

Chronic and Recurrent Abdominal Pain

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Education Gap

The past 20 years have witnessed a transition in clinical understanding of childhood bellyaches. The recently published third iteration of pediatric Rome criteria provides updated and accurate criteria for symptom-based diagnosis of chronic and recurrent abdominal pain. In many cases, primary care clinicians can make symptom-based diagnoses and initiate treatment on the first visit.

Objectives

After completing this article, readers should be able to:

1. Make symptom-based diagnoses of functional abdominal pain disorders.
2. List a variety of treatment options for children with functional abdominal pain.
3. Recognize warning signs that discriminate disease from functional abdominal pain.
4. Understand how psychosocial factors play a role in disability associated with functional abdominal pain.

EPIDEMIOLOGY

By definition, chronic or recurrent abdominal pain must occur at least 4 times each month for at least 2 months. Abdominal pain complaints begin as soon as a child can provide an accurate pain history, usually around age 7 years but occasionally younger. Before that age, children have difficulty separating emotional distress from physical pain. The differential diagnosis of child and adolescent abdominal pain is unrelated to age.

One in 10 children visits a clinician because of chronic or recurrent abdominal pain. (1) How can a clinician screen quickly for disease? The first consideration is the duration of each episode. If the pain lasts less than 5 minutes, even if it occurs many times daily, the pain is unlikely to be worrisome. Abdominal pains lasting just a few minutes may be abdominal wall muscle cramps or high-amplitude-propagating colon contractions. High-amplitude-propagating contractions are waves of muscle contraction starting in the ascending colon, with pressures greater than 60 mm Hg, that move colonic contents through the colon to the rectum. (2) High-amplitude-propagating colon contractions are normal, but they cause an urge to defecate for about 2 minutes several times daily. Children who

AUTHOR DISCLOSURE Dr Hyman has disclosed no financial relationships relevant to this article. This commentary does contain a discussion of an unapproved/investigative use of a commercial product/device.

are sensory-sensitive or children who refuse to defecate may experience abdominal pain with normal high-amplitude-propagating contractions. The second consideration is location. The closer the pain location is to the umbilicus, the less likely it is due to disease. The final consideration is the time of the pain complaints. Children with functional (non-organic) abdominal pain often complain either upon awakening or when going to sleep, but they seem relatively symptom-free during daily activities. Waking up and going to sleep share the characteristic that in those quiet minutes children assess their bodies for discomfort. Once active in the day, healthy children are less aware of body sensations.

Most chronic or recurrent abdominal pain is not caused by disease. In a study of Norwegian children with abdominal pain, 87% met diagnostic criteria for 1 or more functional gastrointestinal disorders (FGIDs) on their first visit (Fig 1). (3) Diagnoses change over time to an organic disease in only 1% to 2% of those diagnosed with an FGID. Inflammatory bowel disease occurs in about 1 in 1,000 children. (4) Celiac disease is found in 1 in 150 children, but most affected children are asymptomatic. (5) Thus, the chances are slim that the next child who comes to the office with a bellyache has a disease.

HISTORY AND PHYSICAL EXAMINATION

A series of simple questions can provide valuable information when taking a history from a patient complaining of pain. The first question should address whether the pain is constant or intermittent. Constant pain is unrelated to

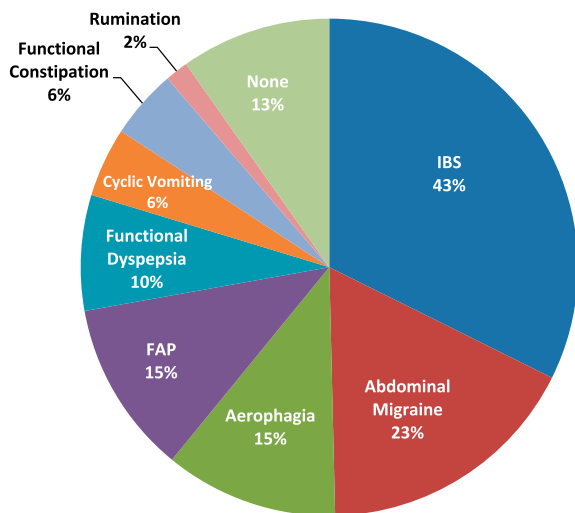


Figure 1. Functional gastrointestinal disorders dominate diagnoses in Norwegian children with abdominal pain. FAP=functional abdominal pain. IBS=irritable bowel syndrome.

