



# Chronic Diarrhea

Karen L. Herbst MD, PhD  
University of Washington



# Diarrhea: Definition

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Increase in the frequency and fluid volume of the bowel movement.

In the USA, the mean daily weight of stool is 100-250 grams (g)

Most patients with diarrhea will produce in excess of 250 g of stool a day

Patients with secretory forms of diarrhea or small bowel malabsorption may pass 1000-5000 g/day of stool



# Mechanisms of Diarrhea

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- 1) Osmotic load within the intestine resulting in retention of water within the lumen
- 2) Excessive secretion of electrolytes and water into the intestinal lumen
- 3) Exudation of fluid and protein from the intestinal mucosa
- 4) Altered intestinal motility resulting in rapid transit through the colon



# Osmotic Diarrhea

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- Occurs when poorly absorbed material retains fluid within the intestinal lumen
- Occurs in patients with malabsorption or lactose intolerance in which undigested sugars accumulate in the intestinal lumen exerting a considerable osmotic load
- Magnesium-containing laxatives and antacids (Maalox) probably produce diarrhea through a similar mechanism

# Secretory Diarrhea

- The intestinal mucosa secretes  $\uparrow$  amounts of water and electrolytes under the stimulation of a variety of substances
- Cholera and enterotoxigenic E. coli
- Bile acids and long chain fatty acids (postileal resection, Crohn's disease, malabsorption syndromes)
- Gastrointestinal hormones (VIPoma, gastrinoma, carcinoid) – treat with octreotide, somatostatin analogue
- Anthraquinone laxatives
- Mechanism: Agents  $\uparrow$  intracellular cAMP  $\rightarrow$   $\uparrow$  secretion ( $\text{Na}^+\text{K}^+$  ATPase is also inhibited)



# Exudative Diarrhea

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- Results from the outpouring of blood protein, or mucus from an inflamed or ulcerated mucosa
- Ulcerative colitis
- Crohn's disease
- Invasive infections
- Infiltrative disorders like Whipple's disease
- Lymphoma



# Motility Disorders

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- May or may not lead to diarrhea
- Irritable bowel syndrome (IBS) – a motor disorder that causes abdominal pain and altered bowel habits with diarrhea predominating
- Diabetes mellitus – neurogenic dysfunction
- Scleroderma – stasis of the bowel with resultant bacterial overgrowth, steatorrhea and diarrhea



# Evaluation of Chronic Diarrhea

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- History
- Physical Exam
- Endoscopy
- Laboratory studies
- Radiological studies
- Other studies



# Evaluation of Chronic Diarrhea

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- Acute diarrhea – lasts longer than 3-4 days
- Chronic diarrhea – lasts longer than 2 weeks
  
- The approach to patients with acute or chronic diarrhea is very much the same
- It is not always possible to identify one particular mechanism to account for diarrhea in a given patient



# History of Irritable Bowel Syndrome

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- Diarrhea dates back many months or years
- No weight loss, anemia, hypoalbuminemia
- Several watery (at times explosive) bowel movements (BM) early in the morning
- No BM the rest of the day; rare nocturnal
- Stool output often <200g/day, rare >500g/day
- Mucus frequent
- Postprandial pain is a feature
- Symptoms wax and wane
- Stress exacerbates the symptoms



# History of Laxative Abuse

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- Healthy patients with large volume diarrhea
- Suspect if melanosis coli is present on proctoscopic examination



# History of Organic Disease

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- 1) Malabsorption – large volume of frothy malodorous stool without blood suggests small bowel diarrhea
- 2) Ulcerative colitis – frequent passage of small volumes of poorly formed bloody stools suggests inflammatory, exudative disorders of the colon
- 3) Pancreatic insufficiency – fat droplets suggests malabsorption



# History of Organic Disease (continued)

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- 4) Floating stools and undigested food are not helpful as they may be seen in functional and organic diarrhea
- 5) The association of diarrhea with milk or hyperosmolar solutions may not be recognized by the patient
- 6) Detailed drug history is important



# Drugs Causing Diarrhea

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- Antibiotics
  - ✓ Clindamycin
  - ✓ Ampicillin
  - ✓ cephalosporins
- Antacids + Mg<sup>++</sup>
- Anti-HTN Agents
  - ✓ Propranolol
  - ✓ Methyldopa
  - ✓ Hydralazine
- Antimetabolites
- CV Agents
  - ✓ digitalis
- Alcohol
- Nutritional Supplements
- Potent Diuretics
  - ✓ Furosemide
  - ✓ Bumetanide



