



## PRACTITIONERS SECTION

### EVALUATION OF DIARRHEA: THE CHALLENGE CONTINUES! PART-I

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Diarrhea and constipation are among the most common patient complaint faced by primary care physicians; and they account for major referrals to gastroenterologists. Although they can be nuisance symptoms, they can signal a serious underlying condition like colorectal cancer, or systemic disorder, like thyroid disease. Most individuals experience diarrhea sometime in their life, with an episode of diarrhea usually lasting for a day or two and subsiding rapidly on its own. However, diarrhea can be a symptom of many other underlying conditions and can be chronic in nature; thus arriving at a proper diagnosis is very important for effective management of diarrhea. Normal Physiology The small intestine and colon perform functions like the secretion and absorption of water and electrolytes, storage and subsequent transport of intraluminal contents aborally, and the salvage of some nutrients after bacterial metabolism of carbohydrate that are not absorbed in the small intestine. Alterations in fluid and electrolyte handling contribute significantly to diarrhea. Alterations in motor and sensory functions of the human colon result in highly prevalent syndromes such as irritable bowel

syndrome, chronic diarrhea, and chronic constipation. Normally, the small intestine and colon absorb 99% of the total fluid load of about 10 L/day presented to it. Approximately, 1 L of residual fluid reaches the colon; the stool excretion of fluid constitutes about 0.2 L/d. The colon has a large capacitance and functional reserve and may recover up to four times its usual volume of 0.8 L/d, provided the rate of flow permits reabsorption to occur. Thus, the colon can partially compensate for intestinal absorptive or secretory disorders. A reduction of water absorption by as little as 1% can result in diarrhea. The distal ileum acts as a reservoir, emptying intermittently by bolus movements. This action allows time for salvage of fluids, electrolytes, and nutrients. Segmentation by haustra compartmentalizes the colon and facilitates mixing, retention of residue, and formation of solid stools. The ascending and transverse colon function as reservoirs while the descending colon acts as a conduit. The colon is efficient at conserving sodium and water, a function that is particularly important in sodium-depleted patients in whom the small intestine alone is unable to maintain sodium balance. Diarrhea or constipation may result from alteration in the reservoir function of the proximal colon, or the propulsive function of the left colon.

#### DEFINITION OF DIARRHEA

The word diarrhea originates from the Greek

terms *dia* (through) and *rhein* (to flow). Diarrhea is considered by most when there is increased liquidity of stool with or without increased frequency of stool. Stool consistency is somewhat an objective parameter, hence, stool frequency or stool weight is used to define diarrhea. Three or more bowel movements per day or stool weight greater than 200 g per day are considered as diarrhea. There may be some exceptions to this definition. For e.g. Indian diet has a high fiber content, and hence they have increased stool weight (> 200 g/day) but do not have diarrhea because they have normal stool consistency and frequency (< 3/day). Conversely, other patients have normal stool weights but complain of diarrhea because their stools are loose or watery (but frequency < 3/day). Two common conditions, usually associated with the passage of stool totaling < 200 g/d, must be distinguished from true diarrhea. *Pseudodiarrhea*, or the frequent passage of small volumes of stool with rectal urgency and accompanies the irritable bowel syndrome or anorectal disorders like proctitis. *Fecal incontinence* is the involuntary discharge of rectal contents and is most often caused by neuromuscular disorders or structural anorectal problems. Diarrhea and urgency, especially if severe, may aggravate or cause incontinence. A careful history and physical examination generally allow these conditions to be discriminated from true diarrhea.

#### PATHOPHYSIOLOGY AND MECHANISMS OF DIARRHEA

Normally, absorption is quantitatively greater than secretion in the intestines. Therefore, either a decrease in absorption or an increase

in secretion can lead to diarrhea. When infectious agents, toxins, or other noxious substances are present within the gut, fluid secretion and motility are stimulated to expel the unwanted material, producing diarrhea. There are four major mechanisms of diarrhea: (1) the presence in the gut lumen of unusual amounts of poorly absorbable, osmotically active solutes (osmotic diarrhea); (2) intestinal ion secretion or inhibition of normal active ion absorption (secretory diarrhea); (3) deranged intestinal motility; and (4) exudation of mucus, blood, and protein from sites of inflammation.

#### OSMOTIC DIARRHEA

Ingestion of poorly absorbed sugars or alcohols (e.g., mannitol, sorbitol) or ions (as found in laxatives - magnesium, sulfate, and phosphate) leads to diarrhea of the osmotic type. Since the intestines cannot maintain an osmotic gradient, these unabsorbed ions in the intestinal lumen cause retention of water to maintain an intraluminal osmolality equal to that of body fluids (about 290 mOsm/kg). Disaccharide (sucrose and lactose) requires disaccharidase for their breakdown before absorption. Lactose intolerance, results due to deficiency of disaccharidase *lactase*, a common clinical situation associated with diseases of the upper small intestine. Lactulose, a synthetic disaccharide cannot be hydrolyzed by the human intestine and cannot be absorbed intact in greater than trace amounts. It thereby causes an osmotic diarrhea when given in sufficient quantity to overwhelm the metabolic capacity of colonic bacteria (about 80 g/day). The essential characteristic of osmotic diarrhea is that it disappears with fasting or cessation of

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ingestion of the offending substance. In contrast, secretory diarrhea typically continues with fasting (though may be slightly reduced).

