

Management of Diarrhea and Constipation (2009)

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Components in the Definition of Constipation

- Symptoms: straining, hard stools, unproductive call to stool, infrequent stools, incomplete evacuation
- Definition of constipation (the "Rome criteria" for functional constipation): 2 or fewer bowel movements per week; stool weight less than 35 g/d, straining on more than 25% of occasions; hard lumpy stools on more than 25% of occasions. Constipation defined by 2 or more symptoms for at least 3 months
- Physiologic measures: colonic transit time
- Patient's opinion

Epidemiology

- Prevalence rate = 15% (10-34% in community-dwelling elderly, 45% in frail home-bound elderly)
- 2.5 million M.D. visits/year (1.2%)
- Cathartics prescribed for > 3 million each year
- \$400 million/year on OTC laxatives
- Low disability and hospitalization rates

Etiology of Constipation

- Neurogenic: MS, Parkinsonism
- Mech. Obstruction: CA, post-surgical
- Metabolic: DM, uremia, hypokalemia, hypercalcemia, hypothyroidism
- Pharmacological: narcotics, stimulant laxative abuse, heavy metals, anticholinergics, psychotherapeutics, antacids, CCBs, Fe, bile acid binders, vinca alkaloids, ondansetron (40% of constipation is due to meds!)

Etiology of Constipation (cont'd)

- Inadequate dietary fiber and/or fluid intake
- Physical inactivity
- Idiopathic

Complications of Constipation in the Elderly

- Cardiac and CV dysfunction: coronary insufficiency, arrhythmias, syncope, transient ischemic attacks
- Fecal impaction
- Megacolon: sigmoid volvulus, ischemic colitis, cecal perforation
- Anorectal: rectal prolapse, hemorrhoids
- Laxative abuse

Therapies for Chronic Constipation

- Identify and treat underlying conditions
- Fluid: 8 x 8 oz glasses/day
- Bran fiber 20 gm/d in adults, (age + 5) gm/d in children \geq 1 y.o. (titrate)
 - ADR: flatulence, abdom. distention, colic due to gas (bacteria), fecal impaction in pts with strictures or bedridden pts, decreased Ca and Fe absorption

Therapies for Chronic Constipation (cont'd)

- Bulk – Formers: psyllium, methylcellulose, cellulose (for pts who cannot consume enough dietary fiber)
- Beware psyllium hypersensitivity in HCW
- Stool – Softeners and Lubricants:
 - Mineral oil
 - Caution: Not for long-term use except peds \geq 1 y.o. (vitamins, lipid pneumonia, leakage)
 - For peds: cool it, choc milk, cubes + OJ, commercial flavored product

Therapies for Chronic Constipation (cont'd)

- Enemas – for intermittent use only (disimpact)
ADR: Electrolyte imbalance, perforation, mucosal toxicity
Tap water, oil retention, saline are safest
- Osmotics –
Na salts-not recommended chronically due to possible electrolyte imbalance (esp. PO_4) (even oral agents)
- Sorbitol 70% or lactulose – ADR: cramps/bloating, taste fatigue; peds
- PEG (Miralax): efficacy > lactulose/sorbitol, minimal ADR

Therapies for Chronic Constipation (cont'd)

- Stimulants – use only infrequently (disimpact)
Chronic opioid recipients : chronically is ok
- Opioid antagonists – for opioid recipients, can use SC methylnaltrexone if all other regimens fail/poorly tolerated – DON'T USE ORAL naloxone, naltrexone (why not?)

Am. Gastroenterol. Assoc. Adult Treatment Recs (Maintenance)

- 1st – fiber + lifestyle + Mg hydroxide
- 2nd – add bisacodyl
- 3rd – add PEG (Golytely)
- 4th – adjust above meds

Pediatric Treatment Recs (Maintenance)

- mineral oil (1-3 mL/kg/d – qd or bid)
- lactulose/sorbitol (1-3 mL/kg/d – bid)*
- magnesium hydroxide (0.5-1 mL/kg/d – bid)*
- PEG (1-1.5 g/kg/d – bid) (supported by RCTs)*
- senna (2.5-7.5 mL/d for 2-6 y.o.; 5-15 mL/d for 6-12 y.o.)
- bisacodyl (5-15 mg/d – qd or bid)
- prn supps – glycerin or bisacodyl
- Most recomm. tx's NOT evid.-based

