Acute Diarrhea

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Disclosures

• I have no financial disclosures
• I have no conflict of interest to declare
Learning objectives

1. Review epidemiology of acute diarrhea

2. Evaluation and management of acute diarrhea and dysentery

Definitions

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Diarrhea</td>
<td>Unformed stool + Increased frequency</td>
</tr>
<tr>
<td>Hyperdefecation</td>
<td>Formed stool + Increased frequency</td>
</tr>
<tr>
<td>Fecal urgency</td>
<td>Feeling of urgent need to have bowel movement with formed or unformed stools</td>
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<tr>
<td>Fecal incontinence</td>
<td>Accidental leakage of stool or gas either without warning or preceded by fecal urgency</td>
</tr>
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**Definitions**

<table>
<thead>
<tr>
<th>Definition</th>
<th>Description</th>
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<tbody>
<tr>
<td>Overflow diarrhea</td>
<td>Liquid stool flowing around hard (often impacted) stool in sigmoid colon or rectum</td>
</tr>
<tr>
<td>Tenesmus</td>
<td>Frequent urge to defecate with no or small amount of stool or mucus</td>
</tr>
<tr>
<td>Acute diarrhea</td>
<td>Duration of diarrhea is less than 2 weeks</td>
</tr>
<tr>
<td>Persistent diarrhea</td>
<td>Duration of diarrhea &gt; 2 but &lt; 4 weeks</td>
</tr>
<tr>
<td>Chronic diarrhea</td>
<td>Duration of diarrhea &gt; 4 weeks</td>
</tr>
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**Bristol Stool Chart**

<table>
<thead>
<tr>
<th>Stool type</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 and 2</td>
<td>Definitely Constipation</td>
</tr>
<tr>
<td>6 and 7</td>
<td>Definitely diarrhea</td>
</tr>
</tbody>
</table>

Image courtesy: https://www.flickr.com/
### Burden of disease in the United States

| **•** Total number of foodborne illnesses | **48 million per year** |
| **•** Foodborne illness without cause | **39 million per year** |
| **•** 31 most common pathogens | **9.5 million per year** |
| **•** Travelers diarrhea cases | **4-17 million per year** |

Cost to US economy: **145 billion dollars per year**

Thus, acute diarrheal illness is a major public health problem.

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### Epidemiology of acute diarrhea

- 90% of the time due to an infection
- Viral infections are most common infectious pathogens in **developed countries**
- Bacteria are the most common pathogens in **developing countries**
- *Enterotoxigenic E.coli* is most common cause of traveler’s diarrhea worldwide
Viral diarrhea

- Most common cause of acute diarrhea worldwide in winter

  - **Rotavirus**: most common cause of diarrhea related hospitalizations worldwide

  - **Norovirus**: Most common cause of outbreaks of gastroenteritis among all age groups

Physiology of water reabsorption by the gut

- Water transport across intestinal epithelial barrier is passive

- Approximately 10 liters of water enters into the small intestine each day

- Small intestine absorbs about 8.5 liters

- Colon absorbs nearly 1.4 out of the remaining 1.5 liters

Thus, **our intestines are highly efficient at absorbing water**—reabsorbing nearly 99% of water from lumen
Osmotic diarrhea

- Unabsorbed osmotically active solutes in the intestinal lumen (e.g. lactose, lactulose) retain water until intra-luminal osmolality is equal to serum osmolality (290 mOsm/kg)
- The excess water makes stools watery
- Stops when intake of solutes stops, i.e. with fasting

Secretory diarrhea

- Excessive secretion of anions (chloride or bicarbonate) or cations (potassium) or
- Inadequate reabsorption of sodium
- Does not stop with fasting

Examples
- Enterotoxins (cholera) or neuroendocrine tumors (e.g. VIPoma) - stimulate secretion
- Congenital chloridoerrhea - loss of chloride transporter
Traveler’s diarrhea

• Diarrhea caused by infectious pathogens when a person travels to places with poor hygiene

