PLEASE CHECK Editing file BEFORE!

Chronic diarrhea & Malabsorption

★ Objectives:

1. Know the definition and different classification of chronic diarrhea
2. Understand the mechanism of chronic diarrhea
3. To learn systematic approach of patient with chronic diarrhea
4. Understand the different mechanisms and causes of malabsorption
5. To be able to recognize the clinical manifestation of malabsorption and approach to patient with malabsorption

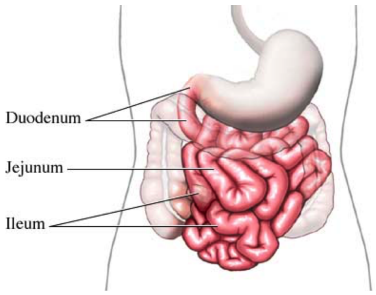
★ Resources Used in This lecture:

Master The boards, Step Up, Slides Mainly,434 pathology teamwork.

Done by: Asmaa Alusaies
Revised by: Reem Labani
Contact us at: InternalMedicineTeam434@gmail.com

Introduction

Absorption of Nutrient



Anatomy:

The digestion and absorption of foods usually take place in Stomach and small intestine through secretion of digestive enzymes that coming from : mouth , stomach , pancreas and small intestine.

Any problem in these structure can lead to malasporbion.

Physiology:

The main purpose of the gastrointestinal tract is to digests and absorbs nutrients (fat, carbohydrate, and protein), micronutrients (vitamins and trace minerals), water, and electrolytes.

Mechanisms of absorption:

1) ***Luminal phase:*** Dietary fats, proteins, and carbohydrates are hydrolyzed and solubilized by secreted digestive enzymes and bile.
2) ***Mucosal phase***: relies on the integrity of the brush-border membrane of intestinal epithelial cells to transport digested products from the lumen into the cells.
3) ***Post-absorptive phase:*** nutrients are transported via lymphatics and portal circulation from epithelial cells to other parts of the body.

Defect in any phases can result in malabsorption.

Malabsorption

Definition

Abnormality in absorption of food nutrients across the gastrointestinal tract.

Characterized

- Defective absorption of fats, (fat- and water-soluble vitamins), proteins, carbohydrates, electrolytes and minerals, and water.
- Impairment can be of single or multiple nutrients depending on the abnormality.
- Presents most commonly as chronic diarrhea.

Causes :

➢ **Congenital defects (rare)**: in the membrane transport systems of the small intestinal epithelium.
➢ **Acquired defect :** in the epithelial absorptive surface.

- Defect in any phases of mechanism of absorption can result in malabsorption.

1. Luminal 2. Mucosal 3.Postabsorptive

Phases	Cause	Example
Luminal	**Reduced Nutrient Availability**	**-Cofactor deficiency:** pernicious anemia, gastric surgery **-Nutrient consumption:** bacterial overgrowth
	Impaired Fat solubilization	**-Reduced Bile salt synthesis:** Hepatocellular disease **-Impaired bile salt secretion:** cholestasis **-Bile salt inactivation:** bacterial overgrowth **-Impaired CCk:** Mucosal disease **- Increased bile salt losses:** terminal ileal disease or resection
	Defect nutrient Hydrolysis	**-Lipase inactivation:** ZE syndrome **-Enzyme deficiency:** pancreatic insufficiency or cancer **-Improper mixing or rapid transient**: Resection, Bypass, Hyperthyroidism
Mucosal phase	**Extensive mucosal loss**	Resection or infarction
	Diffuse mucosal disease	Gluten, tropical, crohn's, radiation, infection,drugs, infiltration.
	Enterocyte defects	-Microvascular inclusion disease -Brush border hydrolase deficiency -Transport defect: Hartnup's cystinuria, B12 and folate uptake. -epithelial processing: alpha-beta lipoproteinemia
Transport phase	**Vascular**	-Vasculitis -Atheroma
	Lymphatic	-Lymphangiectasia,radiation,nodal tumor,cavitation or infiltration.

★ Digestive enzyme inactivation: Zollinger-Ellison syndrome is caused by gastrin secreting tumor of the pancreas that stimulates acid secreting cells of the stomach to maximal activity, with consequent gastrointestinal mucosal ulceration. Hypersecretion of acid → deactivation of small intestine enzymes (which require alkaline media to work) → malabsorption

★ Hartnup disease is an autosomal recessive disorder caused by impaired neutral amino acid transport in small intestine and the proximal tubule of the kidney. Patient present with pellagra, cerebellar ataxia and gross aminoaciduria.

