gadolinium can be used in 2nd and 3rd trimester
- CT scan may be used judiciously with minimum radiation protocols
- Endoscopy in pregnancy endoscopy is safe but should be deferred until the 2nd trimester if possible
- Propofol is safe for endoscopic sedation

Management of biliary disease in pregnancy

- Gallstone pancreatitis is associated with high risk of fetal demise. So it should be managed expedited early with ERCP followed by laparoscopic cholecystectomy
- ERCP can be performed if indicated in pregnant women (e.g. biliary pancreatitis or symptomatic choledocholithiasis or cholangitis). Fetal exposure to radiation is minimized by using a shield

Management of biliary disease in pregnancy

- Untreated cholecystitis is associated with high rate of recurrence up to 60%. This can lead to preterm labor, spontaneous abortions and repeated hospitalizations. So symptomatic cholecystitis should be managed with laparoscopic cholecystectomy

Liver masses in pregnancy

- Asymptomatic hemangioma and focal nodular hyperplasia do not need surveillance during pregnancy
- Hepatic adenomas should be monitored with ultrasound . Patients with large adenomas that is more than 5 cm should be referred for resection prior to pregnancy

Hepatitis B

- Combined active and passive immuno prophylaxis with hepatitis B immunoglobulin and hepatitis B vaccination should be administered to all infants born to hepatitis B virus infected mother's to prevent perinatal transmission
- Woman chronically infected with hepatitis B and high viral load ($>200,000$ IU/ml) should be offered antiviral therapy with tenofovir in the 3rd trimester to reduce perinatal transmission

Hepatitis B

- C-section should not be electively performed in hepatitis B virus positive mother's to prevent fetal infection
- Women chronically infected with hepatitis B should be allowed to breast-feed

Liver disease unique to pregnancy

First trimester

Hyperemesis gravidarum

- Persistent vomiting associated with loss of 5% or more of pre pregnancy body weight, dehydration and ketosis
- Risk factors: molar pregnancy, multiple pregnancies, gestational trophoblastic disease, prior hyperemesis gravidarum and fetal abnormalities (trisomy 21 and hydrops fetalis)
- Mild transaminitis is common but jaundice and hepatic synthetic dysfunction are uncommon
- Treatment: supportive

Liver disease unique to pregnancy

2nd and 3rd trimester

Intrahepatic cholestasis of pregnancy

- typically presents with persistent pruritus involving the palms, soles and rest of the body
- Serum bile acids are elevated and sometimes the only lab abnormality. Complications occur when bile acid levels exceed 40 $\mu\text{moles/L}$
- jaundice is uncommon and should be investigated
- Symptoms resolve with delivery

Liver disease unique to pregnancy

2nd and 3rd trimester

Intrahepatic cholestasis of pregnancy

- Owing to increase risk of fetal complications (preterm labor, prematurity and intrauterine death) early delivery at 37 weeks is recommended
- Ursodeoxycholic acid can be given to symptomatic women

Liver disease unique to pregnancy

2nd and 3rd trimester

Preeclampsia and eclampsia

- Complication: hematoma below the Glisson's capsule and hepatic rupture
- transaminase elevation is due to vaso constriction and fibrin precipitation in the liver
- Deliver after 36 weeks in woman with severe preeclampsia to limit maternal and fetal complications

Liver disease unique to pregnancy

2nd and 3rd trimester

HELLP syndrome (hemolytic anemia elevated liver enzymes and low platelets)

- About 1/3rd of patients develop this in the 1st week postpartum
- Platelet count is less than 100,000
- 1-3% risk of maternal mortality due to hepatic infarction, subcapsular and intra parenchymal hemorrhage
- Managed by prompt delivery especially after 34 weeks of gestation

Liver disease unique to pregnancy

2nd and 3rd trimester

Acute fatty liver of pregnancy

- life-threatening condition characterized by micro vesicular fat deposition in the liver
- Median gestation age at the time of identification is 36 weeks
- Pathophysiology is homozygous absence of enzyme long chain beta oxidation of fatty acid in the mitochondria in the fetus. The unmetabolized long chain fatty acid spills into the maternal circulation and causes liver damage.

Liver disease unique to pregnancy

2nd and 3rd trimester

Acute fatty liver of pregnancy

- Striking elevation in a amino transferases and hyperbilirubinemia that can progress to acute liver failure
- Management: prompt delivery

Liver disease during pregnancy

- Hepatitis E virus can precipitate acute liver failure in pregnant women. Diagnosis is with hepatitis E IgM
- pregnant women with acute hepatitis suspected from HSV should be started on acyclovir. Clues to HSV infection : fever, anicteric severe hepatitis. Both HSV IgM and HSV PCR should be done if HSV hepatitis is suspected.

Liver disease during pregnancy

- Pregnant women with suspected portal hypertension should undergo screening with upper endoscopy in the 2nd trimester
- Those found to have large varices should be treated with band ligation on beta-blockers



Questions & Discussion