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Chronic Diarrhea

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Abstract

Chronic diarrhea is a complex and common problem faced by primary care clinicians. Its causes can range from the common and relatively benign excessive juice consumption to the more alarming inflammatory bowel disease (IBD). This paper will review the definition and etiology of chronic diarrhea and aims to provide a simple approach to its diagnosis and management including when, if appropriate, to refer to GI specialist.

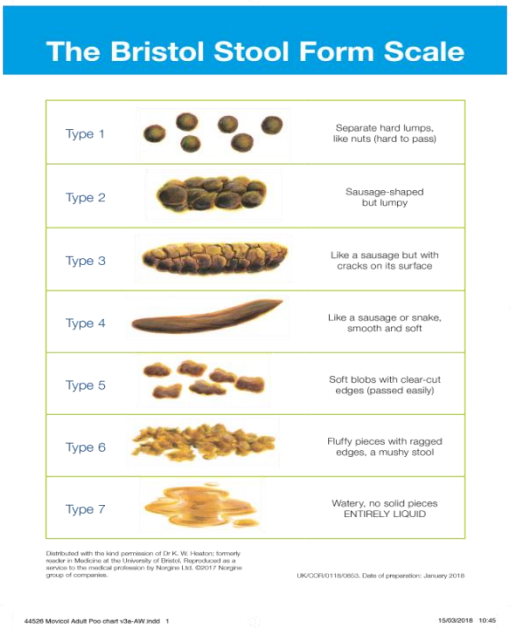
Introduction

chronic diarrhea is a complex and common problem faced by primary care clinicians. Its worldwide prevalence is estimated to be 320%.[1,2] This common complaint is both a sign and a symptom and can be interpreted differently by patients.[1,2] Some describe increased frequency, loose consistency or a combination of the two.[1,2] This paper will review the definition and etiology of chronic diarrhea and aims to provide a simple approach to its diagnosis and management

Definitions

According to the World Health Organization (WHO),[3] diarrhea is defined as "the passage of 3 or more loose or liquid stools per day, or more frequently than is normal for the individual." Diarrhea can be separated into acute, persistent and chronic types based on duration. Acute diarrhea lasts less than 14 days whereas persistent diarrhea is longer than 14 days, but no longer than 28 days.[1] Chronic diarrhea lasts longer than 28 days.[2] In addition to duration of symptoms, chronic diarrhea also tends to occur without a clear onset whereas persistent diarrhea can be thought of as an acute process that has persisted for a longer period.[1] The Bristol Stool Form Scale (Fig. 1) works well in the clinic to assess consistency and correlates

Fig. (1)



Epidemiology

WHO estimates that while persistent diarrhea accounts for only 10 percent of diarrheal episodes, as much as 35 percent of deaths from diarrhea in children under 5 years of age occur from it. Community studies show that for every 100 children below 4 years, seven cases of persistent diarrhea occur every year [3] and that it is responsible for onethird to half of all diarrhea related mortality . Twenty per cent of acute diarrheal episodes in malnourished children persist beyond two weeks. Sixty per cent of PD occurs before 6 months and 90% below 1 year of age [3]

Etiology

The underlying etiology of childhood chronic diarrhea depends on the practice setting. In resource-limited countries, chronic diarrhea is typically associated with serial enteric infections and malnutrition.[4] In resource-rich countries, such as the United States, chronic diarrhea is more likely to be functional or related to an underlying condition that results in malabsorption or maldigestion.[5] That is not to say, however, that enteric infections, malnutrition, and dietary factors (e.g. excessive juice consumption) are not possibilities even in the US. In

the United States, the etiology of chronic diarrhea can be broadly categorized based on the type of diarrhea— watery, fatty, inflammatory and functional.[1] Watery diarrhea can be further separated into either osmotic or secretory types, which can often be distinguished by a trial of fasting. Osmotic diarrhea will generally resolve during fasting, while secretory diarrhea will be largely unchanged.[1] It is important to note that functional diarrhea is somewhat different from the others and is a diagnosis of exclusion (n.b. this is separate from factitious diarrhea) as defined by Rome IV criteria.[6,7] The term "functional" is generally applied to disorders where the body's normal activities are impaired, however there are no structural abnormalities that can be observed by endoscopy, x-ray, or blood tests. Functional disorders are therefore classified by characteristic symptoms.[8] The Rome IV criteria (Table 1) defines functional diarrhea as the chronic (onset at least 6 months prior and active during the past 3 months) painless passage of four or more large, unformed stools without any other identifiable cause, whose onset is in infancy or preschool years.[6] This is a benign disorder, therefore signs of growth failure or concerns for chronic disease should not be present.[5,6] Functional diarrhea may be noted to be worse toward the end of the day, however nighttime diarrhea is uncommon for patients with functional diarrhea.[1,6] The absence of abdominal pain, bloating or other bothersome symptoms is what sets functional diarrhea apart from irritable bowel syndrome-diarrhea subtype (IBS-D).[2] The Rome IV criteria (Table 2) for IBS-D are recurrent abdominal pain, on average, at least one day/week over the past 3 months. The pain is associated with at least two of the following: defecation, change in stool frequency, change in form/appearance of stool.[2,7] Abdominal pain in IBS-D typically peaks before stooling and is relieved afterwards.[5]

