Acute Diarrhea

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Introduction

- Acute gastroenteritis is a major cause of morbidity and mortality.
- Infants and young children are at risk.
- >1000 million cases/year in developing countries, while 38 million cases/year in the US.
- About 3-4 million people/year die coz of diarrhea.

Definition of Acute Diarrhea

- is an increased frequency of defecation (≥3 times per day
- or, at least >200g of stool per day, normal is 100g/d)
- and/or increased liquidity of stool;
- lasting for less than 14 days
- may be accompanied by nausea, vomiting, abdominal cramping, clinically significant systemic symptoms, or malnutrition.

Classification of Ac. Diarrhea

Classified clinically and pathophysiologically as either Inflammatory/or non-inflammatory type.

Inflammatory diarrhea:

- are caused by organism or substances that disrupt the intestinal mucosal barrier through direct invasion or elaboration of cytotoxin.

Non-inflammatory diarrhea:

- are caused by organism or substances that don’t result in disruption or damage to the intestinal epithelium.
- Enterotoxin which may induce hypersecretion of ions.
- or coz of poorly absorbed materials which are osmotically active etc.
- 90% of these cases are mild and self limiting, respond within 5 days to simple rehydration/ and antidiarrheal agents.
- Diagnostic investigation is unnecessary

Difference betn inflammatory and non~Diarrhea

<table>
<thead>
<tr>
<th>Inflammatory D.</th>
<th>Non-inflammatory D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>C/O Small-volume, bloody, lower abdominal cramp, pain; fecal urgency, tenesmus, fever</td>
<td>Large-volume: watery, upper or perianal/bowel pain, cramping, nausea or vomiting</td>
</tr>
<tr>
<td>Fecal WBC yes</td>
<td>no</td>
</tr>
<tr>
<td>Common causes Shigella, campylobacter, Salmonella, E. histolytica, Yersinia, C. difficile, enteroinvasive E.coli, etc</td>
<td>Cholera, giardia, food poisoning St. aureus (Cl, perfingens), norovirus, norwalk virus, enterotoxigenic E.coli</td>
</tr>
</tbody>
</table>
Table 2. Classification of diarrhea

<table>
<thead>
<tr>
<th>Non-inflammatory D.</th>
<th>Inflammatory D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Viral (rotavirus, norwalk)</td>
<td>1. Bacterial disease</td>
</tr>
<tr>
<td>2. Bacterial</td>
<td>Invasive</td>
</tr>
<tr>
<td>Peformed toxin-mediated</td>
<td>- Shigella, Salmonella</td>
</tr>
<tr>
<td>S. aureus, C. Perfringens, Enteroxin production</td>
<td>- Campylobacter, Yersinia</td>
</tr>
<tr>
<td>E. coli (enterotox)</td>
<td>- Volotoxins</td>
</tr>
<tr>
<td>cholera</td>
<td>- Enteroinvasive E. Coli</td>
</tr>
<tr>
<td>3. Protozoal diseases</td>
<td>Toxin mediated</td>
</tr>
<tr>
<td>G. duodenal etc</td>
<td>- Enterohemorrhagic</td>
</tr>
<tr>
<td>4. Medication induced</td>
<td>E. coli</td>
</tr>
<tr>
<td>Antacid, Antibiotics, laxative</td>
<td>2. Protozoal - E. histolytica</td>
</tr>
<tr>
<td>5. Irritable bowel syndrome</td>
<td>3. Mesenteric ischemia</td>
</tr>
<tr>
<td>6. Dietary intolerance (due to cosmetic agent)</td>
<td>4. IBD</td>
</tr>
<tr>
<td>5. Radiation colitis</td>
<td>6. Sporidial</td>
</tr>
</tbody>
</table>

Clinical evaluation of acute diarrhea

- Differentiate potential life threatening and benign
- Self limited diarrhea or need specific treatment

Toxin Mediated diarrhea

- Acute food poisoning with vomiting and diarrhea.
- Incubation period is generally less than 18 h.
- From ingestion of preformed toxin:
  - Staphylococcus aureus, Bacillus cereus (contaminated fried rice, also called “Chinese restaurant syndrome”), and adult Cl. botulinum (in canned foods; toxin blocks the cholinergic nerves).
  - Cl. perfringens, Cl. botulinum (in infants) and Salmonella produce food poisoning after first colonizing the bowels and then release their toxins.

