

Diarrheal Disorders And Diverticular Disease

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Educational Goals

By the completion of the section on diarrheal diseases you should be familiar with:

1. The pathophysiology of different mechanisms of diarrhea.
2. The different types of diarrheal diseases and their specific features.
3. General idea about a clinical diagnostic approach.

By the completion of the section on diverticular disease you should be familiar with:

1. Be familiar with the prevalence of diverticular disease and its potential complications
2. Be familiar with complication rates and treatment

Key Words:

bacillary dysentery	fecal leukocytes
bacterial overgrowth	fecal osmotic gap
bile salt deficiency	ileal resection
cAMP	irritable bowel syndrome
carcinoid syndrome	lactase deficiency
celiac sprue	malabsorption
choleric enteropathy	medullary thyroid cancer
Clostridium difficile	Motility diarrhea
diverticulitis	osmotic diarrhea
diverticulosis	ova and parasites
D-xylose test	secretory diarrhea
exudative diarrhea	steatorrhea
factitious diarrhea	thyrotoxicosis
fecal electrolytes	Vibrio cholera
fecal incontinence	Zollinger Ellison syndrome

Overview of the Diarrheal Diseases

I. Definition of diarrhea – “too frequent passage of too liquid stool”

A. Functional definition (diarrhea as a symptom).

1. Increased frequency (> 3/day) - normal bowel habits range from 3/day to 3/week.
2. Increased looseness or liquidity of stools.
3. Abnormal constituents in the stool - blood, mucus, pus.

B. Specific definition = increased stool weight (diarrhea as a sign): > 250 gm/day.

Daily stool weight in different conditions:

Healthy subjects:

western diet:	< 200 gm
vegetable diet or fiber:	200-500 gm

Diarrheal conditions:

irritable bowel syndrome:	250-500 gm
osmotic diarrhea:	500-1000 gm
secretory diarrhea:	> 750 gm

“Fecal incontinence” is not necessarily diarrhea. Incontinence means the involuntary release of rectal contents.

C. Acute vs. Chronic Diarrhea

1. Chronic diarrhea is defined as a decrease in fecal consistency lasting for more than four weeks
2. Acute diarrhea, therefore is defined as a decrease in fecal consistency lasting less than four weeks

II. Pathophysiology

An excess of water may accumulate in the lumen of the gut by one of two mechanisms:

- A) If digested food substrate cannot leave the lumen and enter the epithelial cell and thereby retains water and electrolytes with it in the lumen (osmotic diarrhea)
- B) If an electrogenic pump of the epithelial cell is pumping too much of a given electrolyte back into the lumen and water is following (secretory diarrhea)

In summary, diarrhea occurs when there is a disorder resulting in either too little epithelial absorption or too much secretion.

III. Four basic pathophysiologic mechanisms of diarrheal diseases:

- A. Osmotic
- B. Secretory
- C. Motility
- D. Exudative

A. Osmotic diarrhea - caused by ingesting solutes that cannot be normally digested or absorbed. This osmotically active solute then draws water into the lumen of the gut.

1. Characteristics:

- a. Daily stool volume usually < 1 liter.
- b. Diarrhea decreases or resolves with fasting.
- c. Fecal Na⁺ is low, the osmotically active solute has replaced Na⁺ in the stool in maintaining the balance with normal blood osmotic balance.
- d. High fecal osmotic gap. Fecal osmoles still equals blood's (approx. 290), but since the abnormal osmotically active solute has replaced sodium, fecal osmolality (~290) - [2 x (Na + K)] > 50
(fecal electrolytes multiplied by 2 to account for anions)

2. Causes

a. Lactase deficiency - is an example of carbohydrate malabsorption due to disaccharidase deficiency. Malabsorption of lactose, which is the sugar in milk.

Incidence of lactase deficiency in adult populations:

- < 15% - White Americans, Northwest Europeans, Scandinavians.
- 60-80% - US blacks, Jews, Indians, and Mexicans.
- 80% - Japanese, Eskimos, Nigerians.

b. Steatorrhea - resulting from maldigestion or malabsorption of fats.

i. pancreatic insufficiency resulting in lipase deficiency.

ii. bile salt deficiency resulting in decreased micelle formation.

