The Diarrhea Persists: 
What to do next

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WCOG 2013 WORKING PARTY REPORT
Chronic diarrhea: Definition, classification, diagnosis

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Definition of Chronic Diarrhea

- **Patients** define diarrhea as passage of loose stools, increased stool frequency or urgency of defecation
- **Physicians** should note precisely what the patient means by “diarrhea”
  - Differentiate from fecal incontinence
- **Chronic diarrhea** when symptoms are present >4 weeks

Creating a Differential Diagnosis

- **Consider** comorbid symptoms and epidemiologic clues
- **Use** Rome Criteria to make a diagnosis of IBS
  - Pain **must** be present; painless diarrhea is **not** IBS
  - Pain increases before BM and decreases after BM
  - Onset of pain associated with change in stool consistency or frequency
- **Take** a good dietary intake history
Think about iatrogenic Diarrhea

- Drugs
- Surgery
- Therapeutic radiation

Drugs Causing Diarrhea

**Common causes**
- Antacids, Proton pump inhibitors
- Antineoplastic drugs
- Broad spectrum antibiotics (especially cephalosporins)
- Colchicine
- Metformin
- Non-steroidal anti-inflammatory drugs, 5-aminosalicylates
- Cholesterol-lowering agents

**Rarer causes**
- Angiotensin converting enzyme inhibitor
- Angiotensin receptor blocking agents
- Beta-adrenergic receptor antagonists, other antiarrhythmics
- Carbamazepine
- Lipase inhibitors
- Lithium
- Prostaglandins
- Vitamin and mineral supplements
Surgeries Causing Diarrhea

- Esophageal, gastric, intestinal, biliary, pancreatic procedures may lead to diarrhea
- Specific syndromes
  - Dumping syndrome
  - Intestinal hurry
  - Bacterial overgrowth
  - Bile acid malabsorption
  - Pancreatic exocrine insufficiency
  - Short bowel syndrome

Stool Characteristics

- Watery stools
  - Osmotic
  - Secretory
- Inflammatory stools
  - Blood or pus
- Fatty stools
  - Maldigestion
  - Malabsorption

DEFINED BY SIMPLE TESTS: Stool Na, K, WBC (or calprotectin), fat content
Diagnostic Testing

- Only when it will impact management
  - Alarm features that mandate further evaluation (e.g., positive fecal occult blood test)
  - When differential diagnosis comes down to two or three entities that can be effectively distinguished by diagnostic tests
  - When differential diagnosis is broad, initial tests to better characterize diarrhea may be helpful
- Therapeutic trials sometimes best approach

Comprehensive Stool Analysis

- Stool weight
- Stool fat content
- Stool electrolytes
  - Na, K
  - Cl, HCO₃
  - pH
- Stool minerals
  - Mg
  - P
- Stool lactoferrin (or calprotectin)
- Reducing substances
- Stool osmolality
- Laxative screening
  - Mg, P
  - Senna
  - Bisacodyl
Fecal Osmotic Gap

- FOG = nonelectrolyte contribution to intraluminal osmolality
- Intraluminal osmolality = plasma osmolality (stool osmolality rises rapidly in vitro)
- Electrolyte contribution = 2 X sum of [Na] + [K] to account for cations + anions
- FOG = 290 – 2 X sum of [Na] + [K]
Interpretation of FOG

- Osmotic diarrhea
  - Low electrolyte concentrations
  - High FOG (>50 mosm/kg)
- Secretory diarrhea
  - High electrolyte concentrations
  - Low FOG (<50 mosm/kg)

Stool Analysis

- Steatorrhea
  - Stool fat excretion >7 g/24h
  - ULN depends in part on stool weight
  - Qualitative analysis (Sudan stain) fairly accurate
- Carbohydrate malabsorption
  - Low stool pH (<6)
  - Increased reducing substances
Post-analysis Taxonomy of Diarrhea

• Secretory diarrhea
• Osmotic diarrhea
• Steatorrhea
• Carbohydrate malabsorption
• Low weight diarrhea

