Gastrointestinal

Clostridium Difficile (Pseudomembranous Colitis): Evidence-Based Approach to Clostridium Difficile Colitis (CME098-099)

Hemorrhoids and Anal Fissure: Anorectal Disease - Diagnosis and Treatment (CME100-101)

Hernia (Abdominal) (CME102-103)

Liver Function Tests: Is Something Wrong With My Liver? (CME104-105)

Probiotics and the GI Tract, What Should A Busy Clinician Know (CME106-107)
Clostridium Difficile (Pseudomembranous Colitis): Evidence-Based Approach to Clostridium Difficile Colitis

Joel Heidelbaugh, MD, FAAFP

ACTIVITY DISCLAIMER

The material presented here is being made available by the American Academy of Family Physicians for educational purposes only. Please note that medical information is constantly changing; the information contained in this activity was accurate at the time of publication. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed. Rather, it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

The AAFP disclaims any and all liability for injury or other damages resulting to any individual using this material and for all claims that might arise out of the use of the techniques demonstrated therein by such individuals, whether these claims shall be asserted by a physician or any other person. Physicians may care to check specific details such as drug doses and contraindications, etc., in standard sources prior to clinical application. This material might contain recommendations/guidelines developed by other organizations. Please note that although these guidelines might be included, this does not necessarily imply the endorsement by the AAFP.

This CME session is supported by an educational grant from Merck.
DISCLOSURE

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflict of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

All individuals in a position to control content for this session have indicated they have no relevant financial relationships to disclose.

The content of my material/presentation in this CME activity will include discussion of unapproved or investigational uses of products or devices as indicated:
- Will discuss the use of fecal microbiota transplantation.

Joel Heidelbaugh, MD, FAAFP

Clinical Professor, Departments of Family Medicine and Urology/Director of Medical Student Education and Clerkship Director, Department of Family Medicine/Director, Patients and Populations Branch, University of Michigan Medical School, Ann Arbor

Dr. Heidelbaugh is a family physician who has 19 years of academic teaching experience. His specialty topics include gastrointestinal disorders, men's health, and primary care urology. He is a member of the American Gastroenterological Association guideline panels for irritable bowel syndrome, inflammatory bowel disease, and Lynch syndrome. He is the co-editor and co-author of the textbook *ROME IV: Functional Gastrointestinal Disorders for Primary Care and Non-GI Clinicians*, published through the Rome Foundation. In addition, he is the consulting editor of *Primary Care: Clinics in Office Practice* and the president-elect of the American Society for Men's Health. Dr. Heidelbaugh believes that increasing awareness and education about gastrointestinal and men's health issues is an important trend in medical education, clinical practice, and research.
Learning Objectives

1. Discuss implementation measures for the clostridium difficile prevention.

2. Review the serologic and radiologic diagnostic criteria for clostridium difficile infection.

3. Identify treatment approaches for clostridium difficile based on severity.

4. Review the usage of supplements and medications associated with the development and prevention of clostridium difficile infections.

Audience Engagement System

Step 1

Step 2

Step 3
Public Health Problem

- Most commonly recognized cause of infectious diarrhea in healthcare settings
- PCR ribotype 027 / North American pulsed field type 1 (NAP1) most prevalent
- Pooled rate healthcare facility onset (HO) - *Clostridium difficile* infection (CDI)
  - 7.4 per 10,000 patient-days
- US (2011) - estimated number of incident CDI cases
  - 453,000 or 147 cases/100,000 persons
  - 293,000 were directly healthcare-associated
- Severity of CDI is highly variable
  - based upon lab data, physical exam findings, ICU stay duration, presence or absence of colectomy
  - mortality with colectomy rates ranges from 0.3 - 1.3%

*Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)*

AES Question # 1

Which of the following is a major risk factor for the development of *Clostridium difficile* infection?

A. A high fat diet
B. Decreased serum creatinine
C. Decreased serum albumin
D. Decrease serum chloride
E. A high carbohydrate diet
Risk Factors

- Advanced age (> 65 years of age), women, white race
- Duration of hospitalization
- Antibiotics - **even a single exposure increases risk**
  - Penicillins, 3rd and 4th generation Cephalosporins
  - Fluoroquinolones
  - Carbapenems
  - Clindamycin
- Cancer chemotherapy / immunosuppression / corticosteroids
- Risk factors associated with complicated diseases
  - Human immunodeficiency virus (HIV)
  - Hypoalbuminemia
  - Leukocytosis
  - Renal failure

Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)

Epidemiology

- Most likely to result from person-to-person spread through fecal-oral route or direct exposure to a contaminated environment
- Prevalence of symptomatic colonization with CD is 3 - 26% among adult inpatients in acute care hospitals
- Prevalence of CD in stool in asymptomatic adults without recent healthcare facility exposure is < 2%
- Meta-analysis found that pooled colonization rate upon hospital admission across 19 studies between 2005-2014 was 8.1% with main risk factor being previous hospitalization
- Routes of transmission - hands of healthcare workers and contaminated environment occupying room of patient with CDI - 10%

Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)
Burden of Illness

- Over 450,000 initial cases
- Over 29,000 associated deaths
- Recurrent CDI
  - 20% to 30% with at least one recurrence
  - 5% to 10% with multiple (2+)
- Hospital costs: $5.9 billion


Clostridium difficile Pathophysiology

- Spore forming bacterium
- Forms hard defensive shell (dies if pH < ~4)
- Lies in a dormant state for long periods of time
- Do not directly cause a concerning infection !!!
- Can easily revert back to the active form of the bacterium and lead to infection if ingested

AES Question # 2

Which of the following medication classes is associated with a higher risk of *Clostridium difficile* infection?

A. Alpha blockers  
B. Beta blockers  
C. HMG Co-A reductase inhibitors  
D. Centrally-acting muscle relaxants  
E. Non-steroidal anti-inflammatory drugs
Medications Implicated in CDI

- Anti-Secretory Therapy
  - Histamine-2 receptor antagonists (H2RAs)
  - Proton pump inhibitors (PPIs)
- Antidepressants
  - Serotonin-specific reuptake inhibitors (SSRIs)
  - Whatever CLASS mirtazapine is .....  
- Anti-inflammatories
  - Non-steroidal anti-inflammatory drugs (NSAIDs)

Anti-Secretory Therapy

- Systematic review and meta-analysis of 42 observational studies with over 313,000 patients
- Studies had to report odds ratios/relative risk of development of CDI or have present comparative data
- Pooled odds ratios
  - H2RA alone - 1.50 (95% CI - 1.23-1.83)
  - Antibiotics alone - 1.97 (95% CI 1.29-3.01)
  - PPI alone - 2.10 (95% CI - 1.66-2.66)
  - PPI + antibiotic - 3.87 (95% CI 2.28-6.56)

Anti-Secretory Therapy

- Retrospective cohort study to determine impact of continuous PPI use on CDI recurrence of patients with hospital-acquired CDI
- 754 patients - 458 PPI users / 296 PPI non-users
- 101 patients had no indication for PPI use
- Adjusted relapse rates of CDI
  - Age $\geq$ 75 years - 1.5 (95% CI 1.1-2.0)
  - Continuous PPI use - 1.5 (95% CI 1.1-2.0)
  - Antibiotic re-exposure - 1.3 (95% CI 0.9-1.7)
  - Length of stay, per day - 1.003 (95% CI 1.002-1.004)

McDonald EG et al., JAMA Intern Med 2015;175(5):784-791.

Anti-Depressants

- Combination of 2 studies
- Study 1: Health and Retirement Study
  - Interview data linked to CMS records
  - Relationship between depression and CDI rates
- Study 2: Hospital Based Case control study
  - Patients with stool + CDI compared to - CDI
  - Medication exposures
  - Depression linked to changes in gut microbiota

Anti-Depressants

<table>
<thead>
<tr>
<th>Medications</th>
<th>Using medication, n</th>
<th>Unadjusted</th>
<th></th>
<th></th>
<th>Adjusted</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR</td>
<td>95% CI</td>
<td>P value</td>
<td>OR</td>
<td>95% CI</td>
<td>P value</td>
</tr>
<tr>
<td>Noradrenergic and specific serotonergic anti-depressants</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mirtazapine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use (versus no use)</td>
<td>99</td>
<td>2.11</td>
<td>1.29 to 3.45</td>
<td>0.003</td>
<td>2.14</td>
<td>1.30 to 3.52</td>
</tr>
<tr>
<td>Doses given, n</td>
<td></td>
<td>1.08</td>
<td>1.01 to 1.16</td>
<td>0.018</td>
<td>1.08</td>
<td>1.01 to 1.16</td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitors</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use (versus no use)</td>
<td>99</td>
<td>1.98</td>
<td>1.20 to 3.26</td>
<td>0.008</td>
<td>1.92</td>
<td>1.16 to 3.17</td>
</tr>
<tr>
<td>Doses given, n</td>
<td></td>
<td>1.06</td>
<td>1.00 to 1.12</td>
<td>0.036</td>
<td>1.06</td>
<td>1.00 to 1.12</td>
</tr>
</tbody>
</table>


Anti-Inflammatories

- Population based case-control study
- CDI in UK GP database 1994-2005
- 1360 cases with 13,072 controls
- Each CDI case matched with ~ 10 controls
- Primary analysis: odds ratio for CDI with NSAID use

### Anti-Inflammatories

#### Table 3
Crude and adjusted odds ratios (RR) of CDAD associated with NSAID exposure in the 90 days prior to the index date

<table>
<thead>
<tr>
<th>NSAIDS exposure in the 90 days prior to the index date</th>
<th>Cases</th>
<th>Controls</th>
<th>Crude RR</th>
<th>Adjusted* RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any traditional NSAID</td>
<td>462 (34.0)</td>
<td>3,709 (28.4)</td>
<td>1.27</td>
<td>0.97</td>
<td>0.86, 1.10</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>96 (7.1)</td>
<td>547 (4.2)</td>
<td>1.63</td>
<td>1.35</td>
<td>1.10, 1.67</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>42 (3.1)</td>
<td>446 (3.4)</td>
<td>0.91</td>
<td>0.85</td>
<td>0.62, 1.15</td>
</tr>
<tr>
<td>Naproxen</td>
<td>12 (0.88)</td>
<td>108 (0.83)</td>
<td>1.06</td>
<td>0.99</td>
<td>0.56, 1.75</td>
</tr>
<tr>
<td>Other traditional NSAIDs</td>
<td>38 (2.8)</td>
<td>262 (2.0)</td>
<td>1.36</td>
<td>1.10</td>
<td>0.79, 1.51</td>
</tr>
<tr>
<td>Cox-2 inhibitors</td>
<td>11 (0.81)</td>
<td>116 (0.89)</td>
<td>0.92</td>
<td>0.77</td>
<td>0.42, 1.39</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>319 (23.5)</td>
<td>2,656 (20.3)</td>
<td>1.18</td>
<td>0.88</td>
<td>0.77, 1.01</td>
</tr>
</tbody>
</table>

*Adjusted for gender, comorbidities, prescription of antibiotics, H2-receptor antagonists, proton pump inhibitors and oral steroids.


