Chronic Diarrhea

Objectives:

- To have an overview regarding chronic diarrhea:
- Definition - Pathophysiology - Classification - Approach
- To discuss common causes of chronic diarrhea:
- Celiac Disease - Whipple Disease - Tropical Sprue - Small Bowel Bacterial Overgrowth
- Exocrine Pancreatic Insufficiency - Bile Salt-Induced Diarrhea

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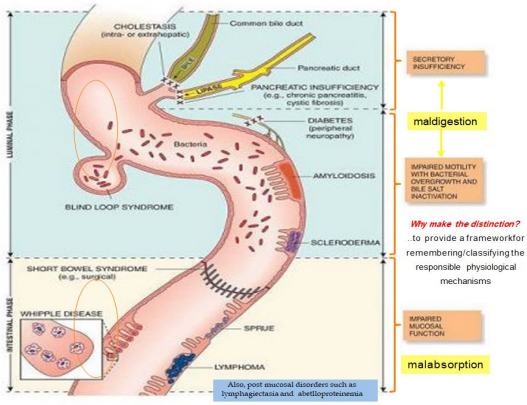
Resources: 436 slides, 435 team, Davidson, kumar & Recall questions step up to medicine.

- Editing file
- Feedback

Introduction

★ If you don't have time to study this lecture, click here

Definitions:



- Diarrhea: >100-200

  organic causes of diarrhea have to be distinguished from **functional causes** (Frequent passage of small volume of stools with stool weights < 250g) Exception distal colon cancer and proctitis are organic causes that present with stool frequency and normal stool volume

  First of all any patient presents with diarrhea you have to **exclude Infection**! By stool cultures and flexible sigmoidoscopy with colonic biopsy if symptoms persist and no diagnosis has been made.

  - **Acute**: common and usually transient, self-limited, Infection related.
  - **Chronic**: A decrease in fecal consistency lasting for 4 weeks or more, usually requires work up,
- Maldigestion; inadequate breakdown of triglycerides.
- Digestion is converting large particles into small particles in the lumen.
- Malabsorption: inadequate mucosal transport of digestion products.
- Absorption is the transition of nutrients from the lumen to portal vein or lymphatic.
- **Fecal Osmotic Gap (FOG)=** 290 (plasma osmolality) − 2 X (stool **Na** + stool **K**) : to
  - ➔ FOG of >50 mosm/kg is suggestive of an **osmotic diarrhea** and a gap of >100 mosm/kg is more specific. (> 100 = osmotic)

Pathophysiology

Each day, 9–10 L of fluid enter the jejunum. You drink about 2-3 L , the remain litre from secretion.

Small intestine absorbs 90% of this fluid load.

- The colon absorbs 90% of the remaining load (about 900 ml/24 hours); leaving approximately 80–100 ml excreted each day in feces.
- A normal colon can compensate by absorbing up to 3000–4000 ml/24 hours

Most of absorption occurs is Small bowel → small bowel disease → large amount of diarrhea

Large bowel disease → small amount of diarrhea

Classification of Diarrhea

(According to Mechanism):

1.Watery:	**A- Osmotic**	**B- Secretory**
Overview	• **poorly absorbed substances** that is osmotically active **remain in the intestine and exert osmotic effect** > obligate retention of water within the lumen by virtue of their osmotic effects • there is actively osmotic agent (lactose)within lumen preventing water from being absorbed this agent will bind to water and increase water content in the stool → diarrhea	• Malabsorption or secretion of electrolytes and water • High stool output : Large volume (>1 L/d).
Effect of fasting One way of differentiating	• Fasting **improve** the condition	• **Lack of response** to fasting.
FOG	• **Fecal osmotic gap** (FOG) of > 50 mosm/kg is suggestive of an osmotic diarrhea and a gap of >100 mosm/kg is more specific (there is loss of hypotonic fluid)	• Low fecal osmotic gap: (loss of isotonic fluid). • Less than 50 mosm/kg
Causes	• **loss of nutrient transporter** (causes Malabsorption) e.g. lactase deficiency, lactose intolerance,celiac disease. • **Ingestion of poorly absorbed agents** (called Osmotic laxatives)eg. Magnesium ,Fructose,Mannitol, Sorbitol , Lactulose ,Phosphate , Sulfate, laxative abuse	**It has a broad DDX, including: ..** • **Infections:** The most common cause is a **bacterial toxin** e.g. (some types of E. coli , cholera) that stimulates the secretion of anions. If acute, may be caused by enteropathogenic virus e.g. (rotavirus and norwalk virus) • **Reduction of mucosal surface area by surgery or disease** bile salts and fatty acids in the colon will draw the water > Diarrhea • Absence of an ion-transport mechanism • Inflammation: Diverticulitis, Microscopic colitis • Dysregulation • **Circulating secretagogues (endocrinopathies)**, as in Addison's disease, Hyperthyroidism, Carcinoid syndrome, Pheochromocytoma, Gastrinoma, VIPoma, Somatostatinoma • Pancreatic Insufficiency