# History of Organic Disease (continued)

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- 7) Arthritis and arthralgias may suggest inflammatory bowel disease, Whipple's disease, Reiter's syndrome
- 8) Weight loss suggests malabsorption, hyperthyroidism or a malignant tumor



# Diarrhea and Abdominal Pain

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- 1) Suggests IBS if pain is in the left lower quadrant or suprapubic region
- 2) Suggests a disease of the small bowel (e.g., Crohn's disease) if the pain is periumbilical or in right lower quadrant
- 3) Gastrinoma (Zollinger-Ellison Syndrome) – peptic ulcers responsible for upper abdominal pain



# Physical Exam

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- General: Weight loss
- Vital signs: Postural hypotension in diabetes with autonomic dysfunction
- Neurology:
  - Peripheral neuropathy 2° to vitamin B deficiency
  - Carpopedal spasm 2° to hypocalcemia
- Skin:
  - Erythema nodosum and pyoderma gangrenosum in inflammatory bowel disease
  - Hyperpigmentation in Whipple's and Addison's disease



# Physical Exam (continued)

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- Musculoskeletal:
  - Non-deforming arthritis - Whipple's disease/IBD
- Abdominal:
  - Hepatosplenomegaly and lymphadenopathy suggest lymphoma or Whipple's disease
  - Arterial bruit or an aortic aneurysm suggests ischemic bowel disease
- Rectal:
  - Perianal disease (e.g., abscess, fistula 2° Crohn's disease)
  - Rectal tumor
  - Fecal impaction



# Endoscopy

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- Perform during the initial visit without a cleansing enema
- Melanosis coli (spotty or diffuse brownish mucosal pigmentation) - laxative abuse
- Obtain stool specimens for microscopic evaluation and culture – leukocytes, blood, fat (Sudan stain), parasites, stool cultures
- Gonococcal proctitis appears similar to ulcerative proctitis and requires direct plating on warm Thayer-Martin medium with prompt incubation



# Laboratory Studies

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Should be selected to support the clinical impression but rarely are able to make or exclude a specific diagnosis



# Radiological Studies

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- Barium enema or Colonoscopy:
  - Blood is a clear indication for either study
  - Patient >40 years with recurrent/chronic diarrhea
  - Not as helpful in the younger patient
  - If IBD is suspected, contrast material should be refluxed into the terminal ileum to rule out Crohn's disease of the terminal ileum
  - A barium enema will interfere with the collection of stool for measurement of volume and fat and with the detection of parasites
  - Delay barium enema for one week after intestinal biopsy to avoid perforation



# 72-Hour Stool Collection

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- Collect all stool in a pre-weighed container for 72 hours; can use a “hat” placed inside the toilet – look for high volume
- Employ early in the workup when initial diagnosis not evident
- Perform before invasive tests or barium studies
- Measure fecal fat

# 72-Hour Stool Collection (continued)

- Measure osmolality and electrolyte concentration
  - Osmotic diarrhea - the measured fecal osmolality is  $> 2X$  the sum of the concentration of fecal  $\text{Na}^+$  and  $\text{K}^+$  because of the presence of unmeasured osmotically active substances
  - Secretory diarrhea – the calculated and measured osmolality are the same
- Fasting (npo) for 48 hours does not change the volume in secretory diarrhea but does  $\downarrow$  volume in osmotic diarrhea



# Radiological Studies (continued)

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- Abdominal plain film
  - Pancreatic calcifications (chronic pancreatitis)
  - Dilated small bowel
  - Abnormal bowel contour suggesting lymphoma or inflammatory bowel disease
- Small bowel series:
  - Distinguishes mucosal disease (celiac sprue), inflammatory conditions (Crohn's disease) and infiltrative processes (Whipple's disease or amyloidosis)
  - Clarifies anatomy in post-surgical patients
  - Detects localized areas of dilation and stasis



# Evaluation of Malabsorption When Steatorrhea is Present

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- <7% of fat is secreted into the stool per day (4-7g on average American diet containing 60-100g fat)
- Causes of steatorrhea:
  - Small intestinal disease
  - Pancreatic disease
  - Hepatobiliary disease
  - Gastric disease