Clinical features *Depend upon the cause and severity of the disease*

★ Malabsorption may either be global or partial (isolated).

1. **Global malabsorption:** results from diseases associated with either diffuse mucosal involvement or a reduced absorptive surface.
2. **Partial or isolated malabsorption:** results from diseases that interfere with the absorption of specific nutrients.

Examples:
Global⟶ celiac disease in which diffuse mucosal disease "villous atrophy" can lead to impaired absorption of almost all nutrients
or Partial⟶ Example: defective cobalamin(B12) absorption, can be seen in patients with pernicious anemia or those with disease resection of the terminal ileum such as patients with Crohn's disease.

Signs and Symptoms

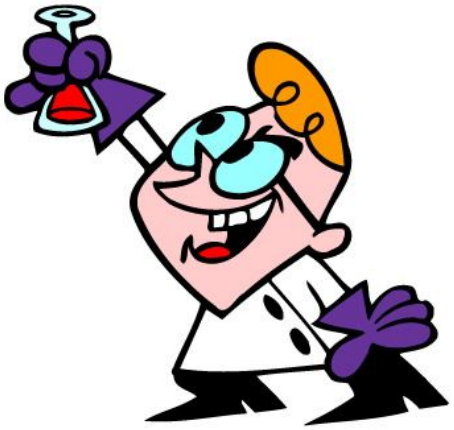
★ Depends on which nutrients is affected:

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
Protein	Edema, muscle atrophy,amenorrhea	Hypoalbuminemia,hypoproteinemia
Carbohydrates	Watery diarrhea, flatulence,acidic stool PH, milk intolerance, stool osmotic gap	Increased breath hydrogen
Vitamin B12	Anemia, subacute combined degeneration of the spinal cord (early symptoms are paresthesias and ataxia associated with loss of vibration and position sense)	Macrocytic anemia, vitamin B12 decreased, abnormal schilling test,serum methylmalonic acid and homocysteine increased.
Folic Acid	Anemia	Macrocytic anemia, serum and RBC folate decreased,serum homocysteine increased.
Vitamin B (general)	Cheilosis[1],painless glossitis,acrodermatitis,angular stomatitis	-
Iron	Microcytic anemia,glossitis,pagophagia	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	Prolonged prothrombin time, vitamin K-dependent coagulation factors decreased

➔ Vitamin B12 needs an intact Bowel wall and pancreatic enzymes to be absorbed.
How can you link the type of anemia to malabsorption?
- ❏ Microcytic anemia (Low MCV) ⟶ Iron deficiency: Caused by celiac or chronic GI chronic loss
- ❏ Macrocytic anemia (high MCV) ⟶ Vit B12/Folate deficiency: caused by celiac, bacterial overgrowth and parasitic infection.

[1] is a painful inflammation and cracking of the corners of the mouth.

Investigations of malabsorption:



1) Laboratory Tests:

➢ **Hematological tests:**
- CBC "to detect anemia"
- Serum iron, vitamin B12 and Folate
- Prothrombin time

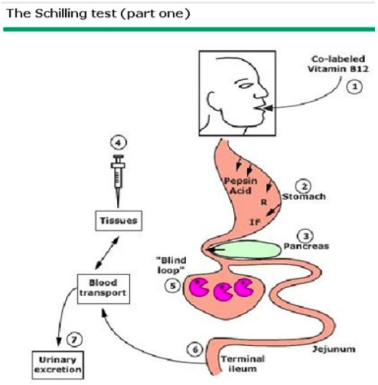
➢ **Electrolytes and chemistries:**
- Hypokalemia, hypocalcemia, hypomagnesemia, and metabolic acidosis.
- Protein malabsorption may cause hypoproteinemia and hypoalbuminemia.
- Fat malabsorption can lead to low serum levels of triglycerides, cholesterol.
- ESR which is elevated in Crohn's disease and Whipple's disease.

➢ **Stool analysis**
- Stool pH may be assessed. Values of <5.6 are consistent with carbohydrate malabsorption
- Stool Culture and Sensitivity. (detect c.difficile in pseudomembranous colitis)
- Pus cells in the stool → IBD, some infections
- Fat in the stool → pancreatic insufficiency, celiac.