Potential Therapies for Chronic Constipation

- Misoprostol 400 mcg tid p.o. (PG)
- Colchicine 0.6 mg tid p.o.
- Lubiprostone p.o.
 - Cl channel activator (adults)
 - 24 mcg bid (↓ to qd if GIAEs – give with food)
 - ? work for opioid constipation
 - cost-prohibitive
- Serotonin agonists – tegaserod withdrawn but several in late phase trials

Constipation in Pregnancy

- Low risk therapy: fiber, stool softeners (surfactants) emollients, osmotics, sorbitol, bisacodyl (latter for intermittent use only)
- Moderate risk: cascara, senna, lubiprostone
- High risk: castor oil (uterotonic), mineral oil (vit. A, D, E, K), misoprostol, colchicine

Diarrhea

- Passage of loose stools (greater water content than normal)
- > 3 movements per day
- Rectal urgency
- Complications – trigger IBD relapse or ppt. new onset IBD, inflammatory reactive arthritis + Reiter's syndrome, post-infection IBS

Normal Infant Stool Patterns

- 0-6 mo
Breast fed: once every 2-3 days to 12 times/day:
yellow to light brown, pH = 5
Formula fed: 1 to 3 times/day (range 1 to 7)
yellow to brown, formed, pH = 7
- 6 mo – 1 year: 2 to 3 per day (range 1 to 7);
brown, formed
- After 1 year: Formed, like adult stools

Possible Underlying Causes of Chronic Diarrhea

- Dietary factors: excessive intake of caffeine and foods containing sorbitol
- Diverticular disease
- Idiopathic secretory diarrhea: collagenous and microscopic colitis
- Infections: amebiasis, giardiasis, opportunistic infections associated with immunodeficiency states, such as AIDS
- Inflammatory Bowel Disease: Crohn's and ulcerative colitis

Possible Underlying Causes of Chronic Diarrhea (cont'd)

- Irritable bowel syndrome (diarrhea-predominant)
- Lactose intolerance
- Malabsorption: bacterial overgrowth; bile-salt deficiency; pancreatic insufficiency; small bowel diseases, such as celiac sprue, short bowel syndrome and Whipple's disease
- Mechanical factors: fecal impaction, post surgical syndromes
- Metabolic disorders: Addison's disease, diabetes, hyperthyroidism

Possible Underlying Causes of Chronic Diarrhea (cont'd)

- Tumors: colon cancer, endocrine tumors, such as carcinoid and gastrinoma, intestinal lymphoma, medullary carcinoma of the thyroid, pancreatic carcinoma, villous adenoma.

Drug-Induced Diarrhea

- Cancer chemo tx (5-FU, Irinotecan)
- Antimicrobials (*C. difficile*, osmotic or secretory diarrhea due to effects on carbohydrate and/or fatty acid metabolism, promotility effect) – incl. chemo drugs
- NSAIDs (3-9%)
- Quinidine, Quinine (8-30%)
- Misoprostol (14-40%)
- Colchicine (80%)
- Oral Gold (40-50%)

Drug-Induced Diarrhea (cont'd)

- Acarbose, miglitol (10-33%)
- Olsalazine (12-25%)
- Orlistat (60%+)
- Acetylcholinesterase inhibitors (up to 14%)
- Chenodeoxycholic Acid (40-50%)

Clinical Assessment of Degree of Dehydration

Feature	Mild	Moderate	Severe
Fluid deficit	< 5%	5-10%	> 10%
Thirst	Slight incr.	Moderate incr.	Great incr.
BP	NL	Decr. (postural only)	Low
Heart rate	Slight incr.	Moderate incr.	Great incr.
Mucous membranes	Moist	Dry	Parched
Urine output	Slight decr.	Moderate decr.	Almost 0

Important Questions to Ask a Patient with Diarrhea

- Character of the stool-small bowel or large bowel, steatorrhea
- Acute Diarrhea-contaminated food, contact with other sufferers, travel, antibiotics, anal-receptive intercourse, HIV risk factors
- Chronic Diarrhea-blood, mucous in stool; diet (dairy products, fat etc), alcohol, drugs, nocturnal diarrhea, associated sx (fever, malaise, wt loss, etc); arthritis, iritis, etc; mouth ulceration, stress, personal and family history.

