

DIARRHEA

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Mphil Pharmacology

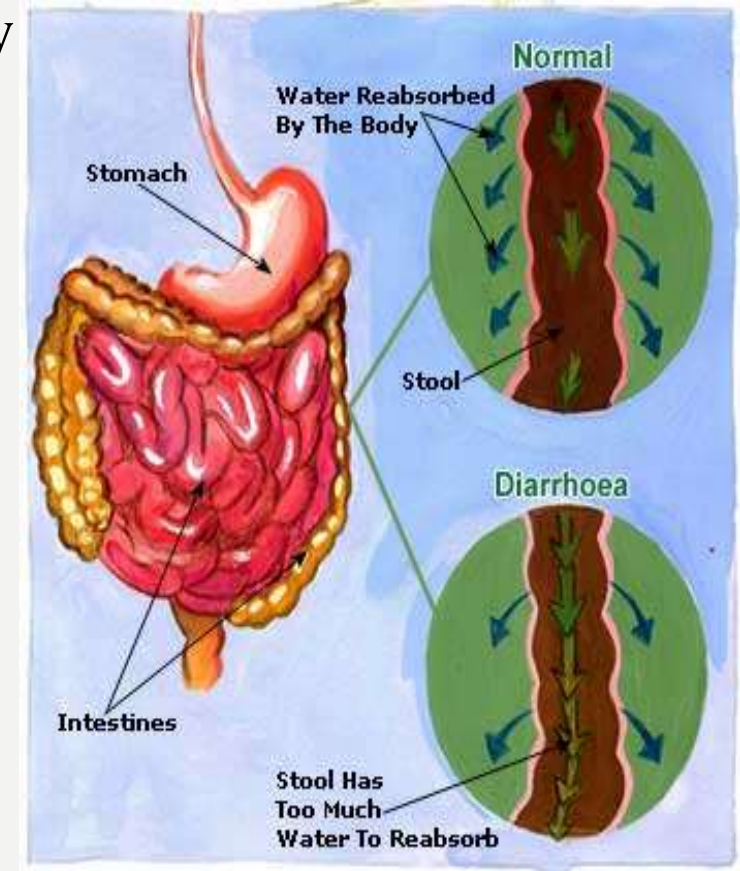
Session 2020-2022

INTRODUCTION

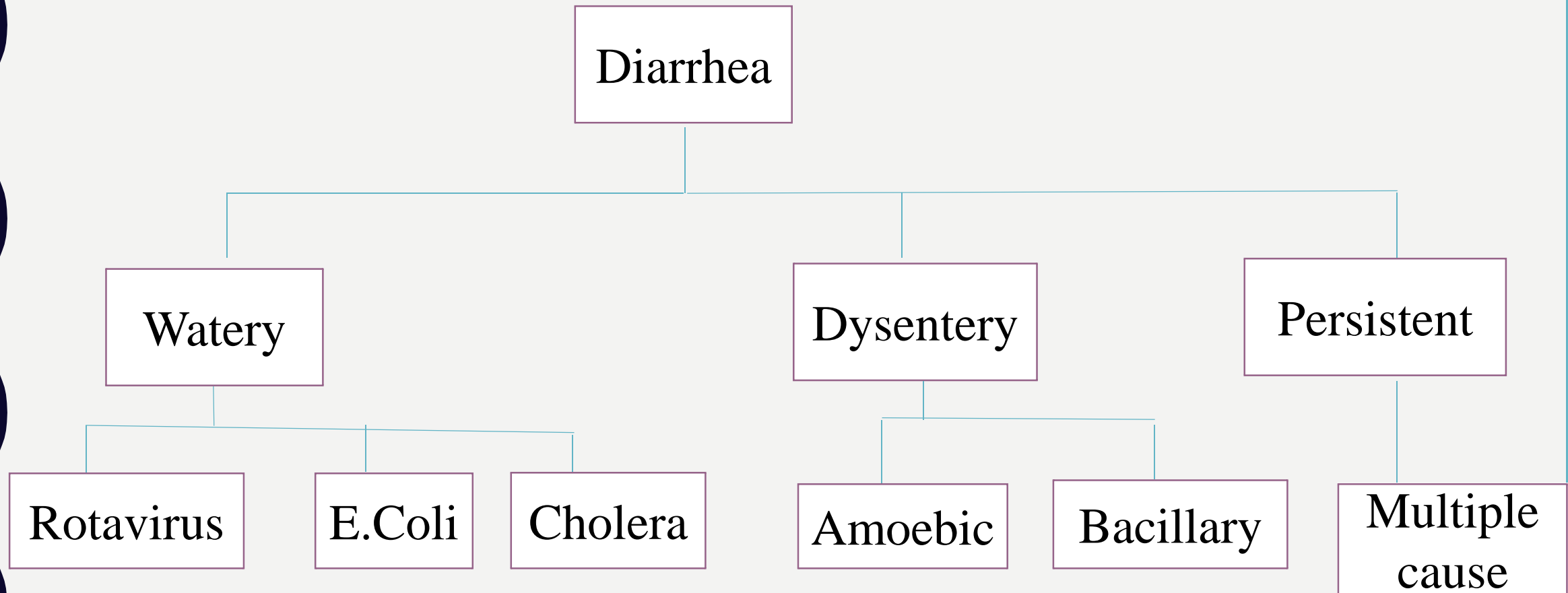
- Diarrhea, a public health concern, is the second leading cause of morbidity and mortality.
- Globally, there are about 2 Billion cases of diarrheal disease every year.
- Today only 39 percent of children with diarrhea in developing countries receive the recommended treatment and limited trend data suggests that there has been little progress since 2000.