physiologic events such as eating or defecation and likely reflects central nervous system (CNS) origins for pain. If the pain comes and goes, ask how often the episodes occur and how long they last. The next question is, “Does eating make your pain better, worse, or no different?” Pain that worsens with eating suggests that the cause is stretching of the stomach (dyspepsia) or the gastrocolonic response increasing pressures in the colon. Next on the question list is, “Does defecation make your pain better, worse, or no different?” If defecation relieves the pain, the diagnosis is likely to be irritable bowel syndrome (IBS). This can be followed with, “Does exercise make your pain better, worse, or no different?” If eating and defecation have no effect but exercise makes the pain worse, the diagnosis may be abdominal wall pain, unrelated to gastrointestinal factors. If the pain is unchanged by eating, defecation, exercise, or any other physiologic event, it is a disorder termed “functional abdominal pain not otherwise specified.” A helpful follow-up question is, “What can you do to make your pain better?” This question provides an opening for discussion of how the patient copes, with possibilities such as medicines, foods, rest, and distractions. It also is important to ask about what makes the pain worse, with possibilities such as food, exercise, academic struggles, bullying, and family stressors (eg, psychological or physical abuse in the home or separation from a loved one by death or relocation).

The patient’s physical appearance is helpful in assessing the degree of distress at the time of examination. Those suffering from chronic pain may appear to be in no distress but when queried, they rate their pain as an 8 or 9 out of 10. Clinicians should never challenge a patient’s pain rating because chronic pain differs from acute pain in its phenotype and challenging the patient’s story can result in a failed therapeutic alliance. The patient who has an acute abdomen appears ill, with tachycardia, flexed legs, and a facial grimace. The patient experiencing chronic pain may look sad but rarely looks acutely ill. The adolescent might state, “No one believes that I am in pain because I look normal.” A comment to facilitate the therapeutic alliance might be, “I am sorry you are feeling so much pain, but maybe I can help.”

PATHOPHYSIOLOGY OF CHRONIC AND RECURRENT ABDOMINAL PAIN

Basic and clinical research has exploded over the past 25 years, resulting in understanding of chronic and recurrent abdominal pain. Chronic pain is often caused by a sensitization of primary visceral afferent nerves to pressure and stretch (primary hyperalgesia) and amplification of pain

messages by deep brain nonspecific arousal systems (secondary hyperalgesia) (6). When the pain impulse in the arousal center is strong enough, pain messages ascend to perception in the sensory cortex on the anterior and mid-cingulate gyrus (Fig 2). In individuals with healthy coping skills, signals from frontal lobes in the brain may reduce pain transmissions from the arousal centers in the midbrain to the sensory cortex. In contrast, past pain experiences, poor coping skills, expectations for pain, anxiety, and depression transmissions from the frontal lobes may increase pain transmission from the deep brain arousal centers and heighten pain perception in the sensory cortex. Children with poor coping skills, academic or social stress, or a coexisting mental health disorder may be at risk of disability from abdominal pain. Treatment for chronic pain may target peripheral or CNS mechanisms or both.

Chronic abdominal pain includes a CNS component, characterized by altered pain pathways and structural changes in the brain. (6)(7)(8) Although evidence exists about how food, infection, inflammation, intestinal permeability, and the microbiome all contribute to triggering symptoms, pain- or nausea-associated FGIDs often respond better to treatments targeting the CNS than drugs working outside the brain. Hypnosis, (9) cognitive behavioral therapy, (10) and citalopram (11) trials in children were more successful than the promotility drugs cisapride and tegaserod, the gastric acid inhibitor famotidine, or the antibiotic used for bacterial overgrowth, rifaximin, (12) for IBS.