### Anti-Inflammatories

#### Table 4
Crude and adjusted odds ratios (RR) of CDAD associated with NSAID exposure in the 90 days prior to the index date in non-hospitalized patients

<table>
<thead>
<tr>
<th>NSAIDS exposure in the 90 days prior to the index date</th>
<th>Cases</th>
<th>Controls</th>
<th>Crude RR</th>
<th>Adjusted* RR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any traditional NSAID</td>
<td>303 (32.6)</td>
<td>2,284 (22.3)</td>
<td>1.43</td>
<td>1.04</td>
<td>0.90, 1.20</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>66 (7.1)</td>
<td>351 (3.8)</td>
<td>1.80</td>
<td>1.43</td>
<td>1.11, 1.84</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>26 (2.8)</td>
<td>302 (3.3)</td>
<td>0.87</td>
<td>0.80</td>
<td>0.54, 1.18</td>
</tr>
<tr>
<td>Naproxen</td>
<td>10 (1.1)</td>
<td>69 (0.7)</td>
<td>1.40</td>
<td>1.12</td>
<td>0.60, 2.10</td>
</tr>
<tr>
<td>Other traditional NSAIDs</td>
<td>29 (3.1)</td>
<td>180 (1.9)</td>
<td>1.54</td>
<td>1.13</td>
<td>0.78, 1.64</td>
</tr>
<tr>
<td>Cox-2 inhibitors</td>
<td>10 (1.1)</td>
<td>73 (0.8)</td>
<td>1.33</td>
<td>1.03</td>
<td>0.55, 1.92</td>
</tr>
<tr>
<td>Acetylsalicylic acid</td>
<td>196 (21.1)</td>
<td>1,569 (16.9)</td>
<td>1.28</td>
<td>0.91</td>
<td>0.77, 1.08</td>
</tr>
</tbody>
</table>

*Adjusted for gender, comorbidities, prescription of antibiotics, H2-receptor antagonists, proton pump inhibitors and oral steroids.

Anti-Inflammatories

- Intestinal toxicity of NSAIDs
  - Intestinal inflammation
  - Increased intestinal permeability
  - Malabsorption of bile salts, D-xylose, fat
  - Exudative enteropathy - hypoalbuminemia
  - Small and large intestinal ulcers
  - Villous atrophy
  - Colitis - microscopic, eosinophilic, segmental ischemic


Current Diagnostic Guidelines:

Infectious Diseases Society of America (IDSA)
Society for Healthcare Epidemiology of America (SHEA)
GRADE Guideline Classification

- **GRADE Methodology**
  - Grading of Recommendations Assessment, Development, and Evaluation System
  - High/Moderate/Low Quality Evidence
  - Strong/Conditional (Weak) Strength of Evidence

- **PICO**
  - Patient Problem or Population
  - Intervention
  - Comparison
  - Outcome(s)

Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)
AES Question # 3

Which patient would be the best candidate for testing for *Clostridium difficile* infection (*none were recently hospitalized*)?

A. An 11-month old male infant with an average of 2 non-bloody loose stools per day over the last 6-7 days
B. A 24-year-old woman with an average of 1 non-bloody loose stool per day for the last 5-7 days
C. A 45-year-old man with an average of 4-5 non-bloody loose stools per day for the last 1 day
D. A 75-year-old woman with an average of 1-2 bloody stools intermittently for the last 6 months
Diagnosis

• Patients with unexplained and new-onset ≥ 3 unformed stools in 24 hours are the preferred target population for testing for CDI
• Use a stool toxin test as part of a multi-step algorithm (e.g. glutamate dehydrogenase [GDH] plus toxin; GDH plus toxin, arbitrated by nucleic acid amplification test [NAAT])
• Do not repeat testing within 7 days during the same episode of diarrhea, and test of cure is not recommended (or needed)
• Do not test asymptomatic patients except for epidemiological studies
• Insufficient evidence to recommend biologic markers in diagnosis
• Because of high prevalence of asymptomatic carriage of toxigenic CD in infants, testing for CDI should never be routinely recommended for neonates or infants < 12 months of age with diarrhea

Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)
Current Therapeutic Guidelines:

- Infectious Diseases Society of America (IDSA)
- Society for Healthcare Epidemiology of America (SHEA)

AES Question # 4

Which of the following is the recommended initial treatment for Clostridium difficile infection?

A. Fidaxomycin  
B. Levofloxacin  
C. Metronidazole  
D. Ampicillin/sulbactam  
E. Cefpodoxime
AES Question # 5

Which of the following is the recommended treatment for a first recurrence of Clostridium difficile infection?

A. Vancomycin standard dose  
B. Vancomycin tapered and pulsed dose  
C. Metronidazole  
D. Ampicillin/sulbactam  
E. Cefpodoxime

Treatment - Adults

- Discontinue therapy with the inciting antibiotic agent(s) as soon as possible, as this may influence risk of CDI recurrence
- Antibiotic therapy for CDI should be started empirically when a substantial delay in laboratory confirmation is expected, or for fulminant cases of CDI
- Either vancomycin or fidaxomycin is recommended over metronidazole for an initial episode of CDI or in fulminant CDI
  - vancomycin 125mg orally QID or fidaxomicin 200mg orally BID for 10 days
- In settings where access to vancomycin or fidaxomycin is limited, use metronidazole for an initial episode of nonfulminant CDI
  - metronidazole 500mg orally TID x 10 days
- Avoid repeated or prolonged courses of treatment due to risk of cumulative and potentially irreversible neurotoxicity

Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)
Treatment - Adults

• If ileus is present:
  • vancomycin 500mg orally QID and 500mg/100ml NS PR Q 6 hours (enema)
  • metronidazole 500mg IV Q 8 hr + vancomycin (oral or enema)
• If surgical management is necessary for severely ill patients, subtotal colectomy with preservation of the rectum should be performed
• Diverting loop ileostomy with colonic lavage followed by integrate vancomycin flushes is an alternative approach that may lead to improved outcomes
• Treat a first recurrence of CDI with oral vancomycin as a tapered and pulsed regimen rather than a second standard 10-day course of vancomycin
• Treat a first recurrence of CDI with a 10-day course of fidaxomycin rather than a standard 10-day course of vancomycin

Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)

Treatment - Adults

• Treat a first recurrence of CDI with a standard 10-day course of vancomycin rather than a second course of metronidazole if metronidazole was used for the primary episode
• Antibiotic treatment options for patients with > 1 recurrence of CDI include oral vancomycin therapy using a tapered and pulsed regimen
• Fecal microbiota transplantation is recommended for patients with multiple recurrences of CDI who failed appropriate antibiotics
• Insufficient data to recommend extending length of anti-CDI treatment beyond recommended course or restarting an anti-CDI agent empirically for patients who required continued antibiotic therapy

Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)
Treatment - Children

- Either metronidazole or vancomycin is recommended for treatment of children with an initial episode or first recurrence of non-fulminant CDI
- For children with an initial episode of severe CDI, oral vancomycin is recommended over metronidazole
- For children with a second or greater episode of recurrent CDI, oral vancomycin is recommended over metronidazole
- Consider fecal microbiota transplantation for pediatric patients with multiple recurrences of CDI following standard antibiotics

Fecal Microbiota Transplantation

- Open-label RCT enrolled 41 immunocompetent older adults who had relapsed CDI after at least 1 course of antibiotic therapy
- Randomized to 3 treatment groups to examine efficacy of FMT:
  - vancomycin, bowel lavage with 4L NG PEG, NG-infused donor feces
  - vancomycin with NG bowel lavage without donor feces
  - vancomycin alone
- Cure = absence of diarrhea or 3 negative stool samples
- 13 of 16 (81%) in the donor feces infusion group were cured with first FMT infusion
- 2 of 3 remaining patients were cured after second donor transplant
- FMT cure rate 94% compared to vancomycin alone 27% - **NNT = 2**

*Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)*
Fecal Microbiota Transplantation

- Open-label RCT of 39 patients compared healthy-donor, fresh FMT given via colonoscopy with vancomycin alone for treatment of CDIs
- Subjects were immunocompetent adults with recurrent CDI after at least 1 course of vancomycin or metronidazole
- Patients in treatment group - short course of vancomycin, bowel cleansing and FMT via colonoscopy, FMT repeated every 3 days until resolution
- Patients in control group - vancomycin for at least 3 weeks
- Cure = absence of diarrhea / 2 negative stool samples at 10 weeks - no relapse
- 13 of 20 patients in the FMT group (65%) achieved cure after first fecal infusion
- 7 remaining patients received multiple infusions and 5 were cured
- FMT cure rate 90% compared to vancomycin alone 26% - **NNT = 2**


Fecal Microbiota Transplantation

- Randomized, double-blind trial compared effectiveness of frozen and thawed FMT with fresh FMT in 219 adult patients with recurrent or refractory CDIs
- Suppressive antibiotics were discontinued 24 to 48 hours prior to FMT then administered 50mL of either fresh or frozen stool by enema
- FMT was repeated with same donor if symptoms didn’t improve within 4 days
- Any patient still unresponsive was offered repeat FMT or antibiotic therapy
- Researchers defined a 15% difference in outcome as clinically important
- Intention-to-treat analysis yielded no significant difference in clinical resolution between groups (75% frozen to 70% fresh; P=.01)

### IDSA and SHEA Guidelines for Treatment of 
*Clostridium difficile* Infection in Adults

<table>
<thead>
<tr>
<th>Initial episode, non-severe</th>
<th>Leukocytosis with a white blood cell count of ≥10,000 cells/mL, and a serum creatinine level &lt;1.5 mg/dL</th>
<th>WIN 125 mg given 4 times daily for 10 days, OR FOX 200 mg given twice daily for 10 days</th>
<th>Strong/Moderate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial episode, severe²</td>
<td>Leukocytosis with a white blood cell count of ≥10,000 cells/mL, or a serum creatinine level &gt;1.5 mg/dL</td>
<td>WIN, 125 mg 4 times per day by mouth for 10 days, OR FOX 200 mg given twice daily for 10 days</td>
<td>Strong/Moderate</td>
</tr>
<tr>
<td>First recurrence</td>
<td>...</td>
<td>WIN 125 mg given 4 times daily for 10 days if metronidazole was used for the initial episode, OR Use a prolonged tapered and pulsed VAN regimen if a standard regimen was used for the initial episode leg, 125 mg 4 times per day for 10–14 days, 2 times per day for a week, once per day for a week, and then every 2 or 3 days for 2–3 weeks, OR FOX 200 mg given twice daily for 10 days if WIN was used for the initial episode</td>
<td>Week/Moderate</td>
</tr>
<tr>
<td>Second or subsequent recurrence</td>
<td>...</td>
<td>VAN in a tapered and pulsed regimen, OR VAN, 125 mg 4 times per day by mouth for 10 days followed by rifaximin 600 mg 3 times daily for 20 days, OR FOX 200 mg given twice daily for 10 days, OR Fecal microflora transplantation³</td>
<td>Week/Moderate</td>
</tr>
</tbody>
</table>

### IDSA and SHEA Guidelines for Treatment of 
*Clostridium difficile* Infection in Children

<table>
<thead>
<tr>
<th>Initial episode, non-severe</th>
<th>Metronidazole x 10 days (PO), OR Vancomycin x 10 days (PO)</th>
<th>75 mg/kg/dose t.i.d or qid 10 mg/kg/dose qid 500 mg tid or qid 125 mg qid</th>
<th>Weak/Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial episode, severe/ fulminant</td>
<td>Vancomycin x 10 days (PO or PR) with or without metronidazole x 10 days (IV)³</td>
<td>10 mg/kg/dose qid 10 mg/kg/dose tid 500 mg tid or qid 500 mg tid</td>
<td>Strong/Moderate</td>
</tr>
<tr>
<td>First recurrence, non-severe</td>
<td>Metronidazole x 10 days (PO), OR Vancomycin x 10 days (PO)</td>
<td>75 mg/kg/dose t.i.d or qid 10 mg/kg/dose qid 500 mg tid or qid 125 mg qid</td>
<td>Weak/Low</td>
</tr>
<tr>
<td>Second or subsequent recurrence</td>
<td>Vancomycin in a tapered and pulsed regimen², OR Vancomycin for 10 days followed by rifaximin³ for 20 days, OR Fecal microflora transplantation</td>
<td>10 mg/kg/dose qid Vancomycin: 10 mg/kg/dose qid; rifaximin: no pediatric dosing 125 mg qid Vancomycin: 500 mg qid; rifaximin: 400 mg tid</td>
<td>Weak/Very low</td>
</tr>
</tbody>
</table>

*Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)*
Probiotic Therapy

- Probiotics - “good bacteria”, or “functional food”
- Antibiotics disturb gastrointestinal microbiota which may lead to reduced resistance to pathogens including *C. difficile*
- Probiotics are live microbial preparations that when administered in adequate amounts may confer a health benefit, and may prevent *C. difficile* infection
- Clinical practice guidelines through 2017 did not recommend probiotic prophylaxis, although probiotics had the highest quality evidence among cited prophylactic therapies