# Evaluation of Malabsorption

## D-Xylose Test

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- Measures absorptive capacity of proximal small bowel
- Distinguishes malabsorption from maldigestion
- Does not require pancreatic enzymes to be absorbed by an intact small bowel mucosa
- Enters the blood and is excreted in urine
- Give 25g D-Xylose; collect urine for 5 hours
- Collect blood one hour after ingestion



## D-Xylose Test (continued)

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- If test abnormal – small bowel biopsy
- Celiac or Whipple's disease – xylose is poorly absorbed with low levels in blood and urine
- Massive bacterial overgrowth – abnormal xylose test may revert to normal after antibiotics
- Dehydration, renal insufficiency, third spacing of fluid, vomiting, hypothyroidism all ↓urine but not serum levels of D-xylose



## D-Xylose Test (continued)

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- If xylose test normal, maldigestion likely due to pancreatic insufficiency
- Pancreatic insufficiency can be confirmed by intubation of the duodenum and collection of intraluminal contents by gastroenterology laboratory
- Bentiramide test – utilizes a non-absorbable synthetic peptide, cleaved by pancreatic enzymes and measured in the urine
- Treat pancreatic insufficiency empirically with pancreatic enzymes (Viokase or Pancrease)



# Evaluation of Malabsorption: Small Bowel Suction Biopsy

- Performed in ambulatory setting
- Topical anesthetic sprayed in pharynx
- Sedation (Valium or Versed IV)
- Pass a small caliber tube by mouth to duodenal-jejunal junction
- Complications – perforation, bleeding
- Disorder's diagnosed by small bowel biopsy:
  - Whipples' disease
  - Intestinal lymphoma
  - Lymphangiectasia
  - Eosinophilic gastroenteritis
  - Sprue
  - Giardiasis
  - Amyloidosis



# Evaluation of Malabsorption: Disorders of the Terminal Ileum

- Schilling test – measures vitamin B<sub>12</sub> absorption which may be impaired despite the presence of intrinsic factor or antibiotics
- Bile salt breath test – measures orally ingested (<sup>14</sup>C)bile salt absorption. If terminal ileum abnormal, bile acid is not absorbed across the terminal ileum, bacteria in colon deconjugate it and <sup>14</sup>CO<sub>2</sub> diffuses across the colon and is excreted in the breath so the level of <sup>14</sup>CO<sub>2</sub> in expired air is abnormally high



# Lactose Intolerance

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- Deficiency/absence of the enzyme lactase in the brush border of the intestinal mucosa → maldigestion and malabsorption of lactose
- Unabsorbed lactose draws water in the intestinal lumen
- In the colon, lactose is metabolized by bacteria to organic acid,  $\text{CO}_2$  and  $\text{H}_2$ ; acid is an irritant and exerts an osmotic effect
- Causes diarrhea, gaseousness, bloating and abdominal cramps



# Lactose Intolerance (continued)

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- Inherited or acquired
- Isolated lactase deficiency is most common in African Americans (50-80% prevalence) and in Asians (75-100% prevalence); 10-20% whites in the US
- Onset of genetic disease is unpredictable and may not occur until adult life
- Small amounts of lactose may produce symptoms in some while ingestion of large amounts may not affect others



# Lactose Intolerance (continued)

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- Lactose tolerance test – measures changes in the concentration of serum glucose at 1 and 2 hours after ingestion of 50g lactose; rise in glucose of 20mg/100ml above fasting is normal; 30% false positive rate
- Hydrogen breath test – easy to perform, more accurate. Unabsorbed lactose is fermented by colonic bacteria and the resultant hydrogen is absorbed and released in the breath where substantial levels are recorded. Requires 2-4 hours in ambulatory setting



# Lactose Intolerance (continued)

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- A 3-week trial of a diet that is free of milk and milk products is a satisfactory trial to diagnose lactose intolerance
- Foods to be avoided – milk products, sausage, creamed or breaded meat, instant hot cereal, prepared bread mixes, soups, cakes, cookies, puddings, canned or frozen fruit prepared with lactose, gravy, caramels, molasses, instant coffee (Folgers okay)



