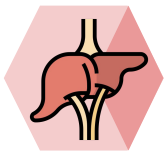
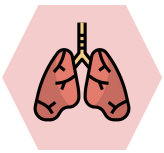
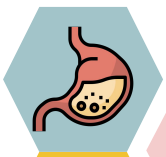
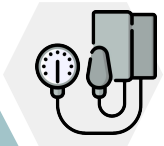
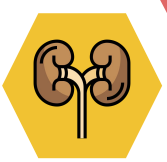
Medicine
TEAM 437

MED437
KING SAUD UNIVERSITY






Chronic Diarrhea

The first 9 slides are FOR YOUR INFORMATION (basic science), just look at red & gold notes. According to the doctor most important thing is from Celiac Disease onwards, and please look at the quiz!! "In the exam I will give you the normal ranges."

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 :

Drs. Slides + Team 436

Lecturer: dr. Suliman Al Shankiti
Same as 436 slides ✔

Introduction:

• Definitions:

- Diarrhea: >100-200

Diarrhea is not the volume of the stool. It's the volume of the **fluid** in the stool. Around **100 ml** of fluid is in the stool (HOW)? **10 L** of fluid pass the small bowel. Most of it come from gastric and small bowel secretion, bile, pancreatic enzymes, sliva and partially from eating and drinking. Small bowel able to absorb up to 90% of this 10 L = **9 L**, so **1 L** will pass the colon. It will absorb 90% of the 1 L = **900 ml**, so **100 ml** will be in the feces.

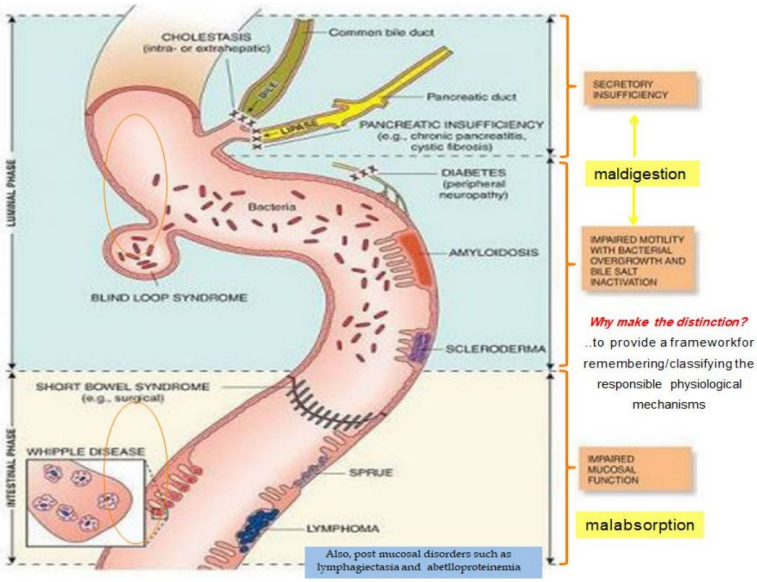
Suppose for some reason, amount of fluid that pass the colon is more than usual whether drinking more water or having small bowel disease. Colon is able to compensate up to **3 L**, more → **diarrhea** will occur.
Based on that **more absorption** occurs in small bowel instead of colon. Patients who has small bowel disease they will complain of **LARGE volume diarrhea** while colonic disease patients will have **small amount diarrhea + more frequent bowel movement**.

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.

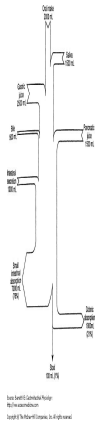
- Acute: common and usually transient, self-limited, Infection related (most common). < 2 weeks.
Chronic: A decrease in fecal consistency lasting for 4 weeks or more, usually requires work up, Can chronic diarrhea caused by infection? Yes especially atypical organism and immunocompromised patients.

- 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

Small bowel doesn't compensate unlike colon.
Most of absorption occurs is Small bowel → small bowel disease → large amount of diarrhea Large bowel disease → small amount of diarrhea

Classification of Diarrhea:

1.Watery

Water-like substances

Large volume, variable presentation.

