Practical Diagnostic Approach to Chronic Diarrhoea

Mashiko Setshedi 01 Feb 2019
Guidelines for the investigation of chronic diarrhoea in adults: British Society of Gastroenterology, 3rd edition

Ramesh P Arasaradnam,1,2,3 Steven Brown,4 Alastair Forbes,5 Mark R Fox,6,7 Pali Hungin,8 Lawrence Kelman,9 Giles Major,10 Michelle O’Connor,9 Dave S Sanders,4 Rakesh Sinha,11 Stephen Charles Smith,12 Paul Thomas,13 Julian R F Walters14

ABSTRACT
Chronic diarrhoea is a common problem, hence clear guidance on investigations is required. This is an updated guideline from 2003 for the investigations of chronic diarrhoea commissioned by the Clinical Services and Standards Committee of the British Society of Gastroenterology (BSG). This document has undergone significant revision in content through input by 13 members of the Guideline Development Group (GDG) representing various institutions. The GRADE system was used to appraise the quality of evidence and grading of recommendations.

These guidelines deal with clinical assessment in primary and secondary care of a patient with diarrhoea, the exclusion of cancer or inflammation, and detecting common disorders such as bile acid diarrhoea, microscopic colitis, lactose malabsorption or post radiation diarrhoea, together with rarer causes of malabsorption and surgical disorders as outlined in figure 1. Options for therapy are not dealt with as it is beyond the remit of this guideline, nor has the need to collect faecal or blood samples for diagnostic purposes been discussed.

Correspondence to
Professor Ramesh
P Arasaradnam, Department of Gastroenterology, University Hospitals Coventry & Warwickshire, Coventry, CV2 2DX, UK; r.arasaradnam@warwick.ac.uk

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For numbered affiliations see end of article.
Chronic diarrhoea is common (3-5% of population)

Considerable diagnostic challenge

Several hundred possible differential diagnoses

### Table 1. Differential Diagnosis of Chronic Diarrhea

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Watery</td>
<td>(often nocturnal; unrelated to food intake; fecal osmotic gap &lt; 50 mOsm per kg*)</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>Bacterial enterotoxins (e.g., cholera)</td>
</tr>
<tr>
<td>Bile acid malabsorption</td>
<td>Brainerd diarrhea (epidemic secretory diarrhea)</td>
</tr>
<tr>
<td>Congenital syndromes</td>
<td>Crohn disease (early ileocolitis)</td>
</tr>
<tr>
<td>Endocrine disorders</td>
<td>(e.g., hyperthyroidism [increases motility])</td>
</tr>
<tr>
<td>Medications (see Table 3)</td>
<td>Microscopic colitis (lymphocytic and collagenous subtypes)</td>
</tr>
<tr>
<td>Neuroendocrine tumors</td>
<td>(e.g., gastrinoma, vipoma, carcinoid tumors, mastocytosis)</td>
</tr>
<tr>
<td>Nonosmotic laxatives</td>
<td>(e.g., senna, docusate sodium [Colace])</td>
</tr>
<tr>
<td>Postsurgical</td>
<td>(e.g., cholecystectomy, gastrectomy, vagotomy, intestinal resection)</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>Neuroendocrine tumors (e.g., gastrinoma, vipoma, carcinoid tumors, mastocytosis)</td>
</tr>
<tr>
<td>Osmotic</td>
<td>Fecal osmotic gap &gt; 125 mOsm per kg*</td>
</tr>
<tr>
<td>Carbohydrate malabsorption syndromes</td>
<td>(e.g., lactose, fructose)</td>
</tr>
<tr>
<td>Celiac disease</td>
<td>Osmotic laxatives and antacids (e.g., magnesium, phosphate, sulfate)</td>
</tr>
<tr>
<td>Sugar alcohols (e.g., mannitol, sorbitol, xylitol)</td>
<td>Small bowel bacterial overgrowth (&gt; 10^8 bacteria per mL)</td>
</tr>
<tr>
<td>Functional</td>
<td>Malabsorption syndrome (damage to or loss of absorptive ability)</td>
</tr>
<tr>
<td>Fatty (bloating and steatorrhea in many, but not all cases)</td>
<td>Lymphatic damage (e.g., congestive heart failure, some lymphomas)</td>
</tr>
<tr>
<td>Inflammatory or exudative (elevated white blood cell count, occult or frank blood or pus)</td>
<td>Invasive infectious diseases</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Crohn disease (ileal or early Crohn disease may be secretory)</td>
</tr>
<tr>
<td>Diverticulitis</td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td>Ulcerative jejunoileitis</td>
<td>Invasive infectious diseases</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>(pseudomembranous colitis–antibiotic history)</td>
</tr>
<tr>
<td>Invasive bacterial infections</td>
<td>(e.g., tuberculosis, yersiniosis)</td>
</tr>
<tr>
<td>Invasive parasitic infections</td>
<td>(e.g., Entamoeba)–travel history</td>
</tr>
<tr>
<td>Ulcerating viral infections</td>
<td>(e.g., cytomegalovirus, herpes simplex virus)</td>
</tr>
<tr>
<td>Neoplasia</td>
<td>Colon carcinoma</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Villous adenocarcinoma</td>
</tr>
<tr>
<td>Radiation colitis</td>
<td>Neoplasia</td>
</tr>
</tbody>
</table>