Physician Evaluation Advised-Adults

- Symptoms of diarrhea exceed 48 h in duration
- Diarrhea is associated with severe abdominal or rectal pain
- Diarrhea is associated with a temperature $\geq 102^{\circ}$ F
- Blood or worms are present in the stool
- Signs and sx of dehydration are present, including dry mouth, excessive thirst, wrinkled skin, little or no urination, dizziness or lightheadedness

Physician Evaluation Advised-Children

- Presence of fever $\geq 100.5^{\circ}\text{F}$ in a child younger than six months of age or $\geq 102^{\circ}\text{F}$ in a child older than six months
- Diarrhea does not improve or continues for more than 24 h
- Vomiting or diarrhea increases
- Presence of blood in the stool
- The child is not drinking adequate amounts of fluid and has signs of dehydration, including dry mouth, excessive thirst, little or no urination, wrinkled skin, dizzy/lightheaded

Intestinal Infections

- Bacterial
- Viral
- Protozoal (parasites)
- Pseudomembranous colitis (*C. difficile*)

Common Enteric Pathogens

- Bacterial: *E. coli* (toxigenic, invasive), *Salmonella* species, *Campylobacter jejuni*, *Yersinia enterocolitica*, *Shigella* species, *Vibrio cholerae*, *Vibrio parahaemolyticus*,
- *C. difficile*
- Viral: *Rotavirus*, Norwalk-like virus
- Parasites: *Entamoeba histolytica*, *Giardia lamblia*, *Cryptosporidia*, *Strongyloides stercoralis*

Epidemiology

- World wide: second only to CV disease, leading cause of childhood death
- USA: > 10,000 deaths/year from diarrhea, 1.5-1.9 episodes/person/year
- Institutions: day-care centers, hospitals, LTCF-hospitals (2.3-7.0 episodes/100 admissions)
- Traveler's Diarrhea: > 50% attack rates over 2-3 wk stay, ***E. Coli* # 1, *Shigella*, *Salmonella*, *Cryptosporidium*, *C. jejuni***
- Food borne and waterborne outbreaks: > 12,000 cases/year in USA (probably 6.5 million!); parasites (*G. lamblia*, *E. histolytica*, *D. latum*, trichinella); **65% due to *Salmonella* (contaminated eggs)**

Summary of the Prevalence Studies of Enteric Pathogens in Patients with HIV Infection

Pathogen	Prevalence
<i>Microsporidia</i>	24-50
<i>Cryptosporidia</i>	10-38
<i>Mycobacterium avium</i> complex (MAC)	5-25
<i>C. difficile</i>	4-19
<i>Cytomegalovirus</i>	8-16
<i>Salmonella</i> species	2-6
<i>Campylobacter</i> species	1-5
<i>Shigella</i> species	1-2
<i>Isospora</i> species	0.2-2
<i>Cyclospora</i> species	Unknown

Pathophysiology of Bacterial Gastroenteritis

- Hygiene
- Gastric acid barrier
- Active and passive immunity (breast milk)
- Normal anaerobic flora
- Enterotoxins (induce intestinal fluid secretion, cytotoxic, neurotoxic)
- Cell invasion

Aspects of Patient History Suggestive of Infectious Diarrhea

- Travel to areas with substandard sanitation
- Exposure to farm animals
- Use of antibiotics
- Camping in desert or mountain areas
- Illness in family or friends

Overview of Therapy of Bacterial Gastroenteritis

- Replacement of lost fluid and electrolytes:
ORS, IV
- Specific antimicrobial therapy for symptomatic patients with inflammatory or parasitic diarrheas-positive fecal leukocytes
 - E. coli* (not 0157)
 - Shigella* and *Salmonella* species
 - C. jejuni*

Treatment of Specific Bacterial GI Pathogens

- *E. coli* 0157 – do not give antibiotics!!! (promotes verocytotoxin release leading to Hemolytic Uremic Syndrome) (TMP/SMX and quinolones esp. bad)
- *E. histolytica* –
 - Metronidazole 750 mg tid x 5-10 d + iodoquinol 650 mg tid x 20 d or paromomycin 500 mg tid x 7 d
- *G. lamblia*
 - Metronidazole 250-750 mg tid x 7-10 d
 - Boil water/filters

Treatment of Specific Bacterial GI Pathogens (cont'd)

- *C. difficile* –
Metronidazole 250 mg qid or 500 mg tid x 10-14 d (DOC) or
Vancomycin 125 mg qid x 10-14 d
- Recurrent *C. difficile* –
 - 1st relapse – repeat initial regimen
 - 2nd relapse – Incr. dose and/or duration, decr. dose scheme over 6 wk., bacitracin, rifampin 300 mg bid or rifiximin 200 mg tid plus metro or vanco, add probiotic
(*S. boulardii* or *Lactobacillus GG*)
Antimotility drugs may be OK but always with concurrent anti-CD therapy