# Fecal Impaction

- At risk - elderly, sedentary or bedridden
- Feces impacted in rectum or rectosigmoid region
- Leaking of colonic fluid around impaction results in frequent, small-volume, watery bowel movements
- Symptoms: rectal fullness, abdominal pain, nausea, headache
- Complications - recurrent UTI from ureter compression, urinary incontinence, intestinal obstruction, perforation of the colon, local ulceration (stercoral ulcer)
- Manual disimpaction best, then enemas
- Prevention - increase fiber, drink > liter of fluid a day, obey urge to defecate, exercise



# Inflammatory Bowel Disease: Ulcerative Colitis

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- A chronic inflammatory disorder of the colonic and rectal mucosa
- Etiology unknown
- Teenagers and young adult at onset; men have 2<sup>nd</sup> peak later in life
- Symptoms: occasional rectal bleeding without diarrhea (50%) to profuse, prurulent and bloody diarrhea with rectal urgency and tenesmus



## Ulcerative Colitis (continued)

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- Severity of initial presentation and extent are useful predictors of the disease course
- 60% mild disease (<4 BM/day, no fever, weight loss, ↓ albumin; colitis usually limited to the rectosigmoid or descending colon)
- 25% moderate disease with bloody diarrhea and crampy abdominal pain
- 10-15% have severe pancolitis, fever, fatigue, weight loss
- 1% present initially with fulminant colitis



# Ulcerative Colitis (continued)

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- Clinical course characterized by periodic exacerbations
- Plain films may demonstrate dilated bowel (“toxic megacolon”)
- Mortality is high in patient’s with severe colitis in which symptoms suddenly worsen
- No specific test or histopathology
- Diagnosis depends on the constellation of symptoms, natural history, endoscopic and histologic appearance of the colonic mucosa and exclusion of other inflammatory disorders

# Ulcerative Colitis (continued)

- Must differentiate acute presentations from other disorders:
  - Bacterial diarrheas – salmonella, campylobacter, yersinia, E.coli O:157:H7, TB, syphilis, chlamydia, amebiasis, C. difficile colitis, CMV or HSV
  - Irritable bowel, lactose intolerance
  - Crohn's disease
  - Ischemic colitis (presents with acute abdominal pain and the passage of bloody stool; disease of middle-age or older with atherosclerosis BUT watch for young woman on OCP)



# Ulcerative Colitis Cancer Risk

- Colorectal cancer risk is  $\uparrow$  5-10X
- Incidence of cancer development is 1%/year
- Common in rectum or rectosigmoid
- Major risk factors:
  - Duration of disease ( $\uparrow$  after 8-10 years)
  - Extent of involvement – no  $\uparrow$  risk with ulcerative proctitis only
  - Age < 25 years
- Yearly evaluations by colonoscopy after 8-10 years of disease
- Colectomy for definite dysplasia



# Ulcerative Colitis

## Extraintestinal Manifestations

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- 1) Improve after treatment:
  - Pyoderma gangrenosum
  - Erythema Nodosum
  - Rheumatoid factor (-) arthritis
- 2) Don't improve after treatment:
  - Ankylosing spondylitis
  - Primary sclerosing cholangitis (5-10%)
  - Uveitis
- 3) Progress independent of colitis
- 4) Occurs in young men < 40 years old
- 5) Insidious with weight loss, pruritis, jaundice



# Ulcerative Colitis Treatment

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## 1) Sulfasalazine (Azulfidine)

- Mild attacks
- Limited value in acute attacks
- Reduces frequency of exacerbations and allows ↓ steroid dosage
- Only works in the colon

## 2) Steroids

- Acute exacerbations
- Not helpful in preventing relapses
- Minority need continuous therapy

# Ulcerative Colitis Treatment

## 3) Mild-moderate, distal (<4BM/day, nl ESR)

- Topical

- Mesalamine suppositories BID – proctitis
- Mesalamine enemas BID - distal colitis
- Steroid enemas QHS – acute disease

- Oral

- Sulfasalazine 4-6g/day                      divided QID
- Mesalamine 2-4g/day                        divided BID

Distal = distal to the splenic flexure

# Ulcerative Colitis Treatment

## 4) Mild-moderate, extensive

- Oral only:
  - Sulfasalazine      4-6g/day      divided QID
  - Mesalamine      4-8g/day      divided QID
- If ineffective:
  - Prednisone      not useful for  
maintaining remission
- If ineffective:
  - 6-MP or Azathioprine