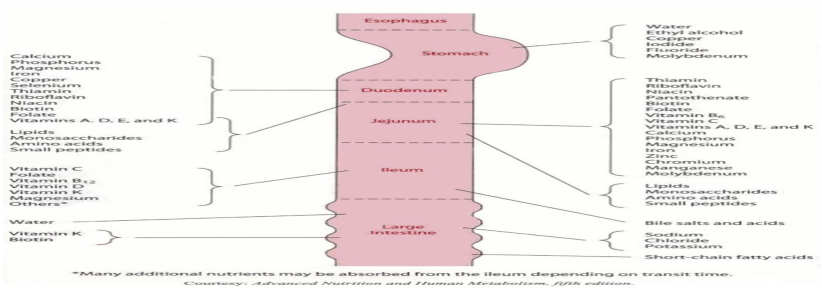
		• **Bile Acid-Induced Diarrhea:** Ileal bile acid malabsorption • Abnormal motility: DM-related dysfunction, IBS, Post-vagotomy diarrhea • Malignancy: Colon CA, Lymphoma, Rectal villous adenoma • Vasculitis • Congenital chloridorrhea • Idiopathic: Epidemic (Brainerd), Sporadic • Medications, stimulant laxative abuse, toxins • Connective tissue diseases (SLE)

2.Inflammatory (Exudative/Mucosal destruction)	• Presents as small volume diarrhea with Blood, mucus, and pus, with abdominal pain and fever. • Positive fecal leukocytes, gross or occult blood, ESR/CRP, leukocytosis , Persists on fasting. **Causes/DDx:** ❖ Inflammatory bowel disease: Ulcerative colitis, Crohn's disease, Diverticulitis, Ulcerative jejunoileitis ❖ Infectious diseases: 1-Pseudomembranous colitis[1] (Clostridium difficile infection) 2-Invasive bacterial infections (e.g., some types of E. Coli, Shigella[2], TB, yersiniosis), 3-Ulcerating viral infections (e.g., cytomegalovirus, Herpes simplex), 4-Invasive parasitic infections (e.g., amebiasis, strongyloides) ❖ Ischemic colitis ❖ Radiation colitis ❖ Neoplasia: Colon cancer, Lymphoma
3. Fatty Diarrhea: (Steatorrhea)	• Present with Bloating, flatulence, greasy malodorous stools that can be difficult to flush, weight loss, s/s[3] of vitamin deficiencies (peripheral neuropathy, easy bruising), Anemia (because of vitamin E deficiency),coagulopathy(because of vitamin K deficiency), hypoalbuminemia, osteopenia (because of vitamin D deficiency). 1. **Malabsorption (inadequate mucosal transport of digestion products):** for absorption we need intac enterocyte and intact lymphatic lumen. Lymphomas of the small bowel causes it. ○ Mucosal diseases (eg, Celiac sprue, Whipple's disease) ○ Mesenteric ischemia ○ Structural disease: Short bowel syndrome, Post-resection diarrhea ○ Small bowel bacterial overgrowth (bile salt deconjugation) 2. **Maldigestion (inadequate breakdown of triglycerides):** We need bile salt and pancreatic lipase for digestion of fat. ○ Pancreatic exocrine insufficiency (chronic pancreatitis, ○ Inadequate luminal bile acid concentration (eg, advanced primary biliary cirrhosis)

[1] An antibiotic-induced colitis
[2] Shigella infections are mainly seen in young children.
[3] Signs and symptoms

Duodenum and jejunum	Ileum	Colon
Carbohydrates / simple sugars, Fats, Amino acids, Iron (iron need low PH to get absorbed), folate ,Fat-soluble vitamins (A, D, E, K), Calcium, Magnesium, Minerals and other vitamins	Vitamin B12, Bile salts and Magnesium	Short-chain fatty acids, Vitamin K (because vitamin K needs bacteria to get absorbed). and Biotin* * In part produced by bacterial gut flora