*Note: Table continues on the next page.*
What is chronic diarrhoea?

? Stool form, frequency, consistency

Objective >200g of stool per day (unreliable)

Accepted definition
> 3 BMs per day
Bristol ≥ 5
Chronic > 4 weeks

N.B: Exclude pseudo-diarrhoea (increased frequency, but normal consistency)

**Bristol Stool Chart**

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Separate hard lumps, like nuts (hard to pass)</td>
</tr>
<tr>
<td>2</td>
<td>Sausage-shaped but lumpy</td>
</tr>
<tr>
<td>3</td>
<td>Like a sausage but with cracks on its surface</td>
</tr>
<tr>
<td>4</td>
<td>Like a sausage or snake, smooth and soft</td>
</tr>
<tr>
<td>5</td>
<td>Soft blobs with clear-cut edges (passed easily)</td>
</tr>
<tr>
<td>6</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td>7</td>
<td>Watery, no solid pieces. Entirely Liquid</td>
</tr>
</tbody>
</table>
Subtypes

<table>
<thead>
<tr>
<th>OLD</th>
<th>NEW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osmotic</td>
<td>Watery (osmotic, secretory, dysmotility)</td>
</tr>
<tr>
<td>Secretory</td>
<td></td>
</tr>
<tr>
<td>Inflammatory</td>
<td></td>
</tr>
<tr>
<td>Fatty</td>
<td>Inflammatory</td>
</tr>
<tr>
<td>Dysmotility</td>
<td>Fatty</td>
</tr>
</tbody>
</table>
Watery

**Secretory** (often nocturnal; unrelated to food intake; fecal osmotic gap < 50 mOsm per kg*)

Alcoholism

Bacterial enterotoxins (e.g., cholera)

Bile acid malabsorption

Brainerd diarrhea (epidemic secretory diarrhea)

Congenital syndromes

Crohn disease (early ileocolitis)

Endocrine disorders (e.g., hyperthyroidism [increases motility])

Medications (see Table 3)

**Microscopic colitis** (lymphocytic and collagenous subtypes)

Neuroendocrine tumors (e.g., gastrinoma, vipoma, carcinoid tumors, mastocytosis)

Nonosmotic laxatives (e.g., senna, docusate sodium [Colace])

Postsurgical (e.g., cholecystectomy, gastrectomy, vagotomy, intestinal resection)

Vasculitis
**Osmotic** (fecal osmotic gap > 125 mOsm per kg*)

- Carbohydrate malabsorption syndromes (e.g., lactose, fructose)
- Celiac disease
- Osmotic laxatives and antacids (e.g., magnesium, phosphate, sulfate)
- Sugar alcohols (e.g., mannitol, sorbitol, xylitol)

**Functional** (distinguished from secretory types by hypermotility, smaller volumes, and improvement at night and with fasting)