A.Osmotic

- poorly absorbed substances that remain in the lumen of the intestine and 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

B. Secretory

- Malabsorption or secretion of electrolytes and water
- High stool output : large volume (>1 L/d).

Effect of Fasting in Watery Diarrhea

A. Osmotic

Fasting improve the condition

Fecal osmotic gap (FOG) of > 50 mosm/kg is suggestive of an osmotic diarrhea and a gap of >100 mosm/kg is more specific

Causes of Osmotic

- **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

B. Secretory

- Lack of response to fasting.

- Low fecal osmotic gap:
  (loss of isotonic fluid).
- Less than 50 mosm/kg

Causes of Secretory

- 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
- Drugs laxative abuse

Causes of Secretory (cont.)

- **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.** Also **tenesmus.**
- Positive fecal leukocytes, gross or occult blood, ESR/CRP, leukocytosis , **Persists on fasting.**

Causes of Inflammatory

IBD

Ulcerative colitis, Crohn's disease, Diverticulitis, Ulcerative jejunoileitis

Ischemic colitis

Radiation colitis

Infections

Neoplasia

Colon cancer
Lymphoma

1-Pseudomembranous colitis (Clostridium difficile infection)
2-Invasive bacterial infections (e.g., some types of **E. Coli, Shigella** , TB, yersiniosis)
3-Ulcerating viral infections (e.g., cytomegalovirus, Herpes simplex)
4-Invasive parasitic infections (e.g., amebiasis, strongyloides)

3. Fatty Diarrhea (Steatorrhea)

(Large amount of fat goes to lymphatic → portal circulation. Unlike proteins + carbs large amount of them go directly to portal vein → liver).

● Present with Bloating, flatulence, greasy malodorous stools that can be difficult to flush, weight loss, s/s 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).

Malabsorption (inadequate mucosal transport of digestion products): for absorption we need intact 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)

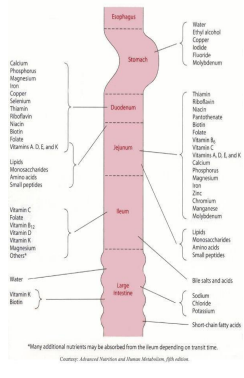
Maldigestion (inadequate breakdown of triglycerides): We need bile salt and pancreatic lipase for digestion of fat.

- ○ Pancreatic exocrine insufficiency (chronic pancreatitis)
- ○ Inadequate luminal bile acid concentration (eg, advanced primary biliary cirrhosis)

Review of Nutrient/Vitamin Absorption:

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) and bile acid diarrhea.



Common Medications and Toxins Associated with Diarrhea

- **Acid-reducing agents (H2 blockers, PPIs)**
- **Magnesium-containing antacids**
- Antiarrhythmics (eg, digitalis, quinidine)
- **Antibiotics.** Very common. (cause Irritation of colon or bowel, disruption of normal flora balance or C. difficile)
- Antineoplastic agents
- Antiretrovirals
- Beta blockers (a lot of cardiac patients use it)
- Colchicine
- Levothyroxine
- SSRIs
- Furosemide
- **Metformin**
- **NSAIDs, ASA**
- Prostaglandin analogs (ie, misoprostol)
- Theophylline
- Amphetamines
- **Caffeine** (especially IBS patients)
- **Alcohol**
- Narcotic/opioid withdrawal (opioid cause constipation , so opioid withdrawal cause diarrhea)