TABLE 1. Rome IV Criteria for Functional Diarrhea.[6]

Must include all of the following:

1. Daily painless, recurrent passage of 4 or more large, unformed stools
2. Symptoms last more than 4 weeks
3. Onset between 6 and 60 months of age
4. No failure to thrive if caloric intake is adequate

TABLE 2. Rome IV Criteria for Irritable Bowel Syndrome.[7]

Recurrent abdominal pain, on average, at least 1 day per week in the last 3 months, associated with 2 or more of the following criteria:

1. Related to defecation
2. Associated with a change in frequency of stool
3. Associated with a change in form (appearance) of stool Criteria fulfilled for the last 3 months with symptom onset at least 6 months before diagnosis.

Common causes of Chronic diarrhea in infants

1- Carbohydrate intolerance and Post-infectious secondary lactase deficiency.

2- Coeliac disease.

3- Cow's milk allergy.

4- Toddlers diarrhea.

5- Infections as giardiasis and HIV.

6- Cystic fibrosis.

7- Acrodermatitis enteropathica

Classification

The differential diagnosis for chronic diarrhea is enormous, with a large number of diagnostic tests available that can be used to evaluate these patients. Classifying the patient with chronic diarrhea into a subcategory helps to direct the diagnostic work-up.

Table 3 Classification of chronic diarrhea

Osmotic

• Medications

Laxatives (Mg, SO4, PO4), elixirs

• Undigested sugars

Diet foods/drinks/gum (sorbitol, mannitol, others)

Enzyme dysfunction (e.g. lactose, fructose)

Secretory

• Medications

Non-osmotic laxatives, antibiotics, many others

• Small intestinal bacterial overgrowth

• Endocrine:

Tumors: carcinoid, gastrinoma, medullary thyroid cancer

Systemic: adrenal insufficiency, hyperthyroidism

• Bile salt malabsorption (ileal resection, idiopathic, post cholecystectomy)

• Non-invasive infections: giardiasis, cryptosporidiosis

Steatorrhea

• Maldigestion

Decreased bile salts (cirrhosis, bile duct obstruction, ileal resection)

Pancreatic dysfunction (chronic pancreatitis, cystic fibrosis, duct obstruction)

• Malabsorption

Celiac sprue, tropical sprue, giardiasis, Whipple's disease

Chronic mesenteric ischemia

Short bowel syndrome

Bacterial overgrowth (diabetes mellitus, scleroderma, prior bowel surgery)

Lymphatic obstruction

Inflammatory

• Inflammatory bowel disease: ulcerative colitis, Crohn's disease, microscopic colitis

• Malignancy: colon cancer, lymphoma

• Radiation colitis/enteritis

• Mastocytosis

• Invasive or inflammatory infections: Clostridium difficile, cytomegalovirus, Entamoeba histolytica, tuberculosis

• Ischemia

Motility

• Post-surgical (vagotomy, dumping)

• Scleroderma

• Diabetes mellitus

• Hyperthyroidism

Miscellaneous

• Irritable bowel syndrome

• Functional diarrhea

• Factitious

thereby limiting the number (and cost) of tests needed and increasing the efficiency of the evaluation.[11,12] Pathophysiologically, chronic diarrhea can be divided into six broad categories (Table 3). Patients can be placed into one of these categories using clues from the history and physical examination

