Lecture 5
Diarrhea

PATHOLOGY TEAM 435

{ ومن لم يذق مرّ التعلُّمِ ساعةً.. تجرع ذلَّ الجهل طوال حياتهِ }

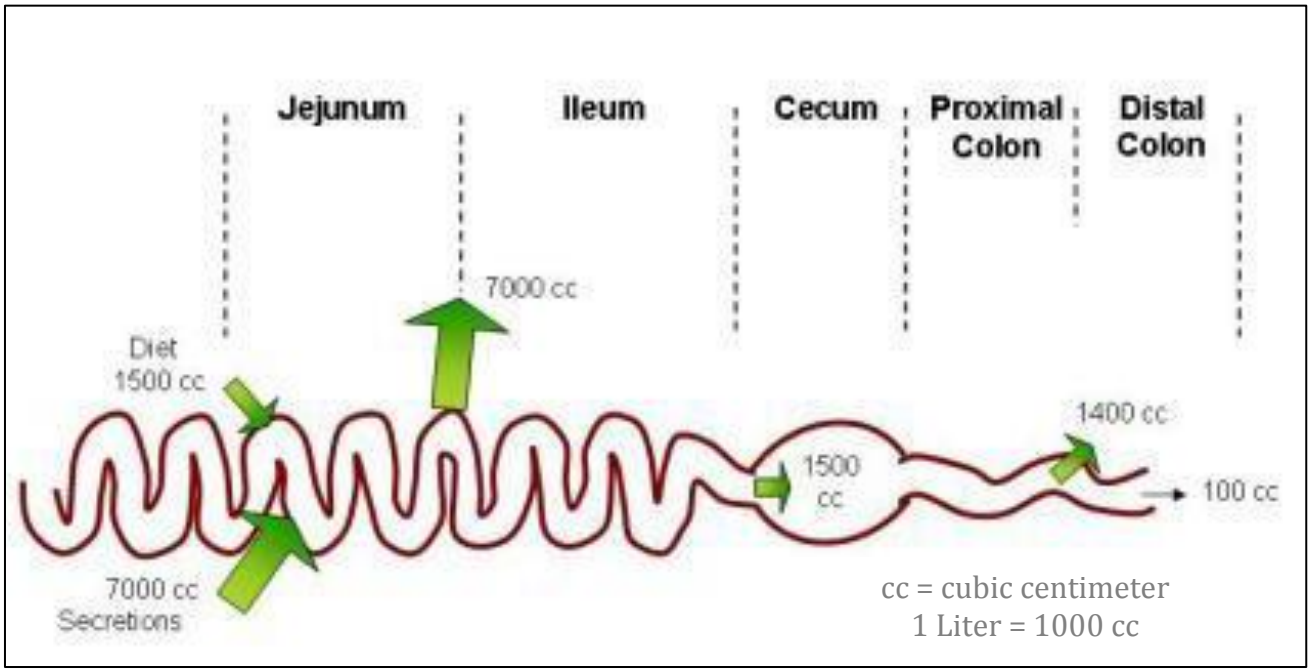
Revised by
خولة العماري & هشام الغفيلي

Red: Important. Grey: Extra Notes Doctors Notes will be in text boxes

Objectives:

- Understand the physiology of fluid in small intestine
  - 1.5-liter food
  - 7 liters' secretions and reabsorbed in small intestine
  - 1.4 reabsorbed in large intestine
- Describe the pathophysiology and causes of various types of diarrhea
  - Secretory Normal stool osmotic gap {bacterial toxin (E. coli, cholera) Endocrine tumors}
  - Osmotic, osmotic gap is high, {Malabsorption, osmotic laxatives}
  - Exudative, blood and pus in the stool, {inflammatory bowel diseases, and invasive infections}
  - Motility-related {Irritable bowel syndrome (IBS)}
- 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), cancer

Physiology of Fluid and small intestine:



Diarrhea:

3 or more loose or liquid stools per day(WHO[1]). There is abnormal high fluid content in the stool more than 200-300 gm/day.