Efferent and afferent nerves connect brain and gut, each modulating the other, which provides a rationale for the use of psychotropic drugs for abdominal pain treatment. Moreover, recent evidence from brain imaging demonstrated

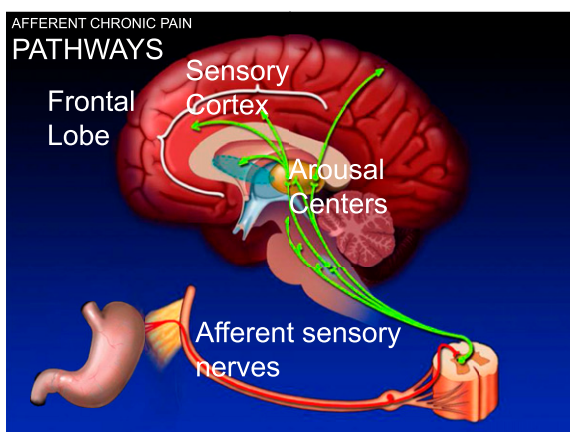


Figure 2. Afferent chronic pain pathways. From Hussain SZ, Hyman PE. Psychotropic medications for pediatric functional gastrointestinal disorders. *J Pediatr Gastroenterol Nutr.* 2014;59(3):280-287. Reprinted with permission from Wolters Kluwer Health.

changes in cortical thickness and white matter pathways associated with chronic pain. (13) CNS amplification of peripheral pain and nausea signals is a feature of chronic pain physiology. Finally, the disability associated with FGIDs may be related to a child's prediction error or catastrophization; that is, the child believes that the symptoms are severe and hopeless. In such cases, patients may exaggerate symptoms and believe that they cannot cope. (14) Improving children's self-efficacy, their belief that they can help themselves get better, may be an important factor in symptom resolution.

Early childhood acute pain events predispose to the later onset of chronic and recurrent abdominal pain. An event as innocuous as passing a nasogastric catheter in the delivery room to aspirate gastric contents was associated with a two-fold increase in hospitalizations for abdominal pain during a child's first decade. (15) Other early life stressors associated with development of FGIDs include cow milk protein hypersensitivity, pyloric stenosis, urinary tract infections, (16) Henoch-Schönlein purpura, and umbilical hernia repair. (17) Acute bacterial gastroenteritis is followed by functional abdominal pain in approximately 30% of children. (18)

Chronic pain in parents also increases the risk of functional abdominal pain in their offspring. Finally, functional abdominal pain may occur together with disease. For example, a teenager with Crohn disease may have coexisting IBS. Despite histologic remission of the Crohn disease, the patient still may suffer with abdominal pain associated with diarrhea that is relieved by defecation.

FUNCTIONAL GASTROINTESTINAL DISORDERS

Most abdominal pain is associated with one or more FGIDs. Functional symptoms are not imaginary or feigned, but they occur without easily discovered pathology. For example, a runner's cramp may cause intense pain and shivering when cold is an uncomfortable sensation, but both of these functional symptoms are within the expected range of normal body functioning. In gastroenterology, functional disorders are defined by symptom-based diagnostic criteria. The first diagnostic criteria for pediatric FGIDs were created in the late 1990s, when a group of international thought leaders met in Rome to create them. Because the meeting was in Rome, the diagnostic criteria are known as Rome criteria. The first pediatric Rome criteria were based on the personal experiences of the experts, but the publication of criteria stimulated an explosion of research, such that scientific evidence is accruing about the validity, epidemiology, pathophysiology, and treatment of FGIDs. Some of the original diagnostic criteria have been modified based on

new data. The Rome 4 criteria for pediatric abdominal pain disorders are listed in Table 1. (19) Rome criteria replaced Apley's concept of recurrent abdominal pain, (1) which had been the standard for 50 years.

In the past, medical schools taught that every symptom had a cause, and the physician's job was to find and fix the cause for pain. Children with chronic or recurrent abdominal pain were thoroughly evaluated, even overinvestigated, for disease. (20) Most of these children were without objective pathology and were labeled as having "recurrent abdominal pain." Families and physicians were often frustrated and dissatisfied with each other when there was no answer as to what was causing the pain other than excluding serious disease. Families rejected the idea that the pain was "all in her head." An alternative to the traditional medical model is the biopsychosocial model, which recognizes that symptoms may be influenced by disease, psychological illness, developmental challenges, social factors, genetics, and functional disorders. Instead of the dualistic approach that implies if there is no disease of the body, then the pain is imaginary, the biopsychosocial model integrates mind-body interactions into an understanding of a whole person. Symptom-based diagnostic criteria are symptom clusters that occur with regularity in a population with functional abdominal pain. Validation studies have proved that the symptom-based criteria "breed true." (21)