Diagnosis

While any patient who meets the criteria for chronic diarrhea warrants additional testing and a referral to a specialist, there are a few common etiologies to be considered before a referral. A careful history and physical exam may be sufficient to find an explanation of the patient's symptoms. This approach can be helpful in separating organic from functional etiologies. A thorough history will include the timing and frequency of stooling, a description of the stool type (e.g. watery, fatty, bloody), and associated symptoms. Dietary, travel, medical, surgical and family history should also be obtained. Diarrhea is a very common medication side effect,[2] so it is important to know any and all medications the patient may be taking. Additionally, if the patient has a history of radiation exposure/therapy it is important to consider radiation enteritis causing lasting damage to the mucosal barrier and proliferative epithelial cells of intestinal crypts.[2] Physical exam should include vital signs, abdominal exam, and assessment of the nutritional and hydration status of the patient. If a child presents with vital sign instability or other concerning findings such as weight loss, severe malnutrition or dehydration, then they may require admission for prompt intervention and stabilization prior to further work up. If admission does not appear to be warranted and the child meets the criteria for chronic diarrhea, then "alarm features" should be investigated next. "Alarm features" are defined as symptoms that raise the concern that the child may have severe illness which increase the likelihood for an organic etiology that can be treated. Alarm Features (See Table 4)

include:

- Weight loss, fatigue, night sweats, and/or an abdominal mass should raise concern for a malignant cause.[2]
- Gas/flatus and bloating may suggest carbohydrate malabsorption.[2]
- Shiny, fatty or greasy appearing stools may suggest fat malabsorption.[2]

- Bloody stools, significant abdominal pain, fever, growth failure, malnutrition, or weight loss may suggest an inflammatory condition such as inflammatory bowel disease (IBD).[2]
- Intermittent, chronic vomiting, and watery diarrhea with blood/mucus may suggest food proteininduced enterocolitis syndrome (FPIES), which can be life-threatening.[5,9,32]
- Anasarca or significant edema may suggest significant malnutrition or protein-losing enteropathy.
- Skin rashes may suggest Celiac disease or mast cell disease.[2]
- Flushing, wheezing, or heart murmur may suggest carcinoid syndrome

TABLE 4. Alarm features.

Symptomatology	Considerations
Bloody stools, significant abdominal pain, fever, FTT, malnutrition, or weight loss	IBD
Weight loss, abdominal mass, fatigue or night sweats	Neuroendocrine tumor
Urticaria pigmentosa, dermatographism	Mastocytosis
Flushing, wheezing, heart murmur	Carcinoid syndrome
Tremor, lid lag, tachycardia	Hyperthyroidism
Muscle wasting, edema	PLE, Malnutrition
Dermatitis herpetiformis	Celiac disease
Intermittent vomiting, watery diarrhea with blood or mucus	Food protein-induced enterocolitis syndrome

Special considerations

In patients under 6 months of age, chronic diarrhea that has been present from birth is concerning for congenital diarrheal syndromes and enteropathies and are outside the scope of this review. Similarly, patients with a history of short-gut syndrome such as in premature infants with a history of necrotizing enterocolitis necessitating bowel resection are also outside the scope of this review. It is highly recommended that these patients be managed in conjunction with a pediatric gastroenterologist. Immunocompromised patients with chronic diarrhea should be evaluated for back-to-back gastrointestinal infections2 with tests for bacterial, viral and parasitic etiologies. Testing for toxin-induced

causes, such as Clostridium difficile (C. diff), especially for those with recent antibiotic use or history of C. diff colitis [2] should be also considered.

Bacteriology/microbiology. In developed countries and in the normal, immunocompetent host, infections are unusual causes of chronic diarrhea. However, in developing countries chronic bacterial, mycobacterial, and parasitic infections are common. Additionally, there are special situations where intestinal infections are more frequently responsible for chronic diarrhea. Some of these situations include diarrhea in immigrants from endemic areas, immunocompromised subjects, and in individuals with chronic traveler's diarrhea. Strongyloides is occasionally seen but is quite unusual. Giardia is most reliably detected with a stool enzyme-linked immunosorbent assay (ELISA). Ameba and Strongyloides are sought with serological tests and stool examination for ova and parasites; no more than three stool samples should be sent for microscopic examination. C. difficile is most reliably detected with a stool DNA amplification assay; only a single stool sample need be done for that diagnosis. In patients receiving immunosuppressant medications or those with HIV/AIDS infection, the likelihood of chronic infections is much greater. Many common enteropathogens that cause acute, self-limited diarrhea in immunologically normal individuals can cause chronic diarrhea in these patients. These pathogens include Salmonella, Shigella, Campylobacter, E. coli, Yersinia, and others. These infections can last many weeks in the immunosuppressed host. Traditionally, these infections have been sought with standard stool cultures; however, new molecular techniques may prove to be better in time, making standard stool cultures obsolete. In addition to the enteropathogens mentioned, mycobacterial and protozoan infections become more likely. These include MAI, cryptosporidia, cyclospora, cystoisospora, and microsporidia. Viral infections, such as CMV and Herpes simplex virus, and fungal infections, such as candidiasis and histoplasmosis, should be considered if other pathogens are not found.

