Acute Diarrhea

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- I have no financial disclosures
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Learning objectives

1. Review epidemiology of acute diarrhea

2. Evaluation and management of acute diarrhea and dysentery

Definitions

Diarrhea	Unformed stool + Increased frequency
Hyperdefecation	Formed stool + Increased frequency
Fecal urgency	Feeling of urgent need to have bowel movement with formed or unformed stools
Fecal incontinence	Accidental leakage of stool or gas either without warning or preceded by fecal urgency

Definitions

Overflow diarrhea	Liquid stool flowing around hard (often impacted) stool in sigmoid colon or rectum
Tenesmus	Frequent urge to defecate with no or small amount of stool or mucus
Acute diarrhea	Duration of diarrhea is less than 2 weeks
Persistent diarrhea	Duration of diarrhea > 2 but < 4 weeks
Chronic diarrhea	Duration of diarrhea > 4 weeks

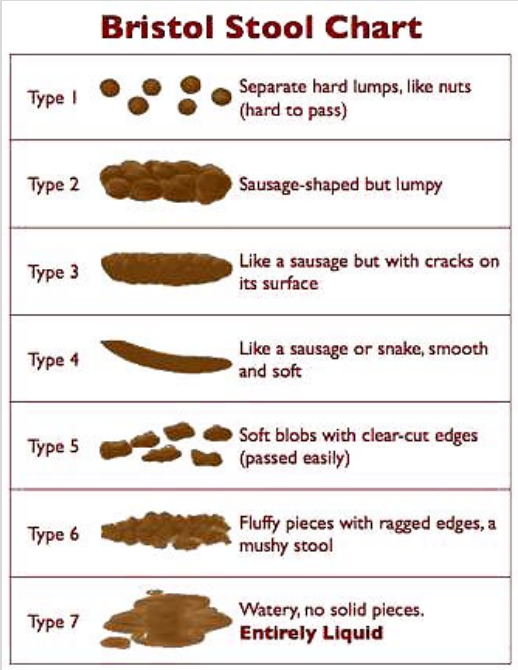


Image courtesy: https://www.flickr.com/

Stool type	Interpretation
1 and 2	Definitely Constipation
6 and 7	Definitely diarrhea

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	

ACG Clinical Guideline, 2016

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

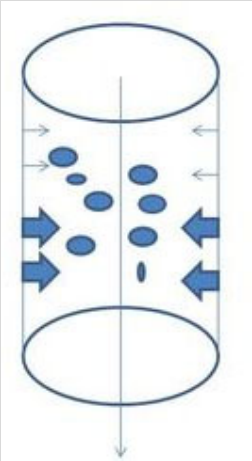
- Most common cause of acute diarrhea worldwide in **winter**
- **Rotavirus**: most common cause of diarrhea related hospitalizations worldwide
- **Norovirus**: Most common cause of outbreaks of gastroenteritis among all age groups

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

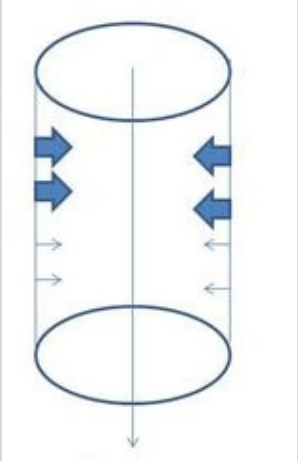
Thus, **our intestines are highly efficient at absorbing water**-reabsorbing nearly 99% of water from lumen

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

Pathogen	**Incubation period**	**Duration of symptoms**
Bacteria and viruses	Incubation period of up to 72 hrs. Symptom onset within hours	Bacterial 3-7 days Viral 2-3 days
Protozoa	Incubation period of up to 2 weeks Exception: *Cyclospora* which can present quickly	Can last weeks to months without treatment