You expect abnormalities when resecting a certain part of the GI, for ex. Resecting terminal ileum with crohn's patients would cause deficiencies of vit. K or B12 (coagulopathy and megaloblastic anemia)

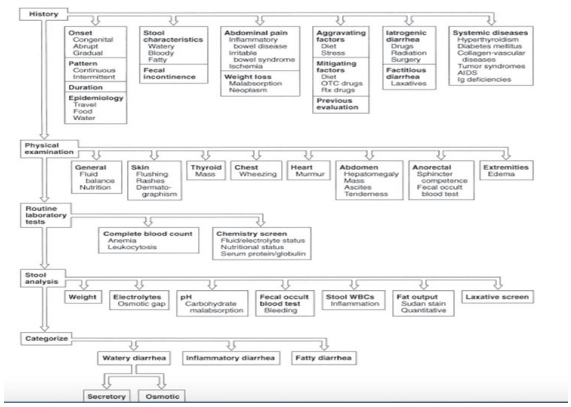


Common Medications and Toxins Associated with Diarrhea :

- **Acid-reducing agents (H2 blockers, PPIs)**
- **Magnesium-containing antacids**
- Anti-arrhythmics (eg, digitalis, quinidine)
- **Antibiotics**. (cause Irritation of colon or bowel, disruption of normal flora balance or C. difficile)
- Anti-neoplastic agents
- Antiretrovirals
- Beta blockers
- Colchicine
- Levothyroxine
- SSRIs
- Furosemide
- **Metformin**
- NSAIDs, ASA
- Prostaglandin analogs (ie, misoprostol)
- Theophylline
- Amphetamines
- **Caffeine**
- Alcohol
- Narcotic/opioid withdrawal (opioid cause constipation , so opioid withdrawal cause diarrhea)

Clinical approach to chronic diarrhea :

- **Epidemiology:**
  - Travel : for how long ? where ?
  - Water : from bottle or حنفية.
- **Fecal incontinence :** same amount but unable to hold it.
- Weight loss indicate malabsorption or malignancy.



Investigation

- **Culture** (more useful only for acute), O&P (ova and parasites), Giardia Ag, C diff toxin, Coccidia, Microsporidia, Cryptosporidiosis
- **Fecal leukocytes** (or marker for neutrophils: lactoferrin or calprotectin)
- **Fecal occult blood** (helpful in inflammatory diarrhea)
- **Stool electrolytes for osmolar gap** = 290 – 2[Na + K]
- **Stool pH** (<6 suggests CHO malabsorption due to colonic bacterial fermentation to CO2, H2, and short chain FA)
  lactase deficiency: patients cannot digest carbohydrate → bacteria will ferment it → produce acids → irritate perianal area. (common in children with diarrhea)
- **Fat content:** Quantitative: 48h or 72h collection of stool (how much fat in stool?)
- Qualitative: Sudan stain (to see there is fat or not ?)
  Laxative screen (if positive, repeat before approaching pt)
  (lactulose , magnesium, phosphate cause osmotic diarrhea)
- **Imaging:** Small bowel series, CT/MRI or CT/MR enterography (looking for malignancy, inflammation)
- **Endoscopy** with small bowel biopsy and aspirate for quantitative culture
- **Colonoscopy**, including random biopsies (looking for malignancy, inflammation)

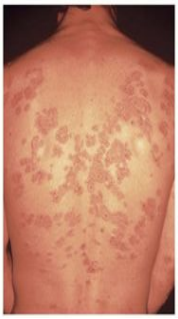
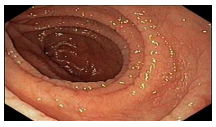
Clinical & Lab finding on malabsorption