S. aureus

- Poor hygiene: transmission via the hands of food handlers to foodstuffs eg dairy products, cheese cooked meats.
- Following ingestion, nausea and profuse vomiting < 1-6 hours.
- Diarrhea may not be marked.
- These toxins act as super-antigens, stimulating a non-specific T-cell activation and a significant neutrophil leucocytosis.
- Rx: Antiemetics and fluid replacement
- Suspected food should be cultured for staphylococci and demonstration of toxin production.

Cl. perfringens

- Spores are widespread in the guts of large animals and in soil.
- If contaminated meat products are incompletely cooked and stored in anaerobic conditions, spores germinate and viable organisms multiply to large numbers.
- Diarrhoea and cramps occur some 6-12 hours following ingestion.
- The illness is usually self-limiting.

Cl. botulinum

Botulism is a syndrome of paralysis and neurological dysfunction produced by the neurotoxins of Cl. botulinum.

This organism may contaminate many different foodstuffs from canned meat and salmon to home-produced and preserved vegetables.

Causes predominately bulbar and ocular palsy (difficulty in swallowing, blurred or double vision, ptosis), progressing to limb weakness and respiratory paralysis.

Management includes assisted ventilation and general supportive measures until the toxin eventually dissociates from nerve endings at 6-8 weeks following ingestion.
Acute watery diarrhea

Rota virus:
- is the most common childhood cause of diarrhea,
- is transmitted by the fecal-oral route,
- it produces a watery, nonbloody diarrhea

Norwalk virus:
- is a common cause of both childhood and adult gastroenteritis,
- a brisk 2-3-day illness with marked nausea, predominant vomiting and little diarrhea.
- illness transmitting step-wise through nurseries and families remains very common.

Cholera:
- severe diarrhoea without pain; succeeded by vomiting,
- begins suddenly; typical "rice-water" material is passed;
- classical cholera produces enormous loss of fluid and electrolytes, leading to intense dehydration with muscular cramps;
- shock and oliguria develop but mental clarity remains.
- ORS or IV fluid is effective. Doxycyclin 300 mg stat.

Giardia:
- diarrhoea, abdominal pain, weakness, anorexia, nausea and vomiting, abdominal distension and tenderness.
- stool is examined for cysts;
- Rx: Tinidazole 2 g stat, or metronidazole 400 mg TDS for 7-10 days.

Traveller’s diarrhea:
- most common illness amongst travellers, affecting 20-50%.
- the risk of ~ varies with destination (highest in Africa, Asia and Latin America), age and mode of travel.
- bacterial pathogens counts 80%. E. coli, Shigella, Campylobacter, E. histolytica, and Giardia are the commonest organisms.
- stool R/E: presence of faecal leucocytes or parasites.
- stool culture: bloody or persistent diarrhoea.
- most travellers' diarrhoea is self-limiting and only ORS is indicated.
- if it is bloody: assess whether the use of antibiotics would be appropriate.
- Ciprofloxacin: shortening the duration of illness.

Inflammatory diarrhea (Invasive diarrhea):

Typhoid fever (enteric fever):
- caused by salmonella typhi, invades peritoneal patches and produce septicaemia (blood c/s 1st week)
- the second week: diarrhoea and classic triad of bradycardia, absolute neutropenia and hepatosplenomegaly.
- it may produce a chronic carrier state (persistence of the organism 1 year post-infection) usually in the gall bladder.
- Quinolones for 5-7 days are effective.

Campylobacter jejuni:
- is one of the common invasive bacterial enterocolitis,
- is contracted by eating contaminated poultry or drinking contaminated milk;
- produces a bloody diarrhea with crypt abscesses and ulcers (mimic ulcerative colitis).
- severe Colicky abdominal pain, plus nausea, vomiting and quite significant diarrhoea frequently blood-stained.
- young adults and are self-limiting after 5-7 days.
- Rx such as ciprofloxacin or a macrolide 500 mg bid for 5 days.

E. coli:
- produces toxin induced and invasive diarrheas;
- Enterotoxigenic strain
  1. produces a heat-labile toxin (LT) stimulating cyclic AMP (secretory diarrhea) or heat-stable (ST) stimulating guanylate cyclase and producing a secretory diarrhea (most common cause of traveler’s diarrheas);
  2. mild and self-limiting after 3-4 days.
- Enteropathogenic strain produces a nontoxin type of mild diarrheas in infants and young children.
**E. Coli (contd)**

- Enteroinvasive strain
  1. an invasive enterocolitis, and similar to Shigella dysentery;
  2. Acute watery diarrhoea, abdominal cramps and some scanty blood-staining of the stool are common;
  3. rarely severe and are usually self-limiting.
- Enterohemorrhagic strain
  1. is associated the O157:H7 serotypes contaminating raw ground beef,
  2. Initial watery diarrhoea becomes frankly and uniformly blood-stained in 70% of cases
  3. a severe and constant abdominal pain;
  4. may produce hemolytic-uremic syndrome and hemorrhagic or pseudomembranous colitis.
  5. Rx TMP-SMZ 160/800 mg bid or quinolones for 3-5 days.