Causative pathogens
• Bacteria- 80-90% of cases
• Intestinal viruses- 5-15% of cases
• Protozoal pathogens- 10%

Source: The CDC Yellow book

Clinical presentations

• Cramps (mild to severe), loose stools, urgency, fever, vomiting, dysentery

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Incubation period</th>
<th>Duration of symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteria and viruses</td>
<td>Incubation period of up to 72 hrs. Symptom onset within hours</td>
<td>Bacterial 3-7 days Viral 2-3 days</td>
</tr>
<tr>
<td>Protozoa</td>
<td>Incubation period of up to 2 weeks Exception: Cyclospora which can present quickly</td>
<td>Can last weeks to months without treatment</td>
</tr>
</tbody>
</table>

Source: The CDC Yellow book
### Epidemiologic associations in Traveler’s diarrhea

<table>
<thead>
<tr>
<th>Situation</th>
<th>Likely pathogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recent trip to St. Petersburg, Russia</td>
<td>Giardia</td>
</tr>
<tr>
<td>Recent trip to Nepal (e.g. climb Mt. Everest)</td>
<td>Cyclospora</td>
</tr>
<tr>
<td>Camping, backpacking, swimming in the wilderness</td>
<td>Giardia</td>
</tr>
<tr>
<td>Outbreak aboard cruise ships</td>
<td>Norovirus</td>
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### Epidemiologic associations in acute diarrhea

<table>
<thead>
<tr>
<th>Situation</th>
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<tbody>
<tr>
<td>Diarrhea after picnic, banquet, or outbreak in a restaurant</td>
<td><em>Salmonella, Shigella, Campylobacter</em> (usually spoilt chicken)</td>
</tr>
<tr>
<td>Undercooked hamburger</td>
<td><em>Enterotoxigenic E.coli</em> (O157:H7)</td>
</tr>
<tr>
<td>Reheated fried rice</td>
<td><em>Bacillus cereus</em></td>
</tr>
<tr>
<td>Spoilt mayonnaise or cheese</td>
<td><em>Salmonella and Staphylococcus</em></td>
</tr>
<tr>
<td>Raw or undercooked eggs</td>
<td><em>Salmonella and Shigella</em></td>
</tr>
<tr>
<td>Raw or undercooked sushi</td>
<td><em>Salmonella, Vibrio species, acute hepatitis A</em></td>
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### Epidemiologic associations in acute diarrhea

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<tr>
<td>Diarrhea in someone who keeps reptiles as pets (lizards, turtles, snakes)</td>
<td>Salmonella</td>
</tr>
<tr>
<td>Raw or undercooked pork products</td>
<td>Yersinia enterocolitica (pain can mimic acute appendicitis)</td>
</tr>
<tr>
<td>Raw or undercooked shellfish</td>
<td>Vibrio cholerae (rice water stools)</td>
</tr>
<tr>
<td>Recent travel to endemic country</td>
<td></td>
</tr>
<tr>
<td>Drinking brackish water</td>
<td></td>
</tr>
<tr>
<td>Recent antimicrobial use</td>
<td>Clostridium difficile</td>
</tr>
<tr>
<td>Recent hospitalization, IBD</td>
<td></td>
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### Epidemiologic associations in acute diarrhea

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<tr>
<td>Diarrhea in someone whose pet puppy or kitten also has diarrhea</td>
<td>Campylobacter, Yersinia</td>
</tr>
<tr>
<td>Diarrhea with tenesmus in AIDS patients, endoscopy shows inflamed rectum (proctitis)</td>
<td>Gonorrhea, syphilis, chlamydia</td>
</tr>
<tr>
<td>Severe sometimes fatal diarrhea in hemochromatosis</td>
<td>Yersinia and Vibrio (raw fish, e.g. sushi)</td>
</tr>
<tr>
<td>Outbreak in daycare attendees and families</td>
<td>Giardia, Shigella, Cryptosporidium, norovirus and rotavirus</td>
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</tbody>
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### Epidemiologic associations in acute diarrhea

