

2ND YEAR / GIT BLOCK

MED TEAMS 431

2012

PATHOLOGY TEAM

Pathophysiology
and mechanisms of

Diarrhea

*D*one by:

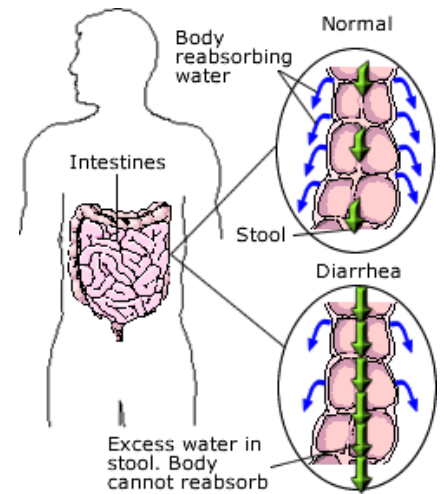
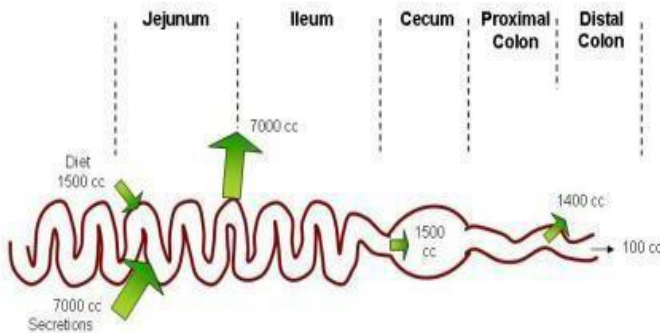
Abdulrahman Aljadoa & Manar Aljebreen

DIARRHEA

Objectives:

1. Define diarrhea
2. Describe the pathogenesis of different types of diarrhea
3. List the causes of chronic diarrhea

Physiology of Fluid and small intestine:



DEFINITION

• World Health Organization:

- 3 or more loose or liquid stools per day

- Abnormally high fluid content of stool
> 200-300 gm/day

Why important?

- The loss of fluids through diarrhea can cause **dehydration** and electrolyte imbalances
- Easy to treat but if untreated, may lead to death especially in children.
- More than 70 % of almost 11 million child deaths every year are attributable to **6 causes**:

1. Diarrhea

2. Malaria
3. neonatal infection
4. Pneumonia
5. preterm delivery
6. lack of oxygen at birth.

CLASSIFICATION

acute	Persistent	Chronic
• if 2 weeks (less than 2 weeks)	• if 2 to 4 weeks	• if 4 weeks in duration (more than 4 weeks)

Pathophysiology:

Categories of diarrhea

1. Secretory
2. Osmotic
3. Exudative (inflammatory)
4. Motility-related

Each category will be explained below

Fecal osmolarity:

- As stool leaves the colon, fecal osmolality is equal to the serum osmolality i.e. 290 mosm/kg.
- Under normal circumstances, the major osmoles are Na^+ , K^+ , Cl^- , and HCO_3^- .

Fecal osmotic gap is calculation performed to distinguish among different causes of diarrhea

$$= 290 - 2 * (\text{stool Na} + \text{stool K})$$

Fecal Osmotic Gap

$$290 \text{ mosm/kg H}_2\text{O} - 2 ([\text{Na}^+] + [\text{K}^+])$$

Osmotic diarrhea: > 125

Osmotic:

• 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, $> 125 \text{ mOsm/kg}$

Can be the result of

1. Malabsorption in which the nutrients are left in the lumen to pull in water e.g. lactose intolerance.
2. osmotic laxatives.

Osmotic diarrhea is characterized by **hypotonic stool** due to presence of osmotically active solutes drawing more water than electrolytes out of the enterocytes . (from USMLE)

Laxatives: are foods, compounds or drugs taken to loosen the stool.

Sufficiently high doses of laxatives may cause diarrhea.

Secretory:

- There is an increase in the active secretion of water.
- High stool output
- Lack of response to fasting
- Stool osmotic gap $< 100 \text{ mOsm/kg}$
- 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
- Also seen in neuroendocrine tumours (carcinoid tumor, gastrinomas)

Bacterial infections that are not associated with invasion of the mucosa only producing toxins

The stool is isotonic

Exudative (inflammatory):

- Results from the outpouring of blood protein, or mucus from an inflamed or ulcerated mucosa.
- Presence of blood and pus in the stool.
- **Persists on fasting**
- Occurs with inflammatory bowel diseases, and invasive infections e.g. *E. coli*, *Clostridium difficile* and *Shigella*

E.coli can be 1)invasive and causing exudative diarrhea
2)toxins producing and causing secretory diarrhea.

Motility-related

- Caused by the rapid movement of food through the intestines (hypermotility).
- **Irritable bowel syndrome (IBS)** – a motor disorder that causes abdominal pain and altered bowel habits with diarrhea predominating.

Occurs with stress and neurological disorders and diagnosed by exclusion of bacterial , viral infections and malabsorption.