➢ **Tests of fat malabsorption:**
- For a quantitative measurement of fat absorption, a 72-hour fecal fat collection
- Qualitative test Sudan III stain of stool (less reliable)

➢ **Endoscopy of the small intestine** (if diagnosis still not known)

➢ **The Schilling test: (**to determine whether the body absorbs vitamin B12 normally.)



Malabsorption of vitamin B12 may occur as a consequence of:
-Deficiency of intrinsic factor (eg, pernicious anemia, gastric resection)
- Pancreatic insufficiency, bacterial overgrowth
- Ileal resection or disease.

Schilling test stages :

-Stage I: Oral vitamin B12
-Stage II: Oral vitamin B12 + intrinsic factor (IF)
-Stage III: Oral vitamin B12 + IF + oral antibiotics

How the test is performed?

➔ This test may be done in four different stages to find the cause of a low vitamin B12 level.

Stage I: Patient is given two doses of vitamin B12 (cobalamin). Then, collect the patient's urine over the next 24 hours. The urine is checked to see if there is normal absorption of Vitamin B12.

Stage II: Radioactive B12 along with intrinsic factor. Test can tell whether a low vitamin B12 level is caused by problems in the stomach, preventing it from producing intrinsic factor.

Stage III: This test is done after the patient has taken antibiotics for 2 weeks. It can tell whether abnormal bacterial growth has caused the low vitamin B12 levels.

Stage IV: This test determines whether low vitamin B12 levels are caused by problems with the pancreas. With

this test, the patient takes pancreatic enzymes for 3 days. Then, a radioactive dose of vitamin B12.

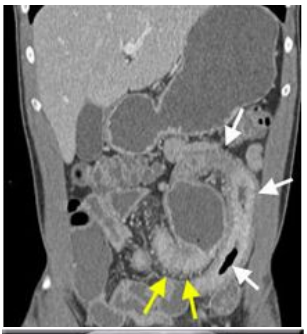
➢ **Bacterial overgrowth:**

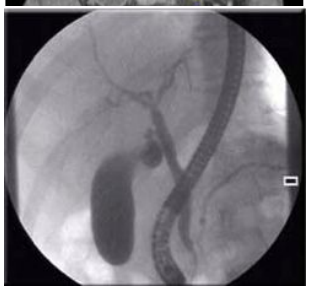
- Bacterial overgrowth cause an early rise in breath hydrogen
- Diagnosed by jejunal culture.
- 14c D–xylose breath test, high sensitivity and specificity

➢ **Serology:**

- No serologic tests are specific for malabsorption
- Serum Anti-TTG and antiendomysial antibodies can be used to help diagnose celiac sprue
- Serum IgA to rule out IgA deficiency
- Determination of fecal elastase and chymotrypsin (2 proteases produced by the pancreas) can be used to try to distinguish between pancreatic causes and intestinal causes of malabsorption.

2) Imaging studies:





➢ Small bowel barium studies :

- Strictures
- Mucosal changes
- Diverticula (bacteria overgrowth usually occurs)

➢ CT scan of the abdomen:

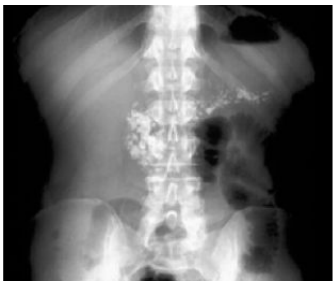
- Strictures, mucosal changes
- Diverticula,wall thickness
- Masses, lymph nodes

➢ Endoscopic Retrograde CholangioPancreatography (ERCP):

- Pancreatitis (duct changes, or calcification in chronic pancretitis)
- Biliary diseases

➢ Plain abdominal x-ray film:

- Pancreatic calcifications are indicative of chronic pancreatitis

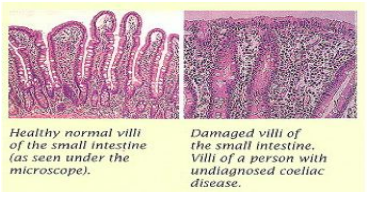


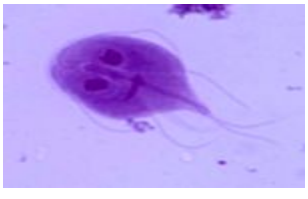
3) Endoscopy:

➢ **Upper endoscopy with small bowel mucosal biopsy:**

Examples:

- Celiac sprue
- Giardiasis
- Crohn's disease
- Whipple's disease
- Amyloidosis
- Lymphoma





➢ **Lower GI endoscopy:**for colonic and terminal ileal pathology (e.g Crohn's disease)

Treatment:

1. Treatment of causative disease: "depends on the etiology"

- A gluten-free diet helps treat celiac disease.
- Similarly, a lactose-free diet
- Protease and lipase supplements are the therapy for pancreatic insufficiency.
- Antibiotics are the therapy for bacterial overgrowth
- Corticosteroids, anti-inflammatory agents, such as mesalamine, and other therapies are used to treat CD.

2. Nutritional support:

- Supplementing various minerals calcium, magnesium, iron, and vitamins.
- Caloric and protein replacement also is essential.
- Medium-chain triglycerides can be used for lymphatic obstruction.
- In severe intestinal disease, such as massive resection and extensive regional enteritis, parenteral nutrition may become necessary.

Celiac (Gluten-sensitive enteropathy)

What is Celiac?

- **An immune reaction to** gliadin fraction of the wheat **protein gluten**
- Gluten is digested by luminal and brush border enzymes into(amino acid,peptide and 33-amino acid gliadin peptide that is resistant to degradation).
- The pathogenic component is **gliadin.**

1-Once absorbed **,gliadin** is deamidated by **tissue transglutaminase (tTG).**
2-Deamidated gliadin is presented → **Antigen presenting cells→ MHC class** 2
3-**CD4 T** cells produce **cytokines** that release matrix proteases causing cell death and degradation in the epithelial cells, resulting in the loss of the villous surface in the small intestine.

- This results in **impaired mucosal function and inability for absorption.**

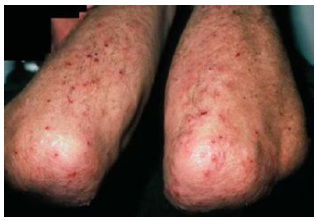
Clinical presentation:

Symptoms begin **after** the introduction of foods that contain gluten → **Wheat, barley, flour.**

1-Typical presentation:

- **GI symptom**s that characteristically appear at age **9-24 months.**
- **Infants and Childhood**: Abdominal distention and diarrhea inadequate rate of weight gain failure to grow.
- **Young adults**: Anemia most commonly chronic diarrhea and bloating
  - ★ Improvement of symptom and mucosal histology on gluten withdrawal from diet.

2- Dermatological manifestations:



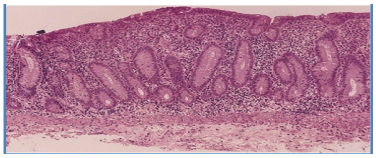
- Pale skin
- Dermatitis Herpetiformis (autoimmune blistering disorder associated with a gluten-sensitive enteropathy).The classic location for the lesions is on the extensor surfaces of the elbows, knees and the back.

3- Neurological manifestations:

- Motor weakness
- peripheral neuropathy

- ataxia (may be present)
- The Chvostek's sign or the Trousseau sign may be evident due to hypocalcemia.

Investigation :



- **Small intestine biopsy** demonstrate villous atrophy.
- **Stool** → ↑Fat
- **Serology** is +ve for IgA to tissue transglutaminase or IgG to deamidated gliadin or anti-endomysial antibodies

★ How to differentiate between Celiac and chronic pancreatitis?

-Both Celiac and chronic pancreatitis cause fat malabsorption, so there will be deficiency of Vit(A,K,E,D) and both of them might cause cause low level of Vit B12 (it needs an intact bowel wall and pancreatic enzymes to be absorbed)
-In case of Celiac there will be iron deficiency in contrast to chronic pancreatitis which is an enzymatic disease (the wall is intact).
Chronic pancreatitis Dx: CT, abdominal x-ray → calcification. (serum amylase & lipase are not helpful, there will be normal)
-Celiac Dx: blood test, biopsy → flattening villi (it is essential to exclude lymphoma)

★ How to differentiate between Celiac and tropical sprue?