# Ulcerative Colitis Treatment

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- 5) Severe Colitis - >6 bloody BM/day,  
↑ESR
- IV prednisone for 7-10 days
  - If ineffective:
    - Colectomy (40%)
    - ?IV cyclosporine 4mg/kg/day



# Ulcerative Colitis Treatment

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## 6) Surgery

- Curative
- Proctocolectomy and ileostomy with stomal appliance
- Koch pouch (continent ileostomy) avoids need for stomal appliance
- Park's procedure – internal pouch from a loop of bowel anastomosed to the anus



# Crohn's Disease

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- Teenagers at onset; rare in elderly
- Common in Caucasians and Jewish; ↑ among Blacks; family incidence 10-30%
- Pathophysiology: Focal, asymmetric “skip” lesions of mucosal inflammation; granulomas not always present; superficial or transmural with fistulas and fissures
- Any part of the alimentary tract affected:
  - Ileocolitis 45%
  - Ileitis 15-35%
  - Colitis 15-30%
  - Oral/gastric rare, isolated



# Crohn's Disease (continued)

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- Presentation
  - Variable and vague
  - Bleeding in only 50%
  - Chronic or nocturnal diarrhea
  - Abdominal pain
  - Anorexia
  - Weight loss, fever
  - Recurrent aphthous ulcers
  - Malabsorption



# Crohn's Disease (continued)

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- Physical Exam
  - Pallor
  - Cachexia
  - Clubbing
  - Abdominal mass
  - Obstruction
  - Perianal disease
  - Extraintestinal manifestations
- Differential diagnosis similar to UC



# Crohn's Disease: Diagnosis

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- 1) Rule out infectious cause: ova and parasites, c.difficile toxin, enteric pathogens; consider amebic serology
- 2) Obtain tissue pathology: biopsy by endoscopy
- 3) Determine extent of disease: If endoscopy insufficient, consider barium, SBFT



# Crohn's Disease (continued)

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- Exacerbants
  - Infections (upper respiratory or enteric)
  - Cigarettes
  - NSAIDS (induction of initial disease or worsening of present)
  - Stress?

# Crohn's Disease (continued)

- Extraintestinal Manifestations:
  - Eyes – uveitis, scleroconjunctivitis (10%)
  - Heme – hypercoagulability, anemia
  - Liver – cholelithiasis (13-34%), sclerosing cholangitis (rare), chronic active hepatitis
  - Rheum –
    - ankylosing spondylitis, sacroiliitis, non-destructive peripheral synovitis (20%)
    - Metabolic bone disease due to  $\downarrow\text{Ca}^{++}$ ,  $\downarrow\text{Vit D}$  (69%), or exogenous steroids
    - Pyoderma gangrenosum, erythema nodosum 10-15% (80% of time with arthropathy)

# Crohn's Disease: Treatment

- 1) Mild-moderate – symptomatic, working, no signs of toxicity
  - Sulfasalazine 3-6g daily
  - 2<sup>nd</sup> line: Mesalamine 3.2-4.8 g daily \$\$
  - Metronidazole 10-20mg/kg daily
  - Gastric location – Omeprazole Beneficial?



# Crohn's Disease: Treatment

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- 2) Moderate – severe: failed therapy, fevers, 10% weight loss, n/v
  - Rule out infection and abscess (CT?)
  - Prednisone 0.5mg/kg with rapid taper to 20mg, then slow over 1-2 months (50% become steroid resistant/dependent)
  - For extensive disease add 6-mercaptopurine or azathioprine
  - Consider surgery for limited disease



# Crohn's Disease: Treatment

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- 3) Severe - fulminant: high fever, vomiting, obstruction
- Inpatient admission with surgery consult
  - U/S or CT
  - 40mg IV prednisone
  - TPN if npo for >7days
  - NG tube to decompress, IV antibiotics if inflammatory mass present, drain abscess if necessary
  - In over 2/3 patients, surgery will eventually be required. 1/3-1/2 require a second surgery.



