Review of the Diseases of the Lower GI Tract

David Glenn Weismiller, MD, ScM, FAAFP

Department of Family and Community Medicine

Kirk Kerkorian School of Medicine

University of Nevada, Las Vegas

david.weismiller@unlv.edu

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Learning Objectives

1. Discuss the diagnosis and treatment of irritable bowel syndrome.
2. Recognize the common forms of malabsorption.
3. Review the diagnosis and treatment of cancer of the small intestine, large intestine, and anus.
4. Summarize other clinical entities of the lower GI tract, including constipation and infections.

1. A 20 yo college student comes to student health services to discuss her 3-year history of abdominal pain and constipation. It has gotten worse since she returned to school this fall. She describes crampy pain and bloating that eases after defecation. Her bowel movements are firm and difficult to pass, and occur about every 4 days on average. She denies vomiting, weight loss, blood in the stool, or melena. Her menses are regular and she is otherwise healthy. She reports using a soluble fiber (psyllium) once daily. Her family history is negative for any gastrointestinal or genitourinary diseases. Her abdominal examination is normal. You diagnose her with irritable bowel syndrome. *Which ONE of the following would be most appropriate at this time?*

A. A therapeutic trial of insoluble fiber intake
B. A therapeutic trial of lubiprostone (Amitiza)
C. Abdominal CT
D. Colonoscopy

Irritable Bowel Syndrome

- **Defined**

  GI syndrome characterized by altered bowel habits and abdominal pain, in the absence of detectable structural abnormalities

  Prevalence

  - 10%-15% in North America

  4 Subtypes

  - IBS-C: constipation-predominant
  - IBS-D: diarrhea-predominant
  - IBS-M: mixed symptoms
  - IBS-U: unsubtyped

Based on patient's report of the frequency of types based on the standard Bristol Stool Scale

Irritable Bowel Syndrome

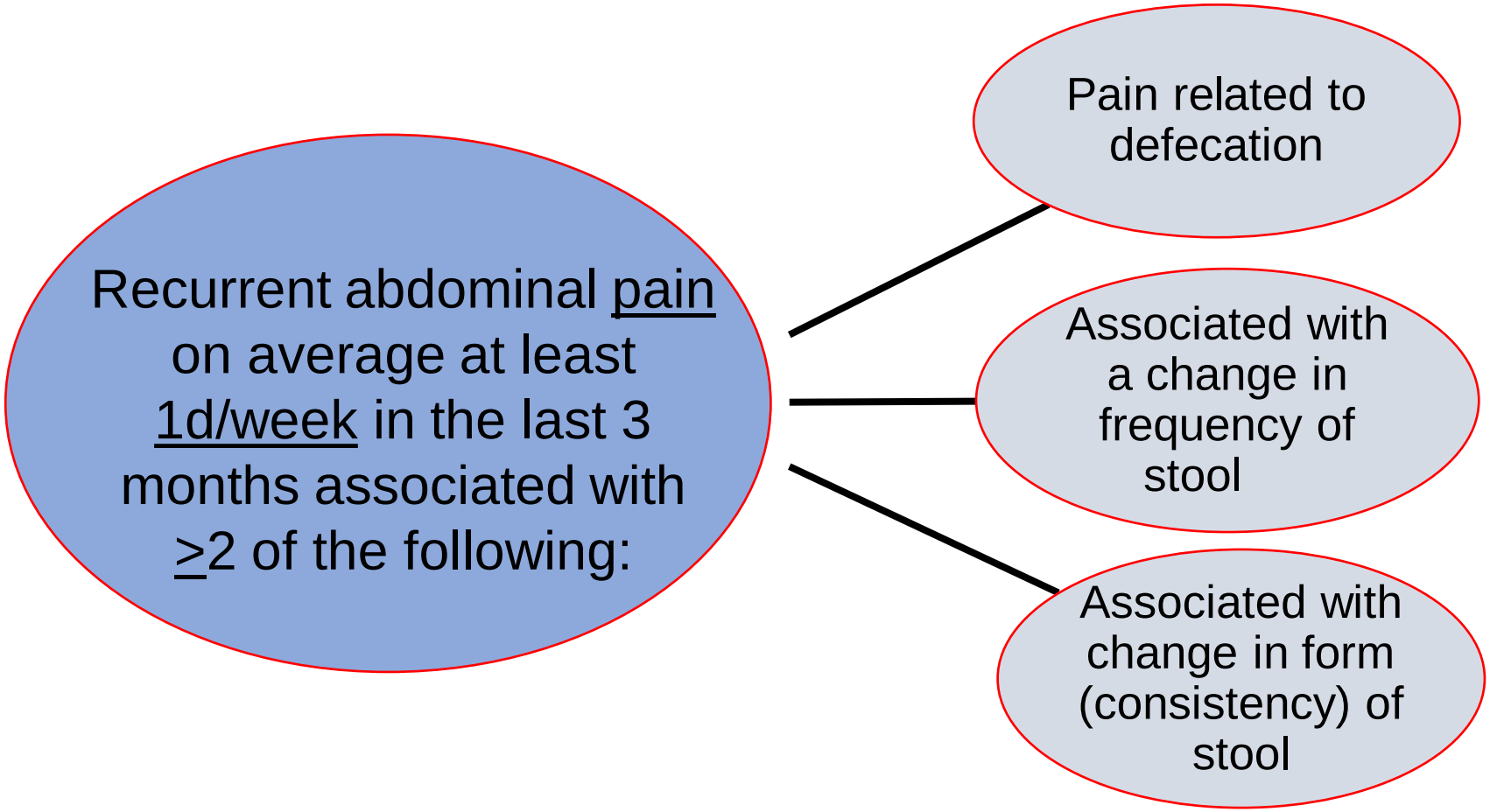
Pathophysiology

- Remains uncertain
- Heredity and environmental factors play a potential role.
- Abnormal myoelectric activity

  Basal rhythm 3 cycles/min in IBS (6 cycles/min is normal)
- Visceral afferent hypersensitivity
- Microscopic mucosal inflammation
- Psychosocial dysfunction

Irritable Bowel Syndrome

Diagnosis – Rome IV Diagnostic Criteria



Gastroenterology, May 2016

Initial Diagnostic Evaluation

Patient History

- Symptom severity/duration
- Family History
- Psychosocial factors

No alarm symptoms or “red flags”

Meets Rome IV Diagnostic Criteria

Further work-up only if clinical evidence suggests organic disease

- Laboratory Tests (CBC, FOBT, ESR, Serum Chemistry, TFTs, stool studies)
- Colonoscopy or sigmoidoscopy

Differential Diagnosis of IBS Symptoms

- Carcinoid Tumor
- Celiac Disease
- Colorectal Cancer
- Diverticular Disease
- Drug Use (Opiate analgesics, calcium channel blockers, antidepressants)
- Gastrointestinal Infection (e.g., *Giardia, Amoeba*, HIV, bacterial overgrowth)
- Hyperthyroidism
- Hypothyroidism
- Inflammatory Bowel Disease
- Ischemic Colitis
- Lactose Intolerance

Am Fam Physician. 2012;86(5):419-426.