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**Inflammatory diarrhea**

**Clostridium difficile**

- the organism associated with antibiotic-induced (most commonly ampicillin and clindamycin) pseudomembranous colitis
- is best diagnosed by toxin assay of stool,
- it is treated with metronidazole 400 mg TDS for 10 days.

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**Bloody diarrhea:**

**Bloody diarrhea:**

are bacillary or amoebic infection.

- **Bacillary dysentery:**
  1. caused by Shigella and Shigella sonnie is the most common cause of shigellosis,
  2. oral-fecal route,
  3. bloody, and purulent diarrhea and pseudomembranous inflammation in the ileum and colon,
  4. low-volume diarrhea with invasion of the intestinal mucosa and production of an inflammatory exudates,
  5. Rehydration and Rx ciprofloxacin 500 mg bid for 3-5 days.

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**Bloody diarrhea:**

**Amoebiasis:**

- Caused by E. histolytica, which is spread between humans by its cysts.
- Diarrhoea alternating with constipation is common, as is mucus, with streaks of blood:
- Often have an offensive odour.
- There may be tenderness along the line of the colon, especially over the caecum and pelvic colon.
- Very frequent motions and the passage of much blood and mucus, simulating bacillary dysentery or ulcerative colitis.
- Motile trophozoites containing red blood cells.
- Movements cease rapidly as the stool preparation cools.

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**Amoebiasis (contd)**

- Sigmoidoscopy may reveal typical flask-shaped ulcers, which should be scraped and examined immediately for E. histolytica.
- Several stools may need to be examined in chronic amoebiasis before cysts are found.
- metronidazole (900 mg TDS for 5 days) or tinidazole (2 g OD for 3 days).
- Diloxanide furoate 500 mg should be given orally 8-hourly for 10 days after treatment to eliminate luminal cysts.

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**Bloody diarrhea:**

- E. coli;
- Campylobacter spp;
- Cl. difficile;
- Salmonella spp (esp non-typhoid)
- But other non-infectious causes like IBD; ischemic colitis etc should be ruled out.
Evaluation and management of diarrhea:

Assess dehydration:
- Note the general appearance and alertness of the patient, the pulse, the blood pressure, the presence or absence of postural hypotension, the mucous membranes and tears, sunken eyes, skin turgor, capillary fillings, and jugular venous pressure.

Treatment:
- Primarily targeted at aggressive volume and electrolyte replacements.

There are three key elements:
- Fluid replacement;
- Antibiotics/antimicrobial therapy; and adjunctive antidiarrheal therapy.

Rehydration:
- Rehydration is usually possible with oral rehydration solution:
  - 3.5g sodium chloride, 2.5g sodium bicarbonate, 1.5g potassium chloride, and 20g of glucose or glucose polymer in 1 L of water.
  - 1 TSF (teaspoon full) salt and 8 TSF of sugar added to 1 L of water to which one cup of orange juice or two bananas can be added for potassium.
- In developing countries, the water residual from boiled rice may be used as excellent source of ORS.

Chronic Diarrhea:
- This is defined as diarrhea persisting for more than 14 days.
- The differential diagnosis can be wide.
- Parasitic and bacterial causes; tropical malabsorption; inflammatory bowel disease and neoplasia should all be considered.
- Osmotic types:
  - due to lactase deficiency (lactose intolerance), are large volume diarrheas that draw water into the lumen; hypotonic diarrheas without mucosal inflammation.
  - Clues:
    1. stool volume decrease with fasting,
    2. increased osmotic gap greater than 50 mosm/L (osmotic gap: 290-stool osmotic pre; normal is <50 mosm/L).
  - Stool osmotic pre: 2(Na +K) of stool.
  - Causes: Antacid; lactulose intolerance; laxative.

Mechanism of acute diarrhea:
- May result from decreased absorption, increased secretion, increased osmolality of luminal content, or a change in gut motility.

Mechanism of Chronic diarrhea:
- Osmotic types:
  - Due to lactase deficiency (lactose intolerance), are large volume diarrheas that draw water into the lumen; hypotonic diarrheas without mucosal inflammation.
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  - Causes: Antacid; lactulose intolerance; laxative.
Mechanism of chronic diarrhea:

**Secretory types:**
- Large volume diarrhea;
- Secondary to stimulation of cyclic AMP mechanism for chloride secretion (cholera toxin, enterotoxigenic E. coli);
- Loss of chloride-rich fluid without mucosal inflammation.