Source: The CDC Yellow book

Epidemiologic associations in Traveler's diarrhea

Situation	Likely pathogen
Recent trip to St. Petersburg, Russia	*Giardia*
Recent trip to Nepal (e.g. climb Mt. Everest)	*Cyclospora*
Camping, backpacking, swimming in the wilderness	*Giardia*
Outbreak aboard cruise ships	Norovirus

Epidemiologic associations in acute diarrhea

Situation	Likely source
Diarrhea after picnic, banquet, or outbreak in a restaurant	*Salmonella*, *Shigella*, *Campylobacter* (usually spoilt chicken)
Undercooked hamburger	*Enterotoxigenic E.coli (O157:H7)*
Reheated fried rice	*Bacillus cereus*
Spoilt mayonnaise or cheese	*Salmonella* and *Staphylococcus*
Raw or undercooked eggs	*Salmonella* and *Shigella*
Raw or undercooked sushi	*Salmonella*, *Vibrio* species, acute hepatitis A

Epidemiologic associations in acute diarrhea

Situation	Likely source
Diarrhea in someone who keeps reptiles as pets (lizards, turtles, snakes)	*Salmonella*
Raw or undercooked pork products	*Yersinia enterocolitica* (pain can mimic acute appendicitis)
Raw or undercooked shellfish Recent travel to endemic country Drinking brackish water	*Vibrio cholerae* (rice water stools)
Recent antimicrobial use Recent hospitalization, IBD	*Clostridium difficile*

Epidemiologic associations in acute diarrhea

Situation	Likely source
Diarrhea in someone whose pet puppy or kitten also has diarrhea	*Campylobacter*, *Yersinia*
Diarrhea with tenesmus in AIDS patients, endoscopy shows inflamed rectum (proctitis)	Gonorrhea, syphilis, chlamydia
Severe sometimes fatal diarrhea in hemochromatosis	*Yersinia* and *Vibrio* (raw fish, e.g. sushi)
Outbreak in daycare attendees and families	*Giardia, Shigella, Cryptosporidium*, norovirus and rotavirus

Epidemiologic associations in acute diarrhea

Situation	Likely source
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**
2. **Opportunistic infections**
   1. *Mycobacterium* species
   2. CMV
   3. HSV
   4. Adenovirus
   5. Protozoa (*Cryptosporidium*, *Isospora belli*, microsporidium, *Blastocystis hominis*)

Campylobacter

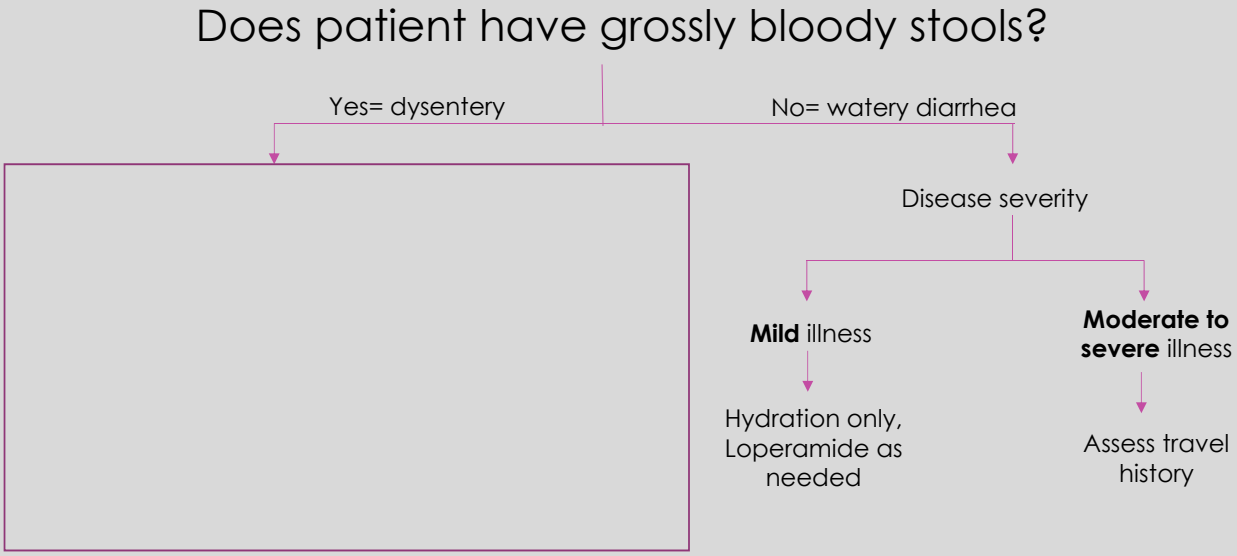
- Mostly causes watery diarrhea, sometimes dysentery
- **Guillain-Barre syndrome** develops in 1:000 people with *C.jejuni* colitis
- Poultry is important source