In our case…

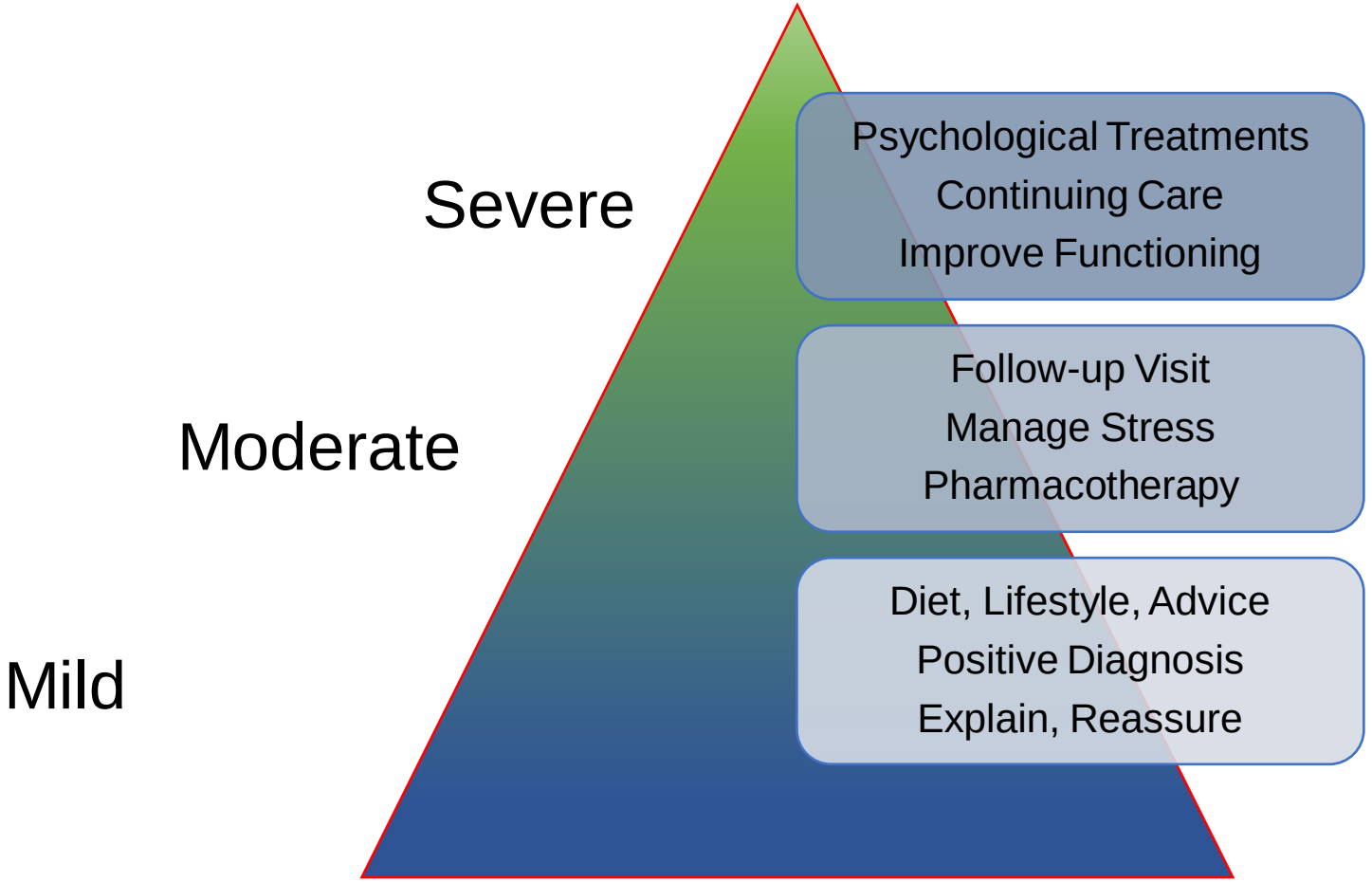
- Patient's symptoms are consistent with irritable bowel syndrome (IBS).
- History, physical examination, and laboratory evaluation did not show any evidence of peptic ulcer disease, celiac disease, thyroid disease, or inflammatory bowel disease.

- No Red Flags
  - Unintentional and unexplained weight loss
  - Rectal bleeding
  - Family history of bowel or ovarian cancer
  - Change in bowel habits persisting MORE than 6 weeks in a person > 60

The patient does not have any of these findings and therefore does not require any additional testing to confirm the diagnosis of IBS.

Model to Individualize Treatment for IBS

Treatment Goals: Symptom Relief and Improved QOL



Diarrhea

- Loperamide
- Alosetron* (5HT3 antagonist)
- Antibiotics
- Bile acid sequestrants

Bloating/Distention

- Probiotics
- Antibiotics
  - Rifaximin (IBS-D or IBS-M)
  - Neomycin (IBS-C)
- Linaclotide
- Lubiprostone

Abdominal Pain/Discomfort

- Antispasmodics
- Antidepressants (TCA/SSRI)
- Linaclotide
- Kubiprostone
- Alosetron
- Antibiotics

Constipation

- Psyllium (soluble fiber)
- Osmotic laxatives
- Linaclotide
- Lubiprostone

Peppermint oil (enteric coated) is superior to placebo in improving global symptoms (SOR B)

*Restricted-use program
SSRI, selective serotonin reuptake inhibitor
Am J Gastroenterol. 2009;104(Suppl):S1.

Symptom-Based Treatment Choices

Fiber

- Water soluble (e.g., oats, apples and pears – skin on, beans, legumes etc.)
  - Gel forming (viscous)
  - Low fermentability
  - A “bulk laxative” –
    - laxative effects but secondary to **increasing fecal size bulk** occurs due to water and gas absorption in small intestine and colon
    - Thus, chyme (made from digested food) has more size and softness
    - Bulk is retained in colon despite microflora as psyllium is poorly fermented (highly fermented fibers may be metabolized by bacteria in the colon, and water retaining properties with the fiber would be lost in this scenario).
- Water insoluble (e.g., whole wheat, whole bran, brown rice, celery, carrots etc.)
  - Prevents constipation - As an indigestible material, it sits in the gastrointestinal tract, absorbing fluid and sticking to other byproducts of digestion that are ready to be formed into the stool.
  - Its presence speeds up the movement and processing of waste, helping prevent gastrointestinal blockage and constipation.

FODMAPs

Fermentable [oligosaccharides, disaccharides, monosaccharides, and polyols] carbohydrates

- Short chain carbohydrates - poorly absorbed in the small intestine - prone to absorb water and ferment in the colon
  - Most FODMAPs are **naturally present in food and the human diet**, but the polyols may be added artificially in commercially-prepared foods and beverages
- **May cause digestive discomfort** in some people -
  - The reasons are hypersensitivity to luminal distension, and/or proclivity to excess water retention and gas production/accumulation
- Restricting FODMAPs (LFD) **might help** to improve digestive symptoms in adults with **IBS** and **other functional GI disorders**
  - A LFD improves symptoms and disease-specific QOL in patients with IBS, particularly IBS-D
- FODMAPs that are present in gluten-containing grains have been identified as a possible cause of gastrointestinal symptoms in people with **non-celiac gluten sensitivity**
- **They do not cause intestinal inflammation**. In fact, naturally occurring FODMAPs may help avert digestive discomfort for some people because they produce beneficial alterations in the gut flora

Irritable Bowel Syndrome

Treatment

- Self-help, patient education, cognitive behavioral treatment
- Soluble (but not insoluble) fiber for the treatment and improvement of **global IBS symptoms**
  - RCTs have found that patients with **IBS-C** benefit from a higher intake of soluble fiber.
- **Lubiprostone (Amitiza) and Linaclotide (Linzess) are effective for constipation-predominant IBS. (SOR B)**
  - Works by increasing the amount of fluid in intestine, making it easier for stool to pass
- Antispasmodics
  - Dicyclomine, tincture of belladonna, hyoscyamine
- Antidepressants (citalopram, fluoxetine, paroxetine; tricyclic antidepressants have been studied) (SOR B)
  - Low dose: Analgesia, mood, colonic transit slowing
- Antidiarrheal agents
  - Diphenoxylate, loperamide; no help with pain

Irritable Bowel Syndrome

Treatment

- Psychological treatment (NNT=4)*
  Hypnotherapy (SOR B)
  Cognitive-behavioral therapy (SOR B)
  Psychotherapy*

essentialevidenceplus.com

**Ford et al. Am J Gastroenterol. 2014;109(9):1350-1365*

AGA

- *For a patient with functional abdominal pain syndrome (as per ROME IV criteria), computed tomography (CT) scans should not be repeated unless there is a major change in clinical findings or symptoms.*

Constipation

- A symptom, not a disease

  Unsatisfactory defecation: Difficult, infrequent, incomplete

  95% of people have at least three BMs per week.

  - ❿2% of people report chronic constipation (M:F 1:3).

  Most common digestive complaint in general population
- Etiologies

Constipation

- **History**
  - Beware of constipation of recent origin.
  - Stool pattern changes or alarm signs/symptoms: Rule out CANCER.

- **Etiologies***
  - Diet
  - Drugs
  - Lack of adequate fluid intake
  - Lack of exercise
  - Irritable bowel syndrome
  - Depression
  - Hypothyroidism
  - Pelvic floor dysfunction
  - Spinal cord injury

* Best Practice 1993;3(1)

Constipation

- **Diagnostic studies**
  - Insufficient evidence to support routine use of blood tests, radiography, or endoscopy in workup without alarm signs/symptoms (CBC, FOBT, TSH)
  - Endoscopy: Flexible sigmoidoscopy or colonoscopy
  - Imaging: Barium enema, ultrasound, CT, colonic transit studies, rectal manometry
- **Physical findings**
  - Rectal exam: Fissures, hemorrhoids, sphincter abnormalities, anal/rectal prolapse, impaction
  - Abdominal exam: Check for abdominal mass.
  - Check for signs of hypothyroidism.