Fecal Osmolarity:

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

Fecal Osmotic Gap

290 mosm/kg H_2O - 2 ([Na^+] + [K^+])

Osmotic diarrhea: > 125

Stool osmotic gap = Stool osmolality - 2 x (stool Na + stool K) ← القانون

Normal value is less than 125

Stool Osmotic Gap: important

- Is a calculation performed to distinguish among different causes of diarrhea.
- A normal gap is between 50 and 100 mosm/kg.
- A low stool osmotic gap (<50 mosm/kg) can imply secretory diarrhea.
- A high gap (>125 mosm/kg) can imply osmotic diarrhea.

secretory diarrhea | Normal gap | osmotic diarrhea

50 mosm/kg 100 mosm/kg

[1] Definition by World Health Organization

- The reason for this is that secreted sodium and potassium ions make up a greater percentage of the stool osmolality in secretory diarrhea, whereas in osmotic diarrhea, molecules such as unabsorbed carbohydrates are more significant contributors to stool osmolality.

TO SUM UP: we have a stool osmolality which is = in value to serum osmolality which ≅ 290 mOsm/kg, so we calculate the difference between stool osmolality (290) and the osmolality of certain ions in the stool from the patient.
Why? to categorize diarrhea to differentiate between the different causes of diarrhea.

Classification:	Acute Diarrhea	Persistent Diarrhea	Chronic Diarrhea
Duration:	< 2 weeks	2 - 4 weeks	> 4 weeks

Why is it Important? (UNICEF)

- 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:
  - Diarrhea
  - Malaria
  - Neonatal infection
  - Preterm delivery
  - Pneumonia
  - Lack of oxygen at birth

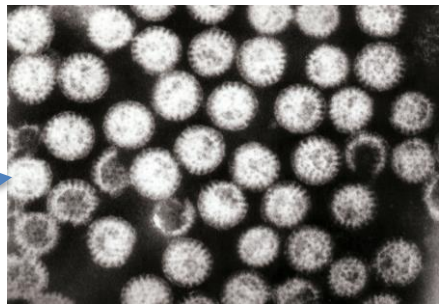
Etiology:

Acute Diarrhea:

Infections and toxins

- 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.
- Food poisoning.
- Drugs.
- Others.

Food positing is caused by performed toxins by (staph aureus, bacillus, clostridium perfringens, clostridium botulinum)



- Majority of acute diarrheas are due to infections,

  and to be specific Viral gastroenteritis is the most common cause.

Rotavirus the cause of nearly 40% of hospitalizations from diarrhea in children under 5

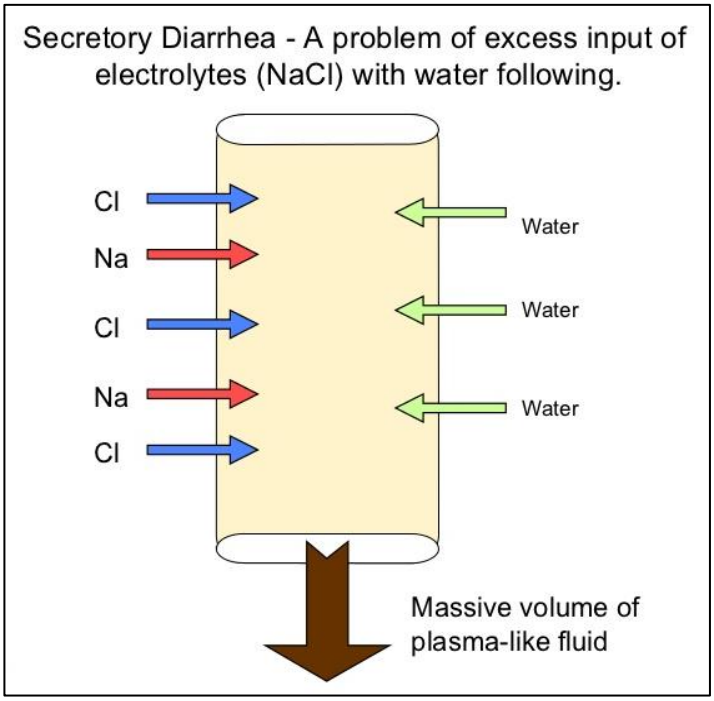
- Clinically person become dehydrated with electrolyte disturbance and low bicarbonate in blood

Pathophysiology: (very important)

Categories of diarrhea:

1. Secretory:

- There is an increase in the active secretion.
- High stool output.
- Lack of response to fasting.
- It has a normal or low stool osmotic gap < 100 mOsm/kg.
- The most common cause of this type of diarrhea is a **bacterial toxin** (E. coli, cholera) that stimulates the secretion of anions.
- Also seen in Endocrine tumors.