Tropical sprue→ Damage to small bowel due to unknown organism result in malabsorption. (Positive culture of bacteria)
➔ Must do biopsy in Celiac disease to exclude Lymphoma.

Chronic diarrhea

Definition A Decrease in fecal consistency lasting for 4 weeks or more.

- (weight of stool and frequency are not reliable)
- Diarrhea <u>is a symptom, not a disease</u> and may occur in many different conditions. (like anemia)

Acute vs Chronic:

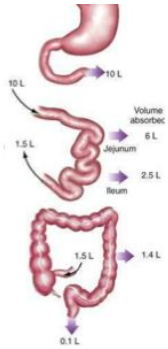
Most of acute diarrhea is due to infectious cause and usually transient and self-limited, while Chronic diarrhea is due to non-infectious cause and requires more work up.

Epidemiological distribution of the common causes :

Developing countries	Developed countries
(usually the infection is high) Chronic bacterial, Mycobacterial, Parasitic infections. Then Functional disorders Malabsorption Inflammatory bowel disease	Irritable bowel syndrome (IBS) Inflammatory bowel disease (IBD) Malabsorption syndromes (such as lactose intolerance and celiac disease) Chronic infections (particularly in patients who are immunocompromised)

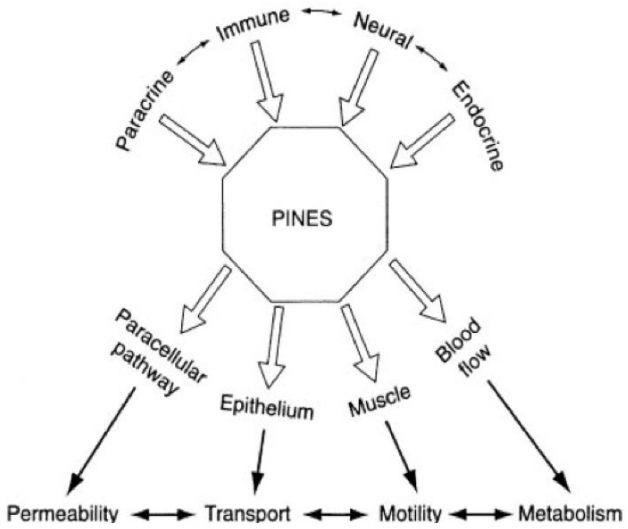
❖ ***Mechanism of diarrhea*** **Change in:**

-Absorption
-Secretion
-Motility of the gut



Fluid from the gut is around 10L but what comes out in the stool is around 0.1 so most of the fluid is normally absorbed in the small intestine and part of it is absorbed in the large intestine.

"PINES" regulatory system in the intestine:



❖ *Classification*

- Time course (acute vs. chronic)
- Volume (large vs. small)
- Pathophysiology (secretory vs. osmotic)
- Stool characteristics (watery vs. fatty vs. inflammatory).
- Epidemiology (epidemic vs. travel-related vs. immunosuppression-related)

❖ *Classification of Diarrhea (According to mechanism)*

Osmotic	Secretory
•**Excess amount of poorly absorbed substances that exert osmotic effect** > water is drawn into the bowels > diarrhea •Stool output is usually not massive •**Fasting improve the condition** •**Stool osmotic gap is high**, > **125 mOsm**/kg (**loss of hypotonic fluid)** **Causes :** • **Malabsorption** in which the nutrients are left in the lumen to pull in water e.g. **lactose intolerance،celiac disease** • **osmotic laxatives**[2]**.**(which work to alleviate constipation by drawing water into the bowels,Ex: Magnesium and phosphate laxatives) • **Hexitols** (poorly absorbed): sorbitol, mannitol, xylitol). • 4-other : distention of the bowel. High-fructose foods	•There is an **increase in the active secretion of water** (or an inhibition of absorption)rather than absorption of electrolyte into intestinal tract. •High stool output : Large volume (>1 L/d) •**Lack of response to fasting** (continues even when there is no oral food intake) •**Stool osmotic gap < 100 mOsm/kg (isotonic)** → normal or low **Causes :** • ***The most common cause of this type of diarrhea is a bacterial toxin (E. coli , cholera) that stimulates the secretion of anions.*** • **Other causes:** –**Enteropathogenic virus e.g**. rotavirus and norwalk virus – **Neuroendocrine tumours** (carcinoid tumor, gastrinomas) –**Rectal villous adenoma**