---

Probiotic Therapy

- 2017 Cochrane Review
- 39 randomized trials with total of 9955 participants
- 31 studies (8672 participants) assessed effectiveness of probiotics for preventing CDAD among participants taking various antibiotics over various durations
- When probiotics were given with antibiotics the risk of developing CDAD was reduced by 60% on average
- In participants at high risk of developing CDAD the potential benefit of probiotics is greater than a 70% average risk reduction

Probiotic Therapy

• 32 studies (8305 participants) assessed risks of adverse effects
• Results suggest that taking probiotics does not increase risk of developing adverse effects
• Most common adverse effects were higher in control groups
  • abdominal cramping, nausea, low-grade fever, soft stools, flatulence, taste disturbance
• Short-term probiotic use is safe/effective when used with antibiotics in patients who are not immunocompromised or severely debilitated
• Probiotics are safe and effective for treating CDAD (NNTB - 42; 95% CI 32 to 58)

NNTB - number needed to treat to benefit


Probiotic Therapy

• Bifidobacterium animalis
• Clostridium butyricum
• Lactobacillus species
• Saccharomyces boulardii
• Streptococcus thermophilus
• Active
• Align
• Culturelle
• DanActive
• Florastor
• MIYAIRI 588
• VSL#3

Strategies for Prevention

- **WASH HANDS (5 mins, warm soapy water) / NO PURELL !!!**
- Healthcare professionals **must use gloves and gowns** on entry to a room of a patient with CDI and while caring for patients with CDI
- Accommodate patients with CDI in a private room with a dedicated toilet to decrease transmission to other patients
- If limited number of private single rooms, then patients should be prioritized with stool incontinence for placement in private rooms
- Cohort patients who are infected with the same organism
  - *Clostridium difficile*
  - Methicillin-resistant *staphylococcus aureus*

*Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)*

---

Strategies for Prevention

- Patients with suspected CDI should be placed on preemptive contact precautions pending CD test results
- Contact precautions should be continued for at least 48 hours after diarrhea has clinically resolved
- Prolong contact precautions until discharge if CDI rates remain high despite implementation of standard infection control measures
- Daily cleaning with a sporicidal agent should be considered in conjunction with other measures to prevent CDI during outbreaks
- Although there is an epidemiologic association between PPI use and CDI, and unnecessary PPI therapy should always be discontinued, there is insufficient evidence for discontinuation of PPIs as a measure for preventing CDI (can’t be appropriately studied, only can be recommended)

*Infectious Disease Society of America Clinical Practice Guidelines CID 2018:66 (1 April)*
Practice Recommendations

- There are many risk factors for CDI:
  - **LIMIT ABX** - even a single exposure of antibiotics increases risk
  - BE CAUTIOUS OF anti-secretory therapy, antidepressants, NSAIDs
  - Test patients with unexplained / new-onset ≥3 unformed stools in 24 hours
  - Use a stool toxin test as part of a multi-step algorithm for diagnosis
  - Do not repeat testing within 7 days during the same episode of diarrhea
  - Consider FMT (higher cure rate compared to vancomycin) **NNT = 2**
  - Use probiotics + antibiotics to reduce risk of CDI by ~60%
  - Wash hands / gown and glove / contact precautions / private isolated rooms

Questions
Contact Information

Joel J. Heidelbaugh, MD, FAAFP, FACG
jheidel@umich.edu
Hemorrhoids and Anal Fissure: Anorectal Disease - Diagnosis and Treatment

Justin Bailey, MD, FAAFP

ACTIVITY DISCLAIMER

The material presented here is being made available by the American Academy of Family Physicians for educational purposes only. Please note that medical information is constantly changing; the information contained in this activity was accurate at the time of publication. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed. Rather, it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

The AAFP disclaims any and all liability for injury or other damages resulting to any individual using this material and for all claims that might arise out of the use of the techniques demonstrated therein by such individuals, whether these claims shall be asserted by a physician or any other person. Physicians may care to check specific details such as drug doses and contraindications, etc., in standard sources prior to clinical application. This material might contain recommendations/guidelines developed by other organizations. Please note that although these guidelines might be included, this does not necessarily imply the endorsement by the AAFP.
DISCLOSURE

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflict of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

All individuals in a position to control content for this session have indicated they have no relevant financial relationships to disclose.

The content of my material/presentation in this CME activity will not include discussion of unapproved or investigational uses of products or devices.

Justin Bailey, MD, FAAFP

Physician, Family Medicine Residency of Idaho, Boise; Assistant Professor of Family Medicine, Department of Family Medicine, University of Washington School of Medicine, Seattle

Dr. Bailey earned his medical degree at the Medical College of Wisconsin, Milwaukee. He completed his residency at Eglin Air Force Base Family Medicine Residency in Fort Walton Beach, Florida, and a teaching faculty development fellowship at the University of North Carolina at Chapel Hill. While active-duty Air Force, he taught full-spectrum family medicine at David Grant U.S. Air Force Medical Center in Fairfield, California, and was deployed to Iraq during the Gulf War and to Haiti after the 2010 earthquake. Dr. Bailey currently teaches full-spectrum family medicine in Boise, Idaho, and serves as the director of the Procedures Institute at the Family Medicine Residency of Idaho, leading resident training in procedures such as endoscopy, procedural musculoskeletal medicine, and skin surgeries. He frequently lectures at national primary care endoscopy conferences on gastrointestinal (GI)-related topics and has published multiple textbook chapters on GI-related disorders. His other interests include hospital medicine, health benefits of relationships, and the care of vulnerable populations.
Learning Objectives

1. Review the anatomical classifications and characteristics of hemorrhoids and anal fissures.

2. Identify the preferred diagnostic approach for hemorrhoids and anal fissures.

3. Discuss prevention methods for hemorrhoids and anal fissures.

4. Review medications and modalities for the treatment of hemorrhoids and fissures.

Audience Engagement System

Step 1
- Dashboard

Step 2
- CME/Events

Step 3
- CME/Event
- Audience Engagement System
- Faculty

CME041 (PBL) Arrhythmias and Dysrhythmias
- Location: 257
- Duration: 12:30-4:30 PM
- Credits: 4
- REPEATS: Saturday at 7:30 AM
- Show more

1. Practice applying new knowledge and skills gained from Arrhythmias and Dysrhythmias sessions, through interactive learning with peers and expert faculty.
2. Identify techniques for better management of arrhythmias and dysrhythmias, within the context of...
Let’s Talk About…

- Hemorrhoids (internal, external)
- Anal fissures
- Other possible differential diagnosis (proctalgia fugax, pilonidal cysts, condyloma)

Hemorrhoids - Epidemiology

- 4% have them M=F
- 40-60 y/o most common
- Uncommon under 20
Hemorrhoids - Pathology

- Dilation of vessels superior hemorrhoidal cushion vs inferior hemorrhoidal cushion

Image courtesy of Visible Body

[Link to image](https://commons.wikimedia.org/w/index.php?curid=4953948)
Evaluation of Hemorrhoids = History

- Painful vs painless (mild vs mod vs I can’t sit)
- Blood?
- BM regularity, consistency, ease of evacuation
- What else are you doing besides the job at hand?
- Straining on the toilet?
- Incontinence, Prolapse

Evaluation of Hemorrhoids = History

- Interventions tried
  - Fiber
  - Stool softeners
  - Wet wipes
  - OTC (witch hazel, hydrocorizone, barrier)
  - Prescriptions
Evaluation: Physical Exam

• Left lateral side, knees bent
• External visual inspection
• Evert the skin
• Digital exam
• Valsalva prolapse
Rectal Exam & Anascope

- Left lateral position
- Well lubed
- Rectal exam form
- Slotted vs not
- Rotation with introducer in place

Dr. Joachim Guntau - www.Endoskopiebilder.de
http://anoscopyhighresolution.blogspot.com/2012/06/miscellaneous-findings.html
CASE #1

- 45 y/o male with extreme pain, refuses to sit down, awaken in the night due to pain. 10/10
- Symptoms started 24 hours ago, after bowel movement. Hard to pass
- No hx of hemorrhoids
- No bleeding
- Feels a lump
AES Question #1

Is this a:

A. Acute thromboses external hemorrhoid
B. Subacute thromboses external hemorrhoid
C. Internal hemorrhoid
D. Anal Fistula

Acute External Treatment (Grade A)

- Excision >
- Watch and wait >
- Incision and Drainage
- Ice, steroid
- Pain Management
S/P 2 Days I&D (Reoccurrence)

Acute Treatment

- RCT n=150 3 arms
- Day 4 pain = Early excision > nitroglycerin > thrombectomy
- Day 30 pain = Early excision = nitroglycerin = thrombectomy
- Hemorrhoid pain resolution excision 3-4 days vs 24 days in conservative management. Fewer reoccurrence.


Elliptical Excision

• Good visualization/light
• Lidocaine with Epinephrine
• Excise ellipse, complete venous complex, to adipose
• Suture closed
• Sitz baths
• Pain control!

CASE #2

• 37 y/o female developed rectal pain 72 hours ago after a difficult to pass bowel movement
• Tried sitz bath, OTC creams, NSAIDS
• Still painful
AES Question #2

• Should you
  A. Elliptical excision?
  B. I&D
  C. Conservation (sitz baths, lidocaine ointment, anti-inflammatory creams)
  D. Refer for surgery

Subacute Thromboses Hemorrhoids: Tx

• Even though you want to cut it off…

• < 48-72 hours excise

• >48-72 hours conservative management favored (expert opinion)

• Don’t forget pain management
Conservative Management

- Education
- Get ride of the constipation and straining
- Relieve symptoms

Fiber (Step 1, Grade A)

- Fiber showed 50% reduction in symptoms (RR = 0.53, 95% CI 0.38-0.73)
- 50% reduced risk of bleeding (RR = 0.50, 95% CI 0.28-0.89)
- Pain, itching and prolapse trended toward significance but individually were non significant
- Results persistent at 6 weeks and 3 months

Symptom Relief - Short Term

• **Oral Venoactive agents** (dobesio, Calcium dobesilate, Hydroxyethylrutosides -not available in the US) (Grade B)
• Analgesics (topical lidocaine)
• Steroid creams (hydrocortisone)
• Antispasmodic (calcium channel blockers)
• Sitz baths/Ice

Med tx- Phlebotonics (where can I buy them)

• Flavanoids, hydroxyethylrutoside, calcium dosbesilate,
• Improve pruritus (OR= 0.23 (95% CI 0.07-0.79)
• Bleeding (OR=0.12 (95% CI 0.04- 0.37))
• Discharge & leakage (OR=0.12 (95% CI 0.12 95% CI 0.04-0.42)
• Overall symptom improvement (OR15.99 (95% CI 5.97-42.84)
Topical (No Data of Benefit)

• Analgesics (topical lidocaine)
• Steroid creams (hydrocortisone)
• Antispasmodic (calcium channel blockers)
• Sitz baths/Ice

External Hemorrhoid Tags

• 34 y/o MSM would like a cosmetically concerning anal skin tag removed
• Mild constipation over lifetime
• Can feel it when he wipes
Excision of External Tag - picture

- Lidocaine with Epi 3-5 cc
- 27-30 gauge needle
- Ligation
- Excision
Case #3

- 52 y/o male, long standing constipation
- Feels something come out with every bowel movement. Sometimes spontaneously resolves, other times stays prolapsed for days. This has been going on for months.
- Intermittent bleeding with it. Sometimes clots in the toilet. Denies any dizziness.
- No hx of colon cancer screening
AES Question #3

• What is the stage of this hemorrhoid?
  A. Stage 1
  B. Stage 2
  C. Stage 3
  D. Stage 4