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| Residents of long term care facilities, nursing homes and hospitalized patients | *Clostridium difficile*  
Overflow diarrhea  
Colonic ischemia  
Tube feeding |
| Medications                                                              | NSAIDs  
Antihypertensives  
Antibiotics |
| History of allogenic stem cell transplant                                | Graft vs host disease (usually accompanied by jaundice, skin rash and upper GI symptoms) |

### Epidemiology of acute diarrhea in immunosuppressed persons

**Conditions**  
1. IgA deficiency  
2. Combined variable immune deficiency  
3. AIDS  
4. Geriatric  
5. Pharmacologic immune suppression  

**1. Common enteric pathogens**  
1. *Mycobacterium* species  
2. CMV  
3. HSV  
4. Adenovirus  
5. Protozoa (*Cryptosporidium, Isospora belli, microsporidium, Blastocystis hominis*)
**Campylobacter**

- Mostly causes watery diarrhea, sometimes dysentery
- **Guillain-Barre syndrome** develops in 1:000 people with *C. jejuni* colitis
- Poultry is important source

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**Classification of acute diarrhea by severity of symptoms**

<table>
<thead>
<tr>
<th>Impact of diarrhea on patient</th>
<th>Severity grade</th>
</tr>
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<tbody>
<tr>
<td>No change in daily activities</td>
<td>Mild</td>
</tr>
<tr>
<td>Able to function but forced to change activities due to illness</td>
<td>Moderate</td>
</tr>
<tr>
<td>Total disability due to diarrhea</td>
<td>Severe</td>
</tr>
</tbody>
</table>
**Algorithm for managing acute diarrhea**

Does patient have grossly bloody stools?

- Yes = dysentery
- No = watery diarrhea

**Disease severity**

- Mild illness
  - Hydration only, Loperamide as needed

- Moderate to severe illness
  - Assess travel history

**Management of moderate to severe diarrhea**

Moderate to severe diarrhea

- Travel to endemic area
- Not associated with travel

Empiric antibiotics
- **Levofloxacin** (500 mg X1d or QD X3 days)
- **Ciprofloxacin** (750 mg X1d or 500 mg QD X3 days)
- **Ofloxacin** (400 mg X1d or QD X 3 days)
- **Azithromycin** (1 gram X1d or 500 mg QD X3 days)
- **Rifaximin** (200 mg TID X 3 days)

**Fever?**

- Fever ≤ 100 F
  - Loperamide for up to 48 hrs.

- Fever ≥ 101 F
  - No
  - Microbial assessment then treat

- < 72 hrs.

- Yes

- > 72 hrs.
Algorithm for managing dysentery

Does patient have grossly bloody stools?

Yes = dysentery

Temperature and disease severity

≤ 100 F or afebrile

Microbial assessment then treat all except STEC

≥ 101 F and severe disease

Assess travel history

Management of severe acute dysentery

≥ 101 F and severe disease

Traveler’s diarrhea

Empiric antibiotic
- Azithromycin (1 gram X1 dose or 500 mg daily X3 days)

Not associated with travel

Microbial assessment then treat
What type of diagnostic test to use?

- Culture independent diagnostic tests (molecular enteric pathogen panels) are recommended over stool culture due to better sensitivity
- If there is suspicion of an outbreak then stool culture is recommended
- Antibiotic sensitivity testing is NOT recommended for routine management of acute diarrheal infection

Are there any stool biomarkers for acute diarrhea?