Other causes:

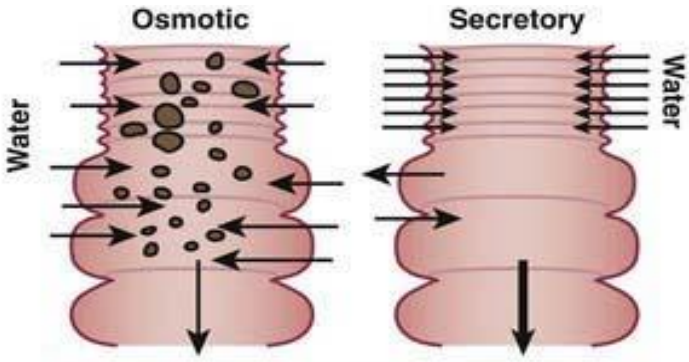
- Enteropathogenic virus e.g. rotavirus and norwalk virus.
- Also seen in neuroendocrine tumors (carcinoid tumor, gastrinomas).
- Rectal villous adenoma. → which is a large tumor that produce protein and high amount of fluid

2. 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 improves the condition.
- Stool osmotic gap is high, > 125 mOsm/kg.
- Can be the result of:
  - Malabsorption in which the nutrients are left in the lumen to pull in water e.g. lactose intolerance.
  - Osmotic laxatives[2] e.g. Lactulose (non-absorbable sugar).
  - Hexitols (poorly absorbed): sorbitol, mannitol, xylitol.

TO SUM UP: osmotic diarrhea results because of the undigested or unabsorbed substances that remain in the lumen of the small intestine and that will lead to change in osmosis and will drag water in the lumen to make the GI tract isotonic

[2] tending to stimulate or facilitate evacuation of the bowels



Stool volume:	Moderately increased	Very large
Response to fasting:	Diarrhea stops	Diarrhea continues
Stool osmolality:	Normal to increased	Normal
Ion gap:	≥ 100 mOsm/kg	< 100 mOsm/kg

3. Exudative (inflammatory):

- Results from the outpouring[3] of blood protein, or mucus from an inflamed or ulcerated mucosa.
- Presence of blood and pus in the stool.
- Persists on fasting (does not improve by fasting).
- Occurs with inflammatory bowel diseases, and invasive infections.
- Some bacterial infections cause damage by invasion of the mucosa. Many cause diarrhea with blood and pus in the stool (**bacterial dysentery**[4]).
- The main organisms that may cause bacterial dysentery are:
  - ***Campylobacter*** invades mucosa in the jejunum, ileum and colon, causing ulceration and acute inflammation. (We didn't mention the duodenum. why? Because the duodenum is more likely to be infected with H. Pylori not campylobacter)
  - ***Salmonella typhi, S. paratyphi A, B,* and *C***
  - ***Shigella*** infections are mainly seen in young children.
  - **Enteroinvasive and enterohemorrhagic *E. coli***

4. 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
  - Increased serotonin: carcinoid syndrome: Serotonin increases bowel motility.
  - No inflammation in bowel mucosa.

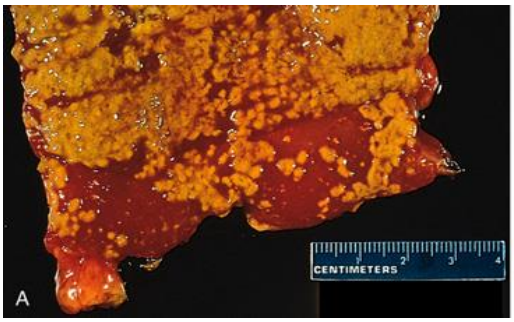
[3] something that streams out rapidly
[4] Painful, bloody, small-volume diarrhea

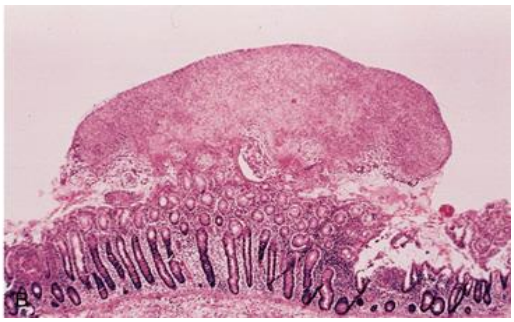
Antibiotic-Associated Diarrheas: (very important)