Prophylaxis and Therapy of Traveler's Diarrhea

Prophylaxis

- Benefits > risks for non pharmacologic (food and water precautions – “boil it, cook it, peel it or forget it”) – no RCTs
- Bi subsalicylate q.i.d. (65% effective)
- Do not use antimicrobials (exceptions: next two slides)
- Begin 1st day in country, cont. for 1-2 days after leaving (3 week max)

Predisposing Factors and Host Factors that Increase Susceptibility to Traveler's Diarrhea or Complicate its Course

Epidemiologic Factors:

- Residence in a highly industrialized region
- No travel to a tropical area in the past 6 mo
- “Adventure” travel, living close to local residents, with recurrent exposure to food and water, and food in unhygienic surroundings
- Higher socioeconomic status
- Lack of adherence to strict principles in selecting food and drink

Predisposing Factors and Host Factors that Increase Susceptibility to Traveler's Diarrhea or Complicate its Course (cont'd)

Host Factors

- Young age (< 6 yr)
- Reduced gastric acidity
- Chronic and active GI disease
- Immunodeficiency disorders

Antimicrobial Prophylaxis in Traveler's Diarrhea (Adults)

- Levofloxacin or ciprofloxacin 500 mg qd (80% effective)
- rifiximin 200 mg bid (72-77% effective)*
- *Lactobacillus GG* (2×10^9 bact./day in 1 daily capsule) (40% effective but not elderly, debilitated, immunosuppressed)
- ? TMP/SMX (resistance) or probiotics in children

Treatment

- Fluoroquinolone or rifiximin or azithromycin if diarrhea occurs (in absence of bloody stools, high fever, severe abdo. pain)
- Antimotility agent (loperamide) – use with caution, although combo with antimicrobial works better than individual drugs – never use alone – start as early as possible (no effect post-48 hr.)

Treatment (cont'd)

Regimens include:

- Ciprofloxacin 500 mg bid or 750 mg qd or levoflox 500 mg qd or rifiximin 200 mg tid, all for 3 days (don't use latter in invasive disease!)
- Pregnancy — Use azithromycin 1 g x 1 dose or 500 mg qd x 3d
- Children — Use azithromycin 10 mg/kg on day 1 then 5 mg/kg on days 2 and 3
- FQ/rifiximin failures — Use azithromycin as above (3 d regimen)
- If symptoms persist, see med. personnel

Home-made ORS (adult)

- Combine 1 qt water, $\frac{3}{4}$ tsp table salt substitute (KCl), $\frac{1}{2}$ tsp baking soda, 2 tbsp white corn syrup, 1 pkt. unsweetened powdered drink mix (Kool-Aid) or desired amt. fruit juice concentrate
- chill slightly, frequent sips, 2 qt./day

"Beware the Medicinal Elixir"

- Sorbitol in "sugar-free" liquid medicines
- Theophylline, acetaminophen, codeine, INH, Li, vitamin, cough syrups

OTC Antidiarrheals

- Polycarbophil
- Attapulgite
- Loperamide
- Opiate combos
- Kaolin+pectin
- Bi subsalicylate
- Watch DI

Diarrhea in Pregnancy

- Low risk-adsorbents, pens, macrolides (eg. azi)
- Moderate risk-loperamide
- High risk-diphenoxylate (teratogen 1st trimester), Pepto-Bismol (ASA), anticholinergics, metronidazole, quinolones, sulfonamides, tetracyclines

"Probiotics"

- Live microorganisms/microbial mixtures → improve microbial balance, esp. GI/vagina
- Saccharomyces boulardii (yeast), Lactobacillus rhamnosus, strain GG or reuteri DSM 12246 (bacteria) and "Activia" (mixture of 3 probiotic organisms)

"Probiotics" (cont'd)

Uses:

- Prevent non-*C. difficile* Abx-assoc. diarrhea (peds > adults) (SB, GG, Activia)
- Prevent *C. difficile* diarrhea (Activia) (adults) (only 1 study)
- Prevent recurrent *C. difficile* (adults) (SB, GG)
- Use *S. boulardii* 1 g/d in adults, Lactobacillus GG $1-2 \times 10^{10}$ CFU/d in peds/adults, 1 bottle daily of Activia in adults for maximum of 3 wks.
- e.g. Culturelle, Florastor, Lactinex (H-), Probiotica, Primacidophilus, Activia