DO NOT USE
- Stool WBCs
- Stool lactoferrin
- Fecal calprotectin
Oral hydration

Does
• Reduce mortality in severe diarrhea especially in infants and elderly

Does NOT
• Reduce severity of diarrhea
• Shorten duration of illness

Oral hydration in acute diarrhea
• Water
• Fruit juices
• Sports drinks
• Soups
• Saltine crackers
• Adequate in nearly 80% of acute diarrheal patients
Loperamide

- Decreases mucosal secretion and intestinal motility
- Advisable in mild-moderate traveler’s diarrhea
- **Dose**: Start with 4 mg then give 2 mg for each watery stool. Do not exceed 8 mg per 24 hrs.
- In combination with antibiotics quickly reduces stool frequency in traveler’s diarrhea

Bismuth subsalicylate

- FDA approved antidiarrheal for symptomatic treatment and chemoprophylaxis of acute diarrhea
- Bismuth moiety provides chemoprophylaxis, salicylate moiety provides antidiarrheal effect
- **Dose**: 30 ml (525 mg) of liquid or 2 tablets (263 mg each) upto four times daily
Bismuth subsalicylate

- **Duration**: No more than 3 weeks
- Warn patients tongue and stool will turn black. This is a harmless side effect

Who should NOT take Bismuth subsalicylate

- Aspirin allergy
- Renal insufficiency
- Gout
- On the following medications: anticoagulants, probenecid, methotrexate
- Active inflammatory bowel disease or HIV- risk of **bismuth encephalopathy** due to excess absorption of bismuth

Crofelemer

- Blocks cystic fibrosis transmembrane regulator chloride channel
- Indication: Non-infectious diarrhea in adult HIV/AIDS patients on anti-retroviral therapy
- Dose: one 125 mg delayed-release tablet twice daily with or without food
- Can cause increase in serum bilirubin

When to use (and not use) antibiotics?

**Use**
- Moderate to severe TD

**Do not use**
- Mild TD
- Community acquired diarrhea as most are due to viruses
Duration of antibiotics in TD

- Usually single dose in effective
- Three days of therapy is recommended if
  - diarrhea does not resolve after a single dose
  - dysentery
  - fever
- Five days therapy is recommended for *Shigella dysenteriae* infection

How do antibiotics help in traveler’s diarrhea?

- Reduce duration of loose stools by 1-3 days
- Combination with Loperamide shortens duration of illness further
**Chemoprophylaxis against TD**

- Non-antibiotic prophylaxis recommended when traveling to high-risk areas
- **Bismuth subsalicylate** is the recommended drug
  - Dose: 2 tablets 4 times daily with meals and at bedtime for upto 3 weeks
  - Can decrease incidence of TD by about 50%
- **Probiotics, prebiotics and synbiotics** - not recommended
- **Indications for antibiotic prophylaxis**
  - a) immunosuppressed
  - b) multiple co-morbidities
  - c) critical trips (e.g. sports events)

**Should I order an endoscopy?**

- Endoscopy is not recommended in **acute diarrhea**
- In **persistent diarrhea** (14-30 days) endoscopy is not recommended if stool tests are negative
- Endoscopy is recommended for **chronic diarrhea**
Summary

• Diarrhea lasting less than 14 days is called acute diarrhea
• Most cases are due to infection
• Severity is determined by impact of diarrhea on patient’s life
• Mild cases- hydration with or without loperamide
• Moderate to severe cases- depends on travel history and co-morbidities
• Dysentery and fever- consider stool testing 1st before antibiotics

Approach to the Patient with Chronic Diarrhea

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Division of Gastroenterology, Hepatology and Nutrition
Women’s Health in IBD Director, OSU Inflammatory Bowel Disease Center
Capsule Endoscopy Director
The Ohio State University Wexner Medical Center
**Definition:**

- Abnormal passage of more than 3 loose stool/day for more than 4 weeks
- Bristol type 5 - 7
- Increased frequency compared to baseline
- Stool weight > 200g/day in US

**Prevalence:**

- 3-5% of the population
- Chronic diarrhea can decrease quality of life
- Direct and indirect costs in USA- $136 million- $524 million per year
## Causes