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

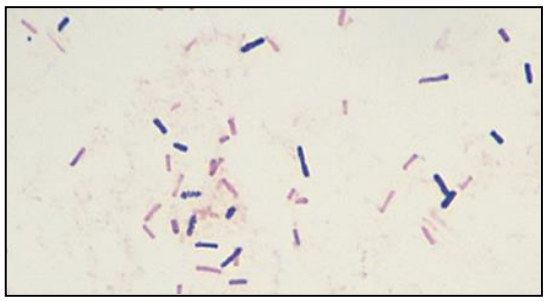
It is fatal if not treated, metronidazole is used for the treatment

Morphological:
1- red mucosa; representing inflammatory exudate
2-white to yellow spots; representing ulcerative necrosis

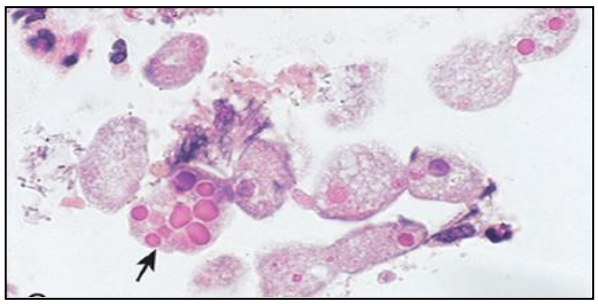




- **Pseudomembranous colitis**
- **Patients received broad-spectrum antibiotics**
- **Caused by *Clostridium difficile***