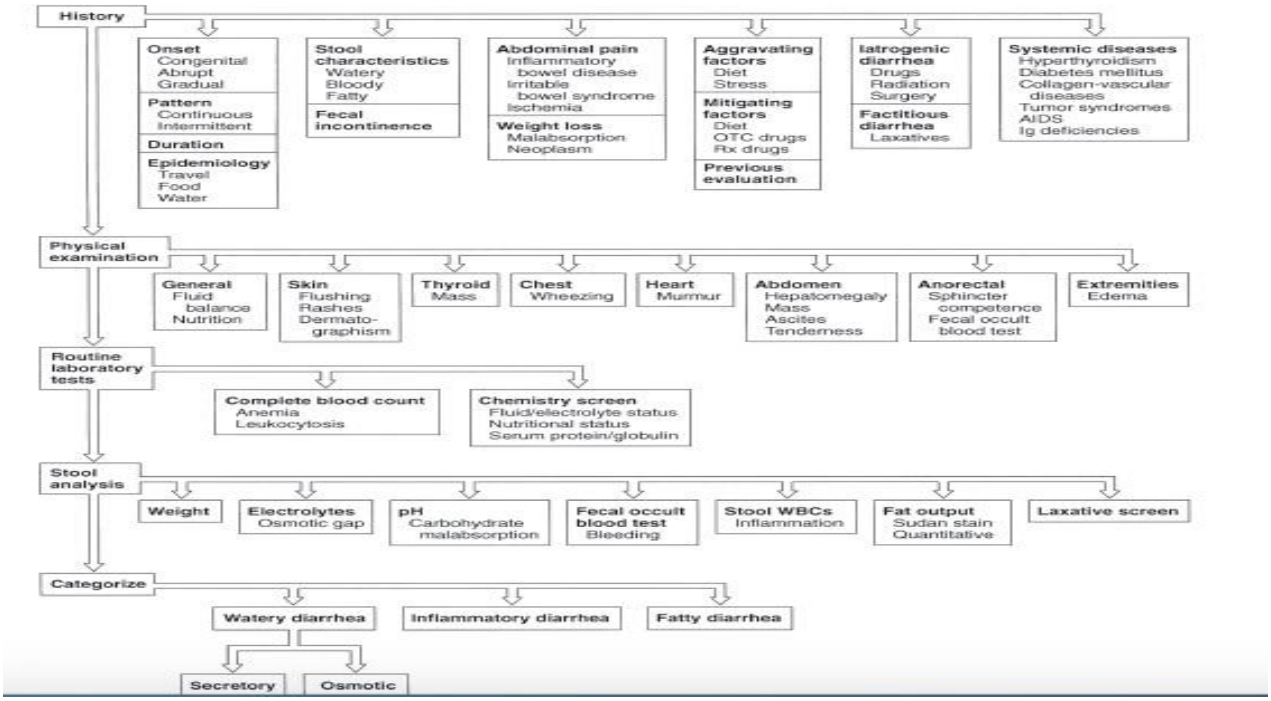
Clinical approach to chronic diarrhea

- 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

- We have 2 ways to differentiate between osmotic and secretory diarrhea:
1) By **history**. If it improve with fasting → osmotic.
2) **FOG**. sending the stool to the laboratory.

- In IBS patients examination should be **fine** with NO MASSES.

- **Anemia** indicates malabsorption either from chronic disease or associated with **malignancy**, NO ONE will have it from IBS.



Investigations

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:

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

(This table is for your information)

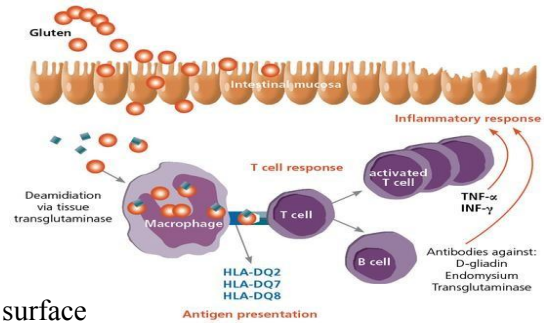
Malabsorption of	Clinical features	Laboratory findings
Calories	Weight loss with normal appetite	-
Fat	Pale and voluminous stool, diarrhea without flatulence, steatorrhea	Stool fat > 6 g/day, low serum levels of triglycerides, cholesterol.
Protein	Edema, muscle atrophy, amenorrhea	Hypoalbuminemia, hypoproteinemia
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 , painless glossitis, 4 acrodermatitis, angular stomatitis Beriberi: nutritional disorder caused by a deficiency of thiamin (vitamin B1)	-
Iron	**Anemia**, glossitis, pagophagia	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)

Celiac Disease:

Introduction:

- Celiac disease is an **autoimmune** disease.
- Gluten intolerance or wheat intolerance are **not the same** as celiac disease because they don't have villous atrophy → not an autoimmune diseases.