(a) Terminal ileal disease or resection - loss of bile salts

(b) Bacterial overgrowth - destruction of bile salts

(c) Hepatic disease - in complete biliary obstruction or advanced liver disease there is an inadequate supply of bile salts.

iii. Small bowel mucosal disease - many causes including small bowel resection, results in malabsorption.

c. Laxatives and antacids - a surprisingly common cause. Examples are: antacids, lactulose, magnesium, phosphates

d. Poorly absorbed carbohydrates used as sweeteners, i.e. sorbitol, manitol, fructose

e. Rapid transit - gastric surgery (dumping syndrome), hyperthyroidism.

B. Secretory diarrhea - classic mechanism is toxin or peptide that increases cAMP in small bowel epithelial cell resulting in increased secretion.

1. Characteristics:

- a. Daily volume usually > 1 liter.
- b. Persists with fasting.
- c. Low fecal osmolality gap.

2. Causes:

a. Toxin-producing infections: *Vibrio cholera* is the classic that results in increased secretion by increasing intracellular cAMP. Importantly, absorption mechanisms remain intact, so that despite the massive secretion and diarrhea, oral solutions with glucose and sodium can be successful treatments.

- E. coli causes "tourist's" diarrhea by toxin that increases cAMP.
 - Staph. and Clostridia cause food poisoning by preformed toxins.
 - b. Hormonal: typically increase secretion by increasing cAMP, cGMP or Ca⁺⁺.
 - i. Pancreatic cholera - due to excess VIP secretion, usually by a pancreatic tumor, resulting in syndrome of watery diarrhea, hypokalemia and achlorhydria.
 - ii. Carcinoid syndrome - excess serotonin (5-HIAA).
 - iii. Medullary thyroid cancer - excess calcitonin and prostaglandins.
 - iv. Zollinger Ellison (ZE) syndrome - excess gastrin, results in excessive gastric secretion overwhelming GI absorption ability. The diarrhea in ZE is often multifactorial - resulting in a mixed secretory and osmotic pattern.
 - c. Bile salt induced increased secretion by the colon.
 - i. Called "choloretic enteropathy"
 - ii. Results from ileal resection or disease.
 - d. Fictitious - cathartic abuse.
- C. Motility
 - 1. Irritable bowel syndrome - functional bowel disorder
 - i. Diarrhea typically associated with abdominal pain which is relieved with bowel a movement
 - ii. Often diarrhea alternating with constipation
 - iii Diarrhea alone, without abdominal pain, is considered "functional diarrhea," which may be a variant of IBS
 - 2. A number of diarrheal conditions that may have a dysmotility component include: diabetic; hyperthyroidism; post vagotomy and others.
- D. Exudative - The mucus, pus and blood contributes to diarrhea but usually not of enough volume to significantly increase stool volume. If there is significant diarrhea it is often caused by another mechanism as well.
 - a. Inflammatory bowel disease
 - b. Carcinoma
 - c. Invasive organisms - shigella, amoeba.

V. Acute Diarrhea – Overview

Definition: Most acute diarrheas last < 10 days. Diarrhea of greater than 4 weeks duration is usually chronic (standard, but arbitrary definition)

Etiology

- Infectious: Mostly spread by oral-fecal route; results in 7 deaths/minute world wide
- Bacteria: E. coli (various types), campylobacter, shigella, salmonella etc.
- Viruses: particularly rotavirus and Norwalk
- Parasites: G. lamblia, E. histolytica, C. parvum
 - Medications: ask patients about new medications (prescription and over-the counter)
 - Foods or toxins: Food sensitivity, food poisoning (usually bacterial toxins, but also organophosphates), sugar substitutes (particularly sorbitol), olestra

VI. Diarrheal disorders classified by clinical presentation

- A. Acute Diarrhea without blood
 - 1. Acute gastroenteritis
 - a. may have associated systemic complaints of arthralgias and myalgias
 - b. most resolve before seeking medical attention
 - c. most commonly are viral in etiology
 - i. Norwalk virus most common in adults
 - ii. Rotavirus most commonly in infants and younger children in daycare
 - iii. symptoms begin more than 16 hours after exposure
 - d. bacterial causes are responsible for most cases of severe diarrhea
 - e. stool cultures are only positive in 1.5% to 5.6% of cases
 - 2. Antibiotic-induced (Clostridium difficile or pseudomembranous colitis)
 - a. most of the time associated with previous hospitalization/exposure