Dr. K.-H. Günther, Klinikum Main Spessart, Lohr am Main

Stage 1 - No prolapse just prominent vessels
Stage 2 - Hemorrhoid prolapse with valsalva but spontaneously resolves
Stage 3 - Prolapse with pressure, requires manual reduction
Stage 4 - Prolapse and unable to reduce
Internal Hemorrhoids- Will They Go Away?
Future Prevention

- Soften your Cleaning
- Soften your stool = the most important 10 min conversation
- Exercise
- Topicals
- Surgery (Don’t take off things that don’t need to come off)
The Most Important Conversation

• 1 soft, easy to pass bowel movement
• “Soft”
• “Easy to Pass”

Stool Softening

• Fiber 25-30 grams a day (slow increase)
• Polyethylene glycol 3350 (nnt=3), lactulose (nnt=6), milk of mag \(^{1}\) (Am J Gastroenterol. 2006 Jan; 101(1):181-8)
• Rescue therapy (stimulant, suppository)
• Docusate -1 tab po bid, then go up
• Probiotics (bifidobacterium)
• Senna (ex lax, laxative teas)
Prevention Chronic Constipation & Hemorrhoids

- Step 1- Education & Partnering
- Step 2- Diet & Exercise
- Step 3- Fiber
- Step 4- Osmotic diuretics
- Step 5- Prokinetics (lubiprostone and linaclotide)
- Step 6- Last resort surgery

Office Based Internal Hemorrhoid Treatment

- Rubber banding
- Infrared Coagulator
- Sclerotherapy
- Laser, Cryo
Rubber Banding
Infrared Coagulator
Office Based Procedures

• Rubber band=93% cure grade 2-3, 11-49% reoccurrence. Less pain and quicker return to work vs rubber band

• IRC - 81% cure in grade 1-2, 28% reoccurrence. Less pain and quicker return to work vs rubber band

• Sclerotherapy- 20% success rate at 1 year in grade 2-3, up to 80% successful in grade 1, agent dependent

Complications

• Perianal sepsis (rare) (worsening pain, fever)
• Urinary dysfunction
• Bleeding (common)
• Pain (misplaced rubber band, burn)
Referral for Surgery (Grade A)

- Grade 3-4
- Rectal prolapse
- Unable to tolerate office procedure
- Improved resolution vs office base in grade 3-4
- Surgery has increased pain and higher complication rates compared to office procedures

What Did We Miss?

- Complete colonic eval?
- Hemorrhoid bleeding most common missed opportunity to establish a colon diagnosis?
- Should all hemorrhoids have a colonoscopy?
- Review any previous endoscopy reports
Indications for Colonoscopy

- >50yrs old
- >40 yrs old or 10 years younger than the age at Dx of 1 or more 1st degree relative with Colorectal cancer or advance adenoma at <60 yrs old
- Positive fecal immunochemical testing
- Positive FIT- fecal DNA test

(Rex Et al. Colorectal cancer screening: recommendations for physicians and patients from US multi-Society task force on Colon cancer, Am J Gastroenterology, 2017; 112:1016-1030.)

Anal Fissure

- 42 y/o male with rectal bleeding and pain with every bowel movement
- “Like crapping a piece of glass”
- Frequent constipation
- Pain lasts for 1-2 hours after bowel movement
- Some bleeding on the toilet paper and in toilet
Physical Exam

- visual inspection
- rectal exam painful

Anal Fissure - Tx Step 1

- Treat constipation (warm baths + fiber healed 50%)
- Fiber 15g + sitz > 7.5 g > lidocaine or hydrocortisone cream
- Lower rate of reoccurrence
- Relaxation of internal sphincter
- Atraumatic passage of stool
- Pain relief
- Sitz baths, fiber, topical anesthetic creams

Anal Fissure - Tx Step 2

- Sphincter relaxation and blood flow
- Topical nitroglycerin > placebo (49% vs 37%, \( p < 0.004 \))
- Topical = Nitroglycerin (58-70%), Diltiazem (70%), Bethanecol (small studies showing benefit)
- Oral = Nifedipine (60%), Diltiazem (38%) Higher reoccurrence rate

Anal Fissures - Step 3

- Injectable = Botox injection (73% - 95%) (when compared side to side botox = topical)
- If other topical treatments failed, Botox low success rate (27%)
- 1/3 of Botox treated patients go on to surgery
Anal Fissures Step 4

• Surgical = Lateral Sphincterotomy (95% healing, 45% with transient incontinence, 6-30% long term)
• Dilation = 4 fingers for 4 min (95% pain relief, recurrence 16%)
• Surgical > Dilation (Efficacy OR = 3.35; 95% CI = 1.55–7.26) and incontinence to flatus or feces (OR = 4.03; 95% CI = 2.04–7.46)

Anal Fissure - Special Consideration

• Chrons
• HIV+ = ulcer vs fissure
Case #4

- 56 y/o male presents for colonoscopy for eval for rectal pain
- Occurs intermittently, usually last 30 min.
- Has left work
- PMHx GAD
- no pain with bowel movements, no itching or burning

Proctalgia Fugax (Acute)

- severe intermittent episodes of rectal pain, self limited (secs - min), not associated with other pelvic pathology
- Dx of exclusion
- Tx- sitz, topical calcium channel blockers, biofeedback, oral anti hypertensives
Case 5

- 34 y/o female with intense anal itching
- work up so far has excluded pin worms (was presumptively treated once), hemorrhoids, or fissures
- Exam shows some lichinification.

Pruiritis Ani

- Itch scratch cycle
- Inflammation, infectious, neoplastic, anorectal disorder, fecal contamination
- Tx based on underlying disorder
Perianal Condyloma

- 30 y/o female with large volume perianal wart. Hygiene difficult, can be painful
- Tx Topical
  - Irritants - Podophylin (20-50%), TCA (20-50%), 5FU+epinephrine (50%)
    - Immunomodulators - Immiqimod 40-70%, Interferon Alpha (25-80%)
      Sinecatechins (55%)
- Surgery
  - Cryo (63%-92%)
  - Infrared Coagulation (61%-74%)
  - Laser Therapy (100%, reoccurrence 45%)
  - Excision (36%)

Practice Recommendations - Tags

- No more then 1/4-1/3 of circumference per visit
- Why do they need to come off?
Practice Recommendation
Internal Hemorrhoids
• Fiber fixes
• 1 Soft easy to pass bowel movement a day
• Symptomatic treatment as needed
• Rubber banding and Infrared Coagulation can easily be done in the office and are well tolerated.

Practice Recommendation – Anal Fissure
• Soften the stool
• Topical nitro +/- topical Calcium Channel blockers
• Oral Calcium Channel blockers
• Botox
• Surgery
Practice Recommendation - Other

• All that hurts is not hemorrhoids and fissures.
Questions

Contact Information

• justin.bailey@fmridaho.org
Hernia (Abdominal)

Joel Heidelbaugh, MD, FAAFP

ACTIVITY DISCLAIMER

The material presented here is being made available by the American Academy of Family Physicians for educational purposes only. Please note that medical information is constantly changing; the information contained in this activity was accurate at the time of publication. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed. Rather, it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

The AAFP disclaims any and all liability for injury or other damages resulting to any individual using this material and for all claims that might arise out of the use of the techniques demonstrated therein by such individuals, whether these claims shall be asserted by a physician or any other person. Physicians may care to check specific details such as drug doses and contraindications, etc., in standard sources prior to clinical application. This material might contain recommendations/guidelines developed by other organizations. Please note that although these guidelines might be included, this does not necessarily imply the endorsement by the AAFP.
DISCLOSURE

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflict of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

All individuals in a position to control content for this session have indicated they have no relevant financial relationships to disclose.

The content of my material/presentation in this CME activity will not include discussion of unapproved or investigational uses of products or devices.

Joel Heidelbaugh, MD, FAAFP

Clinical Professor, Departments of Family Medicine and Urology/Director of Medical Student Education and Clerkship Director, Department of Family Medicine/Director, Patients and Populations Branch, University of Michigan Medical School, Ann Arbor

Dr. Heidelbaugh is a family physician who has 19 years of academic teaching experience. His specialty topics include gastrointestinal disorders, men's health, and primary care urology. He is a member of the American Gastroenterological Association guideline panels for irritable bowel syndrome, inflammatory bowel disease, and Lynch syndrome. He is the co-editor and co-author of the textbook *ROME IV: Functional Gastrointestinal Disorders for Primary Care and Non-GI Clinicians*, published through the Rome Foundation. In addition, he is the consulting editor of *Primary Care: Clinics in Office Practice* and the president-elect of the American Society for Men's Health. Dr. Heidelbaugh believes that increasing awareness and education about gastrointestinal and men's health issues is an important trend in medical education, clinical practice, and research.
Learning Objectives

1. Review the anatomical classifications of common hernias.

2. Differentiate based on examination and presentation those hernias that require urgent versus delayed treatment.

3. Identify the preferred radiological diagnostic test based on hernia location.

4. Review common surgical techniques for hernia repair to assist in patient appropriate referral and education.

Audience Engagement System
Natural History

- 1555 BC - First description of an inguinal hernia appears in the Ebers papyrus
- 460 - 375 BC - Hippocrates mentions hernias of the pubic and umbilical regions
- 1871 - First attempts to reduce the hernial orifice were made
- 1890 - First success with repairing posterior wall of inguinal canal and reducing of the internal inguinal ring
- 1903 - First use of fascia graft to close large hernial orifices
- 1965 - Preperitoneal mesh-implantation for unilateral and bilateral hernias
- 1970 - Mesh first used to bolster the repair of both direct and recurrent hernias
- 1982 - First laparoscopic hernia repair was performed
- 1990 - First series of laparoscopic herniorrhaphies

http://intranet.tdmu.edu.ua/data/kafedra/internal/policlin/classes_stud.../en/med/Ilik/ptn/SURGERY%20IN%20FAMILY%20MEDICINE6/03.%20Principles%20of%20Patients%20Management%20with%20Abdominal%20Hernia.htm

AES Question # 1

Which of the following is TRUE regarding hernias?

A. They are more common in women
B. They are more common in middle aged
C. Obese patients have a lower incidence of herniada
D. Over one-half of men have an identifiable hernia
E. They are more common in shorter women
Epidemiology

- Abdominal / pelvic hernias account for 4.7 million ambulatory care visits annually
- More than 600,000 surgical repairs for inguinal hernias performed annually
- One of the most common surgical procedures performed in the US
- 9:1 male:female predominance
- Highest incidence among men ages 40 to 59
- More than 1:4 US men have a “medically recognizable” abdominal hernia
- Men with hiatal hernia have 2X risk of having inguinal hernia
- Overweight or obese men have lower risk of inguinal hernia
- Risk factors in women
  - Taller height, chronic cough, umbilical hernia, older age, rural residence
  - Neither smoking nor alcohol increase risk of incidence or recurrence

Pathophysiology

- Most common herniae develop in the abdomen, when a weakness in the abdominal wall evolves into a localized "defect" through which adipose tissue or abdominal organs covered with peritoneum may protrude
- Herniae may or may not present with pain at the site, a visible or palpable lump, or by vague symptoms resulting from pressure on an organ which has become "stuck" in the hernia, sometimes leading to organ dysfunction
- Fatty tissue usually enters a hernia first but may be accompanied by an organ (intestine)
Pathophysiology

- Weakening of containing membranes or muscles is usually congenital (familial tendency)
- Can be related to specific conditions:
  - Ehlers-Danlos syndrome or Marfan syndrome
  - Stretching of muscles during pregnancy
  - Significant weight loss (especially if obese)
- Many conditions chronically increase intra-abdominal pressure, (e.g. pregnancy, ascites, COPD, dyschezia, benign prostatic hypertrophy) and may lead to abdominal herniae

http://intranet.tdmu.edu.ua/data/kafedra/internal/policlin/classes_stud.../en/med/11k/ptn/SURGERY%20IN%20FAMILY%20MEDICINE6/03.%20Principles%20of%20Patients%20Management%20with%20Abdominal%20Hernia.htm

What Kind of Hernia?

https://www.webmd.com/digestive-disorders/ss/slideshow-hernia-guide
Examples include:

- **Abdominal wall hernias** (e.g. umbilical, ventral, incisional)
- **Diaphragmatic hernias and hiatal hernias** (e.g. paraesophageal hiatal hernia of the stomach)
- **Pelvic hernias** (e.g. inguinal [96%], femoral [4%])
- **Spigelian hernias** (e.g. lateral ventral hernia)
- **Sports hernias**

---

**AES Question # 2**

Which of the following best reflects characteristics of indirect inguinal hernias?