An important advantage of symptom-based diagnostic criteria is that a clinician may arrive at a diagnosis on the first visit. For example, the clinician may say, "You have had abdominal pains for several hours almost every day for the past 3 months that are associated with straining to defecate and infrequent passage of hard stools. There has been no blood in your stools, no fevers, and no weight loss. Therefore, you meet criteria for a diagnosis of constipation-predominant irritable bowel syndrome. We know what it is. It is not dangerous. It comes and goes. There are options for treatment." A second advantage of symptom-based diagnosis is a reduction in the costs for evaluating the symptoms. (20) Instead of ruling out disease with laboratory tests and endoscopy, it is possible to make a positive diagnosis with symptom-based criteria. The clinician can explain that the patient's symptoms are diagnostic for an FGID, but if symptoms fail to improve with treatment, new symptoms develop, or symptoms change in character, the clinician provides reassurance that he/she is available and always willing to re-evaluate.

TESTING

Sometimes testing is necessary to assess for disease. For example, dyspepsia defined by upper abdominal pain or

other discomfort such as nausea may be due to peptic disease, eosinophilic gastroenteritis, or giardiasis. Endoscopy may be necessary to assess for mucosal disease in dyspepsia. However, 85% of those undergoing endoscopy for dyspepsia have no mucosal disease and are diagnosed with functional dyspepsia. (22) Because most children with dyspepsia have no organic disease, an acceptable approach is to educate the family about dyspepsia and initiate a therapeutic drug trial with a proton pump inhibitor, cyproheptadine, or tricyclic antidepressant. If symptoms resolve in the subsequent month, there is no need for endoscopy. If symptoms persist, an endoscopy and biopsies may be undertaken.

Testing should be limited and focused to rule out a specific diagnosis. Testing is needed when the child presents with alarm features (Table 2) that suggest disease. Testing may be necessary to assuage caregiver fears. On the other hand, each negative result may reinforce caregiver belief that something is being missed.

DIFFERENTIAL DIAGNOSIS

School Phobia and Separation Anxiety

Physical symptoms may arise from emotional distress. School phobia and separation anxiety are two common entities that may present with abdominal pain. Clinicians must obtain a history of when the pain episodes occur and how long they last for both conditions. With school phobia, symptoms are most prominent in the mornings before school and improve as the day progresses. Symptoms may be absent on weekends. The clinician should ask about bullying and assess the patient's sense of academic and social competence. "What is harder for you at school: doing the schoolwork or getting along with the other kids?" Once the source of stress is identified, it can be managed. Communication and collaboration among school, parents, and clinician are helpful in resolving school phobia.

Separation anxiety disorder is an anxiety disorder of middle childhood (peak onset between 7 and 9 years) that is characterized by developmentally inappropriate and exaggerated fear of separation. Gastrointestinal symptoms of periumbilical pain, nausea, and vomiting intensify when separation from the caregiver is imminent. Situations involving loss, such as moving to a new home or school, divorce, or death of a family member; stressors such as academic challenges and difficult peer relationships; and an overprotective parenting style increase the risk for onset or exacerbation of separation anxiety. Children with separation anxiety may develop symptoms and refuse to go to school or camp or spend any time away from their major attachment

TABLE 1. Rome Criteria for the Pediatric Pain-associated Functional Gastrointestinal Disorders (15)*

FUNCTIONAL DYSPEPSIA (FD)

Must include 1 or more of the following bothersome symptoms at least 4 times a month for at least 2 months prior to diagnosis:

1. Postprandial fullness
2. Early satiation
3. Epigastric pain or burning not associated with defecation
4. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

Within FD, the following subtypes are now adopted:

1. *Postprandial distress syndrome* includes bothersome postprandial fullness or early satiation which prevents finishing a regular meal. Supportive features include upper abdominal bloating, postprandial nausea, or excessive belching.
2. *Epigastric pain syndrome* includes all of the following: bothersome (severe enough to interfere with normal activities) pain or burning localized to the epigastrium. The pain is not generalized or localized to other abdominal or chest regions and is not relieved by defecation or passage of flatus. Supportive criteria can include: a) burning quality of the pain but without a retrosternal component and b) commonly induced or relieved by ingestion of a meal but may occur while fasting.