- b. onset of voluminous, foul smelling, watery diarrhea
 - c. antibiotics eliminate "normal" bacterial flora of the bowel, allowing *C. difficile* to flourish
 - d. diagnosed with stool analysis for *C. difficile* toxin A and B
 - e. treated with metronidazole
3. food poisoning
- a. *Staphylococcus aureus*
 - i. incubation period 1-6 hours
 - ii. associated with mayonnaise, meats and dairy products
 - iii. present with vomiting, diarrhea and abdominal pain
 - iv. resolve usually within 24 hours
 - b. *Bacillus cereus*
 - i. incubation time is 6-14 hours
 - ii. associated with rice, meat and sauce
 - iii. present with abdominal pain, diarrhea and vomiting
 - c. *Clostridium perfringens*
 - i. incubation period 8-16 hours
 - ii. associated with meat pie or pork
 - iii. diarrhea, abdominal pain and even shock
4. Parasites
- a. Persistent diarrhea: *Giardia*, *Crypto*, *Entamoeba histolytica*
 - b. Travel: *Giardia*, *Crypto*, *Cyclospora*
 - c. Infants/Daycare: *Giardia*, *Crypto*
 - d. Waterborne outbreak: *Giardia*, *Crypto*
 - e. HIV/AIDS: *Giardia*, *Crypto*
 - f. Bloody stool: amebiasis
 - g. Send sample on consecutive days
- B. Acute diarrhea with blood
- 1. Uncommon and presents in 3%
 - 2. Infectious
 - a. *Salmonella*
 - b. *Shigella*
 - c. *Campylobacter*
 - d. *Yersinia*
 - e. *E. coli* 0157
 - f. diagnosed with stool cultures
 - 3. Ischemic colitis
 - a. usually presents in elderly patient with abdominal pain
 - b. resolves after couple days
 - c. may need to look for cause ie hypotension, thromboembolic event, or arteriosclerotic vascular disease
 - 4. inflammatory bowel disease
 - a. most commonly ulcerative colitis
 - b. acute presentation
 - c. diagnosed with colonoscopy
 - 5. Colon cancer
 - a. may present with some blood in stool, anemia, or lethargy
 - b. usually older than 50 y/o
 - c. important to exclude this from the differential if stool samples are negative
 - d. raises suspicion if family history of colon cancer, colon polyps, or personal history of inflammatory bowel disease
 - 6. Diverticular disease
 - a. usually acute, painless, voluminous, bloody diarrhea
 - b. may bleed several times
 - c. usually self-limited
 - 7. Medications
- C. Chronic diarrhea without blood
- 1. Celiac Sprue

- a. 1:122 persons
 - b. allergy to wheat, rye and barley
 - c. can also present as iron deficiency anemia
 - d. more common in Irish descent
 - e. treatment is dietary avoidance of above
2. Inflammatory bowel disease
- a. usually Crohn's disease
 - b. can have systemic complaints of arthritis, rash, uveitis
 - c. multiple frequent movements throughout the day
 - d. diagnosed with colonoscopy, radiology or capsule endoscopy
3. Lactose intolerance
- a. one of the most common causes
 - b. get diarrhea and cramps after eating dairy
 - c. can diagnose with lactose breath test
 - d. treated with avoidance or lactose replacement (lactaid tablets, or lactaid milk)
4. Infectious
- a. acute infectious etiologies can persist
 - b. HIV (cryptosporidia, isospora, or microsporidia)
5. Diabetes
- a. nocturnal bowel movements
 - b. worse when glucose is elevated
 - c. can be treated with normalization of blood glucose or clonidine
6. Irritable bowel syndrome (IBS)
- a. when entire workup unrevealing with associated abdominal cramps, bloating
 - b. can be either diarrhea or constipation predominant
 - c. usually develop diarrhea and cramps after eating
 - d. pain is relieved with moving bowels
7. Microscopic colitis
- a. usually women over the age of 50
 - b. has been associated with ASA exposure
 - b. slow insidious onset
 - c. due to a deposition of collagen in the subepithelial lining of the colon
 - d. diagnosed with colonic biopsies
 - e. treated with removal of ASA, Imodium, aminosalicylates or even steroids
- (budesonide)
8. Malabsorption
- a. pancreatic insufficiency
 - b. small intestinal bacterial overgrowth
 - c. lactose intolerance
 - d. celiac sprue
- D. Chronic bloody diarrhea
- 1. Ulcerative colitis
 - 2. Colon Cancer
 - 3. Colon polyps