A. Internal inguinal ring may be absent  
B. They are always acquired  
C. Almost all under age 25 are indirect  
D. Lower incarceration risk if extends into the scrotum
**Definitions and Classification**

**The Inguinal Canal**
- Anatomic space beneath the external oblique aponeurosis, between the internal and external inguinal ring
- In men, contains the cremaster muscle and cord structures (vas deferens, testicular vessels, and connective tissues)
- In women, contains the cremaster muscle, round ligament, connective tissues

**Indirect Hernia**
- Sac of peritoneum through internal ring, antero-medial to spermatic cord/round ligament plus omentum or bowel
- Internal ring may be normal or dilated
- Usually congenital, but may be acquired
- Virtually all hernias in patients under age 25 are indirect
- Higher risk of incarceration/strangulation if large and extends into scrotum

**Direct Hernia**
- Bulging due to weakness/attenuation of posterior floor of the inguinal canal, from the internal ring to the pubic bone
- Hernia consists primarily of retroperitoneal fat; a peritoneal sac containing bowel is only infrequently present
- Usually at low (but not zero) risk for incarceration or strangulation
- Rarely occurs in women

**Recurrent Hernia**
- Any inguinal canal hernia which occurs after prior inguinal hernia repair
- Most often direct, but may also be indirect or sliding
Definitions and Classification

**Congenital hernias**
- occur prenatally or in the first year(s) of life, caused by a congenital defect

**Acquired hernias**
- develop later in life, usually from adolescence through adulthood

**Complete or incomplete**
- stomach may partially or completely herniate into the chest

Definitions and Classification

**Intraparietal hernia**
- hernia that does not reach the subcutis, only reaching the musculoaponeurotic layer (e.g. Spigelian hernia)
- may produce less obvious bulging, and may be less easily detected on clinical examination

**Bilateral**
- in this case, simultaneous repair may be considered, sometimes even with a giant prosthetic reinforcement

**Irreducible / incarcerated**
- hernia contents cannot be returned to their normal site with simple physical manipulation
Risks of Hernias

If irreducible, hernias can develop several complications:

Strangulation
- pressure on the hernia contents may compromise blood supply, leading to venous compromise and congestion
- causes ischemia, and later necrosis and gangrene, which may become fatal

Obstruction
- when part of the bowel herniates, bowel contents can no longer pass the obstruction
- results in cramps, and later on vomiting, ileus, absence of flatus and absence of defecation, +/- pain

Dysfunction
- herniated organ itself, or surrounding organs, start to malfunction
- sliding hernia of the stomach causing heartburn
- bowel obstruction as above

http://intranet.tdmu.edu.ua/data/kafedra/internal/policlin/classes_stud.../en/med/lik/ptn/SURGERY%20OF%20FAMILY%20MEDICINE%20/03.%20Principles%20of%20Patients%20Management%20with%20Abdominal%20Hernia.htm

Diagnosis

- Almost all hernias, in all locations, can be adequately diagnosed via physical exam
- Imaging may be useful in cases of:
  - recurrent hernia
  - possible hydrocele
  - uncertain diagnosis
  - surgical complications
  - chronic pain
- US - sensitivity (> 90%), specificity (82-86%)
- CT - under investigation
- MRI - best for differentiating inguinal vs femoral hernias with sensitivity and specificity both > 95%, in cases of pain with no identifiable hernia on exam
  
Physical Examination

The examination should be performed both supine and standing.

**Inspection**
- A visible bulge or asymmetry is present in the region of the inguinal canal
- Measure the diameter of the bulge (in centimeters)
- Does it extend into the scrotum?

**Palpation**
- Palpate abdominal wall along and directly over the inguinal canal from internal to external ring
- Internal ring can be consistently and reliably be found midway between the anterior superior iliac spine and the upper margin of the pubic bone
- Invagination of the scrotum and attempts to insert a finger into the external ring or inguinal canal itself is rarely necessary, always uncomfortable, and frequently misleading
- If a bulge is present, does it reduce?
- If a bulge is present, does it change when the patient strains or coughs?
- If a bulge is not present, does one become palpable when the patient strains or coughs?

Differential Diagnosis of Groin and Scrotal Masses

- Ectopic testis
- Epididymitis
- Femoral adenitis / adenopathy
- Femoral arterial aneurysm
- Femoral hernia
- Hematoma
- Hidradenitis
- Hydrocele
- Inguinal adenitis / adenopathy
- Inguinal hernia
- Lipoma
- Lymphoma
- Metastatic neoplasisa
- Psoas abscess
- Sebaceous cyst
- Testicular torsion
- Varicocele

European Classification

Primary Abdominal Wall Hernia Classification

<table>
<thead>
<tr>
<th>Diameter cm</th>
<th>Small (&lt;2 cm)</th>
<th>Medium (≥2-4 cm)</th>
<th>Large (≥4 cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midline</td>
<td>Epigastric</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Umbilical</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td>Spigelian</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lumbar</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

European Classification

Incisional Hernia Classification

<table>
<thead>
<tr>
<th>Diameter cm</th>
<th>Small (&lt;2 cm)</th>
<th>Medium (≥2-4 cm)</th>
<th>Large (≥4 cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midline</td>
<td>Subxiphoidal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Epigastric</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Umbilical</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Infrasternal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Suprapubic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral</td>
<td>Subcostal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Flank</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Iliac</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lumbar</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Recurrent incisional hernia? | Yes | No | Q

length (cm) | width (cm)

Width (cm) | W1 | W2 | W3
| <4 cm | O | O | O
| 4-10 cm | O | O | O
| ≥10 cm | O | O | O
European Classification

European Classification

http://intranet.tdmu.edu.ua/data/kafedra/internal/policlin/classes_stud.../en/med/lik/ptn/SURGERY%20IN%20FAMILY%20MEDICINE6/03.%20Principles%20of%20Patients%20Management%20with%20Abdominal%20Herna.htm

http://intranet.tdmu.edu.ua/data/kafedra/internal/policlin/classes_stud.../en/med/lik/ptn/SURGERY%20IN%20FAMILY%20MEDICINE6/03.%20Principles%20of%20Patients%20Management%20with%20Abdominal%20Herna.htm
Hernia Anatomy

https://www.webmd.com/digestive-disorders/ss/slideshow-hernia-guide

Anatomy

http://intranet.tdmu.edu.ua/data/kafedra/internal/policlin/classes_stud.../en/med/lik/ptn/SURGERY%20IN%20FAMILY%20MEDICINE/03.%20Principles%20of%20Patients%20Management%20with%20Abdominal%20Hernia.htm
Abdominal Wall Hernias

Umbilical Hernia

https://www.webmd.com/digestive-disorders/ss/slideshow-hernia-guide
Abdominal Wall Hernias

Umbilical hernias
- Fascial opening (umbilical ring) exists to allow passage of umbilical vessels from mother to fetus
- Opening closes after birth with continued growth of rectus abdominis toward each other
- Closure is complete in almost all children by 5 years of age, slower in blacks
- Cross-sectional study of 665 black children showed incidence
  - 4-5 years of age - 14%
  - 6-7 years of age - 4%
  - 8-9 years of age - 3%
  - 10-11 years of age - 2%
- Natural course is closure of umbilical ring, almost all eventually resolve
- Children with large proboscoid (trunk-like) hernias by 2 years of age require closure

Ventral Hernia

https://www.webmd.com/digestive-disorders/ss/slideshow-hernia-guide
Abdominal Wall Hernias

Ventral hernias
- Abdominal wall fascial defects not associated with prior surgery
- Among 2.3 million inpatient abdominal repairs performed between 2000-2010 an estimated 576,000 were performed emergently
- Rate of emergency hernia repairs has increased
  - 2001 - 16.0/100,000 patient/years
  - 2010 - 19.2/100,000 patient/years
- Asymptomatic hernias can be safely observed
  - Mean annual incidence of acute presentation is 2.6% (mean 0-20%)
  - Smoking, obesity, diabetes associated with poor healing, increased complications, recurrence


Incisional Hernia

https://www.webmd.com/digestive-disorders/ss/slideshow-hernia-guide
Abdominal Wall Hernias

Incisional hernias
- Many thousand laparotomy incisions are created each year
- Failure rate for closure of these abdominal wounds is between 10–15%
- Many of these hernias have been neglected and treated with abdominal trusses or inadequately managed with high failure rates
- Comparative, retrospective study of over 400 incisional hernia operations over a 25-year period, estimated that the most important prognostic factor is the surgeon’s experience
- Optimal technique is an all layer closure with absorbable monofilament suture
- Components’ separation - allows a flap of the rectus muscle, anterior rectus sheath, and internal oblique transversus to be advanced in the midline a maximum of 10 cm (e.g. incisional hernia gaps of 20 cm can be closed)
- An alternative method is use of tissue expanders placed in the subcutaneous or submuscular space for months to achieve tissue expansion prior to hernia repair


Diaphragmatic/Hiatal Hernias
AES Question # 3

Which of the following is a key characteristic of diaphragmatic / hiatal hernias?

A. They can be associated with GERD
B. They commonly require surgery
C. Surgery may increase risk of esophageal erosions
D. They are permanent and fixed
Diaphragmatic (Hiatal) Hernias

- Sliding and paraesophageal types
- Often associated with gastroesophageal reflux disease (GERD)
- Difficult to prove direct cause and association
- Most commonly discovered on upper endoscopy
- Surgery rarely required unless significant refractory (GERD) symptoms and erosive esophagitis
- 221 patients underwent laparoscopic repair with biologic mesh
- 3.6% had a documented anatomic hiatal hernia recurrence
- Laparoscopic repair using biologic mesh, both with and without a simultaneous bariatric or antireflux procedure, is efficacious safe therapeutic option for management of hiatal hernia, prevention of recurrence, and relief of symptomatic GERD


Pelvic Hernias
Inguinal Hernia

https://www.webmd.com/digestive-disorders/ss/slideshow-hernia-guide

Inguinal Hernia

https://www.webmd.com/digestive-disorders/ss/slideshow-hernia-guide
Inguinal Hernias

- Direct inguinal hernias account for 30-40% of groin hernias in men
- Protrude at the internal inguinal ring
  - Site where spermatic cord in men and round ligament in women exists
  - Hernia sac located lateral to inferior epigastric artery
- Develop more frequently on the right in both men and women
- More have congenital origin
- “Shutter mechanism”, thought to close internal inguinal ring to a slit, thought to be dysfunctional in patients with a patent processus vaginalis


Femoral Hernia

https://www.webmd.com/digestive-disorders/ss/slideshow-hernia-guide
AES Question # 4

Which of the following is a key characteristic of femoral hernias?

A. They are the most common type of hernia
B. They are more common in women than men
C. Most can be observed expectantly
D. They have low complication rates

Femoral Hernias

• Least common type of all hernias
• More common in women
• 40% present emergently with incarceration or strangulation
• Located inferior to inguinal ligament and protrude through femoral ring
• Medial to femoral vein
• Lateral to lacunal ligament
• Femoral ring can widen with aging and injury
• Surgically challenging to correct with high complication rates

Spigelian Hernias

Spigelian Hernia

https://abdominalkey.com/spigelian-hernia/
Spigelian Hernia

- Estimated at 0.12% of abdominal wall hernias
- Very rare and difficult to diagnose clinically - usually requires US/CT/MRI
- Occurs through slit-like defect in anterior abdominal wall adjacent to the semilunar line
- Most occur in the lower abdomen where the posterior sheath is deficient
- Hernia ring is a well-defined defect in the transverses aponeurosis
- Hernial sac, surrounded by extraperitoneal fatty tissue, is often interparietal passing through the transversus and the internal oblique aponeuroses and then spreading out beneath the intact aponeurosis of the external oblique

Sports Hernias

Sports Hernia (Athletic Pubalgia)

Sports hernias often occur where the abdominals and adductors attach at the pubic bone. Traditional hernias occur in the inguinal canal.