Constipation

Treatment

- Depends on etiology

  Empiric treatment without diagnostic testing can be considered when alarm features are absent.

  Acute

  ⓾ Enemas, suppositories, osmotic laxatives

  Patient education: Lifestyle, exercise, hydration, bowel training

  Diet: High fiber (psyllium, methylcellulose, bran, polycarbophil)

  Laxatives: Mineral oil, lactulose, polyethylene glycol

  Rule out fecal impaction.

  Treat depression, if present.

Hemorrhoids

- **Pathogenesis**

  Dilated sinusoids within anal canal and distal rectum

  External vs internal

  - Determined by origin: Above/below the dentate line

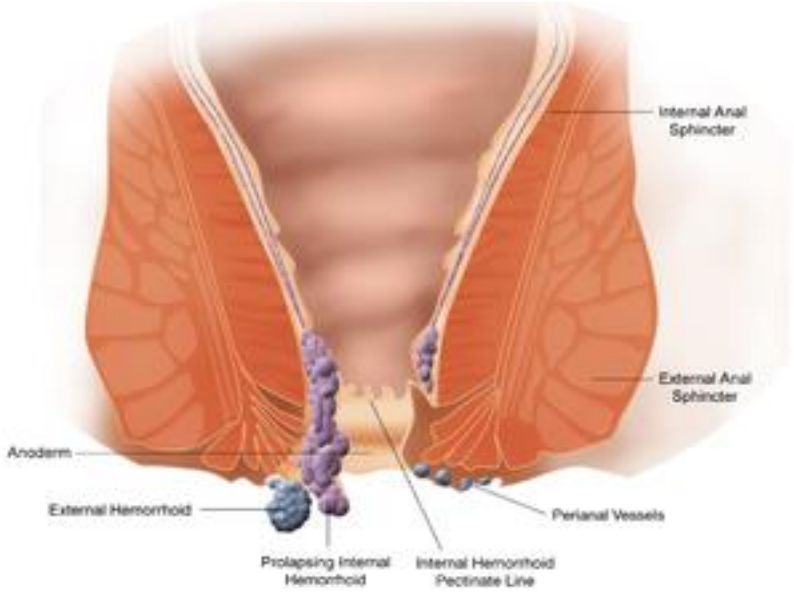
- **History**

  Usually bleeding is the symptom; can experience anal itching (external) or mild pain (internal); severe pain only with thrombosed hemorrhoids.

- **Physical exam**

  Visual exam and digital exam

  Anoscopy and sigmoidoscopy



Source: Mikael Häggström/ Wikipedia

Hemorrhoids

- Treatment
  - High-fiber diet
  - Stool softeners
  - Hot sitz baths
  - Topical agents
  - Ligation
  - Infrared ablation
  - Surgery

Other Common Anal Problems

- Pruritus ani
- Anal fissure

Other Common Anal Problems

- Pruritus ani

  Severe itching around anus

  - Worse with anxiety

  Many causes

  - Fissure, fistula, hemorrhoid, dermatitis
  - Diabetes, STDs, premalignant lesions
  - Parasites, functional

  Diagnosis: Rule out causes above.

  Treatment

  - Improve anal hygiene.
  - Treat constipation and diarrhea.
  - 0.25% hydrocortisone cream

Anal Fissure

- Tear in anal mucosa
- Severe pain with defecation
- Diagnosis
  - Anoscopy
- Treatment

Source: Wikipedia

Treatment

- Botulinum toxin injection
- Surgery
  - Disrupting to internal sphincter
    - 30% have problem controlling flatus.
    - 20% with minor fecal incontinence
- Warm sitz baths
- Anesthetic ointments
- Soften stool.
- Sclerotherapy
- Topical nitrates or CCBs

2. A 19 yo patient presents to your office for follow-up. She reports continued intermittent abdominal cramping and bloating, diarrhea, fatigue, and a 4.5-kg weight loss. She initially was diagnosed with irritable bowel syndrome, but you suspect celiac disease. Which one of the following should be used to establish the diagnosis?

A. Colonoscopy
B. Serologic testing
C. Serologic testing initially, followed by endoscopy if test results are positive
D. Serologic testing initially, followed by colonoscopy

Celiac Disease

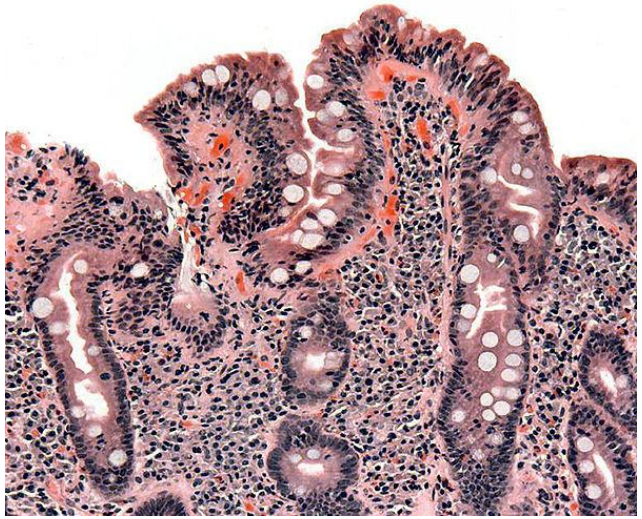
- Chronic intestinal (auto-immune) malabsorption disorder

  Intolerance to the gliadin fraction of gluten in wheat

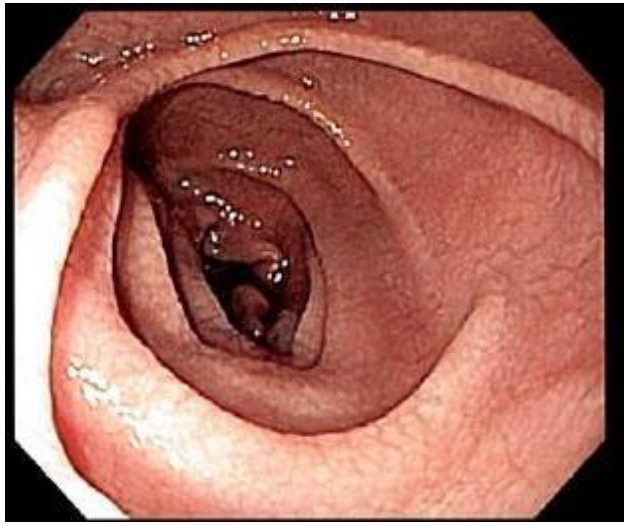
- Features

  scalloping of folds and **"cracked-mud"** appearance to mucosa (Endoscopic)

  Flat small intestine mucosa (with clinical and/or histologic improvement following withdrawal of dietary gluten) [Histologic]



Biopsy of small bowel showing celiac disease manifested by blunting of villi, crypt hypertrophy, and lymphocyte infiltration of crypts



Celiac Disease

❿ Symptoms and signs

- **No typical presentation**
- May be asymptomatic (adults)
- Abdominal distention
- Malabsorption
- Loss of appetite
- Failure to thrive (children)
- Symptoms of various deficiency states

❿ Laboratory

- Fe deficiency anemia in children
- Adults
  - ❿ Iron deficiency
  - ❿ Folate deficiency
  - ❿ Vitamin D deficiency

Celiac Disease

Diagnosis

- Several serologic tests are readily available for diagnosis.

  IgA anti-tissue transglutaminase antibody*§ (sensitivity 79%-90%, specificity 98%)

  Endomysial antibody* (sensitivity 81%, specificity 97%)

  Deaminated gliadin peptide antibody (IgG/IgA) (sensitivity 95%-98%)
- Test while consuming a diet of gluten-containing foods (2-6 weeks).
- **Gold standard**: Histologic assessment of distal duodenum(EGD) – villous flattening/atrophy (SOR: C)

* AGA recommends these tests as initial serologic testing in adults.