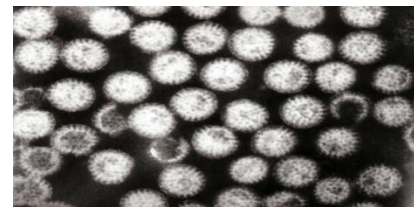
Aetiology:

Acute diarrhea: (less than 2 weeks)

- Approximately 80% of acute diarrheas are due to **infections** (viruses, bacteria, helminths, and protozoa).
- **Viral gastroenteritis** (viral infection of the stomach and the small intestine) is the most common cause of acute diarrhea worldwide.

Rotavirus the cause of nearly 40% of hospitalizations from diarrhea in children under 5 years. (most common cause of diarrhea in children)

- Food poisoning
- Drugs
- Others



Chronic diarrhea:

1. Infection e.g. *Giardia lamblia*. AIDS often have chronic infections of their intestines that cause diarrhea.

Giardia covers the mucosa of the small intestine and interfere with absorption and lead to malabsorption , can be seen in the stool and in mucosal biopsy.

2. Post-infectious Following acute viral, bacterial or parasitic infections

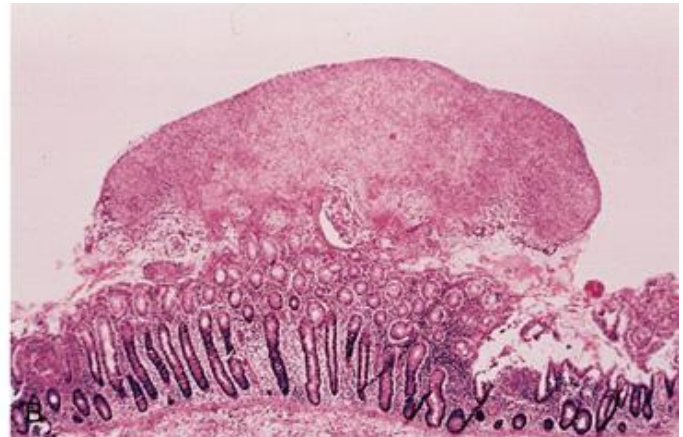
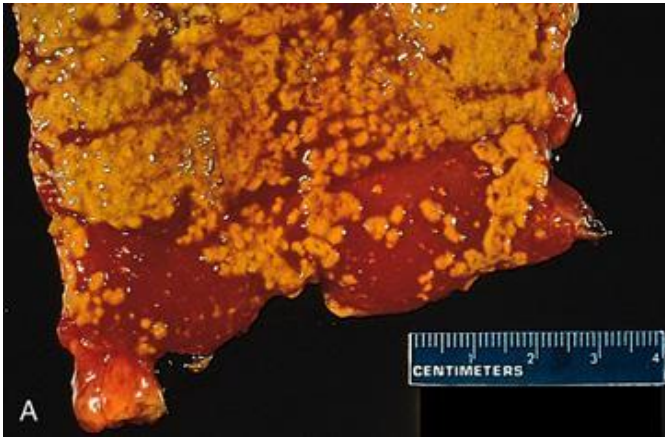
3. Malabsorption investigations for malabsorptions are applied mainly in chronic diarrhea

*to differentiate between the villus atrophy produced by celiac disease and post infections :By the location in celiac disease the atrophy is in the proximal part of the intestine while in post infection it involves the entire intestine.

- 4. Inflammatory bowel disease (IBD)
- 5. Endocrine diseases
- 6. Colon cancer
- 7. Irritable bowel syndrome

Antibiotic-Associated Diarrheas

- Diarrhea occurs in 20% of patients receiving broad-spectrum antibiotics; about 20% of these diarrheas are due to *Clostridium difficile*
- Leading to pseudomembranous colitis



Complications:

1. FluidsDehydration
2. Electrolytes Electrolytes imbalance
3. Sodium bicarbonate..... Metabolic acidosis
4. If persistentMalnutrition