Malabsorption of	Clinical features	Laboratory findings
Calories	Weight loss with normal appetite	-
Fat	Pale and voluminous stool, diarrhea without flatulence, steatorrhea	Stool fat > 6 g/day, low serum levels of triglycerides, cholesterol.
Protein	Edema, muscle atrophy, amenorrhea	Hypoalbuminemia, hypoproteinemia
Carbohydrates	Watery diarrhea, flatulence, milk intolerance.	Increased breath hydrogen, High stool osmotic gap, acidic stool (pH <6)
Vitamin B12	Macrocytic Anemia, peripheral neuropathy,Subacute combined degeneration of the spinal cord (early symptoms include paresthesias and ataxia associated with loss of vibration and position sense)	Vitamin B12 decreased, abnormal schilling test, serum methylmalonic acid and homocysteine increased. Macrocytic Anemia and hypersegmented neutrophils
Folic Acid	Anemia	Macrocytic Anemia and hypersegmented neutrophils, Serum and RBC folate decreased, serum homocysteine increased.
Vitamin B (general)	Cheilosis [4], painless glossitis, acrodermatitis, angular stomatitis Beriberi: nutritional disorder caused by a deficiency of thiamin (vitamin B1)	-
Iron	Anemia, glossitis, pagophagia[5]	Microcytic anemia, Serum iron and ferritin decreased, total iron binding capacity increased
Calcium and vit D	Paresthesia, tetany, pathologic fractures due to osteomalacia, positive Chvostek and Trousseau signs,	Hypocalcemia, serum alkaline phosphatase increased, abnormal bone densitometry
Vitamin A	Follicular hyperkeratosis, night blindness	Serum retinol decreased
Vitamin K	Hematoma, bleeding disorders Coagulopathy	Prolonged prothrombin time (PT) and elevated INR, decreased vitamin K-dependent coagulation factors (2,7,9,10)

Bloody, small amount, fever, high WBC, abdominal pain (inflammatory diarrhea)

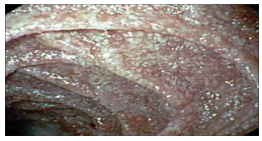
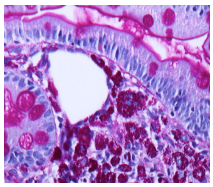
[4] Cheilosis is a painful inflammation and cracking of the corners of the mouth. It also is called cheilitis.
[5] Pagophagia is the compulsive consumption of ice or iced drinks.

Celiac Disease

Introduction	- Celiac disease is: Small intestinal malabsorption (usually duodenum and proximal jejunum)of nutrients following the ingestion of wheat gluten or related proteins from rye and barley. - Villous atrophy of the small intestinal mucosa is a characteristic but not specific - Strict adherence to a gluten free diet Prompts clinical and histologic improvement - Reintroducing gluten > Clinical and histologic relapse.
Pathophysiology	1. The disease affects the mucosa with marked variation > Loss of normal villous structure (flattening) > Intestinal crypts are elongated and open onto a flat absorptive surface. 2. Leaky mucosa with increased permeability due to structural changes of the tight junctions between damaged absorptive cells. 3. Marked increase in cellularity of the lamina propria (plasma cells & lymphocytes)
Who is at risk?	Type 1 DM (3-6%), Autoimmune thyroid disease (6-8%), Down's syndrome, Connective tissue disease and IgA deficiency (2-3%). Generally patients who have autoimmune diseases
Presentations	• Asymptomatic. • Nonspecific GI symptoms: • Nutritional deficiency: 3D (Diarrhea, Distension (Bloating) and Dyspepsia) • Fat soluble vitamin deficiencies: (enterocyte atrophy→ can not secrete secretin and cholecystokinin) -Vit A: poor night vision, follicular hyperkeratosis -Vit D: hypocalcemia, osteoporosis. -Vit K: easy bruising & bleeding, elevated INR. • Dermatitis herpetiformis (itchy rash at elbows,buttock,back. in biopsy you will see antibodies deposit in skin and improved with gluten free diet) • Elevated ALT & AST. (because of fatty liver) • **Malignancy (a complication) : small bowel T-cell lymphoma & Small bowel adenocarcinoma** , could be the first presentation 
Endoscopy	• Normal • **Loss of mucosal folds (Flattening of mucosa)** • **Scalloping of mucosa** • Ulcerations 
Histology	villous atrophy and crypts hyperplasia (duodenum is the 1st option for biopsy)
Serology	• Anti-tTG: Anti-tissue transglutaminase antibody (IgA) is the best marker: Sensitivity 95%; specificity 97.5% • IgG anti-gliadin antibodies (Can be used in IgA deficient patients): Sensitivity 69-85% (~75) Spec 73-90% (~80) not sensitive and not specific • IgA anti-gliadin antibodies, Sensitivity 75-90% (~80) Specificity 82-95% (~85) • Endomysial antibody (IgA), Sensitivity 85-98% (~93) Specificity 97-100% (~99)