NOT MUTUALLY EXCLUSIVE CATEGORIES

Patterns of stool composition¹

STOOL WEIGHT >200 g/24h

<table>
<thead>
<tr>
<th>GROUP</th>
<th>IMPLICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secretory diarrhea without steatorrhea</td>
<td>Microscopic colitis or other secretory diarrheas</td>
</tr>
<tr>
<td>CHO malabsorption without steatorrhea</td>
<td>Ingestion of poorly absorbed carbohydrate</td>
</tr>
<tr>
<td>Steatorrhea with or without CHO malabsorption</td>
<td>Small bowel mucosal disease, SIBO, pancreatic exocrine insufficiency</td>
</tr>
<tr>
<td>Osmotic diarrhea</td>
<td>Ingestion of poorly absorbed ions, PEG</td>
</tr>
</tbody>
</table>

Patterns of stool composition

**STOOL WEIGHT <200 g/24h**

<table>
<thead>
<tr>
<th>GROUP</th>
<th>IMPLICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>No evidence of diarrhea</td>
<td>Change in frequency, fecal incontinence</td>
</tr>
<tr>
<td>Hyperdefecation (increased frequency)</td>
<td>IBS, proctitis, abnormal reservoir function</td>
</tr>
<tr>
<td>Abnormal consistency</td>
<td>IBS</td>
</tr>
<tr>
<td>Elevated fecal osmotic gap</td>
<td>Mild CHO malabsorption, Mg ingestion</td>
</tr>
<tr>
<td>Steatorrhea</td>
<td>Malabsorption or maldigestion</td>
</tr>
</tbody>
</table>


**General Paradigm**

- When diagnosis is difficult, stratifying chronic diarrhea by stool characteristics can facilitate evaluation and focus management

- The key is to consider all the possibilities
Most of the time this will result in a diagnosis...

- When it doesn’t, need to consider “difficult-to-diagnose” diarrhea
  - Common problems that are overlooked because they are not considered
  - Rare syndromes

Diarrhea of Obscure Origin (DOO)

**DEFINITION**

- Chronic diarrhea with negative microbiological studies; no evidence of structural gastrointestinal disease or endocrine disease and no history of gastrointestinal surgery or radiation therapy
DOO: Diagnoses

- Fecal incontinence
- Drug-induced diarrhea
- Surreptitious laxative ingestion
- Microscopic colitis syndrome
- Small bowel bacterial overgrowth
- Carbohydrate malabsorption
- Pancreatic exocrine insufficiency
- Bile acid diarrhea
- Endocrine tumor
- Neuropathy
- Idiopathic secretory diarrhea

Idiopathic Secretory Diarrhea

- Diagnostic criteria
  - Chronic diarrhea (>4 weeks)
  - Persistent loose stools
  - No gastrointestinal surgery
  - No systemic disease
  - Negative diagnostic evaluation
  - Stools with characteristics of secretory diarrhea

Idiopathic Secretory Diarrhea

• Clinical picture
  – Previous good health
  – Abrupt onset
  – Frequent, watery stools (mean 10/day, range 5-25/day)
  – Moderate weight loss soon after onset

• Epidemiology
  – Recent travel
  – Rare household contacts
  – No response to antibiotics

• Course
  – Spontaneous complete resolution in all
  – Gradual offset
  – Mean duration: 15 months (range 7—31)
  – No recurrence
**Idiopathic Secretory Diarrhea**

- Epidemic form (Brainerd diarrhea)
  - Similar history as episodic cases
  - Occurs in outbreaks
  - Associated with common water/milk/food exposure
  - Little secondary transmission
  - Similar time course as episodic cases
  - Infectious agent sought, but not found; ?novel agent

**Chronic Diarrhea**

- Extensive differential diagnosis
- Comprehensive history most useful diagnostic tool
- Stool analysis can provide clues to diagnosis in difficult cases
- Diagnosis is possible in most cases