De Wood, Pooley, USDA, ARS, EMU., Public domain, via Wikimedia Commons

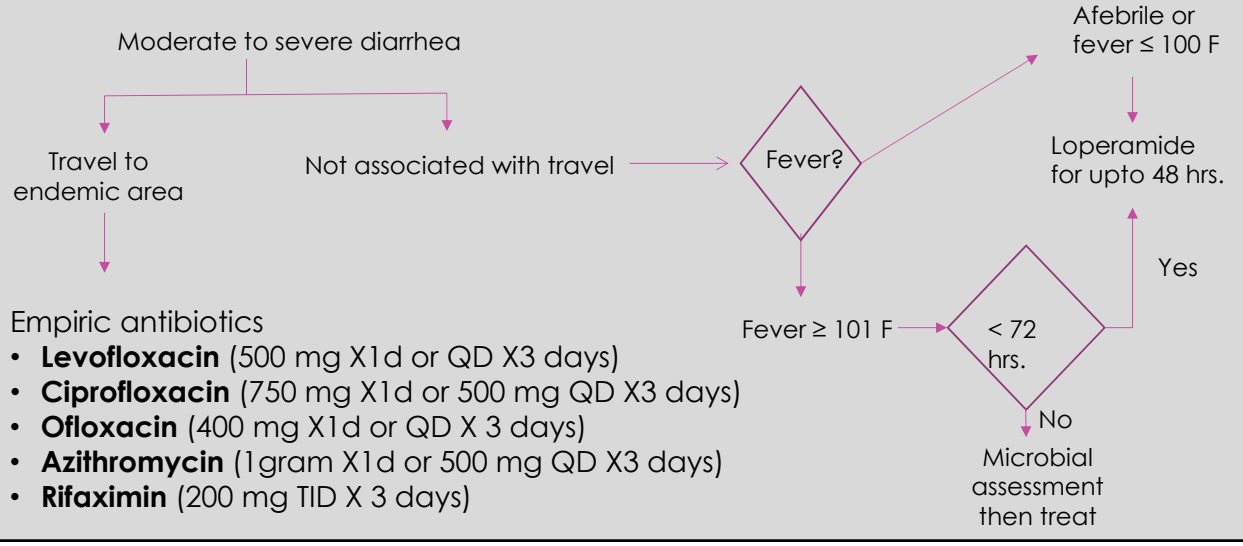
Classification of acute diarrhea by severity of symptoms

Impact of diarrhea on patient	Severity grade
No change in daily activities	**Mild**
Able to function but forced to change activities due to illness	**Moderate**
Total disability due to diarrhea	**Severe**