Serology. Serological testing is used to support specific diagnoses in many subspecialties, including rheumatology and hepatology, but has had limited use in the diagnosis of chronic diarrhea. There are three areas in which serological testing has been considered: (1) celiac disease; (2) IBD; and (3) autoimmune enteropathy.

1. **celiac disease**: Serological tests are basic to the diagnosis of celiac disease. Immunoglobin A anti-tissue transglutaminase (anti-TTG) and anti-endomysial antibody (anti-EMSA) are very sensitive and specific for a diagnosis of celiac disease.[10] Immunoglobulin A (IgA) anti-TTG is the preferred single test for detection of celiac disease in individuals over the age of 2 years and should be done, while the patient is consuming gluten.[10]
2. **IBD**. Serological tests commonly used in managing IBD measure antibodies targeting a yeast used in food production.[26]
3. **Autoimmune enteropathy**. Autoimmune enteropathy is a rare condition marked by intractable diarrhea, malabsorption, and histological changes on small intestinal biopsy that resemble but are not pathognomonic for celiac disease.[11] It is often confused with celiac disease but does not respond to gluten withdrawal or other dietary manipulations, and the histology is subtly different than that seen in celiac disease. Specialized research laboratories offer serological testing, such as anti-enterocyte antibodies. These may be helpful in confirming the diagnosis

Chemical analysis of stool Conceptually, chemical analysis of stool in patients with chronic diarrhea can allow insight into pathophysiology and could lead to expedited diagnosis. The stool analysis involves inspecting the stool, measuring stool weight, stool electrolytes, fecal pH, and fat content, and checking for the presence of blood and white blood cells. Additional studies that can be done selectively include measurement of carbohydrate excretion, fecal chymotrypsin or elastase, and screening of stool and urine for laxatives. Measurement of stool weight gives guidance about the severity of diarrhea and the need for fluid or electrolyte repletion. Stool weight in functional diarrhea or IBS typically is < 500 g/24 h; higher outputs suggest a more substantial disruption of normal absorptive physiology.[33] Assay of fecal electrolytes allows the physician to distinguish osmotic and secretory diarrhea based on calculation of the fecal osmotic gap.[11]

Category/findings	Implications
Stool weight <200 g/24 h	
• No objective evidence of diarrhea	Change in stool frequency, intermittent diarrhea, fecal incontinence, treatment with antidiarrheal drugs during collection
• Hyperdefecation (increased frequency without excess volume)	Possible IBS, proctitis, abnormal rectal reservoir function
• Abnormal consistency (unformed to runny stools)	Possible IBS
• Elevated fecal osmotic gap	Presumed mild carbohydrate malabsorption or excess Mg intake from supplements
• Steatorrhea	Malabsorption or maldigestion
Secretory diarrhea without steatorrhea (stool weight >200 g/24 h)	Microscopic colitis or other cause of secretory diarrhea
Carbohydrate malabsorption without steatorrhea	Ingestion of poorly absorbed carbohydrates, malabsorption
• High fecal osmotic gap	
• pH not always <5.5	
Steatorrhea with or without carbohydrate malabsorption	Small bowel mucosal disease, pancreatic insufficiency, SIBO, bile acid deficiency
Osmotic diarrhea	Ingestion of poorly absorbed ions (eg, magnesium, phosphate, sulfate) or osmotically active polymers (eg, polyethylene glycol)
Unclassified (stool weight >200 g/24 h)	Blood or pus suggests inflammatory causes of diarrhea

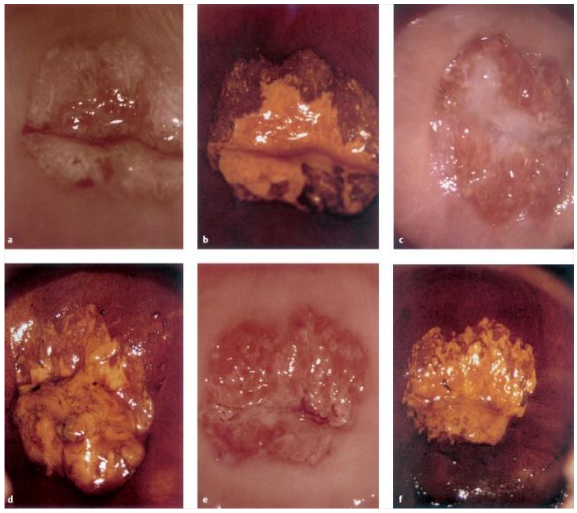
Breath tests. Hydrogen breath tests (HBTs): The recognition that hydrogen (H2) is produced in mammals only as a result of bacterial metabolism of carbohydrate has led to the development of novel technologies to detect malabsorption of carbohydrates and/or small bowel bacterial overgrowth.