IRRITABLE BOWEL SYNDROME (IBS)

1. Abdominal pain at least 4 days per month over at least 2 months associated with 1 or more of the following:
 - a. Related to defecation
 - b. A change in frequency of stool
 - c. A change in form (appearance) of stool
2. In children with constipation, the pain does not resolve with resolution of the constipation (children in whom the pain resolves have functional constipation, not IBS)
3. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

Criteria fulfilled for at least 2 months prior to diagnosis

ABDOMINAL MIGRAINE

Must include all of the following occurring at least twice:

1. Paroxysmal episodes of intense, acute periumbilical, midline, or diffuse abdominal pain lasting 1 hour or more (should be the most severe and distressing symptom)
2. Episodes are separated by weeks to months
3. The pain is incapacitating and interferes with normal activities
4. Stereotypical pattern and symptoms in the individual patient
5. The pain is associated with 2 or more of the following:
 - a. Anorexia
 - b. Nausea
 - c. Vomiting
 - d. Headache
 - e. Photophobia
 - f. Pallor
6. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

Criteria fulfilled for at least 6 months prior to diagnosis

Continued

TABLE 1. (Continued)

FUNCTIONAL ABDOMINAL PAIN – NOT OTHERWISE SPECIFIED
Must be fulfilled at least 4 times per month and include <i>all</i> of the following:
1. Episodic or continuous abdominal pain that does not occur solely during physiologic events (eg, eating, menses)
2. Insufficient criteria for IBS, FD, or abdominal migraine
3. After appropriate evaluation, the abdominal pain cannot be fully explained by another medical condition
Criteria fulfilled for at least 2 months prior to diagnosis
FUNCTIONAL CONSTIPATION
Must include 2 or more of the following occurring at least once per week for a minimum of 1 month with insufficient criteria for a diagnosis of IBS:
1. Two or fewer defecations in the toilet per week in a child of a developmental age of at least 4 years
2. At least 1 episode of fecal incontinence per week
3. History of retentive posturing or excessive volitional stool retention
4. History of painful or hard bowel movements
5. Presence of a large fecal mass in the rectum
6. History of large-diameter stools that can obstruct the toilet
7. After appropriate evaluation, the symptoms cannot be fully explained by another medical condition

*More information is available at <http://theromefoundation.org>.

figure. Many cases resolve with simple interventions from the pediatrician using a rehabilitation approach targeting 3 goals: 1) reducing fear and avoidance of separation, 2) increasing the child's participation in age-appropriate activities, and 3) redirecting attention to the child's competent behavior (participating in school activities, helping others). (23)

The goal of management for both school phobia and separation anxiety is to help the child learn positive methods of coping with and transcending the fear. Caregivers should receive clear instructions from the clinician on how to get the child back to school. The longer the child is out of school, the more difficult becomes the return.

Functional Constipation

Sometimes there may be overlap between constipation-predominant IBS (c-IBS) and functional constipation (Table 1). Many patients have abdominal pain and constipation. If the patient says that the constipation is worse than the pain, the diagnosis is functional constipation. If pain is the most important feature of the illness, the diagnosis is c-IBS.

Abdominal Wall Pain

Approximately 1 in 30 children presenting with bellyaches has abdominal wall pain. Chronic abdominal wall pain is frequently confused with visceral pain, often leading to extensive diagnostic testing before reaching a correct

diagnosis. There may be a history of pain with movement but not with eating or defecation. Stretching exercises, bending, and rotating the trunk may elicit the pain. Carnet's test is said to discriminate anterior cutaneous nerve entrapment syndrome from visceral pain. (24) After localizing an area of maximal tenderness by palpation, the clinician applies pressure to the tender spot and asks the patient to tense the abdominal muscles by lifting head or legs. The examiner releases pressure on the abdomen and reapplies pressure on the same spot. If the pain is from the viscera, the reapplication of pressure fails to cause intense pain. When the pain is from cutaneous nerve entrapment syndrome, pain upon reapplication of pressure is equivalent to that of the first palpation. Abdominal wall pain is usually a benign condition, but if persistent, it may be treated by a pain specialist with injections of local anesthesia and corticosteroids. (25)

Celiac Disease and Non-celiac Gluten Sensitivity

Celiac disease occurs in about 1 in 180 individuals, although the ratio of symptomatic-to-asymptomatic patients is 1:7. The most common presenting complaint in childhood celiac disease is abdominal pain. (26) Screening for celiac disease with serologic testing is reasonable in many children with abdominal pain. Celiac disease is not more frequent in patients with FGIDs than it is in the general population.