Algorithm for managing acute diarrhea



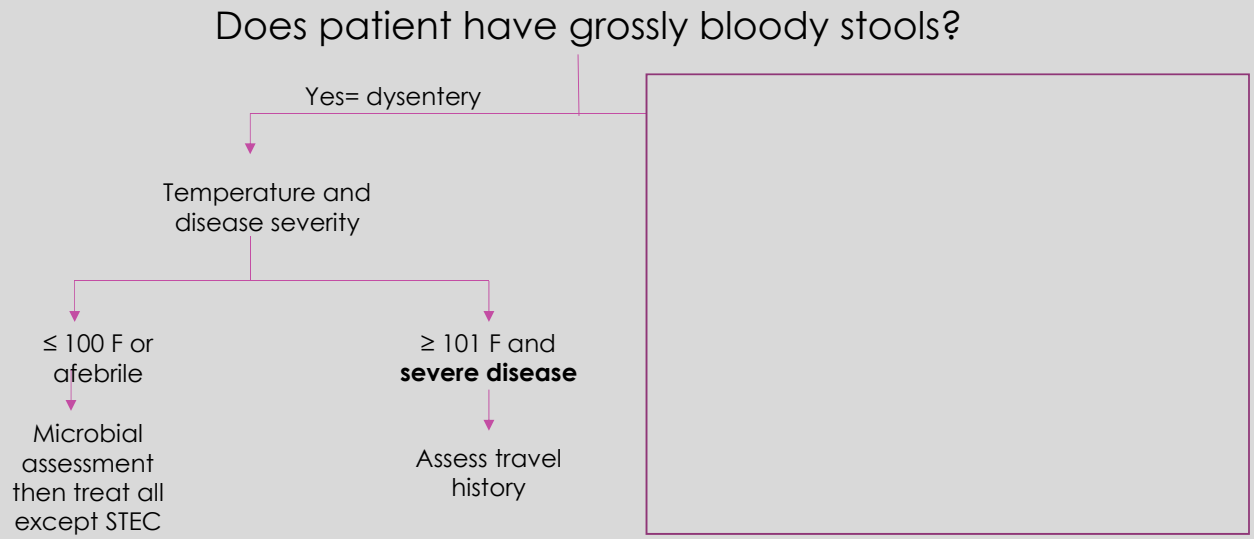
Management of moderate to severe diarrhea



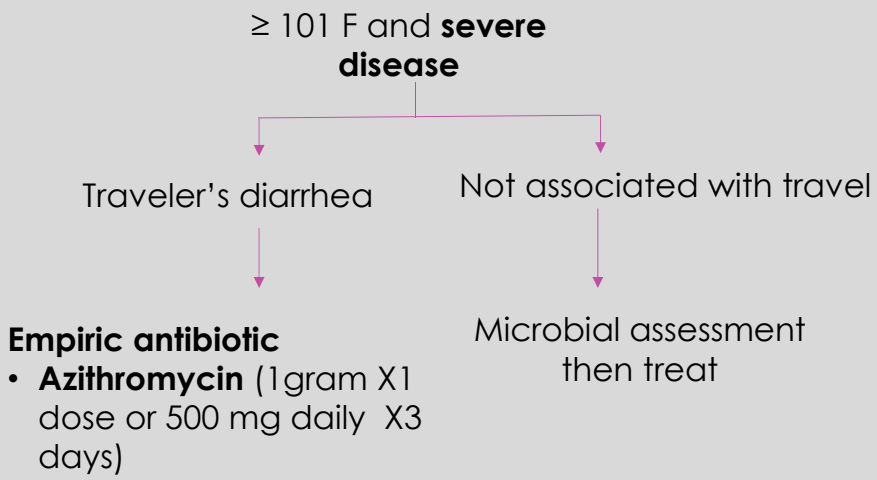
Empiric antibiotics

- **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** (1gram X1d or 500 mg QD X3 days)
- **Rifaximin** (200 mg TID X 3 days)

Algorithm for managing dysentery



Management of severe acute dysentery



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 travelers diarrhea

Bismuth subsalicylate

- FDA approved antidiarrheal for symptomatic treatment and chemoprophylaxis of acute diarrhea
- Bismuth moiety provides chemoprophylaxis, salicyclate 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

https://wwwnc.cdc.gov/travel/yellowbook/2020/preparing-international-travelers/travelers-diarrhea

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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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