§**If you only choose one test, then IgA is first-line test for serologic diagnosis** (SOR: C)

Celiac Disease

Treatment

- Gluten avoidance (SOR: B)
- A gluten-free diet improves the quality of life in those with symptomatic celiac disease (SOR: B)

3. A 32 yo male presents to your office as a new patient and requests a refill of sulfasalazine (Azulfidine) tablets for maintaining remission of his ulcerative colitis. The initial presentation of his disease was at 17 and involved inflammation of the entire colon. He was then started on sulfasalazine, which has worked well for controlling his symptoms. He had one flare when he ran out of medicine two years ago. He cannot recall the last time he saw a gastroenterologist. ***Which one of the following is an appropriate management plan for this patient?***

A. Refill his sulfasalazine and continue usual care unless symptoms recur
B. Attempt to gradually discontinue the sulfasalazine
C. Stop sulfasalazine and start azathioprine
D. Continue sulfasalazine and arrange for colonoscopy to screen for colorectal cancer

Inflammatory Bowel Disease

- Onset
  Usually young adults
  Affects men and women equally
  More common among Caucasians in N. America and N. Europe

Inflammatory Bowel Disease

- **Spectrum**

  Crohn's, indeterminate, ulcerative colitis

  600,000 people in the US have some form of inflammatory bowel disease

- **Pathogenesis**

  Some genetic role

  No identified infectious agent

  Strong evidence for immune role as mediator of tissue injury - unknown trigger

  Serologic markers can be helpful in differentiating UC and Crohn's

⑩ **Laboratory**

  Fecal lactoferrin and calprotectin levels (surrogate markers for bowel inflammation) ***may*** help distinguish between inflammatory conditions and IBS

Ulcerative Colitis

- **Incidence:** 10/100,000, 25% family history
- **Pathology**

  CONFINED TO MUCOSA

  Starts in rectum, moves proximally **WITHOUT** skips
- **Clinical features**

  Mild to severe at start

  Abrupt onset

  Rectal bleeding, diarrhea, fever, cramping pain, weight loss

  Clinical symptoms are inadequate for assessing need for ongoing therapy
- **Serologic marker**

  Perinuclear antineutrophil cytoplasmic antibody is more suggestive of UC

Differential Diagnosis of Ulcerative Colitis and Recommended Testing

Disease	Findings that suggest diagnosis	Evaluation
Amebic dysentery	Travel to endemic areas or exposure to illness	Anti-amebiasis antibodies, microscopy (O&P)
Bacterial colitis	Should be routinely considered; exposure history may increase suspicion	Stool culture, including testing for *E. coli* 0157:H7
Clostridium difficile infection	Recent antibiotic use	Stool studies for *C. difficile* toxin
Crohn's disease	Increased suspicion with disease not limited to colon	Endoscopic biopsy
Ischemic colitis	Risk factors for vascular disease	Endoscopic biopsy
Microscopic colitis	Nonbloody stools	Endoscopic biopsy
Viral or parasite-induced colitis	Immunocompromised	Endoscopic biopsy

Medication	Dosage for active disease	Maintenance dosage	Adverse effects
Sulfasalazine *(first line therapy for UC)*	4-6 g/day divided QID	2-4 g/day	HA, interstitial nephritis, N/V; ***one of most effective agents for remission***
5-Aminosalicylic acid *Oral* *Suppository* *Enema*	 2-4.8 g/d, divided TID 1000 mg/d 1-4g/d	 1.2-2.4 g/d 500 mg 1-2x/d 2-4g daily to every third day	 Interstitial nephritis Anal irritation Difficulty retaining, rectal irritation
Hydrocortisone *Enema* *Foam*	 100 mg 90 mg 1-2X/d	 Not recommended Not recommended	 Rectal irritation Rectal irritation
Prednisone **Methylprednisolone**	40-60 mg/d until clinical improvement, then taper 5-10 mg/w 40-60 mg/d	Not recommended Not recommended	Adrenal suppression, impaired wound healing, PUD, etc.
Infliximab *Anti-tumor necrosis factor agents (biologics)*	5-10 mg/kg weeks 0, 2, and 6	5-10 mg/kg q 4-8 weeks	Increased risk infection, lymphoma
Azathioprine	Not recommended	1.5-2.5 mg/kg/d	Allergic reactions, BM suppression, infection
Cyclosporine	2-4 mg/kg/d	Not recommended	Infection, nephrotoxicity, seizures

Ulcerative Colitis – SORT:

Key Recommendations for Practice

Clinical recommendation	Evidence rating
5-aminosalicylic acid is highly effective for inducing remission and preventing relapse.	**A**
Oral corticosteroids are effective for inducing remission.	B
Infliximab is effective for inducing remission in corticosteroid-refractory UC.	**A**
Azathioprine is effective for preventing relapse.	B
Probiotics *Lactobacillus* GG and *E. coli* Nissle 1917 (Mutaflor) are as effective as 5-ASA in maintaining remission.	B

Am Fam Physician. 2013; 87(10):699-705.

Crohn's Disease

- **Pathology**
  - FULL WALL THICKNESS
  - Any part of GI tract may be affected.
  - Terminal ileum most common site
  - SKIPS
- **Clinical features**
  - Insidious onset
  - Commonly with mild diarrhea and pain
- **Diagnosis**
  - Laboratory

Diagnostic Studies

- Laboratory Testing
  - **Initial**
    - CBC, C-Reactive protein, ESR, BMP, LFTs
    - Stool cultures, testing for *Clostridium difficile* toxin; O&P
  - **Subsequent**
    - Iron studies, Albumin, Vitamin D, Calcium
    - Presence of antibodies to *E. coli* outer membrane porin and *Saccharomyces cerevisiae* is suggestive of Crohn's

Diagnostic Studies

- **Endoscopy and Related Investigations**
  - Colonoscopy and ileoscopy and biopsy
    - Skip lesions, cobblestoning, ulcerations, strictures
  - Capsule endoscopy
  - CT enterography
  - MR enterography
  - EGD
    - Upper GI symptoms
    - Asymptomatic patients with Iron deficiency anemia
    - Active Crohn's with a normal colonoscopy

Crohn's and Treatment

Disease Activity	Medications	Comments
Mild	Mesalamine Products • Sulfasalazine • 5-aminosalicylic acid Budesonide	Pancreatitis and pneumonitis can occur with these agents 5 ASA - **Ineffective** in maintaining remission Budesonide - useful for **treating** disease at the junction of the ileum and colon or ascending colon; **ineffective** for maintaining remission
Moderate	Corticosteroids Azathioprine 6-mercaptopurine Methotrexate Anti-TNF Agents • Infliximab • Adalimumab (Humira) • Certolizumab pegol (Cimzia)	Corticosteroids ineffective in maintaining remission **Azathioprine** is effective for maintenance of remission ***Increasing evidence supports that anti-TNF or Azathioprine may offer corticosteroid sparing benefits for corticosteroid-naïve patients***
Severe	Use of anti-TNF agents is controversial; failure to respond or worsening symptoms may require surgical intervention	

Crohn's - SORT:
Key Recommendations for Practice

Clinical Recommendation (*Am Fam Physician.* 2011; 84(12):1365-1375.)	**SOR**
Ultrasonography, CT, scintigraphy, and MRI are helpful for excluding extramural complications	C
Colonoscopy with ileoscopy and biopsy is a valuable initial test in diagnosis of ileocolonic Crohn's disease	C
EGD is recommended if patients have upper GI symptoms	C
No difference between elemental and nonelemental diets in inducing remission in patients with Crohn's disease	**A**
Budesonide is effective in inducing, but not maintaining, remission	B
Corticosteroids are more effective than placebo and 5-ASA products in inducing remission	**A**
Azathioprine and 6-MP are effective in inducing remission in patients with active disease	**A**
Methotrexate is effective in inducing and maintaining remission	B

Summary – Serologic Tests

IBS	Celiac Disease	IBD
None	• Serum IgA tissue transglutaminase (TTG) antibodies (first–line) • Endomysial antibody	• Fecal lactoferrin and fecal calprotectin are tests of gut inflammation and may be helpful in distinguishing **IBD** and IBS • Presence of antibodies to *E. coli* outer membrane porin and *Saccharomyces cerevisiae* is suggestive of **Crohn's** • Perinuclear antineutrophil cytoplasmic antibody is more suggestive of **UC**

Arch Intern Med. 2009 Apr 13;169(7):651-8.
Aliment Pharmacol Ther. 2010 Jun;31(12):1365-70.
Eur J Gastroenterol Hepatol. 2010 Mar;22(3):340-5.