WHAT IS DIARRHEA?

- Diarrhea is defined as passage of unusually loose or watery stool usually at three times in a 24 hour period.(WHO)
- Alteration in normal bowel movement characterized by decreased consistency and increased frequency.
- It is usually a symptom of an infection in the intestinal tract which can be caused by a variety of bacterial,viral and parasitic organisms
- People of all ages can get diarrhea,but it is more common in children below five years of age.



TYPES & CAUSES BASED ON CLINICAL SYNDROME



PATHOPHYSIOLOGY OF DIARRRHEA:

- Osmotic
- Secretory
- Exudative
- Motility disorder

Pathophysiology of Diarrhea

Classification	Pathophysiology
Osmotic/Malabsorption	Osmotic load in the intestine resulting in retention of fluid in the lumen of the bowel
<u>Secretory</u>	Excess secretion of electrolytes and water into the intestinal lumen
Inflammatory	May have features of secretory diarrhea and/or osmotic diarrhea depending on location of inflammation Stool may have blood, WBC, protein, mucus
Motility	Rapid transit through the colon

ORGANISMS INVOLVED:

Viral infections:

1. Rota virus
2. Norovirus(Adults)
3. Adenovirus types 40 and 41
4. Astroviruses

Bacterial infections:

1. Escherichia coli
2. Salmonellae
3. Shigellae
4. Campylobacter
5. Vibrio Cholera
6. Clostridium difficile

Parasitic infections:

1. Giardia
2. Entamoeba histolytica

SOURCES OF INFECTION

1. Poor personal hygiene
2. Improper sanitation contaminated
3. Water and food
4. Systemic infections
5. Urinary tract infection
 - i. Pneumonia
 - ii. Otitis media
 - iii. Meningitis
 - iv. Septicaemia

NON-INFECTIOUS

1. Malabsorption
2. Cystic fibrosis
3. Coeliac disease
4. Food intolerance or Allergy:
 - i. Lactose intolerance
 - ii. Cow's milk, Protein allergy
5. Drug induced e.g. antibiotics
6. Inflammation e.g. Ulcerative colitis, Crohn's disease
7. Surgical conditions: appendicitis, partial bowel obstruction
8. Hemolytic uraemic syndrome and toddler's diarrhea

TRANSMISSION

- Most of the diarrheal agents are transmitted by the fecal-oral route
- Cholera: water-borne disease transmitted through water contaminated with feces
- Some viruses such as rota virus can be transmitted through air.
- Nosocomial transmission is possible
- Shigellosis(blood dysentery)is mainly transmitted through person to person and also a water-washed disease transmitted more when there is scarcity of water.