[2] ملين

Exudative (inflammatory)	Motility-related
•Results from the o**utpouring of blood protein**, or **damaged mucus** and **microvilli** from an inflamed or ulcerated mucosa. •**Presence of blood and pus in the stool**. mucus can be present •**Persists on fasting** **Causes :** ● **Inflammatory bowel diseases such as** Crohn's disease or ulcerative colitis. ● **Invasive infections** e.g. ***E. coli***, ***Clostridium difficile*** **and** ***Shigella.*** *(not only their toxins)* ● **Some bacterial infections** cause damage by invasion of the mucosa. → diarrhea with blood and pus in the stool caused by → **bacterial dysentery** ● **Ischemic colitis** ● **Radiation colitis** ● **Neoplasia: Colon cancer, Lymphoma** The main organisms are: ❑ Tuberculosis, Yersiniosis ❑ ***Campylobacter*** invades mucosa in the jejunum, ileum and colon, causing ulceration and acute inflammation. ❑ ***Salmonella typhi, S. paratyphi*** *A*, *B*, and *C* ❑ ***Shigella*** **infections** are mainly seen in young children. ❑ **Enteroinvasive and enterohemorrhagic *E. coli*.** ❑ **Invasive parasitic infections** (e.g., amebiasis, strongyloidiasis) ❑ **Pseudomembranous colitis** (Clostridium difficile infection) ❑ **Ulcerating viral infections** (e.g., cytomegalovirus, herpes simplex virus)	•Caused by the rapid movement of food through the intestines (hypermotility) -Decreased contact time of fecal mass with intestinal wall so decreased water absorption from feces. -No inflammation in bowel mucosa. **Causes (motility disorder mainly) :** ● **Irritable bowel syndrome (IBS)** – a motor disorder that causes abdominal pain and altered bowel habits with diarrhea predominating. ● **Carcinoid Syndrome** → Increased serotonin → It increases bowel motility. ● **Gastric / intestinal resection**

★ Fatty Diarrhea:(Steatorrhea)

- **Malabsorption syndromes**
  - Mucosal diseases
  - Short bowel syndrome Post-resection diarrhea
  - Small bowel bacterial overgrowth
  - Mesenteric ischemia
- **Maldigestion:**
  - Pancreatic exocrine insufficiency
  - Inadequate luminal bile acid

Some DDX of chronic diarrhea:

Features	
IBS	Can have diarrhea, constipation or both- pain- relieved by bowel movement- less at night*- No weight loss-
IBD	Blood in stool, fever, weight loss, extraintestinal manifestations (arthralgia,ulcer,..ect)
Carcinoid	Intermittent diarrhea,flushing,wheezing,cardiac abnormalities diagnosis by urinary (5 HIAA[3]), therapy is octreotide.
Celiac	Steatorrhea,floating, abdominal distention,weight loss test:Anti-TTG, antiendomysial Ab, antigliadin (IgA)
Lactose intolerance	No fever, No blood,No deficiency in calories(no weight loss), vitamins and fats and other nutrients are absorbed normally only lactose sugar not absorbed. Remove milk & cheese From diet and he will get better, or give lactase.
Ab associated diarrhea	Clindamycin or any Ab + C.diff
Chronic Pancreatitis	Hx of pancreatitis, most accurate test secretin stimulation test.

IBS is a functional disease not an organic disease, so it does not present while the patient is sleeping (in contrast to IBD).

Approach to patient with diarrhea:

(1) History: (this is important to always keep in mind when pt. has diarrhea)

- What led the patient to complain of diarrhea? (e.g. consistency or frequency of stools, the presence of urgency or fecal soiling)
- Stool characteristics: (e.g. greasy stools that float and are malodorous may suggest fat malabsorption while the presence of visible blood may suggest inflammatory bowel disease)
- Duration of symptoms, nature of onset (sudden or gradual)
- Volume of the diarrhea: (e.g. voluminous watery diarrhea is more likely to be due to a disorder in the small bowel while small-volume frequent diarrhea is more likely to be due to disorders of the colon)
- Occurrence of diarrhea during fasting or at night (suggesting a secretary diarrhea.
- Weight loss, appetite.
- Association of symptoms with specific food ingestion. (such as dairy products or potential food allergens)
- Epidemiological factors, such as travel before the onset of illness, symptoms of nutritional deficiency.
- A history of recurrent bacterial infections (eg, sinusitis, pneumonia), which may indicate a primary immunoglobulin deficiency.
- Systems review: The presence of systemic symptoms: (such as fevers, joint pains, mouth ulcers, eye redness) IBD, CTD, thyroid.
- Family history: IBD.
- Drug Hx: including over the counter medication.