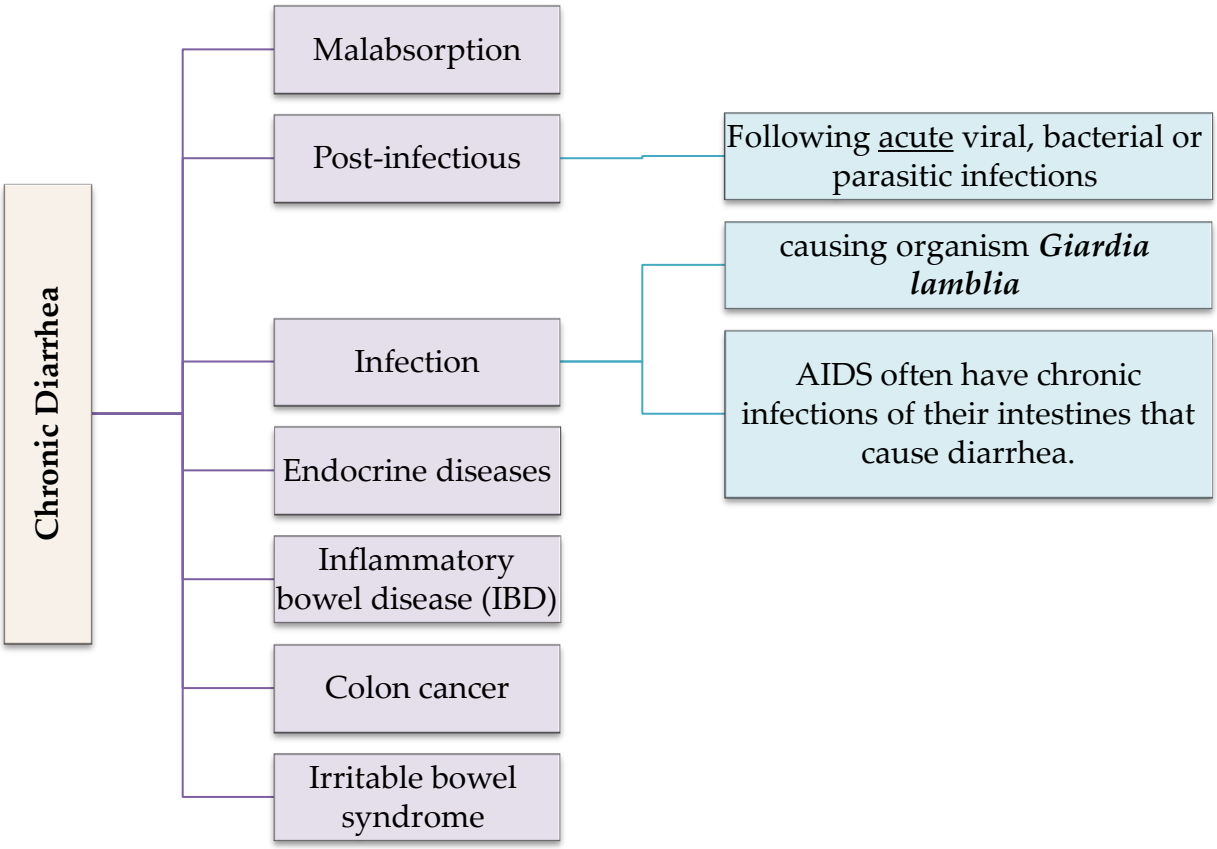
Clostridium species. Gram-positive rods



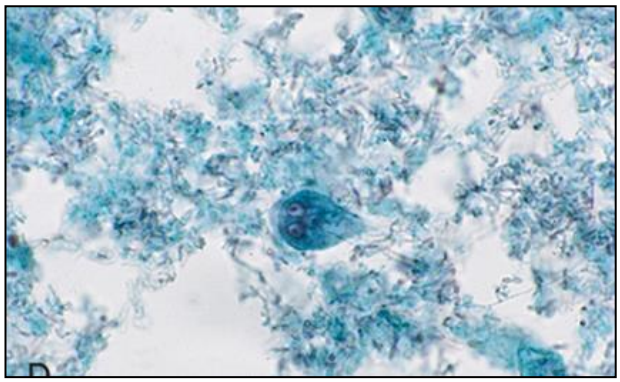
Entamoeba histolytica, Causes Amoebiasis

Entamoeba histolytica; Protozoa, it invades the wall of intestine, and live in the submucosa and secretes inflammatory exudate

Chronic Diarrhea:

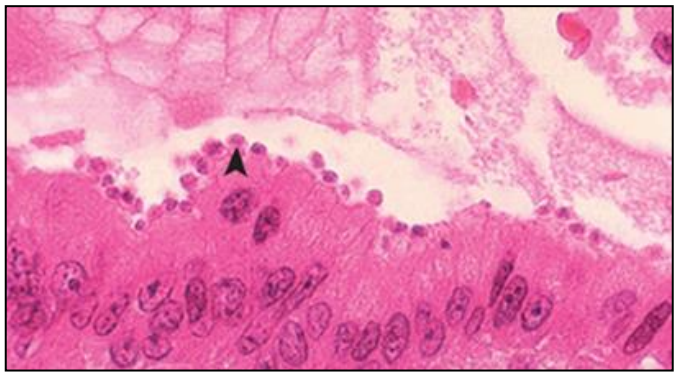


Causes:



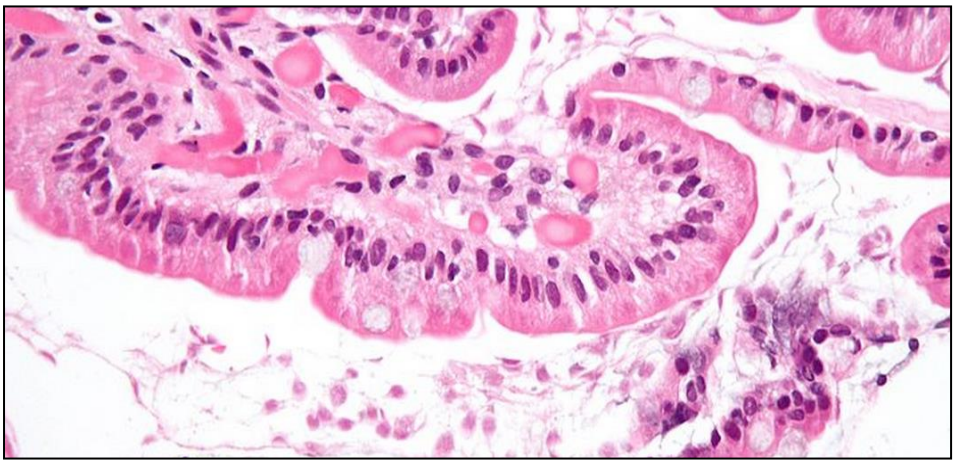
Giardia lamblia

Giardia; Protozoa 'pear shaped'
Giardiasis; affect mainly the duodenum, causes iron deficiency. Because duodenum is the main site of iron absorption