Sports Hernia (Athletic Pubalgia)

• A painful, soft tissue injury that occurs in the groin area
• Most often occurs during sports that require sudden changes of direction or intense twisting movements
• Although a sports hernia may lead to a traditional, abdominal hernia, it is a different injury
• A sports hernia is a strain or tear of any soft tissue (e.g. muscle, tendon, ligament) in lower abdomen or groin area
• Because different tissues may be affected and a traditional hernia may not exist, the medical community prefers the term "athletic pubalgia" to refer to this type of injury


Sports Hernia (Athletic Pubalgia)

• Causes severe pain in the groin area at time of the injury
• Pain typically gets better with rest, but comes back with return to sports activity, especially with twisting movements
• Over time, a sports hernia may lead to an inguinal hernia, and abdominal organs may press against the weakened soft tissues to form a visible bulge
• Without treatment, the injury can result in chronic, disabling pain that prevents resuming sports activities
Sports Hernia (Athletic Pubalgia)

Diagnosis
- Pain during resisted sit-up, tenderness in the groin or above the pubis
- Although a sports hernia may be associated with a traditional, inguinal hernia, in most cases, no hernia can be found by the doctor during a physical examination

Treatment - Nonsurgical

Rest
- In the first 7 to 10 days after the injury, treatment with rest and ice or compression wrap if bulge is present

Physical therapy
- Two weeks after injury, physical therapy exercises can improve strength and flexibility in abdominal and inner thigh muscles

Pharmacotherapy
- Non-steroidal anti-inflammatory drugs, steroid injections

Sports Hernia (Athletic Pubalgia)

Treatment - Surgical

Surgical procedure
- Surgery to repair the torn tissues in the groin can be done as a traditional, open procedure with one long incision, or as an endoscopic procedure
- Some cases of sports hernia require inguinal neurectomy during the surgery to relieve pain

Surgical rehabilitation
- Most athletes are able to return to sports 6 to 12 weeks after surgery

Surgical outcomes
- More than 90% of patients who go through nonsurgical treatment and then surgery are able to return to sports activity
- In some patients the tissues will tear again during sports and the surgical repair will need to be repeated

Additional surgery
- In some cases, pain in the inner thigh continues after surgery
- An additional surgery, called adductor tenotomy, may be recommended to address the pain
- The tendon heals at a greater length, releasing tension and giving the patient a greater range of motion
Management of Asymptomatic Inguinal Hernia

- Systematic review of 41 manuscripts and 2 RCTs evaluating watchful waiting and surgical approaches to asymptomatic inguinal hernia (AIH)
- Data extraction centered on pain, discomfort, general health status, complications, life-threatening events
- No significant difference in pain scores or general health status were reported
- Crossover ratio between 23% and 72% from watching waiting to surgery
- In patients with watchful waiting, rates of AIH strangulation were 0.27% after 2 years of follow-up and 0.55% after 4 years
- In patients who underwent elective surgery, range of operative complications was 0 - 22.3% and recurrence rate was 2.1%
- Both treatment options for asymptomatic inguinal hernia are safe
- Most patients will develop pain over time and require operation


When To Refer...

- Acute pain
- Any evidence of strangulation or incarceration
- Any evidence of sepsis or complication
- Patient concern
  - Offer reassurance
  - Watchful waiting
  - After discussion about short-term and long-term expectations and outcomes
Surgical Treatment

https://www.webmd.com/digestive-disorders/ss/slideshow-hernia-guide

Treatment

• Definitive treatment of all hernias is surgical repair, regardless of hernia origin or type
• Urgent emergency surgical repair is indicated for patients who develop complications
• If undertaken within approximately four to six hours from onset of symptoms, an emergency surgical repair may prevent loss of bowel from prolonged strangulation
• For uncomplicated hernias, optimal timing of repair technique remain controversial
• Currently recommended that symptomatic hernias undergo elective hernia repair
• For patients who are asymptomatic but have risk factors for groin hernia incarceration or strangulation, a hernia repair is generally undertaken as soon as is feasible
• For male patients with minimal symptoms, with a “watchful waiting” approach to treatment, cumulative probability of developing increasing pain, incarceration or strangulation
  • 2.8% at three months
  • 4.5% to 23% at two years
  • 31% at four years

Treatment

• Aim of hernia repair surgery is not only to fix current hernia defect, but also to reduce risk of recurrence
• Recurrence rates for primary hernia repair range from 0.5% to 15% depending on the hernia site, type of repair and clinical circumstances
• Groin hernia repairs can involve the use of a mesh (hernioplasty) or no mesh (herniorrhaphy)
• Prosthetic mesh is being increasingly incorporated into hernia surgery (either open or laparoscopic) as a component of tension-free repair
• Mesh used in hernia repair is typically made from a synthetic polymer (e.g. polypropylene) which is inert and does not cause abnormal inflammation


Treatment

• Meshes may be held in place using partially dissolvable sutures and/or a fibrin glue, of which the glue may produce a more effective seal, or “screws”
• A mesh repair involves covering the hernial defect by placing the mesh on one of the layers of the abdominal wall either using an open approach or a minimal access laparoscopic technique
• The approach to repair depends on a number of factors in each individual case, including the type of hernial defect, patient factors and the surgeon's preference
• With the open approach, the repair is generally anterior to the hernial defect, whereas laparoscopic repair is approached from a posterior aspect

Treatment

- The two main laparoscopic groin hernia repairs are the totally extraperitoneal (TEP) and transabdominal preperitoneal patch (TAPP) repairs, both requiring the use of a mesh
- TEP repair is performed by gaining access to the preperitoneal space (that is, the space between the peritoneum and the anterior abdominal wall) using an anterior approach, without ever actually entering the abdomen
- A TAPP repair, on the other hand, requires the surgeon to enter the peritoneal (abdominal) cavity to access the preperitoneal space


Potential Surgical Complications

- Some of the more significant disadvantages of the TAPP repair include potential injury to adjacent organs and, long-term, adhesions resulting in bowel obstruction
- Common early complications include wound seroma or hematoma, urinary retention, bladder injury and superficial wound infection
- Common later complications include persistent groin pain and post-herniorrhaphy neuralgia, testicular complications, deep wound or mesh infection, recurrent hernia and mesh migration or erosion

Potential Surgical Complications

- The incidence of post-surgical complications is more common following emergent repairs and recurrent hernia repairs.
- While laparoscopic repairs are associated with quicker recovery times and less persistent pain, the procedure itself usually takes longer and has higher rates of bladder and vascular injuries.
- Hernia recurrence post laparoscopic mesh repair was less common compared to open non-mesh repair.
- Main indicator of recurrence related to the use of a mesh rather than the approach itself.


Post-Operative Care

- Wound care
- Required inactivity varies
  - Depends upon surgeon
  - Depends upon patient
  - Depends upon type of hernia and extent of surgical repair
- Most activity permitted
  - Within 10 days for professionals
  - Within 14-28 days for laborers, with caution

Practice Recommendations (SOR C)

• Although imaging techniques such as ultrasonography, computed tomography, and magnetic resonance imaging are rarely needed to diagnose inguinal hernias, they may be useful in certain clinical situations
• Ultrasonography has good sensitivity and specificity for detection of abdominal and inguinal/groin hernias
• Small, minimally symptomatic, first hernias do not necessarily require repair, and these patients may be followed expectantly
• Patients should be counseled on the symptoms of incarceration or strangulation, and to seek prompt evaluation if these occur
• Patients with symptomatic, large, or recurrent inguinal hernias should be referred for repair within one month of detection, or urgently if necessary


Questions
Contact Information

Joel J. Heidelbaugh, MD, FAAFP, FACG
jheidel@umich.edu
Liver Function Tests:
Is Something Wrong With My Liver?

Robert C. Langan, MD, FAAFP

ACTIVITY DISCLAIMER

The material presented here is being made available by the American Academy of Family Physicians for educational purposes only. Please note that medical information is constantly changing; the information contained in this activity was accurate at the time of publication. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed. Rather, it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

The AAFP disclaims any and all liability for injury or other damages resulting to any individual using this material and for all claims that might arise out of the use of the techniques demonstrated therein by such individuals, whether these claims shall be asserted by a physician or any other person. Physicians may care to check specific details such as drug doses and contraindications, etc., in standard sources prior to clinical application. This material might contain recommendations/guidelines developed by other organizations. Please note that although these guidelines might be included, this does not necessarily imply the endorsement by the AAFP.
DISCLOSURE

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflict of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

All individuals in a position to control content for this session have indicated they have no relevant financial relationships to disclose.

The content of my material/presentation in this CME activity will not include discussion of unapproved or investigational uses of products or devices.

Robert C. Langan, MD, FAAFP

Program Director, St. Luke’s Family Medicine Residency Program, Allentown, Pennsylvania; Adjunct Associate Professor, Department of Family and Community Medicine, Temple University, Philadelphia, Pennsylvania

Dr. Langan earned his medical degree from Albany Medical College, New York, and completed his family medicine residency at Naval Hospital Pensacola, Florida. In 2015, he was named the Pennsylvania Academy of Family Physicians Exemplary Teacher of the Year. He is on the editorial board for FP Essentials™ and is a senior author with The Core Content Review of Family Medicine. Dr. Langan has been published in journals including American Family Physician, Osteopathic Family Physician, and The Journal of Family Practice. His interests cover all aspects of family medicine.
Learning Objectives

1. Review the ACG guidelines for evaluation of abnormal liver chemistries.

2. Use a stepwise diagnostic approach to evaluate patients with elevated liver transaminase levels if the history and physical examination do not suggest a cause.

3. Develop a collaborative care plan that involves observation with lifestyle modification is appropriate if the initial history, physical examination, and workup do not suggest a cause of elevated liver transaminase levels.

4. Coordinate referral and follow-up in patients with unexplained elevation of liver transaminase levels for six months or more.

Audience Engagement System
Welcome Back to New Orleans!

Moving Up in the World

- 2014: Prostate
- 2017: Testicles
- 2018: Liver
- 2019: ???
AES Question #1

The most common cause of mildly elevated transaminases is:

A. Nonalcoholic steatohepatitis
B. Nonalcoholic fatty liver disease
C. Alcoholic liver disease
D. Acute hepatitis B
E. Hemochromatosis

A Tour of the Liver

- Transaminases
- Alkaline phosphatase
- Albumin
- Bilirubin
- Prothrombin time

Downloaded from https://en.wikipedia.org/wiki/French_Quarter
What’s a Transaminase?

[Chemical diagrams]


Are All Transaminases Created Equal?

[Diagram showing AST and ALT in various organs]

All images downloaded from [https://commons.wikimedia.org](https://commons.wikimedia.org)
Transaminase Pearls

• “Normal” ALT has been difficult to define
• ACG proposes:
  – MEN: 29 to 33 IU/L
  – WOMEN: 19 to 25 IU/L
• Elevated AST or ALT without risk factors is associated with increased liver-related mortality
• There is a linear relationship between ALT and BMI

Pay Attention to this Slide!