[3] 5 hydroxyindoleacetic

Clarify the patient's definition of diarrhea it might not be actual diarrhea. (Differentiate diarrhea from fecal soiling) Timing in diarrhea is important because if it is a functional disease not an organic disease it does not present while the patient is sleeping (like, IBS).

(2) Physical Examination:

- Rarely provides a specific diagnosis.
- Findings suggestive of IBD (e.g. mouth ulcers, a skin rash, episcleritis, an anal fissure or fistula, the presence of visible or occult blood on digital rectal examination, abdominal masses or abdominal pain)
- Evidence of malabsorption (wasting, physical signs of anemia, scars indicating prior abdominal surgery)
- Lymphadenopathy (possibly suggesting HIV infection)
- Palpation of the thyroid and examination for exophthalmos and lid retraction.
- may provide support for a diagnosis of hyperthyroidism.

(3) Investigations:

- CBC, Look for anemia, WBC elevation
- ESR
- Electrolytes
- Total protein and albumin
- TFT
- Stool: occult blood, C/S (stool culture and sensitivity), ova and parasites C-D toxins (if history is suggestive)
- CT (might be helpful for Diverticulitis and IBD suspected.)
- Colonoscopy/ sigmoidoscopy (if unknown of chronic diarrhea→ due to risk of perforation)

IF fecal leukocyte is positive for leukocyte and patient has moderate to severe diarrhea→ send stool for culture and/or C.Difficile toxin assay → start empiric therapy with antibiotic.

(4) Specific Investigations

The history and physical examination may point toward a specific diagnosis for which testing may be indicated

(5) Treatment

- ➢ Rehydrate; monitor electrolytes and replace if necessary
- ➢ Treat the underlying cause (stop or change the medication, advice lactose free diet). Consider a trial of NPO status to see if diarrhea stops.
- ➢ Consider antibiotics in infectious diarrhea→ 5 day course of ciprofloxacin. Antibiotics are definitely recommended in these following conditions:
  - Patients has fever, bloody stools, or severe diarrhea- give quinolones.
  - Positive stool culture
  - Patients has traveler's diarrhea.
  - C.Difficile infection- Give Metronidazole.
- ➢ Loperamide (Imodium) is an antidiarrheal agent that should only be given is mild to moderate and not recommended in patient with fever of bloody diarrhea.

Summary

Malabsorption = abnormal digestion or small intestinal mucosa

Lactose Intolerance

- absent activity of the enzyme lactase
- Bloating, abdominal discomfort, and flatulence, explosive diarrhea.
- 1 hour to a few hours after ingestion of milk products.
- it can Inherited or lactase deficiency

Celiac disease

- An immune reaction to gliadin fraction of the wheat protein gluten
- Patients have raised antibodies to gluten autoantibodies.
- Highly specific association with class II HLA DQ2 (95% of cases) and, to a lesser extent,

Define acute diarrhea and enumerate its common causes:

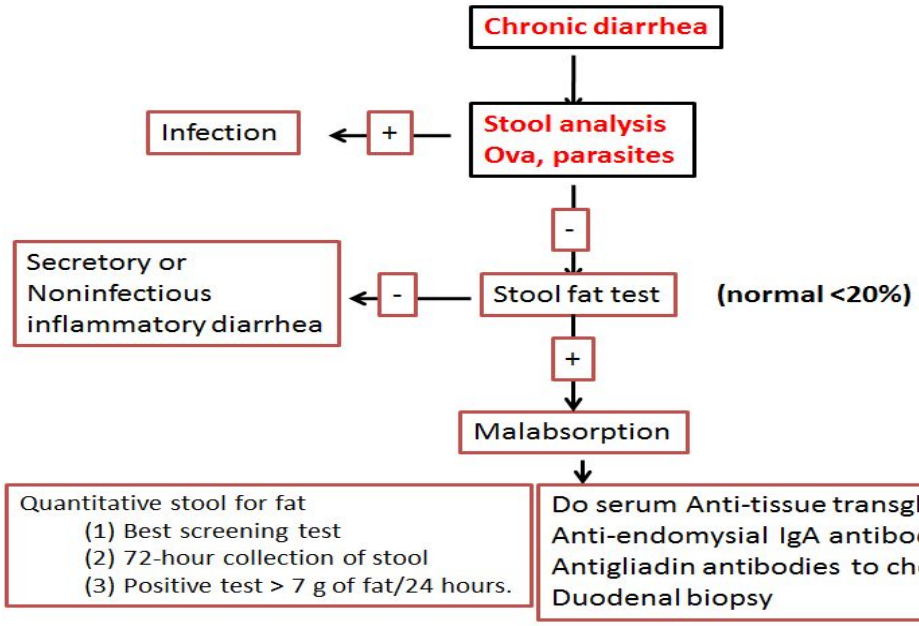
- Less than 2 weeks
- infections (viruses, bacteria, helminths, and protozoa). Food poisoning

Define chronic diarrhea and enumerate its common causes:

- More than one month
- Infection, post Infection malabsorption, Inflammatory bowel disease (IBD),

SUMMARY: TYPES OF DIARRHEA

TYPE	CHARACTERISTICS	CAUSES	SCREENING TESTS
Invasive Inflammatory	Pathogens invade enterocytes Low-volume diarrhea	*Shigella* spp. *Campylobacter jejuni*	Fecal smear for leukocytes: positive in most cases
	Diarrhea with blood and leukocytes (i.e., dysentery)	*Entamoeba histolytica*	Order stool culture & for O&P
Secretory	Loss of isotonic fluid High-volume diarrhea Mechanisms:Laxatives Enterotoxins stimulate Cl^- channels regulated by cAMP and cGMP	Laxatives: melanosis coli with use of phenanthracene laxatives Production of enterotoxins: *Vibrio cholerae* Enterotoxigenic *E. coli*	Stool osmotic gap < 50 mOsm/kg Fecal smear for leukocytes: negative
Osmotic	Osmotically active substance is drawing hypotonic salt solution out of bowel High-volume diarrhea No inflammation in bowel mucosa	Disaccharidase def. Giardiasis, Celiac Dis. Ingestion of poorly absorbable solutes	Fecal smear for leukocytes: negative Stool osmotic gap > 125 mOsm/kg
Motility-related	Rapid movement of food through the Intestines Serotonin increases bowel motility No inflammation in bowel mucosa	Irritable bowel syndrome (IBS) – a motor disorder Increased serotonin: carcinoid syndrome	Increased 5-HIAA



Cases:

22 Y F c/o non bloody diarrhea for 7 months, 6-10 times/ Day, Mild RIF pain, Weight loss 10 kg (49 kg -> 39), O/E cachexia, RIF tenderness (mild), Lab low hb 8, low mcv) High ESR and CRP
What is the most likely diagnosis? RIF pain and high ESR are characteristics for Crohn's disease

18 years old with fatigue, abdominal bloating and diarrhea for 3 months. Itchy skin rash, unremarkable physical examination, except pallor and skin rash over thighs, Has low Hb (low mcv), Serology : anti TTG ab positive. Most likely Celiac (anti TTG ab)

27 years old F, with intermittent diffuse abdominal pain and diarrhea for 3 years. No blood in stool, diarrhea is triggered by fatty food, no nocturnal diarrhea. Symptoms improved with defecation. Symptoms free for weeks, Weight and appetite stable. Examination: N, CBC, ESR: N. Most likely IBS

A 22 year old female with anemia only.

1. Ask about:
   Nutrition, diarrhea, blood loss... etc.
2. Check for the type of anemia

- Macrocytic : diseases in terminal ileum
- Microcytic : diseases in the upper GIT

If her anemia happens to be microcytic hypochromic anemia : iron deficiency anemia
Most likely: Celiac disease "sometimes the only manifestation is anemia".

- ★ An example of luminal phase defects is Zollinger Ellison syndrome, which causes hypersecretion of acidàdeactivation of small intestinal enzymesàmalabsorption
- ★ Types of malabsorption:
  - A) Global
  - B) Partial
- ★ Serological tests of Celiac include: Anti-TTG, antiendomysial ab and antigliadine.