VII. Diagnostic Approach

A. Medical History

Since there are so many causes of diarrhea, it is important to have some method to classify patients, so that the possibilities can be narrowed.

- 1. Duration of symptoms: acute (2-3 weeks) v. chronic (>4 weeks), recurrent?
- 2. Clues about fecal appearance: greasy (malabsorption), bloody (inflammatory), color, etc.
- 3. Volume (large volume is usually a small bowel problem, while small volume, but more frequent is large bowel, particularly left colon and more distal).
- 4. Is the diarrhea bloody? Depending on the site of bleeding, is usually brown diarrhea with blood mixed in (a reddish tinge).

- a. Is it bright red blood or dark black (melena) suggesting that GI bleeding is the problem?
- b. Is it a little streaking of red blood in otherwise non-bloody diarrhea, more suggestive of a perianal excoriation or hemorrhoidal bleed due to the diarrhea and excessive wiping.
- 5. Other symptoms: tenesmus, position of pain (periumbilical suggests small bowel, LLQ suggests recto-sigmoid etc).
- 6. Past medical history
 - a. Prior surgery
 - b. XRT
 - c. Relation to food
 - d. Friends with similar complaints
- 7. Current or recent medications (particularly antibiotics, Mg⁺⁺ containing laxatives, any new medicines), alcohol, OTC drugs.

Medications that can cause diarrhea:

Antacids containing magnesium	Loop diuretics
Antibiotics	Propranolol
Colchicine	Quinidine
Digoxin	Theophylline
Lactulose	Thyroxine

- 8. Dietary history: special diets, dairy products, "sugar-free" foods (sorbitol), raw meat or seafood
- 9. Family history: sprue, IBD
- 10. Travel history: endemic areas, questionable water supply (parasites), spring water
- 11. Social history: sexual orientation, activity

B. Physical examination

Usually better for determining the severity of diarrhea, than the cause: weight loss, dehydration. Some clues are present (see handout).

C. Stool examination

1. Fecal leukocytes
 - a. Best seen with methylene blue stain - positive if more than 50% of the total cells
 - b. Positive in bacterial infections, IBD, ischemic colitis, and others
 - c. Negative in viral infections, IBS, many osmotic and secretory etiologies
2. Culture for enteric pathogens - shigella, salmonella, campylobacter, yersinia
3. Ova and Parasites - amoeba, giardia, hookworm ova, strongyloides
 - a. Can be false neg for giardia, so repeating can improve yield
 - b. Duodenal aspirate is best for giardia
4. Fat - qualitative test
 - a. Stain with Sudan III or IV
 - b. More than 3-5 orange globules/hpf suggests steatorrhea
 - c. Detects > 15 gm/24 hr
5. Electrolytes and osmolality
 - a. Osmotic diarrheas with show unexplained osmotic gap
6. Hemoccult test for blood
7. Alkalinize stool specimen (add 0.1 N NaOH) - will turn red if phenolphthalein is present

D. Role of endoscopy

Allows inspection to rule out inflammatory and neoplastic conditions. Can identify source of bleeding. Allows biopsy to look for histologic abnormalities.

E. Role of x-rays

Barium images of the small and large bowel can be helpful to identify mucosal abnormalities as in IBD, neoplasia, etc.