IBD and Colorectal Cancer

- Patients with IBD have an increased risk of developing dysplasia and CRC
  - Risk appears to be declining possibly related to changes in surveillance or treatment
  - Predictors of risk: disease duration, extent, family history of CRC, and concomitant diagnosis of primary sclerosing cholangitis (PSC)
  - More recent data also show that the degree of inflammation is associated with the risk of colonic dysplasia

Recommendations on Surveillance for Colorectal Neoplasia in Patients With Inflammatory Bowel Diseases (AGA)

- All patients should undergo colonoscopy a **maximum of 8 years after onset of symptoms**, with biopsy to assess extent of inflammation (including Crohn's colitis >1/3 length of colon)
  - Patients with ulcerative proctitis or ulcerative proctosigmoiditis are NOT considered at increased risk
  - Patients with extensive or left-sided colitis should begin surveillance within 1 to 2 years after the initial screening endoscopy
  - **Optimal surveillance interval has NOT been clearly defined. After 2 negative examinations, further surveillance should be performed every 1–3 years.** *Should be performed when in remission, ideally*
  - Patients with PSC should begin surveillance colonoscopy **at the time of this diagnosis and then yearly**
- Considerations for **stopping** surveillance – Age (75), comorbidities, prior inflammatory burden, PSC, prior adenomatous polyps or dysplasia

AGA - 2018

GI Infections

Common GI Infections

- **Goals**

  Replace the fluid lost through diarrhea and vomiting

  Identify and eradicate the causative agent

- **Diagnosis**

  History: Work, travel, eating, others ill, recent antibiotics, immunocompromised, HIV

  Vomiting implies gastric involvement with preformed toxin

  Pain implies distention and inflammation

  Lab: Stool for fecal blood and leukocytes, cultures, O&P*

  Sigmoidoscopy

** Most acute diarrhea is viral and self-limited. Order O&P if history of travel or diarrhea is chronic.*

Rehydration

Recommendations

- **Oral rehydration therapy (ORT)**
  - Recommended by the AAP as "the preferred treatment of fluid and electrolyte losses caused by diarrhea in children with mild to moderate dehydration."
  - WHO reduced-osmolarity oral rehydration solution (ORS) now recommended for all rehydration in children, both cholera-endemic areas and non-cholera endemic.
  - Pedialyte, Rehydrolyte, Ceralyte, Infalyte
  - Sports drinks, diluted fruit juices, watery soups (adults)
- **Intravenous therapy**
  - Parenteral saline and electrolytes
  - Ringer's lactate
- **Dietary adjustments (following rehydration)**
  - Boiled vegetables, starches, soups, yogurt
  - Avoid high fat.
  - Simple sugars as opposed to complex carbohydrates

Gavin N, et al. *Pediatrics.* 1996;98(1):45-51.

4. Which of the following is the most common cause of <u>infectious</u> diarrhea in children both in developed and developing countries?

A. Campylobacter
B. Rotavirus
C. Shigella
D. Norovirus

Common GI Infections

- Rotavirus
- Norovirus
- Campylobacter
- Salmonellosis
- Shigella
- Amebiasis
- Giardiasis
- Cryptosporidium
- Pseudomembranous enterocolitis
- Traveler’s diarrhea
- Vibrio cholerae

(Viral) Gastroenteritis

Majority of Gastroenteritis Is Viral

- Rotavirus
- Norovirus
- Adenovirus
- Astrovirus

- **Rotavirus** is the most common cause in children and produces similar incidence rates in both the developed and developing world.
- **Norovirus** is the leading cause of gastroenteritis among adults in America, causing greater than 90% of outbreaks.

Rotavirus

- Most important viral cause of severe gastroenteritis in children worldwide

  Most common cause in US

  Large-volume diarrhea without blood or leukocytes in stool

  Daycare centers – fecal oral spread
- Dx: Immune-based assays of stool, PCR
- Complications: Necrotizing enteritis, biliary atresia, intussusception, chronic diarrhea

Rotavirus

- Treatment is generally supportive.
- Immunization (SOR A)

  CDC/AAP recommend universal immunization in US with oral PRV vaccine.

  - ❿2 months
    - ✓First dose minimum 6 weeks, maximum < 15 weeks
  - ❿4 months
  - ❿6 months
    - ✓Must complete by 8 months

Norovirus

- Norovirus is the leading cause of gastroenteritis among adults in America, causing greater than 90% of outbreaks.
  - Top pathogen contributing to domestically acquired foodborne illness
  - Second most common foodborne illness resulting in hospitalization
  - Fourth in terms of domestically acquired foodborne illness resulting in death
  - **Abrupt onset** (12-48 hours after exposure) and **prompt resolution** (1-3 days)

5. A 52 yo female with hypertension presents with a 2-day history of profuse bloody diarrhea, moderate to severe abdominal cramping, and fever. She has recently returned from a week-long trip to Singapore. Her stool culture is positive for Campylobacter. Which one of the following is the treatment of choice?

A. Azithromycin (Zithromax)
B. Ciprofloxacin (Cipro)
C. Metronidazole (Flagyl)
D. Rifaximin (Xifaxan)

Bacterial Gastroenteritis

- Adults
  - Salmonella
  - Campylobacter
  - Shigella
- Children
  - Salmonella
  - Campylobacter
  - Shigella

Campylobacter

- 10%-15% of US acute diarrhea
- Animal reservoir
  - Most human cases are contaminated poultry (~50%)
- Severe cramps, bloody diarrhea, anorexia, malaise; rarely, Guillain-Barre, reactive arthritis
- Diagnosis: Culture
- Treatment
  - Spontaneous clearing without antibiotics or
  - **Azithromycin**, erythromycin **if culture proven**
  - FQ > resistance

Shigella

- Bloody diarrhea
- Fecal oral spread
  - Highly contagious
- Principal effect on colon mucosa
  - Low-volume diarrhea
  - Blood
  - Mucus
  - Fever
  - Tenesmus
- Diagnosis
  - Culture

Shigella

- **Clinical**
  - Self-limiting
  - Rarely
    - Rectal prolapse, proctitis, toxic megacolon, perforation, obstruction, seizures in children, HUS
- **Treatment**
  - TMP-SMX (children)
  - **Quinolone**
  - Fluids
  - No vaccine

Salmonellosis

- 10%-15% of US acute diarrhea
  - Second leading cause of acquired foodborne illness in US
  - Top pathogen of domestically acquired foodborne illness resulting in hospitalization and death
- Nontyphoidal starts 6-48 hours after exposure, resolves spontaneously
  - Vomiting
  - Nausea
  - Pain
  - Diarrhea
- Sources
  - Eggs and poultry
  - Pet reptiles

Salmonellosis

- **Clinical**

  Self-limited

  Can cause bacteremia

  - Endocarditis
  - Osteomyelitis
  - Mycotic aneurysm

  Recommended management for patients who have **non-severe** Salmonella infection and are other wise healthy is **NO TREATMENT**

  High risk condition that predispose to bacteremia, and those with severe diarrhea, fever, systemic toxicity or positive blood cultures – treat with **Levofloxacin**, 500 mg q day for 7-10 days (or another **FQ** in an equivalent dosage).

Salmonellosis

- **Typhoid** via fecal-oral contamination, rare in US
  - Constipation and rash early, then diarrhea and pain
  - Diagnosis
    - Culture from blood or stool
  - Treat: **Fluoroquinolone**
  - Vaccine available

E. coli 0157:H7 (EHEC)

- Sporadic and large outbreaks
  - Produces Shiga toxin
  - Diagnose with culture
  - Clinical
    - Dysentery
    - Striking abdominal pain
    - Usually no fever

E. coli 0157:H7 (EHEC)

- Complication
  - **Hemolytic uremic syndrome**
    - ⓾ Check serum Cr
- Source
  - Contaminated meat
- Treatment
  - Supportive
  - Antibiotic NOT indicated

Amebiasis

- 5% reported US carriage rate
- *E. histolytica* mostly
  - Fecal-oral spread
  - Abdominal cramps
  - Chills, fever
  - Liquid BMs with bloody mucus
- Diagnosis
  - Sigmoidoscopy
  - O&P
  - Stool/serum antigen
  - Serology
- Treatment
  - Metronidazole etc.

Giardiasis

- **Common**
  - Mostly from contaminated water
- **Symptoms**
  - Abdominal cramps
  - Malabsorption
  - Nausea and vomiting
  - Watery diarrhea
- **Diagnosis**
  - O&P
  - *Giardia* antigen assay
- **Treatment**
  - Metronidazole

6. Of the following antibiotics, which is the agent recommended for treatment of pseudomembranous enterocolitis in an individual over the age of 60 with a temp of 38.7C and a wbc count of 19.8K?