Cryptosporidiosis in AIDS

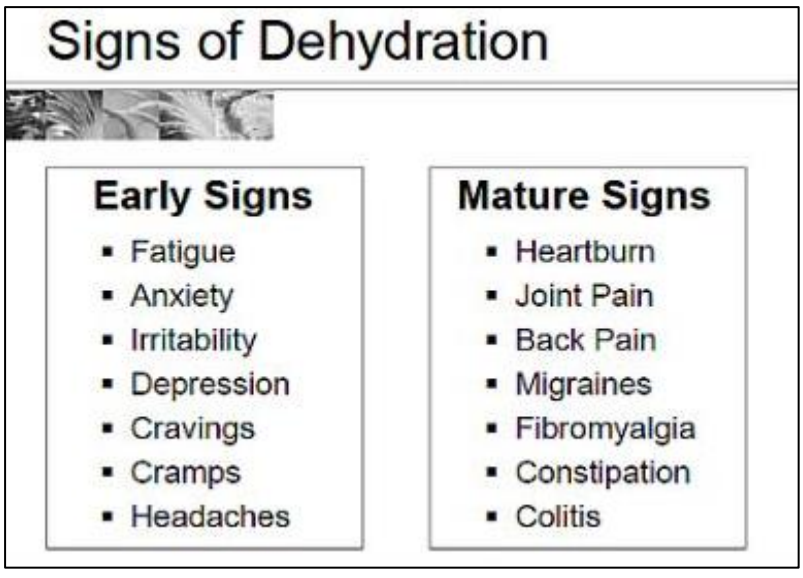
Cryptosporidiosis: is very weak, only causes diseases in immunosuppressive patient.
It wasn't known before AIDS



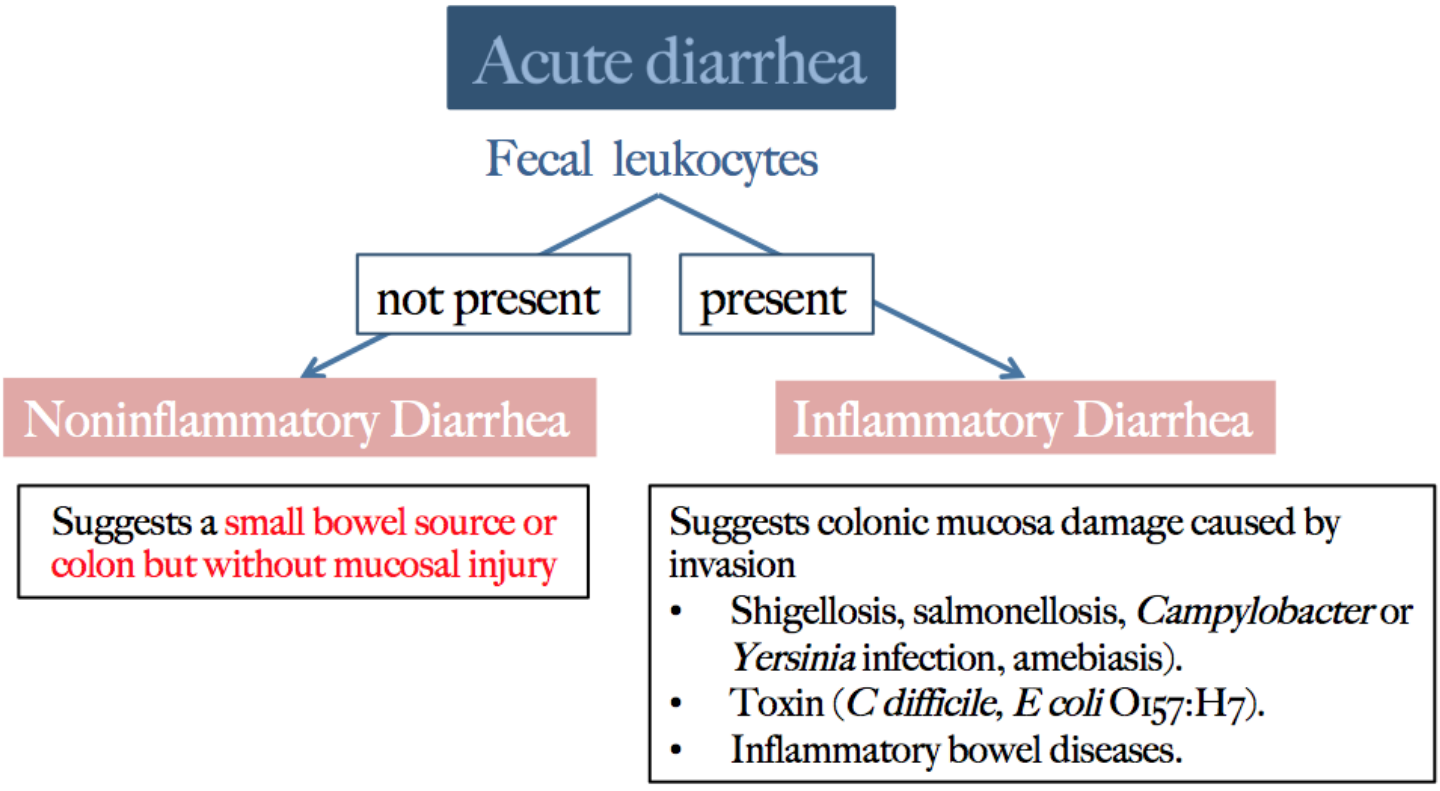
Parasitic and *protozoal* infections affect over half of the world's population on a chronic or recurrent basis.