### Common
- IBS-diarrhea
- Bile acid diarrhea
- Diet
- Colonic neoplasia
- Inflammatory Bowel disease
- Microscopic colitis
- Celiac disease
- Medications
- Overflow diarrhea
- Small bowel bacterial overgrowth
- Mesenteric ischemia
- Lymphoma
- Surgical causes
- Chronic pancreatitis
- Radiation enteritis
- Pancreatic carcinoma
- Hyperthyroidism
- Diabetes
- Giardiasis
- Cystic fibrosis

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## Causes - rare

- Whipple’s disease, tropical sprue, amyloid, intestinal lymphangiectasia
- Hypoparathyroidism
- Addison’s
- Hormone secreting tumors- VIP-oma, gastrinoma, carcinoid
- Autonomic neuropathy
- Factitious diarrhea
- Brainerd diarrhea- possible infectious cause not identified

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Published online 2018 Apr 13. Guidelines for the investigation of chronic diarrhoea in adults: British Society of Gastroenterology, 3rd edition
Clinical assessment - detailed history

• Assess for alarm features
  - unexplained recent change in bowel habits,
  - persistent blood in stool,
  - unintentional weight loss,
  - continuous diarrhea,
  - diarrhea at night

• Rome IV criteria for IBS-D
• Characterize diarrhea- watery diarrhea, bloody, steatorrhea

ROME IV criteria-IBS

Recurrent abdominal pain, on average, at least one day per week in the last three months, associated with two or more of the following criteria:

• Related to defecation
• Associated with a change in stool frequency
• Associated with a change in stool form (appearance)
Clinical assessment - Family history

• Inflammatory Bowel disease
• Celiac disease
• Neoplastic disease

Clinical assessment:

• Previous surgery:
  - Cholecystectomy
  - Small bowel resections- short gut, terminal ileum resection
  - Colon resection
  - Upper GI surgery- Roux-en-Y, Billroth II, vagotomy

• Medical history - Chronic pancreatitis, hyperthyroidism, hypoparathyroid disease, DM, adrenal insufficiency, systemic sclerosis, risk factors for STD, bone marrow transplant

• Previous overseas travels
• Previous use of antibiotics
Clinical assessment - diet/medications

- Alcohol- direct toxic effect on intestinal epithelium, rapid gut transit, decreased activity of intestinal disaccaridases and decreased pancreatic function
- Caffeine intake
- Milk in patients with lactase deficiency
- Food additives- sorbitol
- FODMAP (fermentable oligo-, di-, mono-saccharides and polyols)
- Drugs- magnesium supplements, ACE inhibitors, NSAIDS, antibiotics, antineoplastic drugs

Types of diarrhea

<table>
<thead>
<tr>
<th>Secretory</th>
<th>Osmotic</th>
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</thead>
<tbody>
<tr>
<td>Large volume of watery stool</td>
<td>Less voluminous</td>
</tr>
<tr>
<td>Persists during fasting</td>
<td>Improves during fasting</td>
</tr>
<tr>
<td>Ex- certain enteric infections, carcinoid syndrome</td>
<td>Osmotic gap= 290-2x(stool Na+ stool K)</td>
</tr>
<tr>
<td></td>
<td>Osmotic gap &gt;75</td>
</tr>
</tbody>
</table>
Investigations:

- CBC
- BMP, magnesium
- Liver function tests
- Vitamin B12
- Folate
- Ferritin
- ESR-CRP
- TSH
- TTG Ig A and Ig G
- HIV
- Vitamin D
- Stool tests- fecal calprotectin, c.difficile, ova and parasites, FIT test

Referral to gastroenterologist:

- Alarm features
- Severe diarrhea
- Suspected inflammatory bowel disease
- Inconclusive initial evaluation
- Failure to respond to therapy
The role of endoscopy in evaluation of chronic diarrhea - ASGE