Management	- Education - Gluten-free diet: avoid wheat, barley, rye & oat - Correct nutritional deficiencies (**Iron**, Ca, Vit D) - Anticipate complications: nutritional & malignancy (anemia and osteoporosis)
Notes	Celiac disease is an autoimmune disease vs. gluten intolerance (No microscopic abnormalities or antibodies are found) and the prognosis of the two diseases are not the same

Whipple Disease

Introduction	• Chronic systemic infection by Tropheryma whipplei. • Has GI, CNS, CVS, MSK & skin manifestations. patient with joints pain, myocarditis ,seizure diarrhea and CNS manifestations? Whipple disease!!!!!
Pathophysiology	Caused by bacterial and macrophage-predominant inflammatory cell infiltration of the small intestinal mucosa and obstruction of mesenteric lymph nodes.
Presentations	- Malabsorption – weight loss, diarrhea (watery or fatty) and abdominal pain. - CNS: Progressive dementia, Supranuclear ophthalmoplegia, Altered LOC (level of consciousness), Oculo-masticatory & oculo-facial skeletal dysfunction. - CVS: Endocarditis – MV most common, Myocarditis, Pericarditis. - MSK: Oligo or polyarthralgias - Skin (Common): Hyperpigmentation
Endoscopy	Whitish to yellow plaque-like patches in 75% of patients (representing lipid droplets and/or lymphangiectasia). Any cause of lymphatic obstruction (TB, Lymphoma and malignancy) will cause malabsorption and steatorrhea 
Histology	• **Foamy macrophages on routine H&E** • **Numerous PAS-positive granular particles (pink/purple appearing)** • Lysosomes filled with T. whipplei • **PAS-positive granular particles = Whipple disease** 
Management	• 2 weeks with Antibiotics to cross BBB: Ceftriaxone 2g IV daily monotherapy, or Penicillin G 2 MU IV q4h PLUS streptomycin… • THEN Septra DS tab BID x 1 year (Trimethoprim/sulfamethoxazole)

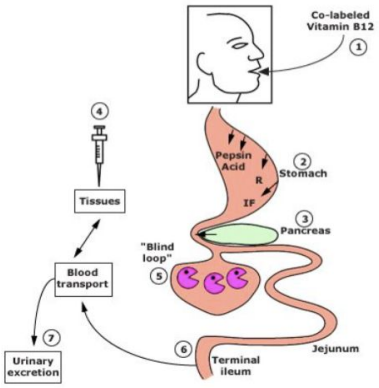
Small Bowel Bacterial Overgrowth (SBBO)

<table>
<tr><td>Normal Microbiome:</td><td colspan="2">1. Stomach 0-10^3 CFU/ml
2. Jejunum 0-10^4 CFU/ml:
Gram + aerobes (oral streptococci, lactobacillus); no gram –ve aerobes
3. Ileum 10^5-10^9 CFU/ml
4. Colon 10^{10}-10^{12} CFU/ml
Anaerobes: bacteroides, peptostreptococcus, lactobacillus, bifidobacterium, clostridium
Facultative aerobes: e. coli, enterococcus, staphylococcus</td></tr>
<tr><td rowspan="7">Normal barriers that prevent SBBO and their abnormalities</td><td>Mechanism to prevent SBBO</td><td>Possible causes of SBBO</td></tr>
<tr><td>Gastric acid & pancreatic enzymes</td><td>chronic pancreatitis, low HCl due to surgery or PPI (proton pump inhibitors)</td></tr>
<tr><td>Intact bowel structure</td><td>Surgery, diverticulum</td></tr>
<tr><td>Cleansing effect of bowel motility – interdigestive migrating motor complex</td><td>dysmotility</td></tr>
<tr><td>Gut immunity – intraluminal secretory IgA</td><td>Immunodeficiency</td></tr>
<tr><td>Competent ileocecal valve</td><td>scarring from inflammation, removal/injury by surgery</td></tr>
<tr><td>Competition by other bacteria</td><td>Antibiotics (broad spectrum antibiotics)</td></tr>
<tr><td>Effect of SBBO:</td><td colspan="2">• Bile acids metabolism – deconjugated bile acids
• Bilirubin metabolism – deconjugated bilirubin
• CHO metabolism – C02, H2, D-lactic acid, organic acids (short chain fatty acids)
• Lipid metabolism – short chain fatty acids
• Protein metabolism – amines, ammonia</td></tr>
<tr><td>Presentations</td><td colspan="2">• Bloating, diarrhea(steatorrhea), abdominal pain, weight loss, neuropathy
• B12 deficiency – utilized by bacteria for nutrition
• Elevated folate level - produced by bacteria
• Bacteria will produce folate and it will consume B12
• Vitamin A,D,E,K deficiency
• Iron deficiency
• Hypoproteinemia, hypoalbuminemia
• Fat and CHO malabsorption</td></tr>
<tr><td>Investigations</td><td colspan="2">• Jejunal aspirate and culture – gold standard
• C^{14}-labeled bile acid breath test.
• C^{14}-xylose breath test
• H breath test
• Schilling's test (Malabsorption of vitamin B12) See the next slide</td></tr>
</table>