TABLE 2. Alarm Signs and Symptoms Prompting Testing for Disease

- Pain localized to the right upper or right lower quadrants
- Blood in the stools
- Weight loss
- Slow or delayed growth and delayed puberty
- Odynophagia
- Dysphagia
- Persistent vomiting
- Family history of inflammatory bowel disease or celiac disease
- Fevers
- Arthritis
- Perianal disease: skin tags, fissures, fistulae

Some patients report symptoms caused by wheat and/or gluten ingestion, even though they do not have celiac disease or wheat allergy, as indicated by negative celiac disease serologies and immunoglobulin E-mediated assays. Most of these patients report both gastrointestinal and non-gastrointestinal symptoms, and all report symptom improvement with a gluten-free diet. This condition has been named non-celiac gluten sensitivity. The clinical response to a gluten-free diet may be caused by a variety of mechanisms, including placebo effect, FODMAP (fermentable oligo-di-monosaccharides and polyols) reduction, and gluten sensitivity. Thus, a diagnosis of non-celiac gluten sensitivity should be approached with caution and not be based on a short-term improvement in symptoms on a gluten-free diet.

Peptic Ulcer Disease and *Helicobacter pylori* Infection

Peptic ulcer disease is uncommon during childhood, with prevalence estimates of 1 in 2,000 children. Ulcers may present with abdominal pain, although 50% of childhood ulcers present with a complication of bleeding, obstruction, or perforation.

Gastric *H pylori* infection is the most common bacterial infection worldwide. It is most prevalent in low-income populations. *H pylori* is associated with acute and chronic gastritis, duodenal ulcer disease, and increased risk for gastric cancer. *H pylori* antigens in a stool sample are 95% accurate for diagnosis. It is prudent to eradicate the infection with a course of acid suppression and multiple antibiotics. However, *H pylori* may be an incidental finding in patients with functional abdominal pain, and eradication of *H pylori* may not result in pain reduction. There are evidence-based guidelines for assessing and treating *H pylori* in children. (27)

Lactase Deficiency

Carbohydrate malabsorption causes pain because the osmotic load of luminal carbohydrate draws in water from the intestinal walls, thus increasing the luminal volume, stretching the bowel wall, and activating stretch and pain receptors located in the bowel wall. Fermentation of unabsorbed carbohydrate in the colon results in gas and another osmotic load, drawing more water into the lumen and stretching the colon wall, causing pain and diarrhea.

Certain ethnic groups (everyone except Northern Europeans) may develop a relative lactase deficiency in the late first or second decade. If milk causes pain, substitutes such as soy milk do not cause symptoms. Lactase deficiency may be diagnosed by a breath hydrogen test using lactose as a substrate.

Sucrase Deficiency

Less common than lactase deficiency in late childhood is congenital sucrose deficiency, which may cause pain and other symptoms indistinguishable from IBS. (28) Sucrase deficiency may be detected by a breath test using sucrose as a substrate.

Fructose Malabsorption

Fructose malabsorption is less common than lactase deficiency and is a cause of diarrhea and gas. (29) Fructose deficiency may be diagnosed with a breath test using fructose as the substrate.

Biliary Dyskinesia

Biliary dyskinesia is defined in most pediatric studies by 3 criteria: chronic upper abdominal pain, delayed excretion of radionuclide on a gallbladder emptying study, and absence of gallstones. Biliary dyskinesia is treated by cholecystectomy. A growing trend in many communities is to refer children and adolescents to surgeons for evaluation of chronic or recurrent upper abdominal pain. However, chronic and recurrent abdominal pain is not the same as biliary colic, the intense episodic pain required for a biliary dyskinesia diagnosis in adults. Moreover, there is no evidence that hepatobiliary iminodiacetic acid (HIDA) scan results are valid or reliable for diagnosing biliary dyskinesia in children. In adults, IBS and functional dyspepsia are associated with delayed gallbladder emptying, but there are no data in children. Pediatric studies of biliary dyskinesia use symptoms consistent with functional dyspepsia to diagnose biliary dyskinesia. Leaders in the pediatric gastroenterology community stress that dyspepsia responds to nonsurgical treatment. In the author's opinion, clinicians should avoid screening for biliary dyskinesia and instead treat chronic and recurrent upper abdominal pain or nausea as dyspepsia.