- Small intestinal malabsorption of nutrients following the ingestion of wheat gluten or related proteins from rye and barley. Duodenum + proximal jejunum get affected more.
- A characteristic, though not specific, **villous atrophy** of the small intestinal mucosa.
- Prompt clinical and histologic improvement following strict adherence to a gluten free diet.
- Clinical and histologic relapse when gluten is reintroduced



Pathophysiology:

- The disease affect the mucosa with marked variation
- Loss of normal villous structure - flattening
- Intestinal crypts are elongated and open onto a flat absorptive surface
- Leaky mucosa with increased permeability due to structural changes of the tight junctions between damaged absorptive cells because of the inflammation.
- Marked increase in cellularity of the lamina propria – plasma cells and lymphocytes because it's an autoimmune disease.

Presentation:

Non-specific GI symptoms:

Diarrhea - Bloating
Dyspepsia

Nutritional deficiency:

- **Anemia (Iron & folate)**
- Osteoporosis

Asymptomatic

We diagnose them accidentally by screening

Elevated ALT & AST

Malignancy

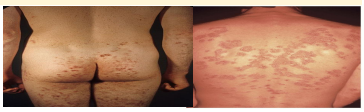
T-cell lymphoma
Small bowel adenocarcinoma

If you don't control the celiac disease you can't escape it!

Fat soluble vitamin deficiencies:

Vit A: poor night vision, follicular hyperkeratosis
Vit D: hypocalcemia, osteoporosis
Vit K: easy bruising & bleeding, elevated INR

Dermatitis herpetiformis



Blister, crusty, mostly on extensor surface

At Risk:c

Already having an autoimmune disease is a MAJOR risk factor to develop other autoimmune diseases

- Type 1 DM (3-6%)
- Autoimmune thyroid disease (6-8%)
- Down's syndrome
- Connective tissue disease
- IgA deficiency (2-3%)

Serology

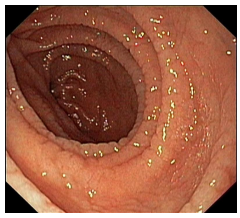
(Negative serology doesn't rule out celiac disease!)
In IgA deficiency patients, Anti-tissue transglutaminase antibody (IgA) would be **NORMAL** why? because they don't have IgA. In this case we will order Anti-tissue transglutaminase antibody (**IgG**).

- **Anti-tissue transglutaminase antibody (IgA)** **(MOST SENSITIVE + SPECIFIC)**
  - Sensitivity 95%; specificity 97.5%
- Endomysial antibody (IgA)
  - Sensitivity 85-98% (~93) Specificity 97-100% (~99)
- IgA anti-gliadin antibodies
  - Sensitivity 75-90% (~80) Specificity 82-95% (~85)
- IgG anti-gliadin antibodies
  - Sensitivity 69-85% (~75) Spec 73-90% (~80)
  - Can be used in IgA deficient patients

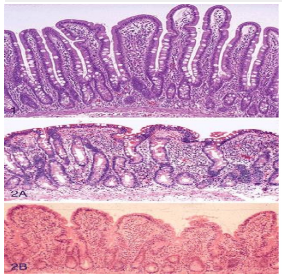
Endoscopy:

(Normal endoscopy doesn't rule out celiac disease!)
You need to take **biopsy** and do **serology**. All complementary to each other.

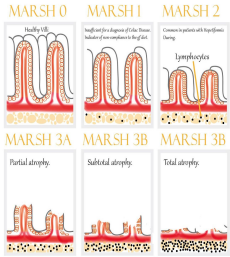
- Normal
- Loss of mucosal folds
- Flattening of mucosa
- Scalloping of mucosa
- Ulcerations



Histology:



★ Villous atrophy
★ Crypt hyperplasia



(Grading system) you don't have to memorize it.