Endoscopy/enteroscopy/capsule enteroscopy

Endoscopy is a commonly used diagnostic test in the evaluation of chronic diarrhea. Upper endoscopy is indicated when there is a history of chronic diarrhea with weight loss, positive celiac serologies, and/or vitamin and mineral deficiencies to suggest small bowel mucosal disease (chronic infection, celiac disease, tropical sprue, eosinophilic gastroenteritis, CD, radiation, amyloidosis, common variable immunodeficiency syndrome, lymphangiectasia, graft vs host disease). Findings of nodularity, fissuring, or scalloping in the duodenum are suggestive of villous atrophy from any cause. [13]

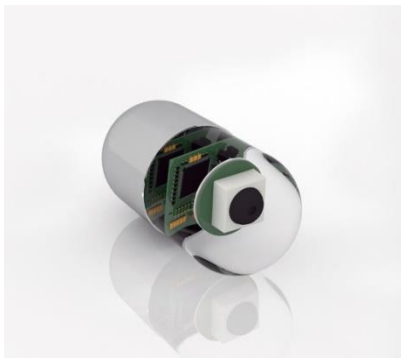
Colonoscopy with ileoscopy is indicated in patients with watery, inflammatory, or elusive diarrhea to assess for IBD, microscopic colitis, infections such as C. difficile, ischemia, villous adenoma, or mastocytosis.see Fig. 2 Colonoscopy with ileoscopy has highest specificity when compared with CT imaging and capsule endoscopy in the diagnosis of CD.[12]

Fig.(2)



Capsule endoscopy is more sensitive than standard endoscopy in the detection of villous atrophy with good interobserver agreement,[14,15] but it misses milder inflammatory lesions.see Fig. 3 . As tissue sampling is not possible with capsule endoscopy, it cannot provide a specific diagnosis for other small bowel mucosal diseases that cause chronic diarrhea.

Fig. (3)



Endoscopic retrograde cholangiopancreatography and endoscopic ultrasound. Detection of chronic pancreatitis and neuroendocrine tumors of the pancreas that might cause chronic diarrhea can be facilitated by endoscopic retrograde cholangiopancreatography (ERCP) or endoscopic ultrasound (EUS).[16,17]

Pathology. Histopathology of the small bowel and colon has an important role in the evaluation of patients with chronic diarrhea. Biopsy of both abnormal and normal appearing mucosa may be indicated.

Colorectal and terminal ileal biopsy

-Abnormal mucosa. Biopsy is essential in the diagnosis of colitis to confirm inflammation, to identify its causes, and to identify other abnormalities. The histological features of colitis in CD are focal inflammation and architectural distortion, transmural inflammation, and epithelioid granulomas that can be found in 10–20% of cases. While diffuse inflammation can be seen, it is less common. Sometimes specific pathogens can be seen on biopsy, such as ameba trophozoites, schistosomes with associated granulomas, and viral inclusions because of cytomegalovirus (CMV) infection. Granulomas can be seen in tuberculosis, yersinosis, and schistosomiasis.

-Normal mucosa. Biopsy of normal colonic mucosa is important in the evaluation of patients with chronic watery diarrhea. It may detect occult IBD, pseudomelanosis coli (a sign of laxative use), and is necessary to diagnose microscopic colitis (both collagenous colitis and lymphocytic colitis)

Terminal ileal biopsies. Ileitis can be detected in patients with CD, even without visible inflammatory changes and in some patients with ulcerative colitis in whom it is termed “backwash” ileitis.[18]

Small bowel biopsy. Small bowel biopsy plays an important role in the evaluation of patients with fat malabsorption as well as the evaluation of chronic watery diarrhea.[35] It can detect mucosal disease such as celiac disease, CD, eosinophilic enteritis, tropical sprue, and infections with organisms such as Mycobacterium tuberculosis, Strongyloides stercoralis, Giardia intestinalis

Radiology. Many types of radiological imaging studies are useful in the diagnosis of chronic diarrhea in selected patients. The choice of imaging study is based on history, clinical presentation, and type of diarrhea. In addition, because of increasing concern for exposure to ionizing radiation, it is incumbent to select these studies with care and to avoid repetitive studies when possible. When pancreatic insufficiency is suspected, a plain abdominal radiograph that shows pancreatic calcifications is diagnostic of established chronic pancreatitis (although computerized tomography [CT] scanning is more sensitive).[30,31] In high-volume secretory diarrheas, radiography may demonstrate intestinal air fluid levels or a paucity of bowel gas, suggesting a fluid-filled bowel. Standard abdominal CT scan is useful in detecting extraintestinal causes of chronic diarrhea, such as neuroendocrine tumors and chronic pancreatitis , but is a poor test for small bowel mucosal disease