Irritable bowel syndrome
Fatty (bloating and steatorrhea in many, but not all cases)

**Malabsorption syndrome** (damage to or loss of absorptive ability)

- Amyloidosis
- Carbohydrate malabsorption (e.g., lactose intolerance)
- Celiac sprue (gluten enteropathy)—various clinical presentations
- Gastric bypass
- Lymphatic damage (e.g., congestive heart failure, some lymphomas)
- Medications (e.g., orlistat [Xenical; inhibits fat absorption], acarbose [Precose; inhibits carbohydrate absorption])

**Mesenteric ischemia**

- Noninvasive small bowel parasite (e.g., *Giardia*)
- Postresection diarrhea
- Short bowel syndrome
- Small bowel bacterial overgrowth (> $10^5$ bacteria per mL)
- Tropical sprue
- Whipple disease (*Tropheryma whippelii* infection)

**Maldigestion** (loss of digestive function)

- Hepatobiliary disorders
- Inadequate luminal bile acid
- Loss of regulated gastric emptying
- Pancreatic exocrine insufficiency
Inflammatory or exudative (elevated white blood cell count, occult or frank blood or pus)

Inflammatory bowel disease
- Crohn disease (ileal or early Crohn disease may be secretory)
- Diverticulitis
- Ulcerative colitis
- Ulcerative jejunoileitis

Invasive infectious diseases
- *Clostridium difficile* (pseudomembranous) colitis–antibiotic history
- Invasive bacterial infections (e.g., tuberculosis, yersiniosis)

Invasive parasitic infections (e.g., *Entamoeba*)—travel history

Ulcerating viral infections (e.g., cytomegalovirus, herpes simplex virus)

Neoplasia
- Colon carcinoma
- Lymphoma
- Villous adenocarcinoma
- Radiation colitis
Describe diarrhoea
Onset?
Pattern
- continuous
- intermittent
- nocturnal symptoms
Associated features (pain, fever, gas etc)
Alarm features (new-onset diarrhoea, persistent blood in stool, unintentional LOW)
Approach - history

**Describe diarrhoea**
- Onset?
- Pattern
  - continuous
  - intermittent
  - nocturnal symptoms
- Associated features (pain, fever, gas etc)
- **Alarm features** (new-onset diarrhoea, persistent blood in stool, unintentional LOW)
Approach - history

Describe diarrhoea
Onset?
Pattern
- continuous
- intermittent
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Associated features (pain, fever, gas etc)
Alarm features (new-onset diarrhoea, persistent blood in stool, unintentional LOW)

Associations
- travel, food (dairy, sweeteners, FODMAPS, gluten, alcohol, caffeine, liquorice)

Past medical history
Family hx (IBD, coeliac disease)
Other medical conditions - thyroid, DM, collagen vascular disease, pancreatic disease
Previous surgery (e.g. SB resection, cholecystectomy)
Previous radiotherapy