A. Amoxicillin
B. Ciprofloxacin
C. Vancomycin
D. Metronidazole

Pseudomembranous Enterocolitis

- Common in “postantibiotic” setting
  - Amoxicillin is most common offending antibiotic.
  - Occurs with most antibiotics
- Etiology
  - Toxin from *Clostridium difficile*
- Diagnosis
  - Cytotoxin assays
  - Immunoassays to toxin
- Treatment
  - Stop antibiotic – use **Vancomycin**
  - Fluids
- Relapse and carrier rates are possible (10%-25%)

Traveler's Diarrhea

- Multiple causes
  - Enterotoxigenic *E. coli (***most common),** *Campylobacter jejuni, Shigella* spp, *Salmonella* spp
- Prophylaxis
  - **NOT** recommended by CDC
  - Routine prophylaxis increases the traveler's risk for adverse reactions and for infections with resistant organisms.
- Strict adherence to preventive measures
  - Handwashing (alcohol-based hand sanitizer also effective) has been shown to reduce the risk by 30%
  - Avoiding street vendor foods, tap water, ice, and raw foods has NOT been shown to reduce the risk
- Usually self-limited

Traveler's Diarrhea (TD)

If Treatment Is Needed …

- Travelers who develop ≥ 3 loose stools in an 8-hour period – especially if associated with nausea, vomiting, abdominal cramps, fever, or blood in stools
- Antibiotics*
  - Fluoroquinolones are drugs of choice when needed single dose or 1 day ***(increasing resistance)***
  - ***Alternative: Azithromycin (500 mg q day for 1-3 days)***
  - **NO** trimethoprim-sulfamethoxazole or doxycycline because of high levels of resistance
- Bismuth subsalicylate may also be used for treatment.
  - One fluid oz or two 262 mg tablets q 30 minutes for up to eight doses in a 24-hour period
- *The antimotility agent loperamide is a well-established antidiarrheal agent.*
  - *Its effective and safe use as an adjunct to antibiotics in the treatment of TD has been demonstrated in several studies. No other nonantibiotic treatment for TD has significant guideline or clinical trial support.*

* *CDC Health Information for International Travel 2012.* New York: Oxford University Press; 2012.

Vibrio Cholerae

- In the developing world, especially sub-Saharan Africa and Asia, cholera is a common cause of gastroenteritis.
  - Contaminated water or food
- In US, generally associated with travel
  - Asia
  - China
  - South/Central America

  OR consumption of contaminated seafood

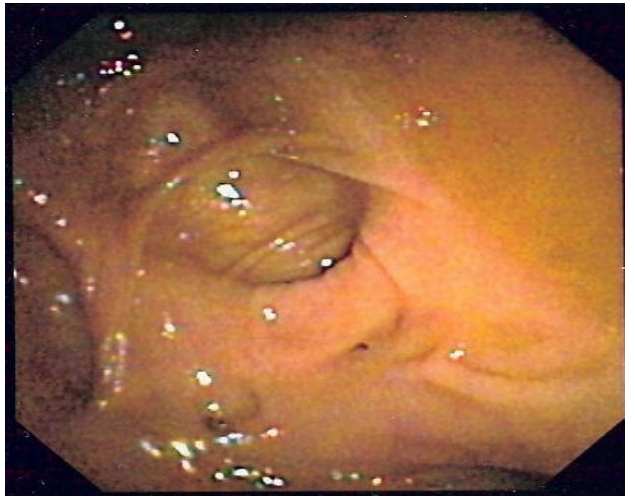
  OR recent consumption of contaminated imported foods
- **Treatment**
  - Vigorous rehydration
  - Doxycycline

Key Learning Points: Diarrhea

- **Rotavirus** is the leading cause of infectious diarrhea in children in the US.
- **Norovirus** is the leading cause of foodborne disease in US and the leading cause of gastroenteritis in US adults.
- **Salmonalla** is the most common cause of bacterial diarrhea in adults in the US.
- Antibiotics are not indicated for treatment of *E. coli 0157:H7.*
- Amoxicillin is most common offending antibiotic for pseudomembranous enterocolitis.
- Prophylaxis for traveler's diarrhea is NOT recommended.

Diverticular Disease

- Symptoms
  - 90% asymptomatic
  - Intermittent LLQ abdominal pain
  - Irregular defecation
- Exam
  - Tender LLQ
  - (−) rectal exam without occult blood
- Diagnosis
  - Flexible sigmoidoscope and barium enema
- Treatment
  - High-fiber diet (unprocessed bran, hydrophilic bulk laxatives)



Source: Wikipedia

Diverticulitis

- Clinical presentation
  - Acute lower abdominal pain
  - Fever (usually below 102º F)
  - Tachycardia
  - Physical findings
    - ❿ Tender lower abdomen, possibly with rebound
      - —Tenderness only in the LLQ significantly increases the likelihood of diagnosis ([+] LR = 10.4)
    - ❿ Acute abdomen is possible

Diverticulitis

Diagnostic Studies

- CBC: Leukocytosis with “left shift”
  - 55% will have leukocytosis
- BMP
  - Assess electrolytes and renal function.
- Consider C-reactive protein
  - LLQ tenderness **AND** a CRP > 50 mg/L, in the absence of vomiting, likelihood of acute diverticulitis significantly increased ([+] LR = 18).
- UA: Sometimes WBC and RBC
- Plain films: Sometimes free air
- US: Sometimes abscess
- *CT: Evolving as preferred method*
  - Quite a bit of controversy with CT scan regarding the use of contrast agents: Intravenous, oral, or rectal contrast agents versus giving no contrast agents at all, CT KUB.
- AVOID endoscopy and BE in acute setting
  - Colonoscopy 4-6 weeks post-resolution of symptoms in patients with complicated disease

Diverticulitis

Treatment

- **General**

  Depends on severity

  May require only clear liquids and oral antibiotics

  - Can be done outpatient with follow-up in 2-3 days
  - Ciprofloxacin and/or metronidazole

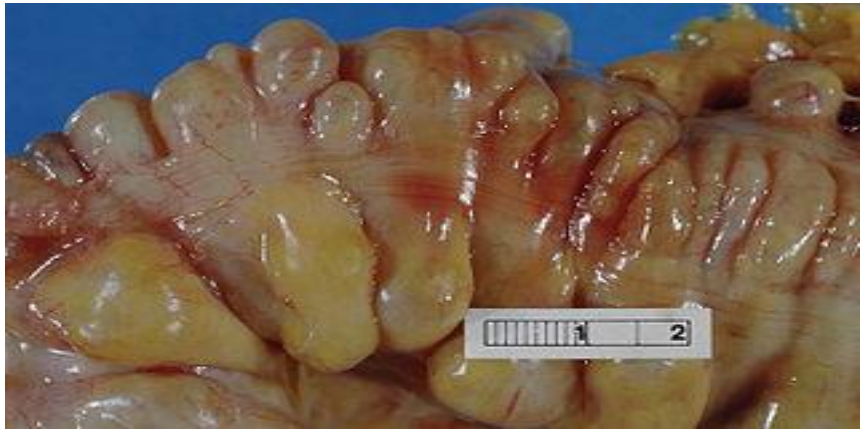
  OR MAY NEED (hospitalization)

  - NPO
  - NG suction
  - IV fluids
  - IV antibiotics
    - Ampicillin + aminoglycoside + metronidazole OR
    - Imipenem/cilastatin OR
    - Piperacillin/tazobactam

Diverticulitis

Treatment

- **Surgery**
  - 15%-30% admitted for acute diverticulitis will need surgical intervention during the admission.
  - For peritonitis, perforation, unresolved obstruction, and colovesical fistula
  - Avoid for uncomplicated diverticulitis
- **Bleeding *(Diverticulosis)***
  - 15%-40%
  - Profuse, painless
  - Generally self-limited