Gut. 2018 Aug; 67(8): 1380–1399. Published online 2018 Apr 13. Guidelines for the investigation of chronic diarrhoea in adults: British Society of Gastroenterology, 3rd edition

Causes - rare

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

Gut. 2018 Aug; 67(8): 1380–1399. 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, hypo parathyroid 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

Secretory

- **Large volume of watery stool**
- **Persists during fasting**
- **Ex- certain enteric infections, carcinoid syndrome**

Osmotic

- **Less voluminous**
- **Improves during fasting**
- **Osmotic gap= 290-2x(stool Na+ stool K)**
- **Osmotic gap >75**

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

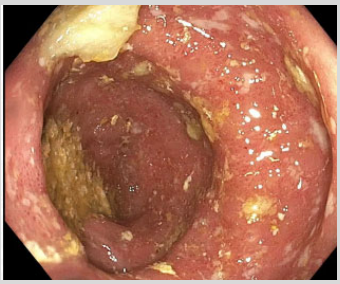
Referral to gastroenterologist:

- Alarm features
- Severe diarrhea
- Suspected inflammatory bowel disease
- Inconclusive initial evaluation
- Failure to respond to therapy

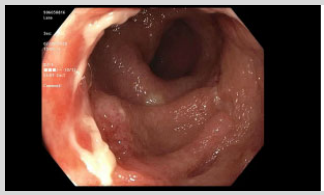
The role of endoscopy in evaluation of chronic diarrhea - ASGE

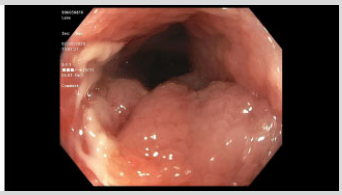
- Colonoscopy with biopsies in both right and left colon even if mucosa is normal. Terminal ileum intubation and biopsies of abnormal mucosa
- Flexible sigmoidoscopy may be used in certain cases, but it can miss right sided organic disease
- Upper endoscopy in patients with negative colonoscopy and patients 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

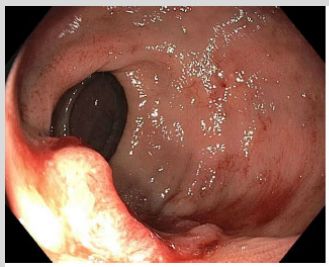
Ulcerative colitis

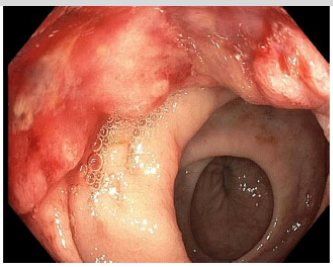


Crohn's disease



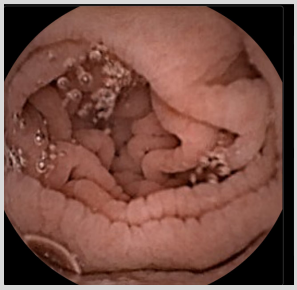






Adenocarcinoma

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

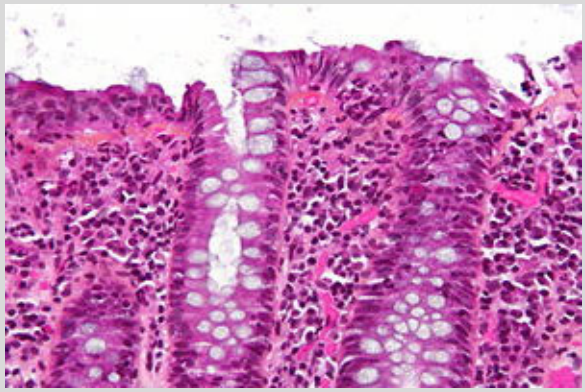
- 1/3 of patients labelled with diarrhea predominant IBS have bile acid diarrhea
- Post- cholecystectomy syndrome, patients with ileal disease, terminal ileum resection
- SeHCAT testing- nuclear medicine, not widely available
- Trial of bile acid sequestrants

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