**Choles:**
1. Large volume (>1L/d);
2. Little change with fasting; normal stool osmotic gap.
3. Causes: Endocrine tumors (stimulating intestinal/pancreatic secretion); bile salt mal-absorption (stimulating colonic secretion) and laxative abuse.

**Mechanism of chronic diarrhea:**

**Motility disorders:**
- Abnormal intestinal motility secondary to surgery or systemic disorder (as in DM, hyperthyroidism), irritable bowel syndrome.

**Choles:**
- Significant history; chronic in nature.

**Malabsorptive conditions:**
- Intestinal mucosal diseases (Crohn’s disease etc.), lymphatic obstruction, pancreatic diseases or SI bacterial overgrowth.

**Choles:**
- Weight loss; fecal fat greater than 7-10g/24h stool collection; anemia, hypoalbuminemia, chronic in nature.

**Significant diarrhea in the absence of weight loss is not likely to be due to malabsorption.**

**Mechanism of chronic diarrhea:**

**Inflammatory conditions:**
- Diarrhea is present in most pt. with IBD, lymphoma, post-radiation.

**Choles:**
- Abdominal pain; fever; weight loss; hematochezia.

**Chronic infections:**
- Acute parasitic infections may cause diarrhea through different mechanism. Giardia, E. histolytica; intestinal metaplasia; immunocompromised patients are susceptible to CMV, Cyclospora, Mycobacterium avium etc.

**Factitious diarrhea:**
- 15% of patients have factitious diarrhea caused by surreptitious laxative abuse or dilution of stool.

**Evaluation**

- Routine Blood test: CBC; electrolytes; LFT; Ca; P; albumin; TSH; Anemia occurs in malabsorption syndromes.
- Other Lab. Test: Secretory diarrheas may be due to neuroendocrine tumors (check: serum vasoactive intestinal peptide; gastrin; glucagon)
- Endoscopy/mucosal biopsy of Upper GI; large intestine; barium radiograph of small intestine etc.
- CT abdomen: no pancreatic diseases.

**Evaluation**

- Stool analysis:
  1. 24h stool collection for weight and fat (>300g/d confirms diarrhea; >1L/d suggest secretory; fecal fat >10g/d malabsorption disorder).
  2. Stool osmotic gap.
  3. Stool laxative screen (stool Mg; phosphate; and sulphate level measured).

**Evaluation**

- Exclude: Causes of acute diarrhea; Lactose intolerance; Postvomitus gastritis or drug reaction; Parasitic infection; Medication like laxative, muscles, Systemic disease.

<table>
<thead>
<tr>
<th>Fecal leukocytes</th>
<th>stool OB</th>
<th>sigmoidoscopy</th>
<th>upper GI endoscopy</th>
<th>biopsy exams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abnormal</td>
<td>Normal</td>
<td>Cancer</td>
<td>Stool electrolytes; osmoticity; stool weight/24h; fat</td>
<td></td>
</tr>
<tr>
<td>Increased osmotic gap</td>
<td>Normal osmotic gap</td>
<td>Normal stool wt</td>
<td>Increased wt</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Normal stool wt</td>
<td>Increased wt</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrine tumors</td>
<td>Insulinoma</td>
<td>Diabetes</td>
<td>Cancers</td>
<td>Laxative</td>
</tr>
<tr>
<td>Bacterial overgrowth</td>
<td>Lactose intolerance</td>
<td>Norbital,lactose</td>
<td>Laxative</td>
<td></td>
</tr>
</tbody>
</table>

- Chronic diarrhea
Treatment

- A number of antidiarrheal agents but opioids are safe in most patients with chronic, stable symptoms.
- Loperamide: 4 mg stat; then 2 mg after each stool (max:<16mg/d)
- Diphenoxylate with atropine: one tab TID/QID
- Codeine and deodorized tincture of opium: used only for the chronic and intractable diarrhea. Potential of habituation. Codeine: 15-60mg Q4H; tincture of opium: 10-25 drops/Q6h.

Treatment contd

- Clonidine: α2 agonist inhibit intestinal secretion. 0.1-0.6mg Bid
- Octreotide: somatostain analog stimulates intestinal fluid and electrolyte absorption. Is used for secretory diarrhea. 50-250 ug SC TID.
- Cholestyramine: bile salt binding resin is useful for bile salt induced diarrhea secondary to intestinal resection. 4g QD-TID.