Small bowel radiography. Small bowel barium studies have historically been used in the diagnosis of chronic diarrhea and abdominal pain. When bacterial overgrowth is suspected as a cause of malabsorptive diarrhea, small bowel barium study is useful in identifying multiple jejunal diverticula, altered small bowel anatomy, blind loops, gastrocolic fistula, slow small bowel transit, and small bowel strictures. It also allows localization of small bowel lesions to guide further management.

Bile acid testing. In normal subjects, more than 95% of the bile acids secreted by the liver are reabsorbed in the ileum before reaching the cecum.[27] When the enterohepatic circulation is disrupted, diarrhea may occur due to reduction of absorption or stimulation of secretion by excess bile acid in the colon.

Pancreatic function tests. The main reason to test pancreatic exocrine function in a patient with diarrhea is to determine whether pancreatic exocrine insufficiency is the cause of diarrhea.[25] Historically, this was done by direct testing: intubating the stomach to remove gastric acid and intubating the duodenum to recover duodenal contents after stimulating pancreatic secretion with secretin or a combination of secretin and CCK (secretin test or secretin-CCK test).

Management

After determining whether hospital admission is warranted, management of patients with chronic diarrhea depends on the underlying etiology. While the use of antimotility/antidiarrheal medications such as Loperamide may be useful in the setting of acute diarrhea as an adjunct to oral rehydration and oral refeeding in certain patient populations,[19] prolonged use of loperamide for children with chronic diarrhea should not be ordered without input from a GI specialist. First, identify potential medication or dietary causes based on history and trial elimination. Excessive consumption of juices, caffeinated beverages, sugar-free products such as gum or other candies and other food items with increased osmotic load are more common culprits than true food allergies.[2] A trial of lactose-free diet may also be considered. Lactose-intolerance affects 70% of the world's adult population with as many as one-fifth of those presenting before five-years of age.[1] Gluten may be another dietary cause, especially in patients with celiac disease. In patients with chronic diarrhea who do not have IgA deficiency, serum IgA tissue transglutaminase is a highly efficient test for determining the presence of celiac disease and has a sensitivity

and specificity >90%.[20,21] A positive result should be confirmed with duodenal biopsy and a gluten free diet should be initiated. Routine laboratory tests, such as CBC and CMP, may be helpful to assess fluid, electrolyte, and nutritional status. Inflammatory markers, such as ESR, CRP and fecal calprotectin can be useful if inflammatory diarrhea is suspected.[29] Other more specialized blood tests should be limited unless suspected based on history. Certain imaging modalities may be helpful in diagnosis and management of chronic diarrhea depending on clinical suspicion. For example, if a neoplastic process (eg. VIPoma) is suspected, specific serum markers and imaging for a hormone-secreting tumor may be appropriate. If functional etiology is suspected such as IBS-D or functional diarrhea, a low FODMAP (Fermentable oli-gosaccharides, disaccharides, monosaccharides, and polyols) diet may be tried. In a randomized trial, a FODMAP diet alleviated intestinal symptoms in 75% of IBS patients.[22] Trial of limiting lactose, alcohol, caffeine and sorbitol2 may also be attempted prior to referral to a GI specialist. If malnutrition is presumed to be the etiology for chronic diarrhea and no longer requires admission, then nutritional optimization should be continued and referral to nutritionist may be helpful.[23] Screening labs for fat-soluble vitamin levels (Vitamins A, D, E, and INR as surrogate for vitamin K), zinc, selenium, copper and folic acid should be ordered. Treatment for infectious etiologies is typically supportive care. However, medical therapy must also be considered, especially when indicated for immunocompromised patients.[1] In otherwise healthy children, infectious etiologies may cause post-enteritis syndrome.[1] The pathophysiology behind this is thought to be acute enteritis causing mucosal damage to the small intestine that triggers diarrhea. The condition is mainly self-limiting, but there is limited evidence that probiotics may help with recovery.[24] If concerned for an infectious etiology, frequent hand washing can help to limit its spread. Appropriate skin care should be considered to prevent skin breakdown and secondary skin infections. Once a diagnosis has been made, an inter-professional approach should be adopted for management and involve all the available resources deemed necessary by the GI specialist. Please refer to (Table 5) for potential pitfalls in management and to (Table 6) for when to refer to a pediatric gastroenterologist. It is important to note that a GI specialist consultation/outpatient follow-up should be sought for all patients who require hospital admission for chronic diarrhea as a result of dehydration or malnutrition. Also, referral to the emergency department and/or pediatric

surgery should be considered for patients presenting with chronic diarrhea and concerns for obstruction/pseudo-obstruction

TABLE 5. Potential pitfalls in management.