A NORMAL ALT MAY NOT EXCLUDE SIGNIFICANT LIVER DISEASE!
Specific Causes of Elevated AST/ALT

- Viral Hepatitis
- Alcohol
- Genetic Disorders
- NAFLD
- Medications

Non-Alcoholic Fatty Liver Disease

- Most common cause of borderline (<2x ULN) and mild (2-5 x ULN) ↑ AST and ALT
- 25-51% of cases
- AST<ALT (+LR 80 for a ratio less than 1)
- Associated with metabolic syndrome
  - Obesity, diabetes, dyslipidemia, hypertension
- RUQ u/s can be used to show fatty infiltration
NAFLD versus NASH

Non-Alcoholic Steatohepatitis (NASH)
- Subset of NAFLD (3-5%)
- Inflammation, fibrosis
- May progress to cirrhosis
- No blood test to distinguish NASH from NAFLD
- Gold standard for dx: biopsy

NAFLD fibrosis score can be used to assess the risk of developing NASH
- Includes age, ALT, AST, BMI, DM or glucose intolerance, platelet count, albumin
- [http://nafldscore.com/](http://nafldscore.com/)
- Recommended over other noninvasive tests by ACG (liver elastography, serum cytokeratin 18)
NAFLD Score

Low
- Low Likelihood of NASH
- Lifestyle Modifications

Intermediate
- Intermediate Likelihood of NASH
- Consider Biomarkers, Elastography

High
- High Likelihood of NASH
- GI evaluation
- Liver Biopsy

Lifestyle Modifications for NAFLD

<table>
<thead>
<tr>
<th>INTERVENTION</th>
<th>NOTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight Loss</td>
<td>Aim for 7%-10% weight loss if overweight/obese</td>
</tr>
<tr>
<td>Alcohol Consumption</td>
<td>Limit to less than 2 drinks/day (M), 1 drink/day (F)</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>150-200 minutes/week of moderate to vigorous intensity</td>
</tr>
<tr>
<td>General Nutrition</td>
<td>No specific dietary approach is recommended</td>
</tr>
<tr>
<td>Fructose Intake</td>
<td>Avoid high-fructose foods</td>
</tr>
</tbody>
</table>

WEIGHT LOSS AND PHYSICAL ACTIVITY REDUCE INCIDENCE AND EFFECTS OF NAFLD!
Primary Care of NASH

- Lifestyle modifications
- Pioglitazone (improved steatosis, inflammation but not fibrosis; caution with HF)
- Vitamin E (non-diabetic patients only)
- Not recommended to treat NASH:
  - metformin, ursodeoxycholic acid, statins, omega-3 fatty acids

NASH and HCC

- Hepatocellular carcinoma occurs more frequently in NASH, but not as frequently as in cirrhosis
- Risk factors: DM, obesity, metabolic syndrome
- Optimal screening strategy not known
Alcoholic Liver Disease

- The primary cause of liver-related mortality in U.S.
- ↑ AST>ALT (rarely >300 IU/L)
  - The higher the ratio, the more likely it is due to alcohol (+ LR of 17)
- ↑ GGT suggests alcoholic liver disease, but is not diagnostic

Alcoholic Liver Disease

- Ask all patients about alcohol intake
- Significant alcohol consumption (ACG):
  - MEN: >30 grams/day
  - WOMEN: >20 grams/day
- 14 grams of alcohol:
  - 12 oz. of beer, 5 oz. of wine, or 1.5 oz. liquor
Alcoholic Liver Disease

- Considerable overlap between alcoholic liver disease and NAFLD radiologically and histologically
- Consider using alcoholic liver disease/NAFLD index to differentiate between the two (+LR of 12)
- Includes AST, ALT, MCV, height, weight, gender

Medication-Induced Liver Disease

- Medications and supplements are frequent causes of mild elevations of AST/ALT
- It may be necessary to do several trials of discontinuation and reevaluation in order to isolate the specific agent
- ALT >1000 IU/L → think of acetaminophen
- Statins are safe to use with chronic liver disease
Medication-Induced Liver Disease

- Analgesics (APAP)
- Antihypertensives (ACE-I, ARB)
- Antimicrobials (INH, azoles, TCN)
- Chemotherapy (MTX)
- Psychiatric (SSRI, SNRI)
- Supplements (chaparral, ephedra, green tea extract)

Viral Hepatitis Testing (ACG)

- In patients with elevated AST/ALT, consider screening for viral hepatitis if RF are present:
  - HEPATITIS A: possible fecal-oral exposure
  - HEPATITIS B: born in endemic areas, MSM, IVDA, dialysis, HIV+, close contact with HBV+
  - HEPATITIS C: IVDA, tattoos, body piercings, blood transfusions, high risk sexual behavior, born between 1945 and 1965
Viral Hepatitis Testing (ACG)

- HEPATITIS A: IgM HAV
- HEPATITIS B: HBsAg & IgM anti-HBc (acute)
  HbsAg (chronic)
- HEPATITIS C: anti-HCV, confirmed by HCV-RNA

Viral Hepatitis Pearls

<table>
<thead>
<tr>
<th></th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Symptoms</td>
<td>Anorexia, N/V, Fever, Fatigue, Jaundice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Acute Infection</td>
<td>70-80%</td>
<td>30-50%</td>
<td>20-30%</td>
</tr>
<tr>
<td>Incubation</td>
<td>28 days</td>
<td>120 days</td>
<td>45 days</td>
</tr>
<tr>
<td>Screening?</td>
<td>N/A</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Complications</td>
<td>Rarely fatal</td>
<td>1800 deaths/year</td>
<td>20,000 deaths/year</td>
</tr>
<tr>
<td>Treatment</td>
<td>Supportive</td>
<td>Supportive</td>
<td>Antivirals</td>
</tr>
<tr>
<td>Vaccine?</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
AES Question #2

Which of the following pairs is correctly matched?

A. α-1 antitrypsin disease: type 1 diabetes mellitus
B. Hemochromatosis: abnormal copper metabolism
C. Autoimmune hepatitis: Lyme disease
D. Wilson’s disease: ↓ ceruloplasmin
E. Extrahepatic: chronic kidney disease

Uncommon Disorders

- Hemochromatosis (UNCOMMON)
- α-1antitrypsin deficiency (RARE)
- Wilson’s disease (RARE)
- Autoimmune hepatitis (RARE)
- Extrahepatic causes (RARE)
Hemochromatosis

- Increased iron absorption
- Autosomal recessive
- 1 in 150-250 Northern European
- Screen:
  - TRANSFERRIN SATURATION >45%
  - FERRITIN >300 ng/mL (MEN)
  - FERRITIN >200 ng/mL (WOMEN)
- Confirmation: HFE gene testing
- Treatment: phlebotomy, chelators

Uncommon Disorders Review

- α-1antitrypsin deficiency
  - Rare in adults, young COPD, 1:2500 Caucasians
- Wilson’s disease
  - Abnormal Cu metabolism; 1:30,000, ↓ ceruloplasmin
- Autoimmune hepatitis
  - Associated with autoimmune d/o; 1:6000; + ANA/anti-SM
- Extrahepatic causes
  - Celiac disease, Hypothyroidism, Rhabdomyolysis, Lyme
Alkaline Phosphatase

• Metalloproteinase that catalyzes the hydrolysis of phosphate esters at an alkaline pH
• Found in the liver, kidneys, bone, placenta, and colon

Alkaline phosphatase is located on the canalicular membranes of the hepatocytes, not the bile duct proper.
Elevations of Alkaline Phosphatase

- Usually indicates biliary obstruction
- May occur BEFORE elevations of bilirubin
- Elevated GGT suggests that isolated elevation is hepatic, but is not specific for hepatic disease
- Can be fractionated into hepatic, non-hepatic subtypes
- Consider RUQ U/S in patients with isolated elevations
- Conditions that elevate AST/ALT can also elevate it (NAFLD, alcoholic liver disease)

Non-Hepatic Elevations of Alkaline Phosphatase

- Pregnancy: mild isolated elevation of alkaline phosphatase commonly seen (placental in origin)
- Children: higher levels are due to rapid bone growth
- Elderly: higher levels due to more bone turnover, especially in women
- Other causes: Paget’s disease of the bone, neoplasm with bony metastases, heart failure, ulcerative colitis
**Albumin**

- Marker of hepatic FUNCTION
- Plasma protein exclusively synthesized in the liver
- Half life of 3 weeks
- Levels ≤ 3.5 g/dL usually indicate liver disease of >3 weeks
- Any significant illness may decrease albumin

**PROTHROMBIN TIME**

- Marker of hepatic FUNCTION
- More sensitive marker than albumin
- Severe liver disease <24 h may cause elevation in PT
  - Hepatocellular disease: Factors 1, 2, 5, 7, 9 and 10
  - Cholestasis: Factors 2, 7, 9, 10 (no vitamin K absorption)
- Differential: warfarin, heparin bolus, DIC, hypothermia
AES Question #3

Common medications that cause hyperbilirubinemia do NOT include:
A. Trimethoprim-sulfamethoxazole
B. Atorvastatin
C. Tramadol
D. Isoniazid
E. Oral contraceptives

BILIRUBIN METABOLISM

• Hemoglobin breaks down to UNCONJUGATED bilirubin, tightly bound to ALBUMIN, and is water-insoluble
• In the liver, bilirubin is made water-soluble (CONJUGATED), and excreted in the bile
• Bilirubin is metabolized by gut bacteria to UROBILINOGEN, which is excreted in stool & urine
BILIRUBIN TERMINOLOGY

INDIRECT
- UNCONJUGATED

DIRECT
- CONJUGATED

TOTAL
- UNCONJUGATED AND CONJUGATED

BILIRUBIN

↑ CONJUGATED BILIRUBIN:
- Hepatocellular
- Cholestasis

↑ UNCONJUGATED BILIRUBIN:
- RBC enzyme disorders (G6PD)
- Autoimmune hemolytic anemia
- Sickle cell disease
- Myeloproliferative disorders
- Gilbert’s disease

Image downloaded from https://commons.wikimedia.org
MEDICATIONS CAUSING HYPERBILIRUBINEMIA

<table>
<thead>
<tr>
<th>MECHANISM</th>
<th>EXAMPLES</th>
<th>INDIRECT/DIRECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>↑ bilirubin</td>
<td>TMP/SMX, nitrofurantoin (G6PD deficiency)</td>
<td>I</td>
</tr>
<tr>
<td>↓ hepatic uptake</td>
<td>Choramphenicol, probenecid, rifampin</td>
<td>I</td>
</tr>
<tr>
<td>↓ conjugation</td>
<td>Ethinyl estradiol</td>
<td>I</td>
</tr>
<tr>
<td>Hepatocellular dysfunction</td>
<td>APAP, amiodarone, INH, NSAID, statin</td>
<td>D</td>
</tr>
<tr>
<td>Intrahepatic cholestasis</td>
<td>Amoxicillin/clavulanic acid, steroids, OCP, phenothiazines</td>
<td>D</td>
</tr>
</tbody>
</table>

INDIRECT HYPERBILIRUBINEMIA

1. Check transaminases and alkaline phosphatase
2. Review medications that might cause ↑ indirect bilirubin
3. Evaluate for hemolysis
4. If other liver chemistries are normal and there is no evidence of hemolysis, most likely represents GILBERT’S DISEASE
   A. Genetic defect of UDP-glucuronyltransferase
DIRECT HYPERBILIRUBINEMIA

1. Check transaminases and alkaline phosphatase
2. Review medications that might cause ↑ direct bilirubin
3. Consider cirrhosis, biliary obstruction, sepsis
4. Obtain RUQ U/S to evaluate for cholestasis
   A. Duct Dilation: consider ERCP, MRCP
   B. No Duct Dilation: consider AMA, ANA, SMA
5. If associated with abnormal AST/ALT or worsening, may need liver biopsy

Practice Recommendations
Practice Recommendations

• Borderline (<2x ULN)/mildly elevated (2-5x ULN) transaminases:
  – Confirm elevation
  – Discontinue alcohol use
  – Assess for risk factors for:
    • NAFLD (DM, obesity, dyslipidemia, hypertension)
    • Viral Hepatitis (A/B/C)

Practice Recommendations

• NAFLD:
  – RUQ U/S, lifestyle modifications, screen for NASH
• Viral Hepatitis:
  – Supportive care, antivirals, vaccination
• Alcohol/Drug Related
  – Abstinence
• Negative Workup
  – Observation versus looking for rare causes
Moderately elevated (5-15 x ULN) transaminases:
- Significant overlap with etiologies of borderline/mild elevations
- Initial steps are the same, but have a lower threshold for evaluating a broader differential (obstruction, hepatitis, autoimmune liver disease, unusual causes) and GI referral

Severely elevated (>15x ULN) transaminases:
- Admit, broad workup, screen for APAP ingestion

Practice Recommendations

Isolated elevation of alkaline phosphatase: biliary obstruction
Decreased albumin, increased INR: significant hepatic disease
Isolated indirect hyperbilirubinemia: think hemolysis, Gilbert’s disease
Isolated direct hyperbilirubinemia: think cholestasis versus hepatic disease
REFERENCES


REFERENCES


Questions

Contact Information

Robert Langan
Robert.Langan@sluhn.org
Probiotics and the GI Tract, What Should A Busy Clinician Know

Daniel Merenstein, MD
Ruben Hummelen, MD, PhD

ACTIVITY DISCLAIMER

The material presented here is being made available by the American Academy of Family Physicians for educational purposes only. Please note that medical information is constantly changing; the information contained in this activity was accurate at the time of publication. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed. Rather, it is intended to present an approach, view, statement, or opinion of the faculty, which may be helpful to others who face similar situations.