Management:

- Education they have to change the whole life style
- Gluten-free diet: avoid wheat, barley, rye & oat
- Correct nutritional deficiencies (Iron, Ca, Vit D)
- Anticipate complications

- Patient **above 50** years old has **iron deficiency anemia** you will think about colon cancer while **young patient celiac disease.**

Whipple Disease:

Introduction:

- Chronic systemic infection by Tropheryma whipplei
- Has GI, CNS, CVS, MSK & skin manifestations
- Malabsorption – weight loss, diarrhea (watery or fatty) and abdominal pain

Pathophysiology:

Caused by bacterial and macrophage-predominant inflammatory cell infiltration of the small intestinal mucosa and obstruction of mesenteric lymph nodes.

Presentation:

CNS

Progressive dementia
Supranuclear ophthalmoplegia
Altered LOC (level of consciousness)
Oculo-masticatory & oculo-facial skeletal dysfunction

CVS

Endocarditis – MV most common
Myocarditis
Pericarditis

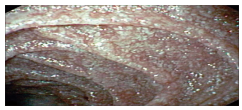
MSK

Oligo or polyarthralgias

Skin

(common)
Hyperpigmentation

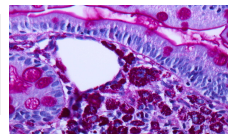
Endoscopy



Whitish to yellow plaque-like patches in 75% of patients (representing lipid droplets and/or lymphangiectasia)

Stasis of lymphatic fluid.

Histology



- Foamy macrophages on routine H&E
- Numerous PAS-positive granular particles (pink/purple appearing)
- Lysosomes filled with T. whipplei

Management

2 weeks with Abx to cross BBB: Ceftriaxone 2g IV daily monotherapy or Pen G 2 MU IV q4h) PLUS streptomycin…THEN…Septra DS tab BID x 1 year.

You need medications that can cross BBB because it can affect the CNS.

Small Bowel Bacterial Overgrowth (SBBO)

Normal Microbiome:

- ➔ Stomach 0-103 CFU/ml
- ➔ ejunum 0-104
  - ◆ Gram + aerobes (oral streptococci, lactobacillus); no gram –ve aerobes
- ➔ Ileum 105-109
- ➔ Colon 1010-1012
  - ◆ Anaerobes: bacteroides, peptostreptococcus, lactobacillus, bifidobacterium, clostridium
  - ◆ Facultative aerobes: e. coli, enterococcus, staphylococcus

Normal barriers that prevent SBBO and their abnormalities

Mechanism to prevent SBBO	Possible causes of SBBO
Gastric acid & pancreatic enzymes	chronic pancreatitis,low HCl due to surgery or PPI (proton pump inhibitors)
Intact bowel structure	Surgery, diverticulum or abnormal anatomy.
Cleansing effect of bowel motility – interdigestive migrating motor complex	dysmotility
Gut immunity – intraluminal secretory IgA	Immunodeficiency
Competent ileocecal valve Doesn't let fecal contents get back to small bowel.	scarring from inflammation, removal/injury by surgery. crohn's disease.
Competition by other bacteria	Antibiotics (broad spectrum antibiotics)

Effect of SBBO:

- ❖ 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

Presentation:

Patients who has **malabsorption** caused by crohn's disease, cancer, celiac disease and resection usually present with: ↓ **B12** + ↓ **Folic acid** why? Because you don't absorb both of them

- Bloating, diarrhea, abdominal pain, weight loss, neuropathy
- **B12 deficiency** – utilized for nutrition B12 activate folate
- **Elevated folate level** - produced by bacteria
- Vitamin A,D,E,K deficiency (fat soluble vitamins) – therefore bruising, night blindness, bone diseases because bile acid deconjugated, so no absorption of fat.
- Iron deficiency
- Hypoproteinemia, hypoalbuminemia
- Fat and CHO malabsorption

investigation:

1. Jejunal culture – gold standard;
2. C14-labeled bile acid breath test
3. C 14 -xylose breath test
4. H breath test
5. Schilling's test — I will not ask about it in the exam

- 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. (you see it in imaging)

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:

- Stage I: + IM vitamin B126 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