TYPES

Acute diarrhea:

90% caused by infectious agents

Remaining 10% is caused by

1. Medications
2. Toxic ingestions
3. Ischemia

Causes:

Medications

Ischemic colitis

Toxins

Approach To Patients With Acute Diarrhea

- Most episodes of acute diarrhea are mild and self limited
- Indication for evaluation include:
 1. Profuse diarrhea with dehydration
 2. Grossly blood stools
 3. Fever 38.5°C(101 °F)
 4. Duration >48h without improvement
 5. Recent antibiotic use
 6. New community outbreak
 7. Elderly (70 years)
 8. Immuno-compromised patient

INVESTIGATIONS:

The cornerstone of diagnosis in those suspected of severe acute infectious diarrhea is microbiologic analysis of stool:

Workup includes:

- a. Cultures for bacterial and viral pathogens
- b. Direct inspection for ova and parasites
- c. Immunoassays for certain bacterial toxins(C.Difficile), viral antigens(rota virus), and protozoal antigens (Giardia,E.Histolytica)
- If stool studies are unrevealing,flexible sigmoidoscopy with biopsies and upper endoscopy with duodenal aspirates and biopsies may be indicated
- Structural examination by sigmoidoscopy , colonoscopy,or abdominal CT scanning may be appropriate in patients with uncharacterized persistent diarrhea to exclude IBD.

CHRONIC DIARRHEA

- Diarrhea lasting > 4 weeks
- In contrast to acute diarrhea, most of the causes of chronic diarrhea are non-infectious

CAUSES

- 1) Secretory causes
- 2) Osmotic Causes
- 3) Steatorrheal causes
- 4) Inflammatory Causes
- 5) Dysmotility causes
- 6) Factitial Causes

I. Secretory causes:

- Due to derangements in fluid and electrolyte transport across the entero-colonic mucosa.
- Characterized clinically by watery, large volume fecal outputs
- Typically painless
- Persist with fasting

1. Medications (causes)

- Bacterial toxins (cholera, E.coli)
- a broad range of drugs (e.g. some types of asthma medications, antidepressants, cardiac drugs, Laxatives, Antacids)
- certain metals, organic toxins, and plant products (e.g. arsenic, insecticides, mushroom toxins, caffeine)

2.Bowel resection, Mucosal disease or entero-colic Fistula:

- Inadequate surface for reabsorption of secreted fluids and electrolytes
- Tends to worsen with eating.
- With disease (e.g.Crohn's ileitis) or resection of <100 cm of terminal ileum, dihydroxy bile acids may escape absorption and stimulate colonic secretion (cholorrheic diarrhea)
- May contribute to so-called **Idiopathic secretory diarrhea**,in which bile acids are functionally malabsorbed from a normal appearing terminal ileum

3.Hormones:

- **Metastatic gastrointestinal carcinoid tumors**

1. Watery diarrhea,episodic flushing wheezing,dyspnea and right sided valvular heart disease
2. Diarrhea is due to release into the circulation of potent intestinal secretagogues

- **Gastrinoma**

1. Diarrhea due to fat maldigestion owing to pancreatic enzyme inactivation by low intraduodenal pH

- **VIPoma:**

1. Watery diarrhea hypokalemia achlorhydria syndrome,also called **pancreatic cholera.**
2. Due to non-cell pancreatic adenoma,referred to as a VIPoma
3. Secretes VIP and a host of other peptide hormones,pancreatic polypeptide,secretin,gastrin and prostaglandins.