The AAFP disclaims any and all liability for injury or other damages resulting to any individual using this material and for all claims that might arise out of the use of the techniques demonstrated therein by such individuals, whether these claims shall be asserted by a physician or any other person. Physicians may care to check specific details such as drug doses and contraindications, etc., in standard sources prior to clinical application. This material might contain recommendations/guidelines developed by other organizations. Please note that although these guidelines might be included, this does not necessarily imply the endorsement by the AAFP.
DISCLOSURE

It is the policy of the AAFP that all individuals in a position to control content disclose any relationships with commercial interests upon nomination/invitation of participation. Disclosure documents are reviewed for potential conflict of interest (COI), and if identified, conflicts are resolved prior to confirmation of participation. Only those participants who had no conflict of interest or who agreed to an identified resolution process prior to their participation were involved in this CME activity.

The following individual(s) in a position to control content for this session have disclosed the following relevant financial relationships

Daniel Merenstein, MD
- Consultant or Advisory Board: Dannon (Probiotics); Pharmavite (Probiotics); Sanofi (Probiotics); Debevoise & Plimpton (Probiotics); Reckitt Benckiser (probiotics); and Bayer (Probiotics)

All other individuals in a position to control content for this session have indicated they have no relevant financial relationships to disclose.

The content of my material/presentation in this CME activity will not include discussion of unapproved or investigational uses of products or devices.

Daniel Merenstein, MD

Professor, Family Medicine, Georgetown University, Washington, D.C.

Dr. Daniel Merenstein teaches two undergraduate classes, a research capstone and a seminar on evaluating evidence-based medical decisions. He has been funded by the National Institutes of Health (NIH), the U.S. Department of Agriculture (USDA), various foundations, and industry groups. The primary goal of Dr. Merenstein's research is to provide answers to common clinical questions that lack evidence and improve patient care. Dr. Merenstein is a clinical trialist and has recruited more than 1,700 participants for eight probiotic trials since 2006. He is an expert on probiotics, antibiotic stewardship in outpatient settings and also conducts HIV research in a large women’s cohort. He sees patients three shifts a week. In addition to his role at Georgetown, Dr. Merenstein has a secondary appointment in the undergraduate Department of Human Science, in the School of Nursing and Health Studies.
Ruben Hummelen, MD, PhD

Associate Professor of Family Medicine, Northern Ontario School of Medicine, Thunder Bay, Ontario, Canada

Dr. Hummelen cares for patients in 33 remote, fly-in locations in Northwestern Ontario as part of a team of generalists working for the Sioux Lookout First Nations Health Authority. His practice involves obstetrics, hospitalist medicine, emergency medicine, and addiction care. He is also a primary care researcher focusing on improving maternal and child outcomes. He earned a medical degree at Erasmus University Rotterdam in the Netherlands. During his medical training, he also earned a PhD, with a focus on the microbiome of women in Tanzania living with HIV.

Learning Objectives

1. Understand key concepts of probiotic effectiveness including strain selection, dosage and viability.

2. Correctly identify evidence based probiotic products for gastrointestinal conditions using online tools, apps and websites.

3. Educate patients on selecting an appropriate probiotic and how fermented foods may impact health.
Audience Engagement System

After this session you will have:

- Understood the difference between fermented food, prebiotics and probiotics
- Reviewed the evidence of probiotics for gastrointestinal indications
- Gained skills to prescribe effective products
Your microbes weigh 4-6 lbs of your body mass

Benno et al. 2016 RIKEN Research

**Number Needed to Treat**

- ASA to prevent first heart attack/stroke: 1667
- Mediterranean diet to prevent first heart attack/stroke: 61
- Antibiotics to treat sinusitis: 15

- Probiotics to prevent *C. difficile*: 40
- Probiotics to prevent antibiotic-associated diarrhea in pediatrics: 9
- Probiotics to treat colic: 4

www.thennt.com
A randomized synbiotic trial to prevent sepsis among infants in rural India

Pinaki Panigrahi1,2, Sailajanandan Parida3, Nirmal C. Nanda4, Radhanath Satpathy5, Lingaraj Pradhan6, Dinesh S. Chandel7, Lorena Baccaglini8, Arjit Mohapatra9, Subhranshu S. Mohapatra5, Pravas R. Misra5, Rama Chaudhry8, Hegang H. Chen9, Judith A. Johnson10, J. Glenn Morris Jr10, Nigel Paneth11 & Ira H. Gewolb12

- 4,556 newborns randomized
- Placebo group 206 deaths vs 123 in probiotic group (risk ratio 0.60)
- NNT=27

Panigrahi et al. 2017 Nature

A Tipping Point?

156% increase in probiotic usage in the U.S. in last 10 years

“Not all supplements, of course, lack evidence of efficacy. Many supplements, including vitamins, minerals, and probiotics, are important components of modern health care.”

Cohen et al. 2016 JAMA
Graph courtesy of Dr. M.E. Sanders
AES Question #1

Probiotics that are refrigerated are better

A. True
B. False

AES Question #2

More strains = more effectiveness

A. True
B. False
AES Question #3

What is the most important thing to look for when choosing a probiotic?

A. To have the most bacteria
B. To be clinically studied
C. To have Lactobacillus
D. To be bacteria originated from humans

Live microorganisms that, when administered in adequate amounts, confer a health benefit on the host

$ 91
Lactobacillus rhamnosus HA 111
0 research studies
0 indications

$ 30
Lactobacillus rhamnosus GG
2773 research studies
>10 indications

Fermented Foods

Made through controlled microbial growth and enzymatic conversions

Foods such as yogurt, wine, beer, sauerkraut and kimchi, historically used because of their improved shelf life, safety, and of course taste

Marco et al. 2017 Curr Opin Biotech
Prebiotics

‘Substrate that is selectively utilized by host microorganisms conferring a health benefit’

Need to be shown to have a health effect and impact the microbiota

Gibson et al. 2017 Nat Rev Gastro Hepa

AES Question #4

What is the main reason you use probiotics?

A. For metabolic indications, Weight loss, DM, HTN etc
B. For gastrointestinal indications, diarrhea, IBS etc
C. For preventive health
D. Never recommend probiotics
Antibiotic-associated diarrhea

- 10-25% of children on antibiotics develop AAD
- Episode last 4 days
- Incidence of AAD is higher in children <2y (18%)
- More common with administration of amoxicillin/clavulanate (23%)

Turck et al. 2003 J Pediatr Gastroenterol Nutr
Bauer et al. 2011 Lancet

BMJ Open  Can probiotic yogurt prevent diarrhoea in children on antibiotics? A double-blind, randomised, placebo-controlled study

Multisite, RCT (N=70)
Probiotic (LGG/BB-12/LA-5) or yogurt
Less diarrhea in probiotic group (HR 0.14)

Fox et al. 2015 BMJ Open
Cochrane Probiotic Pediatric AAD

23 RCT’s (n=3938)
AAD probiotic group 8% (163/1992) vs 19% placebo (364/1906)

NNT= 9

Goldenberg et al. 2015 Cochrane
**Clostridium difficile**

- Cephalosporin, fluoroquinolone, carbapenem, clindamycin high risk
- Risk increases with age, duration of hospitalization, IBD, CKD
- Risk of recurrence 25%
- Mortality 4.5 – 5.7%

---

**Meta-analyses**

31 RCTs (n = 8672)
Probiotic group 1.5% (70/4525)
Control group 4.0% (164/4147)

**Number Needed to Treat = 40**

---

**McDonald et al. 2018 IDSA Guidelines**

**Goldenberg et al. 2017 Cochrane**
AES Question #5

Probiotics in your hospital?

A. Yes I know which one they have
B. I have no idea if they have
C. There are no probiotics on hospital formulary
Fecal Microbiota Transplant for *C. Difficile*

- 7562 original articles, not studies
- 4 double-blind RCTs (n = 249) for C. difficile
- Effectiveness 44 – 96%
- Adverse Events 29%
- Array of interventions fresh vs frozen vs route administration

Hota 2018 Open Forum Infect Dis

IDSA Guideline

‘insufficient data at this time to recommend administration of probiotics for primary prevention of CDI’

*27 Clinical trials total 8672 participants*

‘Fecal microbiota transplantation is recommended for patients with multiple recurrences of CDI who have failed appropriate antibiotic treatments’

*3 Clinical trials total 219 participants*

McDonald *et al.* 2018 IDSA Guidelines
Colic

- Crying excessively >3 days a week, >3 hours a day for >1 week
- Peaks at 6-8 weeks and resolves at 3-4 months
- Less frequently colonized with *Lactobacillus* species

Probiotics for Colic

- Four double-blind RCTs (*Lactobacillus reuteri DSM 17938*), n = 345
- Decreased crying -25.4 minutes [95% CI: -47.3, -3.5]
- In breastfed NNT=2.6
- No adverse events reported in any trials

*Sung et al. 2018 Pediatrics*
Recurrent abdominal pain

- One episode per week for 2 months
- 4-25% of school-aged children
- Associated with school absence, admissions, emotional disorders

Newglove-Delgado et al. 2017 Cochrane

Dietary interventions for recurrent abdominal pain in childhood (Review)


13 RCTs on probiotics, 3 on fiber, 2 on diet

NNT=8

Newglove-Delgado et al. 2017 Cochrane
Irritable bowel syndrome

- Rome III: recurrent abdominal pain 3 days/month, last 3 months.
- Obstipation, diarrhea, mixed, unclassified.
- 11% of people and 23% of patients referred to gastroenterology.
- FODMAP, 5-HT4 receptor agonist, opioid receptor modulators, anti-depressants etc.

Probiotics in IBS

Meta-analyses 21 RCT’s (n = 1639) 20 products
Probiotics associated with
- improvement in overall symptoms (RR 1.82)
- quality of life (Mean difference 0.29)
- not in individual IBS symptoms

Yan Zhang et al. 2016 BMC Gastroenterology
Functional constipation
14% of adults
3.2 million visits to medical centers in the US

Effect of the probiotic strain *Bifidobacterium animalis* subsp. *lactis*, BB-12®, on defecation frequency in healthy subjects with low defecation frequency and abdominal discomfort: a randomised, double-blind, placebo-controlled, parallel-group trial

RCT, 3-arms, (n=1248)
No effect on GI well being

Eskesen *et al.* 2015
British Journal of Nutrition
Safety

- Systematic review, 662 studies included, 24615 participants exposed to probiotics
- No increased risk of the overall number of experienced adverse events (RR 1.00)

Hempel et al. 2011 Evid Rep Technol Assess

Practice Recommendations

- Recommend a probiotic when prescribing antibiotics
- Probiotics for colic and recurrent abdominal pain in pediatrics
- Become familiar with 1-2 evidence based probiotics for your indications
- Expect small changes
May the good bugs be with you

Questions
Contact Information

Dan Merenstein
djm23@georgetown.edu

Ruben Hummelen
rubenhummelen@gmail.com