Management	- Treat underlying cause e.g. discontinue acid suppressive meds, treat inflammatory Crohn's disease, remove strictures, etc… - Nutrition: replace fat soluble vitamins and B12, follow Low CHO diet to limit bacteria substrate - 7 – 10 days of antibiotics: Metronidazole, Amox/Clav, Tetracycline, Doxycycline, Amoxicillin (May need to cycle Abx to avoid resistance) - Bowel cleanse with PEG (Polyethylene glycol) نغسلها - Prokinetic to stimulate motility > bacterial cleansing - Octreotide – at low dose, has a promotility effect; (causes hypomotility at higher doses) - Probiotics – minimal evidence

The Schilling test:

- B12 deficiency is caused by multiple things, so the idea here is to exclude one by one.
- B12 metabolism: saliva (R factor binds B12) > stomach "IF" > duodenum (get exposed to pancreatic enzymes "trypsin" > trypsin releases R factor from B12 > then IF will bind B12 > terminal ileum > absorption.



Malabsorption of **vitamin B12** may occur as a consequence of:

- Deficiency of intrinsic factor (eg, pernicious anemia (improved with intrinsic factor), gastric resection)
- Pancreatic insufficiency (improved with pancreatic enzyme)
- Bacterial overgrowth (improved with antibiotic)
- Ileal resection or disease.

To distinguish between these causes of fat malabsorption, the Schilling test is performed on 4 stages,

Radiolabeled B12 is given orally, in each stage you'll add one of the following and then measure B12 absorption using a urine sample:

TABLE 350e-1 DIFFERENTIAL RESULTS OF THE SCHILLING TEST IN SEVERAL DISEASES ASSOCIATED WITH COBALAMIN MALABSORPTION

	^{58}Co-Labeled Cobalamin	With Intrinsic Factor	With Pancreatic Enzymes	After 5 Days of Antibiotics
Pernicious anemia	Reduced	Normal	Reduced	Reduced
Chronic pancreatitis	Reduced	Reduced	Normal	Reduced
Bacterial overgrowth	Reduced	Reduced	Reduced	Normal
Ileal disease	Reduced	Reduced	Reduced	Reduced

- Stage I: + IM vitamin B12[6] if B12 levels are normal then the cause of its deficiency was decreased intake
- Stage II: + intrinsic factor (IF) if B12 is normal after supplement of IF then the cause was pernicious anemia
- Stage III: + oral antibiotics if B12 is normal after Antibiotics then the cause was bacterial overgrowth
- Stage IV: + supplement of pancreatic enzymes if B12 is normal after supplement of pancreatic enzyme (trypsin) then the cause was pancreatic insufficiency

- if B12 is not normal after all of these stages the cause of deficiency might be ileal disease

Schilling Test - Stages 1 to 4 (mnemonic) 0:36 minutes - **read more**

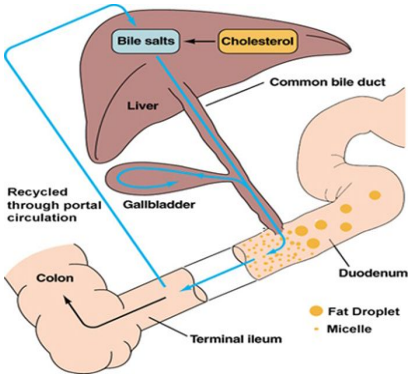
[6] This is not enough to replete or saturate body stores of B12. The purpose of the single injection is to temporarily saturate B12 receptors in the liver with enough normal vitamin B12 to prevent radioactive vitamin B12 binding in body tissues (especially in the liver), so that if absorbed from the G.I. tract, it will pass into the urine.