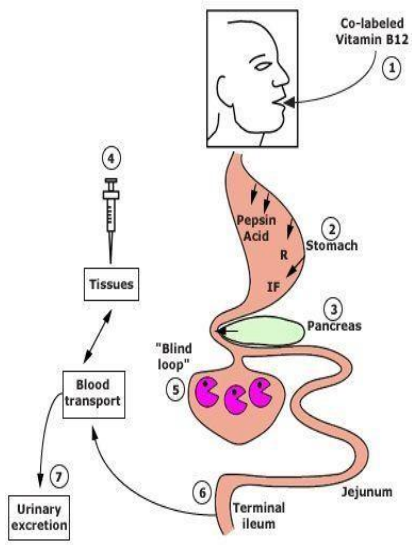


TABLE 350e-1 DIFFERENTIAL RESULTS OF THE SCHILLING TEST IN SEVERAL DISEASES ASSOCIATED WITH COBALAMIN MALABSORPTION

	^{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

Management:

- **Treat underlying cause**
  - e.g. discontinue acid suppressive meds, treat inflammatory Crohn's disease, remove strictures, etc…
- **Nutrition** –
  - replace fat soluble vitamins, B12
  - 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
- Prokinetic increase movement of small bowel
- Octreotide –
  - at low dose, has a promotility effect; causes hypomotility at higher doses
- Probiotics – minimal evidence

Tropical Sprue (Infectious diarrhea)

Introduction:

- Is characterized by villous atrophy and crypt hyperplasia
- Most tropical regions of Asia, Africa, the Middle East, the Caribbean and Central and South America traveling there for months/years (1 week not included) or living there.
- It is an acquired defect – not present in newborns. Travelers from the industrialized world may develop it. Not genetic

Cause

- Not known, but seems to be due to continuous bacterial contamination of the upper small bowel and nutritional deficiency

Presentation:

- Chronic diarrhea often with steatorrhea, anorexia, abdominal cramps, bloating
- B12 and folate deficiency

investigation:

- If suspicion is high – jejunal aspirate and biopsy

Management:

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

Bile Acid-Induced Diarrhea

Increased with people who did **cholecystectomy** because the bile doesn't store in the gallbladder anymore → will pass small bowel → more of it will be in the colon → diarrhea.

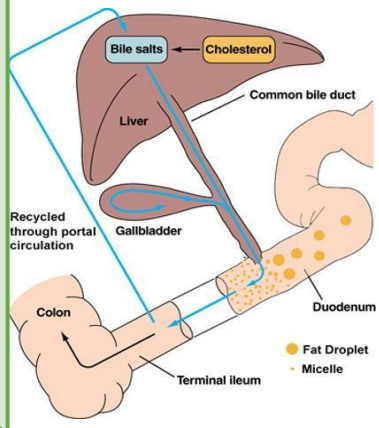
- Watery diarrhea
- Improves with cholestyramine (it binds to bile acids thus reducing its irritant effects)

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

Trypsin is the first enzyme released from pancreas and it activates the rest pancreatic enzymes.

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

(Pancreatic enzyme supplements) can be **diagnostic** + **therapeutic** at the same time.

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

Fieker A, et al. *Clin Exp Gastroenterol.* 2011;4:55-73.

Take Home Messages

- Chronic diarrhea (>4 weeks) can be osmotic, secretory, inflammatory or fatty diarrhea.
- Fecal osmotic gap is helpful to point toward osmotic diarrhea
- Iron, Ca & folate are absorbed in proximal bowel; while B12 is absorbed in ileum.
- Celiac disease:
  - Should always be suspected in patients with iron-def anemia, diarrhea or dyspepsia.
  - Anti-TTG is most helpful.
  - Biopsy shows villus atrophy.
  - Gluten-free diet
  - Watch for complications: nutritional & malignancy
- Whipple Disease:
  - Chronic systemic infection by Tropheryma whipplei
  - Has GI, CNS, CVS, MSK & skin manifisations
  - Biopsy: Foamy macrophages & PAS-positive granular particles
- SBBO:
  - Look for & treat underlying causes
  - B12 def
  - Schilling's test
- Tropical Sprue:
  - Hx of travel to tropical area for long period
- Exocrine pancreatic insufficiency:
  - Mainly in patients with chronic pancreatitis
  - Steatorrhea
  - Improves with pancreatic enzymes replacement therapy
- Bile acid-induced diarrhea:
  - Watery diarrhea
  - Improves with cholestyramine

