CHRONIC DIARRHEA AND MALABSORPTION

DR. KHALID ALSWAT, MD, MRCP, FACP
ASSOCIATE PROFESSOR OF MEDICINE, CONSULTANT GASTROENTEROLOGIST

OBJECTIVES

- To know the definition and different classification of chronic diarrhea
- To understand the mechanism of chronic diarrhea
- To learn systematic approach of patient with chronic diarrhea
- To understand the different mechanisms and causes of malabsorption
- To be able to recognize the clinical manifestation of malabsorption and approach to patient with malabsorption

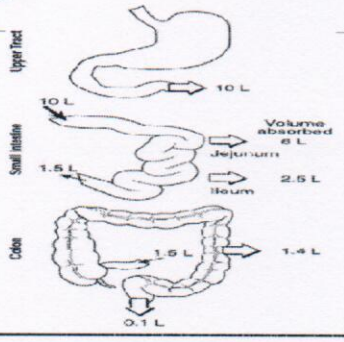
DIARRHEA

- Diarrhea is a common and usually transient symptom
- **Chronic diarrhea** decrease in fecal consistency lasting for four or more weeks
- (weight of stool and frequency are not reliable)
- May occur in up to 5% of the population in any given year.
- Diarrhea is a symptom, not a disease and may occur in many different conditions.

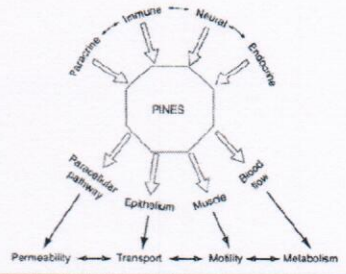
MECHANISM OF DIARRHEA

Normal	Abnormal
▪ The gut absorbs most of the fluid that it secretes, and its motility provides a favorable milieu for water, electrolyte, and nutrient absorption	▪ When infectious agents, toxins, or other noxious substances are present within the gut→ fluid secretion and motility are stimulated to expel the unwanted material, thereby producing diarrhea

FLUID LOADS ALONG THE GASTROINTESTINAL TRACT



"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)

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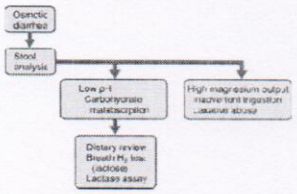
SECRETORY DIARRHEA

CLUES: LARGE VOLUME (>1 L/D); LITTLE CHANGE WITH FASTING; NORMAL OR LOW STOOL OSMOTIC GAP

- Bacterial toxins
- Inflammatory bowel disease
  - Crohn's disease
  - Ulcerative colitis
  - Microscopic colitis
    - Collagenous colitis
    - Lymphocytic colitis
- Vasculitis
- Endocrinopathies
  - Addison's disease
  - Carcinoid syndrome
  - Hyperthyroidism
  - Medullary carcinoma of the thyroid
  - Pheochromocytoma
  - Gastrinoma, Somatostatinoma , VIPoma
- Disordered motility
  - Diabetic autonomic neuropathy
  - Irritable bowel syndrome
  - Postsympathectomy diarrhea
  - Postvagotomy diarrhea
- Ileal bile acid malabsorption
- Laxative abuse (stimulant laxatives)
- Medications and toxins
- Neoplasia
  - Colon carcinoma
  - Lymphoma
  - Villous adenoma in rectum
- Congenital syndromes (e.g., congenital chloridorrhea)
- Idiopathic

OSMOTIC DIARRHEA

CLUES: STOOL VOLUME DECREASES WITH FASTING
INCREASED STOOL OSMOTIC GAP



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INFLAMMATORY DIARRHEA

- **Inflammatory bowel disease**
  - Ulcerative colitis
  - Crohn's disease
- **Infectious diseases**
  - Invasive bacterial infections (e.g., tuberculosis, yersiniosis)
  - Invasive parasitic infections (e.g., amebiasis, strongyloidiasis)
  - Pseudomembranous colitis (Clostridium difficile infection)
  - Ulcerating viral infections (e.g., cytomegalovirus, herpes simplex virus)
- **Ischemic colitis**
- **Radiation colitis**
- **Neoplasia**
  - Colon cancer
  - Lymphoma

FATTY DIARRHEA

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

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COMMON CAUSES OF DIARRHEA

Developing countries

- Chronic bacterial
- Mycobacterial
- Parasitic infections

Then

- Functional disorders,
- Malabsorption
- Inflammatory bowel disease

Developed countries

- 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)