Tropical Sprue

Introduction	• Is characterized by villous atrophy and crypt hyperplasia BUT DUE TO INFECTIOUS CAUSE (celiac : autoimmune) • It is an acquired defect – not present in newborns. Travelers from the industrialized world to most tropical regions of Asia, Africa, the Middle East, the Caribbean and Central and South America may develop it. • Hx of travel to tropical area for long period
Cause	Not known, but seems to be due to continuous bacterial contamination of the upper small bowel and nutritional deficiency.
Presentations	• Chronic diarrhea often with steatorrhea, anorexia, abdominal cramps, bloating • **Both** B12 and folate deficiency
Investigations	If suspicion is high – jejunal aspirate and biopsy
Management	1) Folate & B12 Supplement 2) Tetracycline for 3-6 months.

Bile Acid-Induced Diarrhea

- Watery diarrhea
- Improves with cholestyramine (it binds to bile acids thus reducing its irritant effects)



Bile acids get synthesized in the liver and secreted into the bowel (95% get absorbed in the terminal ileum and only 5% go to the colon). If the small intestine is resected and bile is not absorbed, free bile acid is very irritant to the colon.

Bile salts which overflow into the colon causes secretion of water and electrolytes > Diarrhea, increased oxalate absorption > renal oxalate stones

- Limited resection > watery diarrhea (Secretory not osmotic)
- extensive resection > fatty diarrhea.
- Treatment:

  Cholestyramine (it binds to bile acids thus reducing its irritant effects)

Exocrine Pancreatic Insufficiency

1. Mainly in patients with chronic pancreatitis (most common cause is alcohol), Steatorrhea

2. Improves with pancreatic enzymes replacement therapy (Protease and lipase supplements)
   Hx of abdominal pain, high alcohol intake for long time, diarrhea = pancreatic insufficiency

Enzyme secretion of pancreas and role in digestion

Secretion	Site of action	Active enzyme	Substrate and products
Pancreatic juice	duodenum	pancreatic amylase	starch → maltose
		trypsin	protein → peptides
		chymotrypsin	protein → peptides
		pancreatic lipase	fats → fatty acid + glycerol

Diseases and Mechanisms Associated With Exocrine Pancreatic Insufficiency

Disease or Condition	Pathologic Mechanism
Chronic pancreatitis, CF, diabetes, sequelae of acute necrotizing pancreatitis, hereditary pancreatitis	Loss of pancreatic parenchyma (responsible for most cases of EPI)
Periampullary tumors, IPMN, pancreatic head carcinoma, benign pancreatic tumors	Obstruction of main pancreatic duct
Celiac disease, Crohn disease, Schwachman-Diamond syndrome	Decreased pancreatic stimulation
Zollinger-Ellison syndrome	Acid-mediated inactivation of pancreas enzymes
Gastrectomy, gastric bypass, extensive small bowel surgery	Gastrointestinal/pancreatic surgery

Summary

- **Classification of Diarrhea:**

Type	Description
1. Watery	**A- Osmotic:** Caused by: loss of nutrient transporter or Ingestion of poorly absorbed agent (laxative) • Fasting improve the condition • Fecal osmotic gap (FOG) of > 50 mOsm/kg
	B- Secretory: Caused by: Infections, reduction of mucosal surface area by surgery or disease, circulating secretagogues (endocrinopathies) and others. • Lack of response to fasting. • Low fecal osmotic gap: < 50 mOsm/kg
2. Inflammatory	• Small volume diarrhea with Blood, mucus, and pus, with abdominal pain and fever • Persists on fasting. • Caused by: Infection (E. Coli, Shigella), Inflammation, Ischemia, and Malignancy.
3. Fatty Diarrhea (Steatorrhea)	• Present with Bloating, flatulence, greasy malodorous stools that can be difficult to flush. Associated with vitamins deficiencies (A,E,D and K) • Caused by: 1. Malabsorption e.g. Celiac sprue, Whipple's disease 2. Maldigestion e.g. Inadequate bile acid , Pancreatic exocrine insufficiency

- **Common Causes of Chronic Diarrhea:**

1- Celiac disease

Small intestinal malabsorption of nutrients following the ingestion of wheat gluten or related proteins from rye and barley (autoimmune).