- **Medullary carcinoma of the thyroid:**

Watery diarrhea caused by calcitonin, other secretory peptides or prostaglandin

- **Colorectal villous adenomas**

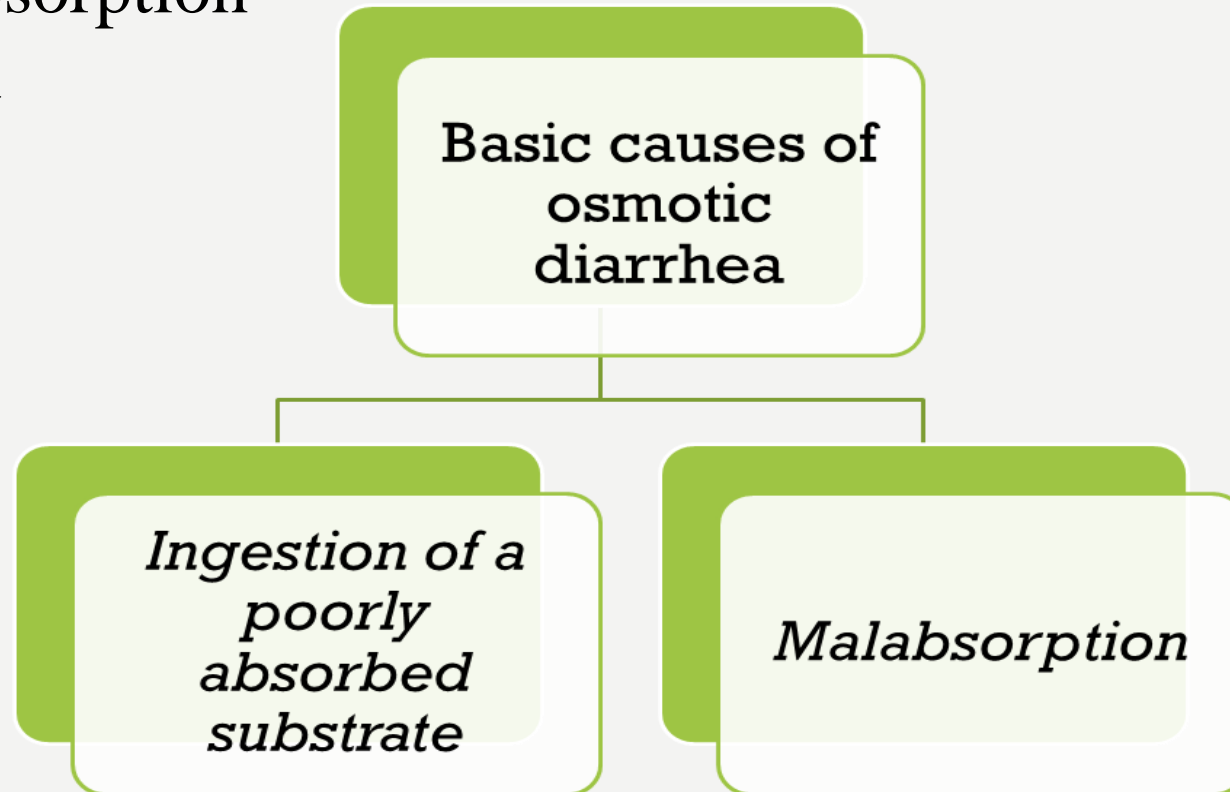
4. Congenital defects in Ion absorption:

Defects in specific carriers associated with ion absorption

II. OSMOTIC CAUSES

- If excessive amounts of solutes are retained in the intestinal lumen, water will not be absorbed and diarrhea will result
- Carbohydrate malabsorption

E:g lactase deficiency



III. Steatorrheal causes:

Fat Malabsorption

Greasy ,foul smelling difficult-to-flush diarrhea often associated with weight loss and nutritional deficiencies.

IV. Inflammatory Causes:

Accompanied by pain fever bleeding or other manifestation of inflammation.

The unifying feature on stool analysis is the presence of leukocytes or leukocyte derived proteins such as cal-protectin.

Disruption of the epithelium of the intestine due to microbial or viral pathogens causes diarrhea

Destruction of the epithelium results not only in exudation of serum and blood into the lumen but often is associated with widespread destruction of absorptive epithelium. In such cases, absorption of water occurs very inefficiently and diarrhea results.

Example: ulcerative colitis

Causes:

Bacteria: Salmonella, E. coli, Campylobacter

Viruses: rotaviruses, norovirus

Protozoa: Cryptosporium, Giardia

V. Dysmotility causes:

- In order for nutrients and water to be efficiently absorbed, the intestinal contents must be adequately exposed to the mucosal epithelium and retained long enough to allow absorption. Disorders in motility that accelerate transit time could decrease absorption, resulting in diarrhea.
- Example: Irritable bowel syndrome.

VI. Factitial Causes:

Accounts for upto 15% of unexplained diarrheas referred to tertiary care centres

Hypotension and Hypokalemia are common co-presenting features.

Approach To Patient With Chronic Diarrhea

Features:

Fecal incontinence

Fever

Weight loss

Pain and exposure e.g.travel,medications,

Family history of IBD

Physical Findings:

Hemodynamic status

Thyroid mass

Wheezing

Heart murmurs

Edema

Abdominal masses

Lymphaadenopathy'

Perianal fistulas or
anal sphincter laxity.



Thank

You