- Colonoscopy with biopsies in both right and left colon even if mucosa is normal. Terminal ileum intubation and biopsies of abnormal mucosa
- Flexible sigmoidoscopy may be used in certain cases, but it can miss right sided organic disease
- Upper endoscopy in patients with negative colonoscopy and patients with positive celiac serology
- Capsule endoscopy is not recommended for routine evaluation of chronic diarrhea
- Deep enteroscopy/ push enteroscopy are not indicated for routine evaluation of chronic diarrhea
- If GVHD is suspected- flexible sigmoidoscopy +/- EGD

Ulcerative colitis

Crohn’s disease

Adenocarcinoma
Capsule endoscopy:

- Celiac disease
- Ulceration

Imaging:

- Small bowel follow through, barium enteroclysis are not recommended
- MR enterography is preferred to CT enterography for evaluation of the small bowel
- Imaging of the pancreas with dedicated pancreatic protocol CT
Bile acid diarrhea

• 1/3 of patients labelled with diarrhea predominant IBS have bile acid diarrhea
• Post-cholecystectomy syndrome, patients with ileal disease, terminal ileum resection
• SeHCAT testing - nuclear medicine, not widely available
• Trial of bile acid sequestrants

Microscopic colitis

• Chronic, non bloody diarrhea with no endoscopic abnormalities
• Inquire about use of PPI, NSAIDS, sertraline
• Can be associated with bile acid diarrhea
• Two forms:
  - collagenous colitis
  - lymphocytic colitis
• Treatment - withdrawal of the offending drug if possible, budesonide, bile acid sequestrants, in steroid refractory cases - immunosuppressives
Microscopic colitis

Collagenous colitis  
Microscopic colitis

Collagenous colitis – Wikipedia  
Lymphocytic colitis - Wikipedia

Small bowel bacterial overgrowth

• Definition- GI symptoms (abdominal pain, bloating, gas, distension, flatulence, diarrhea) caused by excessive numbers of bacteria in the small bowel.

• Predisposing factors- diabetes mellitus, scleroderma, prior surgeries (especially the surgeries involving a blind loop), diverticulosis, strictures of the small bowel, achlorhydria

• Diagnosis- hydrogen breath test
Diarrhea related to pancreas

• First line imaging- dedicated CT of the pancreas, MRI of the pancreas
• Other imaging modalities- EUS, secretin enhanced MRCP
• Stool for fecal elastase

• Diarrhea improves with pancreatic enzymes supplementation

Fecal incontinence

• Risks factors- age, obstetric trauma, pelvic surgery, obesity, diabetes, stroke
• Attention to overflow diarrhea
• Physical exam is important- evaluate sphincter tone, fecal impaction, rectal prolapse
• Further evaluations- anal manometry, endoanal ultrasound
Post-surgical diarrhea

• Vagotomy
• Upper gi procedures creating a blind loop- Billroth II or Roux –en-Y anastomosis
• Jejuno ileal bypass, IPAA
• Small and large bowel resection

Neuroendocrine tumors

• Rare causes of diarrhea- studies to be ordered if other etiologies were excluded and the patient is not responding to treatment
• Gastrinoma – gastrin levels much higher than 150pg/ml- close to 1000 pg/ml
• VIP-oma – large volume secretory diarrhea (>1 liter per day), dehydration and hypokalemia
• Carcinoid syndrome- measure 24 hours urinary 5-hydroxyindoleacetic acid
Factitious diarrhea

• Laxative abuse
• Spurious adding of water or urine to stool specimens

• Measure osmololal gap, screen for laxative abuse, consider admitting the patient when there is high suspicion of factitious diarrhea

Conclusions:

• Test for celiac disease early in investigations
• Patients<40 years old with no alarm symptoms, low fecal calprotectin (<50micrograms/gram), typical functional bowel symptoms, normal labs and physical exam- positive diagnosis of IBS
• Suspicion of malignancy- colonoscopy
• Colonoscopy with terminal ileum intubation and biopsies in the right and left colon
• MRE rather than CTE for evaluation of small bowel
• Push enteroscopy, deep enteroscopy for targeted lesions