Medications (over 700 implicated)
### Table 3. Drugs Associated with Diarrhea

<table>
<thead>
<tr>
<th>Osmotic</th>
<th>Motility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrates, phosphates, sulfates</td>
<td>Macrolides (e.g., erythromycin)</td>
</tr>
<tr>
<td>Magnesium-containing antacids and laxatives</td>
<td>Metoclopramide (Reglan)</td>
</tr>
<tr>
<td>Sugar alcohols (e.g., mannitol, sorbitol, xylitol)</td>
<td>Stimulant laxatives (e.g., bisacodyl [Dulcolax], senna)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Secretory</th>
<th>Malabsorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antiarrhythmics (e.g., quinine)</td>
<td>Acarbose (Precose; carbohydrate malabsorption)</td>
</tr>
<tr>
<td>Antibiotics (e.g., amoxicillin/clavulanate [Augmentin])</td>
<td>Aminoglycosides</td>
</tr>
<tr>
<td>Antineoplastics</td>
<td>Orlistat (Xenical; fat malabsorption)</td>
</tr>
<tr>
<td>Biguanides</td>
<td>Thyroid supplements</td>
</tr>
<tr>
<td>Calcitonin</td>
<td>Ticlopidine</td>
</tr>
<tr>
<td>Cardiac glycosides (e.g., digitalis)</td>
<td>Pseudomembranous colitis (Clostridium difficile)</td>
</tr>
<tr>
<td>Colchicine</td>
<td>Antibiotics (e.g., amoxicillin, cephalosporins, clindamycin, fluoroquinolones)</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs (may contribute to microscopic colitis)</td>
<td>Antineoplastics</td>
</tr>
<tr>
<td>Prostaglandins (e.g., misoprostol [Cytotec])</td>
<td>Immunosuppressants</td>
</tr>
<tr>
<td>Ticlopidine</td>
<td></td>
</tr>
</tbody>
</table>
Vital signs
General appearance – anorexia/bulimia
Oedema, lymph nodes
Thyroid mass
Skin rashes (DH), flushing
Abdomen – scars, tenderness, masses, organomegaly
Rectal exam - sphincter tone and squeeze, fistulae
Diagnostic objective

Make a positive diagnosis with minimal investigations

Exclude cancer or inflammation

Detect common but underdiagnosed disorders such as bile acid diarrhoea, microscopic colitis, lactose malabsorption or post-radiation diarrhoea
Initial approach

Hb, Fe if anaemic, CRP, albumin, TSH, coeliac serology **AND**
Stool MCS, ova, cysts, parasites, faecal calprotectin (>50g/g), consider FIT

If negative, and < 40, and no alarm features and meets Rome IV

Confirm IBS. If needs be, flexible sigmoidoscopy

**Consider**
Coeliac disease (g-scope + duodenal biopsies)
Microscopic colitis (colonoscopy + biopsies)
Bile salt diarrhoea (empiric bile acid sequestrants)

If troublesome symptoms despite treatment for IBS
Who should be investigated further?

Abnormal initial tests
Normal first-line investigations with severe symptoms severe enough to impair QOL
No response to initial treatment/ongoing symptoms
Suspected organic disease

Watery
Inflammatory
Fatty
Other
### Watery

- **Osm > 125 mmol/kg**
  - OSMOTIC
  - History osmotic laxatives
  - Worse with dairy products
  - Hydrogen breath test
  - Consider coeliac disease

- **Normal Osm**
  - DYSMOTILITY
  - Apply Rome IV
  - IBS or functional diarrhoea
  - Exclude coeliac disease

- **Osm < 50 mmol/kg**
  - SECRETORY
  - Stool analysis
  - Colonoscopy (microscopic colitis ≥ 8 biopsies)
  - MRI/CT
  - TSH/ACTH
  - Tests for hormone-secreting tumours
  - Laxative screen

- **Osm > 400 mmol/kg**
  - CONTAMINATION/SPURIOUS
Stool analysis positive for RBCs, WBCs

Colonoscopy + biopsies ± FCP

Confirm IBD or infectious e.g. pseudomembranous, amoebic, CMV colitis

YES

Treat appropriately

NO

Investigate other causes
Fatty

Malabsorption

Gastroscopy + duodenal biopsies
MRE
VCE
DBE
SBBO – trial antibiotics

Maldigestion

Faecal elastase
MRI pancreas (CT if MRI unavailable)

Hb, Alb, Fe, Vit B12, folate
If all else fails, think constipation!

**N.B:** with overflow diarrhoea
Exclude faecal incontinence
- KUB
- anal manometry
- endoanal US
7-step approach

1. Is it diarrhoea? Establish that it is.
2. Is it functional or organic?
3. Is it colonic, small bowel or pancreatic disease?
4. Is it inflammatory, watery, fatty?
5. Determine specific cause.
6. Could it be constipation/pelvic pathology?
7. Could it be factitious (4-20%)?
Learning Points

It begins with a **focused**, comprehensive **history**

Minimal/non-invasive step-wise investigations to arrive at a diagnosis

Test **early** for coeliac disease

Most chronic diarrhoea is due to colonic abnormalities and generally not infectious

Some conditions are more common than we think