# Crohn's Disease: Treatment

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- 4) Perianal disease – metronidazole alone
- 5) Maintenance:
  - Mesalamine
  - Do not use steroids or sulfasalazine
  - Azathioprine 2.5mg/kg – 3-6 months for benefit
  - 6MP 1.5mg/kg – CBC weekly, then every 3 months
- 6) 20% colonized by *Clostridium difficile*; check toxin, not culture



# Crohn's Disease: Prognosis

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- In Copenhagen study, all patients relapsed at 10 years
- 75% will be in remission at 1 year with treatment
- 15-20% will have devastating disease
- Life expectancy is reduced somewhat, particularly in the first years after diagnosis
- Complications:
  - Small bowel – obstruction, malabsorption
  - Ileocolonic – fistulas and abscesses
  - Colonic: toxic megacolon



# Antibiotic-Induced Diarrhea

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- Range from a mild ↑ frequency and volume to toxic, life threatening
- May develop during the course of antibiotics or up to 3 weeks after discontinuation!!
- Ampicillin, tetracycline, clindamycin, cephalosporins
- Clinical Pearl: MOST antibiotics



# *Clostridium difficile* colitis

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- Bloody diarrhea
- Abdominal cramps
- Endoscopy reveals pseudomembranes = raised, yellowish plaques on edematous, friable mucosa. Collections of fibrin, mucin, leukocytes.
- Due to *Clostridium difficile* and its toxin



# *Clostridium difficile* colitis

- Diagnosis: The toxin can be assayed in the stool and is more sensitive than cultures which are difficult to grow
- Therapy:
  - Discontinue antibiotics
  - Bismuth subsalicylate while awaiting toxin results
  - Metronidazole (Flagyl) 500mg QID 7 days
  - Relapses have been reported → vancomycin 125-500mg QID 7 days
- *C. difficile* (+) toxin stools in nursing home residents without symptoms do not need to be treated



# Postsurgical Diarrhea

- 1) Short bowel syndrome – diarrhea after extensive small bowel resections
  - Limited ileal resection (<100cm)
    - Sufficient bile acid pool - no steatorrhea
    - Diarrhea from bile acids delivered to the colon
    - Bind bile acids with Cholestyramine 4g QID
  - Extensive ileal resection (>100cm)
    - Steatorrhea
    - Do not use cholestyramine – depletes bile acids
    - Treat: medium chain triglycerides (Portagen)



# Postsurgical Diarrhea (cont)

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## 2) Gastric surgery with vagotomy

- Altered intestinal motility
- Increases concentration of fecal bile acids
- May unmask latent lactase deficiency
- May unmask celiac disease (rare)
- Blind loop syndrome with bacterial overgrowth
- Gastrocolic fistula
- Therapy with cholestyramine has been successful



# Postsurgical Diarrhea (cont)

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## 3) Cholecystectomy

- Increased fecal bile acids
- Cholestyramine effective

## 4) Subtotal colectomy with ileal-rectal anastomosis (for multiple polyposis)

- Diminishes with time
- Treated with antidiarrheal medications



# Symptomatic Antidiarrheal Therapy

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Avoid with acute infectious diarrhea since suppression of BM prolongs the course

- 1) Hydrophilic bulk-forming agents – psyllium (Metamucil, Konsyl)
  - Improve consistency of ileostomy and colostomy effluent
  - Useful in constipation
  - Useful in irritable bowel syndrome



# Symptomatic Antidiarrheal Therapy

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- 2) Adsorbents – adsorb factors in the intestinal lumen causing diarrhea
- Kaolin and pectin (Kaopectate)
  - Bismuth salts (Pepto-Bismol) – useful for traveler's diarrhea
  - Aluminum hydroxide (Amphogel)
  - Cholestyramine (Questran) – treats bile-acid diarrhea after ileal resection, vagotomy or cholecystectomy; **CAUTION:** binds digoxin, warfarin and levothyroxine, etc. ↓ absorption

# Symptomatic Antidiarrheal Therapy

- 3) Opioid derivatives – most effective antidiarrheal medication
- Delay transit of intraluminal contents through the intestine
  - Tincture of opium 6 gtts every 4-6 hours
  - Codeine 15-30mg every 4-6 hours
  - Central effect cannot be excluded
  - Lomotil (diphenxylate-atropine)
  - Imodium (loperamide) – more favorable GI vs central effects and longer duration of action
  - Risk: megacolon, prolongation of symptoms, pseudomembranous colitis