Source: Wikipedia

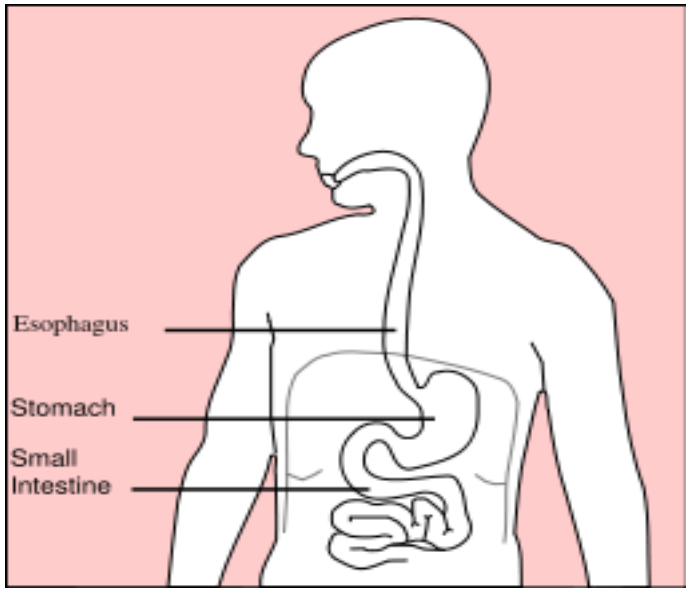
SORT: Key Recommendations for Practice

Clinical Recommendation	Evidence Rating
Antibiotics may not be necessary in patients with uncomplicated diverticulitis who are being treated in the outpatient setting.	B
There is NO clear evidence that avoiding nuts, corn, or popcorn decreases the risk of diverticulosis or diverticular complications, such as diverticulitis.	B

Wilkins T, Embry K, and George R. Diagnosis and Management of Acute Diverticulitis. *Am Fam Physician.* 2013;87(9):612-20.

Cancer of Small Intestine

- Rare
  - Most commonly seen in Crohn's
- Adenocarcinoma: 46%
  - Others: Lymphoma, carcinoid
- Diagnosis
  - Usually imaging study
- Treatment
  - Usually surgery



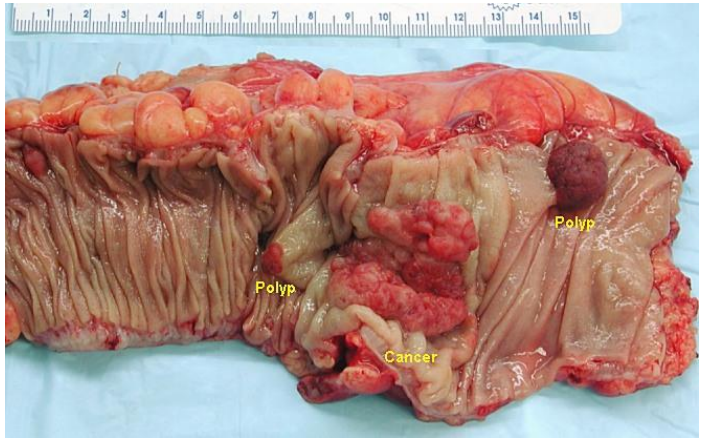
Source: Henry W. Schmitt/Wikipedia

Cancer of Large Intestine

- Most frequent internal neoplasm in the US
  - 5%-6% lifetime risk (1 in 17)
  - Third most common cause of cancer and cancer-related deaths in men and women in the US
  - More common in Western nations
  - Equal frequency in men and women
  - African Americans and Caucasians equally affected
    - African Americans have a higher mortality

Cancer of Large Intestine

- Histology
  - 95% Adenocarcinoma
    - ➓ Progression from adenoma (adenomatous polyp) to carcinoma – may take 10 years
- Polyps
  - < 1 cm: < 1% chance of CA
  - 1-2 cm: 10%−20% chance of CA
  - > 2 cm: 30%−50% likelihood
  - Detecting and removing polyps early CAN PREVENT much colon cancer
- Early Detection of CRC – decreased mortality



Source: Emmanuelm@en.wikipedia

Risk Factors

- **Nonmodifiable**
  - Family or personal history of CRC or advanced adenomas
  - Personal history of IBD
  - Personal history of hereditary polyposis syndromes
- **Modifiable**
  - Smoking
  - Obesity
  - Inactivity
  - Heavy Alcohol Use
  - Red meat consumption (500 g/week)

CA Cancer J Clin. 2014;64(1):9-29.
Gastroenterol Clin North Am. 2002;31(4):925-943.

Diagnosis of Cancer of the Large Intestine

- Symptoms: Variable and nonspecific
  - Rectal bleeding
  - Lower abdominal pain
  - Change in bowel habits
- Physical findings
  - Abdominal mass
  - Enlarged liver
- Lab
  - Stool for occult blood
- Endoscopy
  - Flexible sigmoidoscopy
  - Colonoscopy
- Imaging
  - Barium enema
  - CT
  - Rectal ultrasound

7. A 54 yo male sees you for a health maintenance visit. He inquires about the options for colorectal cancer screening. He has not had any screening tests performed in the past and has no personal or family history of colon cancer. You explain to him that there are several alternatives, but according to the U.S. Preventive Services Task Force, recommendations regarding the optimal screening intervals vary by test. He opts for fecal occult blood testing. You recommend he repeat this test at which one of the following intervals?

A. Yearly
B. Every 3 years
C. Every 5 years
D. Every 10 years

Recommendation *Colorectal Cancer Screening* *USPSTF May 2021*

Recommendation Summary

Population	Recommendation	Grade
Adults ages 50 to 75 years	The USPSTF recommends screening for colorectal cancer in all adults ages 50 to 75 years. See the "Practice Considerations" section and Table 1 for details about screening strategies.	A
Adults ages 45 to 49 years	The USPSTF recommends screening for colorectal cancer in adults ages 45 to 49 years. See the "Practice Considerations" section and Table 1 for details about screening strategies.	B
Adults ages 76 to 85 years	The USPSTF recommends that clinicians selectively offer screening for colorectal cancer in adults ages 76 to 85 years. Evidence indicates that the net benefit of screening all persons in this age group is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the patient's overall health and prior screening history.	C

- Screening tests – equally acceptable (general population)
- Recommendation focuses on BEING SCREENED as opposed to screening test to be used
- Because of limited available evidence, the USPSTF recommendation does **NOT** include serum tests, urine tests, or capsule endoscopy for consideration in screening

Stool-Based Tests

http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/colorectal-cancer-screening2

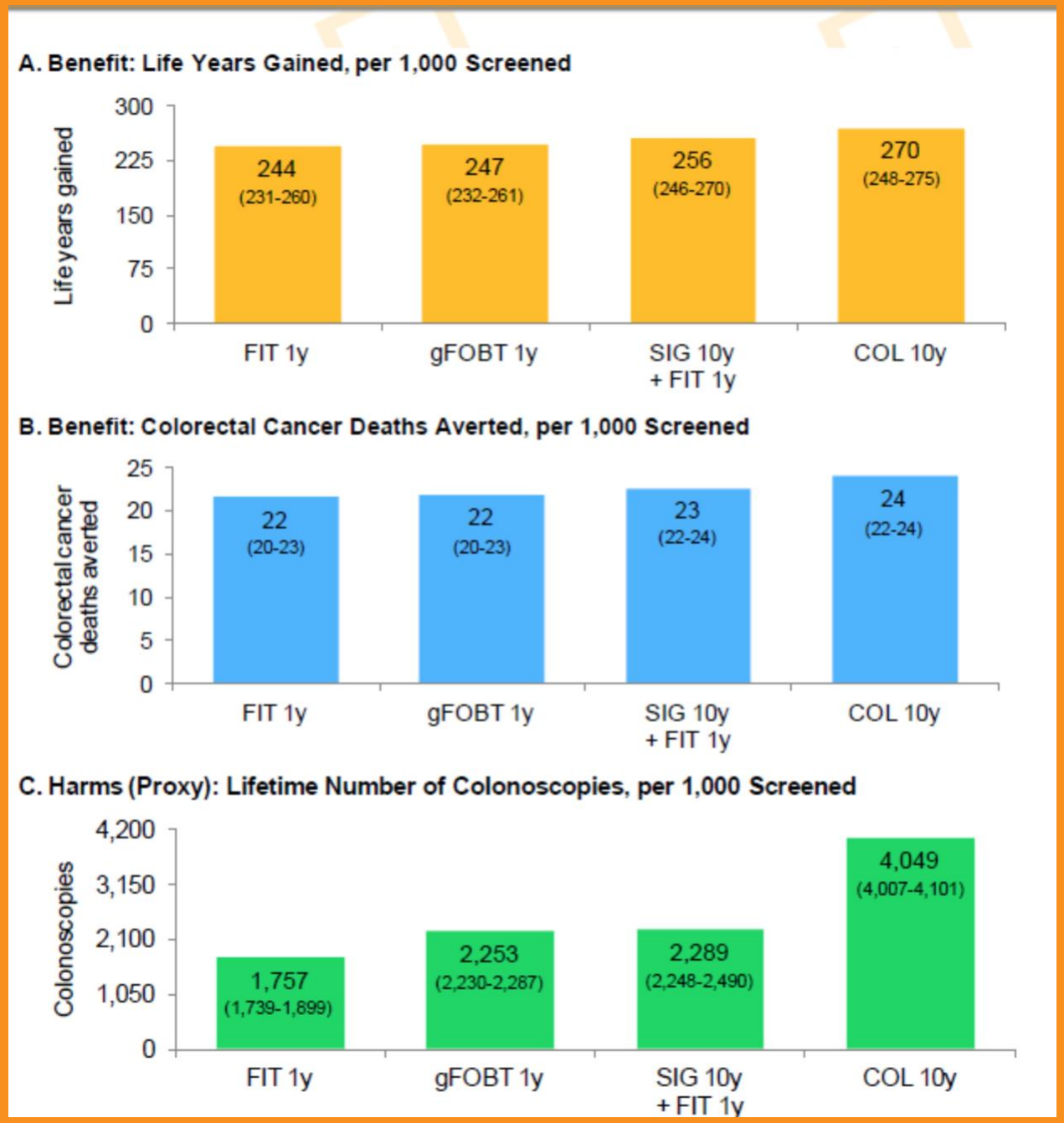
Screening Method	Frequency	Evidence of Efficacy	Other Considerations
High-sensitivity gFOBT	Every year	RCTs with mortality end points: High-sensitivity versions (eg, Hemoccult SENSA) have superior test performance characteristics than older tests (eg, Hemoccult II)	Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT	Every year	Test characteristic studies: Improved accuracy compared with gFOBT Can be done with a single specimen	Does not require bowel preparation, anesthesia, or transportation to and from the screening examination (test is performed at home)
FIT-DNA	Every 1 or 3 y	Test characteristic studies: Specificity is lower than for FIT, resulting in more false-positive results, more diagnostic colonoscopies, and more associated adverse events per screening test Improved sensitivity compared with FIT per single screening test	There is insufficient evidence about appropriate longitudinal follow-up of abnormal findings after a negative diagnostic colonoscopy; may potentially lead to overly intensive surveillance due to provider and patient concerns over the genetic component of the test