Presentation

1. Asymptomatic
2. Nonspecific GI symptoms: 3D (Diarrhea, Distension and Dyspepsia)
3. Nutritional deficiency: Anemia and Osteoporosis
4. Fat soluble vitamin deficiencies (A,E,D and K)
5. Dermatitis herpetiformis (itchy rash at elbows)
6. Elevated ALT & AST
7. Malignancy: small bowel T-cell lymphoma & Small bowel adenocarcinoma

Investigations

- Endoscopy: Normal or Loss of mucosal folds, scalloping of mucosa.
- Histology: villous atrophy and crypts hyperplasia
- Serology: Anti-tTG: Anti-tissue transglutaminase antibody (IgA)

Management

- Education
- Gluten-free diet: avoid wheat, barley, rye & oat
- Correct nutritional deficiencies (Iron, Ca, Vit D)
- Anticipate complications

2- Whipple disease

Chronic systemic infection by Tropheryma whipplei, Has GI, CNS, CVS, MSK & skin manifestations.

Presentations

- Malabsorption : weight loss, diarrhea and abdominal pain.
- CNS: Altered Level of consciousness.
- CVS: Endocarditis.
- Skin : Hyperpigmentation.

Investigations

- Endoscopy: Whitish to yellow plaque-like patches .
- Histology: Foamy macrophages + Numerous PAS-positive granular particles

Management

- Antibiotics to cross BBB.

3- Tropical Sprue

- Is characterized by villous atrophy and crypt hyperplasia.
- History of travel to tropical area for long period.

Presentations

- Chronic diarrhea often with steatorrhea.
- Both B12 and folate deficiency

Investigations

- jejunal aspirate and biopsy

Management

- Folate & B12 Supplement
- Tetracycline for 3-6 months

4- Small Bowel Bacterial Overgrowth (SBBO)

- **Possible causes of SBBO:**
  - chronic pancreatitis, low HCl due to surgery or PPI
  - Surgery, diverticulum
  - Dysmotility
  - Immunodeficiency
  - scarring from inflammation
  - Antibiotics

Presentation

- Bloating, diarrhea..
- B12 deficiency, Elevated folate level and hypoalbuminemia.

Investigations

- Jejunal aspirate and culture – gold standard
- C^{14}-labeled bile acid breath test, C^{14}-xylose breath test, H breath test
- Schilling's test

Management

- Treat underlying cause.
- Nutrition.
- Antibiotics.

Examine Yourself

MCQs:

1. You see a 25-year-old woman who presents with a 24-hour history of watery diarrhoea. She states that she had her bowel movement 11 times since her onset of symptoms. Associated symptoms include nausea and vomiting with abdominal cramps and pain which started in the evening following a barbeque meal in the afternoon that day. The patient is alert and oriented and her observations include a pulse rate of 69, blood pressure of 124/75 and temperature of 37.1°C. On examination, her abdomen is soft, there is marked tenderness in the epigastric region and bowel sounds are hyperactive. The patient is normally fit and well with no past medical history. The most likely diagnosis is:

A. Irritable bowel syndrome
B. Gastroenteritis
C. Ulcerative colitis
D. Laxative abuse
E. Crohn's disease

2. A 35-year-old woman presents with a 24-hour history of watery diarrhoea. She has opened her bowels nine times since the onset of her symptoms. You diagnose gastroenteritis after learning that the patient and her family all ate at a new restaurant and the rest of her family have had similar problems. The most appropriate management is:

A. Oral rehydration advice, antiemetics and discharge home
B. Oral antibiotic therapy and discharge home
C. Admission for intravenous fluid rehydration
D. Admission for intravenous antibiotic therapy
E. No treatment required

3. A 56-year-old man presents with a 2-week history of diarrhoea which has not settled following an episode of 'food poisoning'. Which of the following would be the most appropriate investigation?

A. Full blood count
B. Urea and electrolytes
C. Stool sample for microscopy, culture and sensitivities
D. Abdominal x-ray
E. Liver function tests

4. A 34-year-old white woman is treated for a UTI with amoxicillin. Initially she improves, but 5 days after beginning treatment she develops recurrent fever, abdominal bloating, and diarrhea with six to eight loose stools per day. What is the best diagnostic test to confirm your diagnosis?

A. Identification of Clostridium difficile toxin in the stool.
B. Stool for white blood cells (fecal leukocytes)
C. Detection of IgG antibodies against C difficile in the serum
D. Visualization of gram-positive rods on microscopic examination of stool

5. **PAS-positive granular particles are a histopathologic feature for :**

A. Ulcerative colitis
B. Tropical Sprue
C. Crohn's disease
D. Whipple disease
E. celiac disease

Answers : 1.B / 2. A (Gastroenteritis is usually a self-limiting disease that often does not require pharmacological therapy. The mainstay of treatment is to advise patients to increase oral fluid intake) / 3.C / 4.A / 5.D