### SECRETORY DIARRHEA

In this form, either net secretion of chloride or bicarbonate or inhibition of net sodium absorption is the mechanism for diarrhea. The most common cause for secretory diarrhea is infection. Infectious agents (bacteria, parasites and viruses) produce enterotoxins that interact with receptors and lead to increased anion secretion or these enterotoxins may block specific absorptive pathways (e.g. Na-H exchange). Peptides produced by endocrine tumors such as vasoactive intestinal peptide or calcitonin cause secretory diarrhea by stimulating secretion by epithelial cells. Even though there is a large reserve absorptive capacity in both the small intestine and the colon, significant loss of surface area of intestines (e.g. after resective surgery, inflammatory bowel disease), may compromise water absorption and cause diarrhea. In some cases the problem is temporary, because over time the intestine may improve its capacity for absorption by the process of *adaptation*.

**Deranged Motility** Because rapid transit prevents adequate time for absorption, diarrhea results despite intact mucosal absorptive capacity. In disorders such as *diabetes mellitus*, *postvagotomy diarrhea*, *postprandial diarrhea* and *irritable bowel syndrome*, intestinal hurry has been linked to abnormal enteric nervous system function. Many endocrine diarrheas, such as those due to *peptide-secreting tumors* or *hyperthyroidism*,

may lead to diarrhea not only by effects on intestinal electrolyte transport but also by accelerating intestinal motility. Conversely, slow intestinal transit may lead to a secretory diarrhea by promoting bacterial overgrowth in the small intestine. Excess bacteria in the small intestine disrupt digestion and may alter electrolyte transport (e.g. diabetes mellitus and scleroderma).

**Exudation** Disruption of the integrity of the intestinal mucosa due to inflammation and ulceration (bacillary dysentery, ulcerative colitis) results in discharge of mucus, proteins, and blood into the bowel lumen. In such conditions the colonic absorption of water and electrolytes is severely impaired.

### COMPLEX DIARRHEA

Rather than being produced by a single pathophysiologic mechanism (osmotic or secretory), most diarrheas are complex; and are produced by a combination of mechanisms. For example, a patient with malabsorption syndromes might have diarrhea because of the osmotic effects of unabsorbed carbohydrates and secretory diarrhea because of inhibition of colonic absorption by the unabsorbed long-chain fatty acids.

### CLINICAL CLASSIFICATION

Clinically, it may be useful to classify diarrhea: by time course (acute vs. chronic), by volume (large vs. small), by pathophysiology (secretory vs. osmotic), by epidemiology, and by stool characteristics (watery vs. fatty vs. inflammatory).



### ACUTE VERSUS CHRONIC

Acute diarrheas (<4 weeks) usually are due to infections, most of which are self-limited or are easily treatable by antibiotics. Although there are a few infectious agents that cause prolonged diarrhea in immunocompetent individuals (such as *Giardia lamblia* or *Yersinia* spp.), chronic diarrhea is usually due to some other cause.

### LARGE-VOLUME VERSUS SMALL-VOLUME STOOLS

Normally rectum and sigmoid colon functions as a storage reservoir. When this reservoir capacity is compromised by inflammatory or motility disorders involving the left colon, frequent small-volume bowel movements ensue. If the source of the diarrhea is upstream in the right colon or small bowel and if the rectosigmoid reservoir is intact, bowel movements are fewer, but larger. Thus, frequent, small, painful stools may point to a distal site of pathology, whereas painless large-volume stools suggest a right colon or small bowel source. The daily total stool output may also provide etiologic hints. Irritable bowel syndrome often results in normal or only slightly elevated 24-hour stool weights, whereas diarrheas due to etiologies like

VIPomas or medullary thyroid carcinoma may produce fecal output of greater than 1L/day.

### OSMOTIC VERSUS SECRETORY

Because osmotic diarrhea is due to ingestion of some poorly absorbed substance, it abates with fasting. Secretory diarrheas typically continue during fasting, although stool output may decrease somewhat due to reduced endogenous secretions. Measurement of stool electrolyte concentration, osmolality and osmotic gap will also help differentiate between secretory and osmotic diarrhea.

### WATERY VERSUS FATTY VERSUS INFLAMMATORY

*Watery* diarrhea implies a defect primarily in water absorption due to increased electrolyte secretion or reduced electrolyte absorption (*secretory diarrhea*) or ingestion of a poorly absorbed substance (*osmotic diarrhea*). *Fatty* diarrhea implies defective absorption of fat in the small intestine. *Inflammatory* diarrhea implies the presence of one of a limited number of inflammatory or neoplastic diseases involving the gut.

(Part-II will include clinical evaluation and management of diarrhea).