Direct Visualization Tests

http://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/colorectal-cancer-screening2

Screening Method	Frequency	Evidence of Efficacy	Other Considerations
Colonoscopy	Every 10 y	Prospective cohort study with mortality end point	Requires less frequent screening. Screening and diagnostic follow-up of positive results can be performed during the same examination.
CT colonography	Every 5 y	Test characteristic studies:	There is insufficient evidence about the potential harms of associated extracolonic findings, which are common
Flexible sigmoidoscopy	Every 5 y	RCTs with mortality end points: Modeling suggests it provides less benefit than when combined with FIT or compared with other strategies	Test availability has declined in the United States
Flexible sigmoidoscopy with FIT	Flexible sigmoidoscopy every 10 y plus FIT every year	RCT with mortality end point (subgroup analysis)	Test availability has declined in the United States Potentially attractive option for patients who want endoscopic screening but want to limit exposure to colonoscopy

USPSTF COLORECTAL CANCER SCREENING



Assessment of Risk

- Age is one of the most important risk factors for colorectal cancer
  - incidence rates increasing with age
  - 94% of new cases of colorectal cancer occurring in adults ≥45 years
- **All adults 45 years or older** should be offered screening, even if risk factors are absent
- Risk factors (rates of colorectal cancer incidence are higher)
  - Black adults and American Indian and Alaskan Native adults,
  - Persons with a family history of colorectal cancer (**even in the absence** of any known inherited syndrome such as Lynch syndrome or familial adenomatous polyposis)
  - Men
  - persons with other risk factors (e.g., obesity, diabetes, long-term smoking, and unhealthy alcohol use)

Colonoscopy Screening Recommendations Based on Risk

Risk Factor	Age to Initiate Screening	Interval if normal (years)
Single first-degree relative with CRC or an **advanced adenoma** diagnosed at ≥ 60 years of age	45 years	10
Single first-degree relative with CRC or an **advanced adenoma** diagnosed at <60 years of age	40 years or 10 years younger than affected relative's age when diagnosed, whichever is earlier	5
Two first-degree relatives CRC or an **advanced adenoma** diagnosed at any age	40 years or 10 years younger than the youngest affected relative's age when diagnosed, whichever is earlier	5

* An ***advanced adenoma*** is defined as an adenoma that is 10 mm or larger, has villous elements, or has high-grade dysplasia.

Am Fam Physician. 2015;91(2):93-100.

AGA

Choosing Wisely®
An initiative of the ABIM Foundation

- *Do not repeat colorectal cancer screening (by any method) for 10 years after a high-quality colonoscopy that does not detect neoplasia.*

8. One week after a complete and adequate baseline screening colonoscopy, a 51 yo female with no history of previous health problems visits you to review the pathology report on the biopsy specimen obtained from the solitary 8-mm polyp discovered in her sigmoid colon. The report confirms that this was a hyperplastic polyp. Her family history is negative for colon cancer. Which one of the following is the most appropriate interval for follow-up colonoscopy in this patient?

A. 1 year
B. 3 years
C. 5 years
D. 10 years

Polyps

Br J Surg. 2002;89 (7):845-860.
Gastroenterology. 1990;98(2):371-379.
Gastroenterology. 2012;143(3):844-857.
Gastroenterology. 2010;139(5):1497-1502.

Polyp	Risk	Follow-up
Adenomatous • Tubular adenoma (most common) • Tubulovillous adenoma • Villous adenoma	Malignant potential 4.8% malignant transformation rate 19% malignant transformation rate 38.4% malignant transformation rate	See next slide
Hyperplastic (50% of polyps found)	**No** increased risk for CRC	Routine surveillance guidelines
Serrated	Principle precursor of hypermethylated gene cancers; 20-30% of CRCs from this pathway; difficult to detect during colonoscopy as flat and indiscrete	See next slide

Guidelines for *Follow-up Surveillance* Colonoscopy

Initial Colonoscopy Findings	Follow-up Interval
Normal – No polyps or normal biopsy results	10 years
Hyperplastic polyps – small (<10 mm) hyperplastic polyps in rectum or sigmoid	10 years
Low-risk polyps • 1 or 2 small (<10 mm) tubular adenomas • Small sessile serrated polyp (<10 mm) without dysplasia	 5-10 years 5 years
High-risk polyps • 3-10 tubular adenomas • Tubular adenoma or serrated polyp ≥ 10 mm • Adenoma with villous features or high-grade dysplasia • Sessile serrated polyp with cytologic dysplasia • Traditional serrated adenoma	3 years

Am Fam Physician. 2015;91(2):93-100.

AGA

Choosing Wisely®
An initiative of the ABIM Foundation

- *Do not repeat colonoscopy for at least five years for patients who have one or two small (<1cm) adenomatous polyps, without high-grade dysplasia or villous histology, completely removed via a high-quality colonoscopy.*

Treatment of Cancer of the Large Intestine

- Surgical excision with 5 cm margin
- Clearing colonoscopy at time of diagnosis; thereafter, q 3-5 years
- 40%-50% of patients have long-term survival after resection
- Chemotherapy with 5-FU produces partial tumor remission in 15%-20%
- New agents: Irinotecan and oxaliplatin
- Radiation therapy useful for symptomatic metastases

Key Recommendations

CRC Screening

Recommendation	SOR
Colorectal cancer screening should begin at 45 years of age in average-risk individuals	**B**
Average-risk patients with normal findings on colonoscopy should have repeat colonoscopy in 10 years	**C**
Patients with small, distal hyperplastic polyps are considered to have a normal colonoscopy result and should have repeat colonoscopy in 10 years	**C**
Repeat surveillance colonoscopy in 5 to 10 years for low-risk polyps	**C**
Repeat surveillance colonoscopy in 3 years for high-risk polyps	**C**

Am Fam Physician. 2015;91(2):93-100.

Cancer of the Anus

- Uncommon

  Only 2%-3% as frequent as colon CA

  50%-60% squamous cell CA

  - ❿ Associated with chronic inflammation of anus, especially inflammatory bowel disease

  Diagnosis: Biopsy

  Treatment: Excision and radiation

THANK YOU