Tests useful in the evaluation of diarrhea

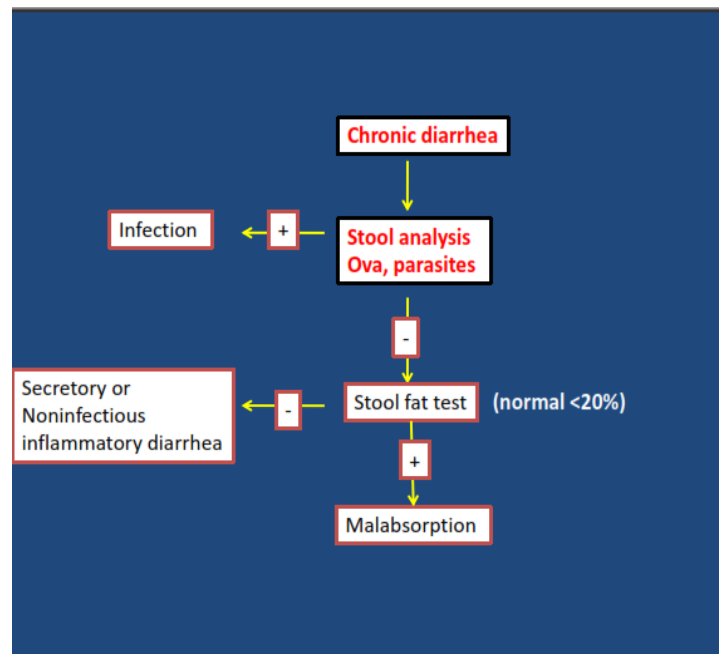
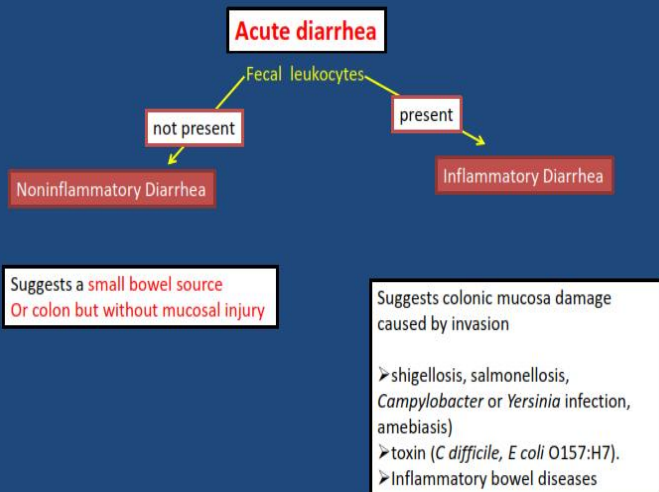


Table 14-3. Defects in Malabsorptive and Diarrheal Disease

Disease	Intraluminal Digestion	Terminal Digestion	Transēpithelial Transport	Lymphatic Transport
Celiac disease		+	+	
Tropical sprue		+	+	
Chronic pancreatitis	+			
Cystic fibrosis	+			
Primary bile acid malabsorption	+		+	
Carcinoid syndrome			+	
Autoimmune enteropathy		+	+	
Disaccharidase deficiency		+		
Whipple disease				+
Abetalipoproteinemia			+	
Viral gastroenteritis		+	+	
Bacterial gastroenteritis		+	+	
Parasitic gastroenteritis		+	+	
Inflammatory bowel disease	+	+	+	

Summary

- Diarrhea is one of the most common causes of death in children all over the world; it causes dehydration, electrolyte imbalance and death if not treated.
- The diarrhea is divided according to the pathophysiology into:
 - a. **Secretory**: caused by bacterial toxin and endocrine tumors with normal osmotic gap.
 - b. **Osmotic**: result from malabsorption and osmotic laxatives with high osmotic gap
 - c. **Exudative**: caused by invasive infection(ex. Shigella and salmonella) and inflammatory bowel disease with present of pus and blood in stool.
 - d. **Motility-related**: Irritable bowel syndrome (IBS)
- Diarrhea is divided according to the aetiology into:
 - Acute** diarrhea (2 weeks): most common caused by viral gastroenteritis.
 - Chronic** diarrhea: it results from many causes like e.g. *Giardia lamblia*, and AIDS.

1- Which type of diarrhea is associated lactose intolerance:

- a) Secretory
- b) Osmotic
- c) Exudative (inflammatory)
- d) Motility-related

Answer: b

2- all of the following are causes of acute diarrhea except:

- a) Viral gastroenteritis
- b) Food poisoning
- c) Inflammatory bowel disease
- d) Antibiotic-Associated Diarrheas

Answer: c

3- A 10-month-old, previously healthy male infant develops a severe, watery diarrhea 2 days after visiting the pediatrician for a routine checkup. The most likely diagnosis is :

- a) Rotavirus infection
- b) Enterotoxigenic *E. coli* infection
- c) *Entamoeba histolytica* infection
- d) Lactase deficiency
- e) Ulcerative colitis

Answer : a

Rotavirus accounts for estimated 130 million cases and 0.9 million deaths worldwide per year, and constitute about 60% of children enterocolitis in the United States. The affected population is children 6 to 24 months of age; spread is by fecal-oral contamination. The prodrome of development of diarrhea after infection is 2 days, and the disease last 3 to 5 days. (from Robbins)

A 44 year-old man is admitted to the hospital with an acute upper GI bleed due to several gastric and duodenal ulcers seen on an urgent upper endoscopy. One of the duodenal ulcers is in the 3rd portion of the duodenum. The patient also complains of a 1 year history of frequent non-bloody diarrhea. A fecal osmotic gap is very low.

- What type of chronic diarrhea does this patient have?
 - Secretory
- What is the most likely cause?
 - Zollinger-Ellison syndrome due to a gastrinoma
- What is the mechanism to explain the diarrhea?
 - Acid inactivation of pancreatic enzymes and bile salts
 - Excess intestinal fluid
- What blood test can you check to make the diagnosis?
 - Gastrin level