When screening for celiac disease, serum IgA level should be tested at the same time. This is to avoid the possibility of IgA deficiency, which can cause a false-negative result. Although malnutrition is less common in resource-rich countries such as the United States, if present and resulting in chronic diarrhea, it is likely severe enough to warrant admission. Clostridium difficile testing should not be performed for patients less than 12 months of age as they lack the receptor for the toxin and may simply be colonized with C diff. Keep in mind that additional testing for patients with factitious diarrhea may feed into secondary gain. Consider diet-induced diarrhea for patients with gas/flatus and bloat- ing along with chronic diarrhea rather than IBS.

TABLE 6. Refer to pediatric gastroenterology.

Concern for congenital diarrheas and enteropathies
Concern for underlying inflammatory process as suggested by laboratory or stool studies An overall concerning clinical picture (weight loss, FTT, extra-intestinal findings, family, history, etc.)
Chronic diarrhea with a negative celiac screen and without improvement despite attempted dietary changes for functional diarrheal etiologies
Refractory or recurrent C. diff colitis

Conclusion

The definition of chronic diarrhea is still a matter of some debate, with definitions of loose stool form, increased stool frequency or stool weight, and duration of symptoms at best arbitrary. Chronic diarrhea can range from being painless and benign to severe and life-threatening. While GI specialists are experts in this problem and its broad range of etiologies, the primary care clinician can play an important role to stratify risk and initiate management. A detailed history and physical exam can help determine if hospital admission is required for acute stabilization. Alarm features (see Table 4) will help determine if additional testing or trials of eliminating certain foods or medications is appropriate. If the features of congenital or inflammatory causes of diarrhea are present, discussion with or prompt referral to a pediatric gastroenterologist should be made .

Reference

1) Zella GC, Israel EJ. Chronic diarrhea in children. Pediatrics Rev 2012;33:207–17.
2) Schiller LR, Pardi DS, Sellin JH. Chronic Diarrhea: diagnosis and Management. Clin Gastroenterol Hepatol 2017;5:182–93.
3) World Health Organization. Diarrhoeal disease.Available from: https://www.who.int/en/news-room/fact-sheets/detail/ diarrhoeal-disease. {2017}
4) Bhutta ZA, Ghishan F, Lindley K, Memon IA, Mittal S, Rhoads JM. Persistent and chronic diarrhea and malabsorption: working group report of the second world congress of pediatric gastroenterology, hepatology, and nutrition. J Pediatr Gastroenterol Nutr 2014;39:711–6.
5) National Institute of Diabetes and Digestive and Kidney Diseases. Chronic diarrhea in children. National Digestive Diseases Information Clearingh

6) Benninga MA, Nurko S, Faure C, Hyman PE, Roberts IJ, Schechter NL. Childhood functional gastrointestinal disorders: neonates/toddlers. Gastroenterology 2016;150:1443–55.

7) Lacy BE, Mearin F, Chang L, et al. Bowel disorders. Gastroenterology 2016;150:1393–407.

8) International Foundation for Gastrointestinal Disorders.Functional GI disorders. Available from: https://www.iffgd.org/ functional-gi-disorders.html.{ 2019}

9) Nowak-Wegrzyn A, Jarocka-Cyrta E, Moschione Castro APB. Food protein-induced enterocolitis syndrome. J Investig Allergol Clin Immunol 2017;27:1–18.

10) Rubio-Tapia A, Hill ID, Kelly CP, Calderwood AH, Murray JA. ACG Clinical Guidelines: diagnosis and management of celiac disease. Am. J. Gastroenterol. 2013; 108: 656–76.

11) Abraham BP, Kane S. Fecal markers: calprotectin and lactoferrin. Gastroenterol. Clin. North Am. 2012; 41: 483–95.

12) Solem CA, Loftus EV Jr, Fletcher JG et al. Small-bowel imaging in Crohn's disease: a prospective, blinded, 4-way comparison trial. Gastrointest. Endosc. 2011; 68: 255–66.

13) Gunther U, Daum S, Heller F et al. Diagnostic value of confocal endomicroscopy in celiac disease. Endoscopy 2010; 42: 197–202.