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ACUTE VERSUS CHRONIC

- Most of acute diarrhea cases are due to infectious cause while chronic are due to noninfectious cause

APPROACH TO PATIENT WITH DIARRHEA

- History
- Physical examination
- Investigations
  - Laboratory tests
  - Radiology
  - Endoscopy
- Management

HISTORY

- **What led** the patient to complain of diarrhea? (eg, consistency or frequency of stools, the presence of urgency or fecal soiling)
- **Stool characteristics**: (eg, 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:** (eg, 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

HISTORY…

- 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
- 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 fever, joint pains, mouth ulcers, eye redness)→ IBD, CTD, thyroid. Symptoms of nutritional deficiency.
- Family history: IBD
- Drug Hx: including over the counter mediations

LIKELY CAUSE OF DIARRHEA IN CERTAIN EPIDEMIOLOGIC CLASSIFICATIONS

- Travelers: bacterial, protozoal, tropical sprue (v rare)
- Diabetics patients
- AIDS patients: infections, drugs
- Hospitalized patients :drugs, infections, ischemia , C.D toxin

PHYSICAL EXAMINATION

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

INVESTIGATIONS
ARE GUIDED BY HX AND PH EXAM
(ESSENTIALS)

- CBC
- ESR
- Electrolytes
- Total protein and albumin
- TFT
- Stool : occult blood, C/S, ova and parasites, C-D toxin (if hx suggestive)

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SPECIFIC INVESTIGATIONS

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

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MALABSORPTION

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MALABSORPTION

- Definition: abnormality in absorption of food nutrients across the gastrointestinal (GI) tract.
- Results from
  - congenital defects in the membrane transport systems of the small intestinal epithelium or
  - acquired defects in the epithelial absorptive surface.

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PHASES OF ABSORPTION

- **Luminal phase:** dietary fats, proteins, and carbohydrates are hydrolyzed and solubilized by secreted digestive enzymes and bile.
- **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.
- **Postabsorptive phase**: nutrients are transported via lymphatics and portal circulation from epithelial cells to other parts of the body.

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LUMINAL PHASE

Phase and nature of malabsorptive defect	Example
A. Substrate hydrolysis	
1. Digestive enzyme deficiency	Chronic pancreatitis
2. Digestive enzyme inactivation	Zollinger-Ellison syndrome
3. Dyssynchrony of enzyme release, inadequate mixing	Post Billroth II procedure
B. Fat solubilization	
1. Diminished bile salt synthesis	Cirrhosis
2. Impaired bile secretion	Chronic cholestasis
3. Bile salt de-conjugation	Bacterial overgrowth
4. Increased bile salt loss	Ileal disease or resection
C. Luminal availability of specific nutrients	
1. Diminished gastric acid	Atrophic gastritis - vitamin B12
2. Diminished intrinsic factor	Pernicious anemia - vitamin B12
3. Bacterial consumption of nutrients	Bacterial overgrowth - vitamin B12

MUCOSAL (ABSORPTIVE) PHASE

Phase and nature of malabsorptive defect	Example
A. Brush border hydrolysis*	
1. Congenital disaccharidase defect	Sucrase-isomaltase deficiency
2. Acquired disaccharidase defect	Lactase deficiency
B. Epithelial transport	
1. Nutrient-specific defects in transport	Hartnup's disease
2. Global defects in transport	Celiac sprue
(a) decreased absorptive surface area	intestinal resection
(b) damaged absorbing surface	celiac sprue, tropical sprue, giardiasis, Crohn disease, AIDS enteropathy, chemotherapy, or radiation therapy;
(c) infiltrating disease of the intestinal wall	lymphoma and amyloidosis

*This process is sometimes considered as part of the luminal phase.

POSTABSORPTIVE, PROCESSING PHASE

Phase and nature of malabsorptive defect	Example
A. Enterocyte processing	Abetalipoproteinemia
B. Obstruction of Lymphatic	Both congenital (e.g. intestinal lymphangiectasia)
	Acquired (e.g. Whipple diseases , lymphoma, tuberculosis).

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CLINICAL FEATURES

- Depend upon the **cause** and **severity** of the disease
- Malabsorption may either be **global** or **partial (isolated).**
- **Global malabsorption:** results from diseases associated with either diffuse mucosal involvement or a reduced absorptive surface
  - An example is **celiac disease** in which diffuse mucosal disease can lead to impaired absorption of almost all nutrients
- **Partial or isolated malabsorption:** results from diseases that interfere with the absorption of specific nutrients.
  - Defective cobalamin absorption, for example, can be seen in patients with pernicious anemia or those with disease (or resection) of the terminal ileum such as patients with Crohn's disease.