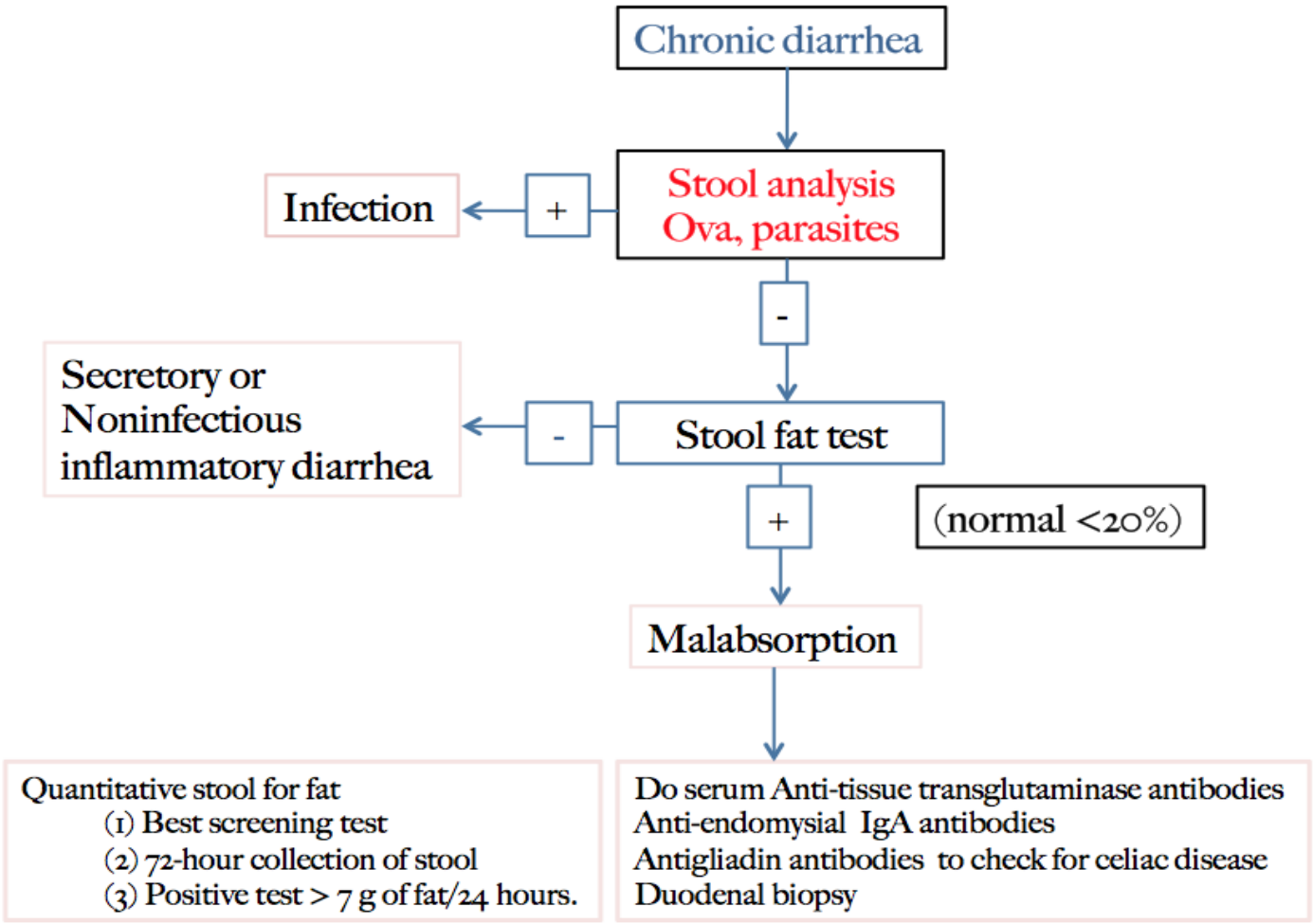
Complications:

- Fluids → Dehydration. (because of evacuating of fluids)
- Electrolytes → Electrolytes imbalance. (electrolytes will travel with the water)
- Sodium bicarbonate → Metabolic acidosis.
- If persistent → Malnutrition.



Tests useful in the evaluation of diarrhea:





Summary

- **Understand the physiology of fluid in small intestine:**
  - 1.5 liter from food.
  - 7 liters secretions and reabsorbed in small intestine.
  - 1.4 reabsorbed in large intestine.
  - And 100 ml liter excreted with feces.

- **Describe the pathophysiology and causes of various types of diarrhea:**

Pathophysiology	
Secretory	▪ Normal stool osmotic gap. ▪ Bacterial toxin (E. coli, cholera). ▪ Endocrine Tumors.
Osmotic	▪ Osmotic gab is high. ▪ Malabsorption. ▪ Osmotic Laxatives.
Exudative	▪ Blood and pus in the stool. ▪ IBD. ▪ Invasive infections.
Motility Related	▪ IBS.

- **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), cancer

This table is extra but very helpful to sum it all up

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

Check Your Understanding

MCQs:

1. **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
2. **A 30-year-old woman presents with 2 days of abdominal cramping and diarrhea. Her temperature is 38°C (101°F), Stool culture shows a toxigenic Escherichia coli infection. Which of the following best explains the pathogenicity of this organism in this patient?**
   A.Destruction of Peyer's patches
   B. Invasion of the mucosa of the colon
   C.Invasion of the mucosa of the ileum
   D.Stimulation of acute inflammation in the superficial bowel mucosa
   E. Stimulation of fluid transport into the lumen of the intestine
3. **3/A 1-year-old girl is brought to the emergency room by her parents who report that she had a fever and diarrhea for 3 days. The child's temperature is 38°C (101°F). The CBC shows a normal WBC count and increased hematocrit. Which of the following microorganisms is the most likely cause of diarrhea in this young child?**
   A. Cytomegalovirus
   B. Rotavirus
   C. Salmonella typhi
   D. Shigella dysenteriae
4. **A 53-year-old woman complains of acute diarrhea and severe abdominal pain. She was recently treated with broad-spectrum antibiotics for community acquired pneumonia. A CBC shows increased WBC count. The patient subsequently develops septic shock and dies. A portion of her colon is shown at autopsy. These findings are typical of which of the following gastrointestinal diseases?**
   A. Crohn disease
   B. Diverticulitis
   C. Ischemic colitis
   D. Pseudomembranous colitis

1: A 2: E 3: B 4: D

Scenario 1

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 endoscopy. The patient also complains of a 1 year history of frequent non-bloody diarrhea. A fecal osmotic gap is very low.

1. **What type of chronic diarrhea does this patient have?**
2. **What is the most likely cause?**
3. **What is the mechanism to explain the diarrhea?**
4. **What blood test can you check to make the diagnosis?**

Scenario 2:

5. **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

Answers:

1. **Secretory.**
2. **Zollinger-Ellison syndrome due to gastrinoma.**
3. **Acid inactivation of pancreatic enzymes and bile salts. Excess intestinal fluid.**
4. **Gastrin level.**
5. **A.**

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قال ﷺ: {من سلك طريقًا يلتمس فيه علمًا سهَّل الله له بهِ طريقًا إلى الجنة}

دعواتنا لكم بالتوفيق