Summary

Classification of Diarrhea:

Watery Large volume, variable presentation.	**Osmotic**: Malabsorption due to loss of nutrient transporter e.g. lactase deficiency or Ingestion of poorly absorbed agent(Laxatives) -Fasting improve the condition -fecal osmotic gap (FOG) of > 50 mosm/kg
	Secretory:due to Infections,Reduction of mucosal surface area by surgery or disease,Circulating secretagogues (endocrinopathies),Bile Acid-Induced Diarrhea… -Lack of response to fasting -Low fecal osmotic gap: < 50 mOsm/kg
Inflammatory	-Presents as small volume diarrhea with Blood, mucus, and pus, with abdominal pain and fever., -Persists on fasting. -Causes: Infection(E. Coli, Shigella), Inflammation, Ischemia, and Malignancy.
Fatty Diarrhea	-Present with Bloating, flatulence, greasy malodorous stools "steatorrhea" that can be difficult to flush, weight loss, vitamin deficiencies -Causes:Malabsorption(eg, Celiac sprue, Whipple's disease),Maldigestion(eg, Pancreatic exocrine insufficiency)

Celiac Disease:

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

- **Presentation:**
  -Asymptomatic
  -Non-specific GI symptoms(Diarrhea,Bloating Dyspepsia)
  -Nutritional deficiency:Anemia (Iron & folate),Osteoporosis
  -Fat soluble vitamin deficiencies(Vit A,D,K)
  -Dermatitis herpatiformis
  -Elevated ALT & AST
  - Malignancy T-cell lymphoma Small bowel adenocarcinoma
- **Investigations:**
  - Endoscopy: Normal ,Loss of mucosal folds (Flattening of mucosa),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

Whipple Disease:

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

- **Presentation:**
  -Malabsorption:weight loss, diarrhea and abdominal pain.
  - CNS: Progressive dementia,, Altered LOC (level of consciousness).
  - CVS: Endocarditis
  - Skin (Common): Hyperpigmentation
- **Investigations:**
  -Endoscopy:Whitish to yellow plaque-like Patches
  -Histology:Foamy macrophages,Numerous PAS-positive granular Particles.
- **Management:** Abx to cross BBB:

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
  -hypoalbuminemia
- **Investigations:**
  -Jejunal aspirate and culture – gold standard
  -C14-labeled bile acid breath test, C14-xylose breath test
  -H breath test
  -Schilling's test
- **Management:**
  -Treat underlying cause
  -Nutrition
  -Abx

Tropical Sprue :

-Is characterized by villous atrophy and crypt hyperplasia
- Hx of Travelers to tropical regions.

- **Presentation:**
  -Chronic diarrhea often with steatorrhea, bloating
  - B12 and folate deficiency
- **Investigations:**
  -jejunal aspirate and biopsy
- **Management:**
  -Folate & B12 Supplement
  -tetracycline for 3-6 months

MCQs: SO IMPORTANT!!!!

1-25-year-old man came to your clinic complaining of chronic diarrhea accompanied by joint pain. Upon physical examination you noticed splinter hemorrhage, as well as a pansystolic murmur in the mitral area. The patient also seemed disoriented, and changed his answer to your questions multiple times. Based on these findings, what could be the correct diagnosis?

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

2-From the previous case, if you were to take an endoscopic biopsy from the patients' small bowel-what do you expect to see?

A. Atrophy of villi
B. Increased plasma cells and lymphocytes
C. Normal
D. Foamy macrophages on routine H&E & Numerous PAS-positive granular particles (pink/purple appearing)

3-Which of the following serology tests is the most sensitive and specific test for celiac disease?

A. Anti-TTG
B. Endomysial antibody (IgA)
C. IgA anti-gliadin antibodies
D. IgG anti-gliadin antibodies

4- Your celiac patient came to the clinic with a flare up of his symptoms. You discover he does not adhere to his change of his diet (gluten free diet). What is the most serious complication he may develop if he does not change his diet and continues to experience flare ups?

A. T cell lymphoma
B. B cell lymphoma
C. A&D
D. Small bowel adenocarcinoma

1-D 2-D 3-A 4-C