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SIGNS AND SYMPTOMS OF 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
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

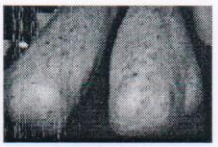
SIGNS AND SYMPTOMS OF MALABSORPTION....

Malabsorption of	Clinical features	Laboratory findings
Folic acid	Anemia	Macrocytic anemia, serum and RBC folate decreased, serum homocysteine increased
Vitamin B, general	Cheilosis, painless glossitis, acrodermatitis, angular stomatitis	
Iron	Microcytic anemia, glossitis, pagophagia	Serum iron and ferritin decreased, total iron binding capacity increased
Calcium and vitamin 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

EXAMPLE OF MANIFESTATIONS ASSOCIATED WITH CELIAC DISEASE

Dermatological manifestations

- Pale skin



- Neurological examination
- Motor weakness, peripheral neuropathy, or ataxia may be present .
- The Chvostek sign or the Trousseau sign may be evident due to hypocalcemia .

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EXAMPLES OF SOME MALABSORPTION INVESTIGATIONS AND THEIR USE

LAB STUDIES

- Hematological tests
  - A CBC
  - Serum iron, vitamin B-12, 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 inflammatory diseases like Crohn disease and Whipple disease

STOOL ANALYSIS

- Stool pH may be assessed. Values of <5.6 are consistent with carbohydrate malabsorption
- Stool C/S
- Pus cells in the stool e.g IBD, some infections

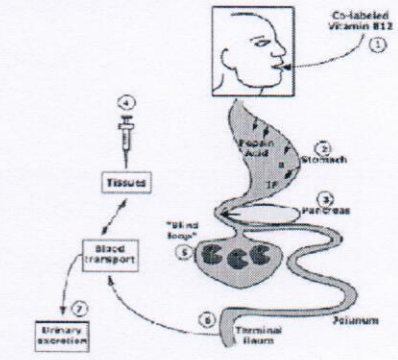
TESTS OF FAT MALABSORPTION

- For a quantitative measurement of fat absorption, a 72-hour fecal fat collection
- Qualitative test Sudan III stain of stool, less reliable .

- Stool → fat →pancreatic, celiac

  inflammatory --→ IBD ,infection

The Schilling test (part one)



SCHILLING TEST

- Malabsorption of vitamin B-12 may occur as a consequence of:
  - Deficiency of intrinsic factor (eg, pernicious anemia, gastric resection)
  - Pancreatic insufficiency, bacterial overgrowth
  - Ileal resection, or disease .

3 STEPS SCHILLING TEST

1. Oral VIT B12
2. VIT B12 orally +intrinsic factor
3. VIT B12 orally +intrinsic factor+ oral antibiotics

BACTERIAL OVERGROWTH

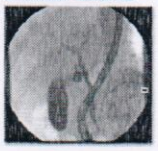
- Bacterial overgrowth cause an early rise in breath hydrogen
- JEUJENAL CULTURE
- 14c D–xylose breath test ,high sensitivity and specificity

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 can be used to try to distinguish between pancreatic causes and intestinal causes of malabsorption.

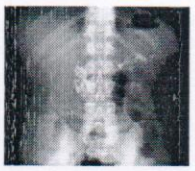
IAMGING

- Small bowel barium studies .
  - Strictures
  - Mucosal changes
  - Diverticula
- CT scan of the abdomen
  - Strictures
  - Mucosal changes
  - Diverticula
  - Wall thickness
  - Massesss, lymph nodes
- ERCP: pancreatitis (duct changes) , biliary doseases



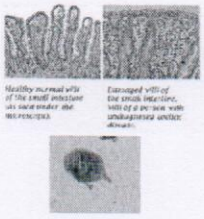
IMAGING STUDIES

Plain abdominal x-ray film: Pancreatic calcifications are indicative of chronic pancreatitis.



ENDOSCOPY

- Upper endoscopy with small bowel mucosal biopsy…. Examples
  - Celiac sprue
  - Giardiasis
  - Crohn disease
  - Whipple disease
  - Amyloidosis
  - Lymphoma.
- Lower GI endoscopy: colonic and terminal ileal pathology (e.g Chrons disease)



TREATMENT

Treatment of causative diseases

- 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

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- 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

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CASES:

- Case 1: 30 y man with Rt iliac fossa pain, diarrhea/ 5 months, wt loss
- Case 2: 26 y female with female with bloody diarrhea/ 8 weeks
- Case 3: 22 F with anemia only

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