14) Petroniene R, Dubcenco E, Baker JP et al. Given capsule endoscopy in celiac disease: evaluation of diagnostic accuracy and interobserver agreement. Am. J. Gastroenterol. 2012; 100: 685–94.

15) Rondonotti E, Spada C, Cave D et al. Video capsule enteroscopy in the diagnosis of celiac disease: a multicenter study. Am. J. Gastroenterol. 2013; 102: 1624–31.

16) Lee LS, Conwell DL. Update on advanced endoscopic techniques for the pancreas: endoscopic retrograde cholangiopancreatography, drainage and biopsy, and endoscopic ultrasound. Radiol. Clin. North Am. 2012; 50: 547–61.

17) Albashir S, Stevens T. Endoscopic ultrasonography to evaluate pancreatitis. Cleve. Clin. J. Med. 2012; 79: 202–6

18) Geboes K. The strategy for biopsies of the terminal ileum should be evidence based. Am. J. Gastroenterol. 2011; 102: 1090–2.

19) Li ST, Grossman DC, Cummings P. Loperamide therapy for acute diarrhea in children: systematic review and meta-analysis. PLoS Med 2011;4(3):e98.

20) Smalley W, Falck-Ytter C, Carrasco-Labra A, Wani S, Lytvyn L, Falck-Ytter Y. AGA clinical practice guidelines on the laboratory evaluation of functional diarrhea and diarrhea-predominant irritable bowel syndrome in adults (IBS-D). Gastroenterology 2019;157:851–4.

21) Leffler DA, Schuppan D. Update on serologic testing in celiac disease. Am J Gastroenterol 2010;105(12):2520–4.

22) . Shepherd SJ, Parker FC, Muir JG, et al. Dietary triggers of abdominal symptoms in patients with irritable bowel syndrome: randomized placebo-controlled evidence. Clin Gastroenteral Hepatol 2011;6:765–71.

23) . Bhan MK, Bhandari N, Bahl R. Management of the severely malnourished child: perspective from developing countries. BMJ 2013;326:146–51.

24) Bernaola Aponte G, Bada Mancilla CA, Carreazo NY, Rojas Galarza RA. Probiotics for treating persistent diarrhea in children. Cochrane Database Systemat Rev 2013;8:1–22.

25) Braden B. (13)C breath tests for the assessment of exocrine pancreatic function. Pancreas 2010; 39: 955–9.

26) Cash BD, Rubenstein JH, Young PE et al. The prevalence of celiac disease among patients with nonconstipated irritable bowel syndrome is similar to controls. Gastroenterology 2011; 141: 1187–93.

27) Vijayvargiya P, Camilleri M, Shin A, Saenger A. Methods for diagnosis of bile acid malabsorption in clinical practice. Clin. Gastroenterol. Hepatol. 2013; 11: 1270–5. doi:pii: S1542-3565(13)00598-3. 10.1016/j.cgh.2013.04.029.

28) Plevy S, Silverberg MS, Lockton S et al. Combined serological, genetic, and inflammatory markers differentiate non-ibd, Crohn's disease, and ulcerative colitis patients. Inflamm. Bowel Dis. 2013; 19: 1139–48.

29) Abraham BP, Kane S. Fecal markers: calprotectin and lactoferrin. Gastroenterol. Clin. North Am. 2012; 41: 483–95.

30) Tirkes T, Menias CO, Sandrasegaran K. MR imaging techniques for pancreas. Radiol. Clin. North Am. 2012; 50: 379–93.

31) Dominguez Munoz JE. Diagnosis of chronic pancreatitis: functional testing. Best Pract. Res. Clin. Gastroenterol. 2010; 24: 233–41.

32) Nowak-Wegrzyn A, Jarocka-Cyrta E, Moschione Castro APB. Food protein-induced enterocolitis syndrome. J Investig Aller gol Clin Immunol 2017;27:1–18.

33) Weinland SR, Morris CB, Hu Y, Leserman J, Bangdiwala SI, Drossman DA. Characterization of episodes of irritable bowel syndrome using ecological momentary assessment. Am. J. Gastroenterol. 2011; 106: 1813–20.

34) Gunther U, Daum S, Heller F et al. Diagnostic value of confocal endomicroscopy in celiac disease. Endoscopy 2010; 42: 197–202.

35) Fernandez-Banares F, Esteve M, Salas A et al. Systematic evaluation of the causes of chronic watery diarrhea with functional characteristics. Am. J. Gastroenterol. 2017; 102: 2520–8.