VIII. Approach to specific types of diarrhea diseases

- A&B. Acute non-bloody diarrhea - Usually self-limited and doesn't present to physician. If they present I do the following:
1. Stool for enteric pathogens; fecal leukocytes; if recent antibiotic use or other risk factor then add C. difficile toxin; consider ova and parasites
 2. Maintaining adequate hydration is the key, oral is usually adequate. If they are unable to maintain proper hydration usually because of associated vomiting then give IV fluid
 3. If culture for enteric pathogens is negative and diarrhea is persisting, give trial of Imodium or Lomotil
- C&D. Acute bloody diarrhea - Should present to physician and an etiology should be looked for and found:
1. Stool for enteric pathogens and C. difficile toxin routinely
 2. Of course if significant GI bleeding manage as you would a GI bleeding patient.
 3. Early flex sig. or even colonoscopy
- E&F. Chronic bloody diarrhea – Colonoscopy often needed
- G&H. Chronic non-bloody diarrhea - can be very challenging
1. Start with easy things:
 - a. Lactose-free diet trial
 - b. Thyroid function tests
 - c. Stool for WBC's, O & P, even enteric culture (just to be sure)
 2. Consider colonoscopy to evaluate for colonic polyps (villous adenoma is a classic), mild IBD, collagenous colitis, microscopic colitis
 3. Very useful is to fast patient for 48 hours (this is often best way to start when patient is admitted to hospital for proper w/u), is near impossible to do as outpatient. Osmotic diarrhea will markedly decrease, while secretory diarrhea should not change
 4. If malabsorption/maldigestion is suspected (presents as steatorrhea), proper w/u is:
 - a. 72 hr (or 24 hr) fecal fat collection (must be on 100 gm fat diet): normal is < 7gm fat/24 hours
 - b. D-xylose test - if abnormal suggests small bowel malabsorption, if normal suggests other than small bowel etiology, most likely pancreatic
 - c. If pancreatic insufficiency is suggested: look for pancreatic calcifications, trial of pancreatic enzyme replacement, bentiramide test, secretin test
 - d. If small bowel malabsorption is suggested: small bowel biopsy endoscopically to look for diffuse small bowel disease, classics are celiac disease, Whipple's, a long list of others, small bowel barium x-ray to look for an anatomic abnormality
 - e. Tests for bacterial overgrowth: Breath tests - hydrogen, bile salts, Schilling test, trial of antibiotic
 - f. Schilling test - B12 absorption
 - g. Screening studies - cholesterol, prothrombin time, carotene, albumin, calcium

Diverticular disease

I. Introduction and Epidemiology

- A. Very common problem in the US especially in the elderly
- B. Although worldwide, there has been a higher incidence in developed countries
- C. 5th most important GI disease due to direct and indirect costs
- D. Mortality rate is 2.5 per 100,000 per year.
- E. 50-66% in patients >85 years of age

II. Pathogenesis

- A. Poorly understood but related to intestinal motility, colonic structure, diet and genetics
- B. Has been correlated with a low residue diet (higher incidence in those with reduced fiber intake and lower in vegetarians)

- C. May be related to muscular hypertrophy of colon and ability of increase intraluminal pressure
- D. Prolonged colonic transit, decreased fecal fiber, and increased in intraluminal pressure

III. Clinical Aspects of Diverticular Disease

- A. Classification of disease
 - 1. Symptomatic uncomplicated disease
 - 2. Recurrent symptomatic disease
 - 3. Complicated disease
 - 4. Hemorrhage, abscess, phlegmon, perforation, purulent and fecal peritonitis, stricture, fistula, small bowel obstruction from adhesive disease
- B. Natural History
 - 1. 80-85% of people with diverticular disease are asymptomatic
 - 2. 15-20% present with abdominal pain
 - 3. 1-2% will require hospitalization
 - 4. 0.5% will require surgery
 - 5. Little data on risk factors, preventative measures
- C. Symptoms
 - 1. Abdominal pain and impaired bowel function
 - 2. Fever
- D. Treatment of acute diverticulitis
 - 1. Intravenous antibiotics
 - 2. Oral antibiotics
 - 3. Low fiber diet
 - 4. 50-70% of patients with one episode of diverticulitis will not have another episode
 - 5. Then high fiber diet after 6-8 weeks
- E. Treatment of symptomatic diverticulosis
 - 1. High fiber diet +/- trial of oral antibiotics

Suggested Reading:

Starr J. . Clostridium difficile associated diarrhoea: diagnosis and treatment. BMJ. 2005 Sep 3;331(7515):498-501

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