TREATMENT FOR FUNCTIONAL ABDOMINAL PAIN

Treatment for abdominal pain varies with the style of the clinician, patient/caregiver preferences, and availability of the variety of modalities. The clinician should establish a therapeutic alliance with the family before the family will accept a symptom-based diagnosis and agree to suspend the search for disease. Treatment of functional abdominal pain disorders should always include reassurance, empathy, and education. Children and families should be assured that the clinician believes the pain is real. The clinician explains that in children, abdominal pain without disease is more common than abdominal pain with disease. Although pharmacologic treatment is common, cognitive behavioral therapy (CBT) and hypnotherapy have been shown to be effective for abdominal pain. The success of psychological interventions as well as the powerful effect of placebos demonstrates the complementary influences between the brain and the gut and the importance of the CNS in the pathophysiology of abdominal pain.

Education

Making a symptom-based diagnosis and providing a lucid explanation for symptoms is usually sufficient to reduce the spoken and unspoken fears that prompted the visit. Patients and families want to know the answers to 4 questions: What is wrong? Is it dangerous? Will it go away? What can we do about it? The clinician should state the answers to each question clearly. In gastroenterology clinic, 9% of families are satisfied with a clear diagnosis and a promise of continuing availability, and they decline other treatment. (30)

Diet Changes

A minority of patients identifies specific foods as a source for pain, such as fried foods, red sauces, and milk. Patients should eliminate the offending foods from their diets. There is no evidence that a lactose-, gluten-, histamine-, or carbonic acid-free diet; increased fluid intake; or prebiotics have effects on pain-associated FGIDs. Probiotics have generally been ineffective for abdominal pain with 2 exceptions in adult studies. Probiotics VSL#3 (31) and *Lactobacillus* GG (32) may be effective in some cases of abdominal pain associated with bloating and diarrhea. Extra fiber is not helpful in most cases.

Pharmacologic Treatment

There are no drugs approved by the U.S. Food and Drug Administration (FDA) for treatment of abdominal pain in children, but that does not hamper prescribing. Proton pump inhibitors and histamine-2 receptor antagonists appear to be the most prescribed drugs, despite symptom improvement rates being similar to those for placebo. The rationale for prescribing gastric acid suppression may relate to the

excellent safety profile of the drugs and the need to relieve concerns that the pain may be caused by esophagitis, gastritis, duodenitis, or peptic ulcer disease. Narcotics that are a mainstay of treatment for acute pain, including abdominal migraine, should not be used for chronic and recurrent abdominal pain. Aspirin, ibuprofen, and other nonsteroidal anti-inflammatory drugs should not be prescribed for abdominal pain because they may disrupt the gastric mucosal barrier and cause gastritis and ulcers. A recent systematic review of pediatric randomized, placebo-controlled drug trials for functional abdominal pain (33) found 8 studies, low numbers of study participants, and many limitations and biases. Meta-analyses suggest that tricyclic antidepressants and serotonin reuptake inhibitors are effective for adults with abdominal pain. Data supporting anticholinergic, "antispasmodic" drugs are less robust. Overall, the quality of evidence for pharmacologic therapy in children with chronic or recurrent abdominal pain is low to very low.

In randomized clinical trials, responses to placebos for functional abdominal pain are usually about 40%. (34) For some clinicians who are learning what works for their patients, a 40% response rate may condition them to continue to prescribe drugs that are essentially no better than placebos. (35) These clinicians' learned responses might be slow to extinguish because a 40% response rate reinforces their prescribing habits.

Psychological Treatment

A recent review of nonpharmacologic treatment of functional abdominal pain concluded that hypnosis and CBT were more effective than placebo for pediatric abdominal pain. (36) However, limited access to mental health services is common in many communities. Identifying the stressors triggering symptoms and working to eliminate such stressors may be a key to successful management.

One study found that CBT reduced pain better than an identical time for education and support (attention control). In this trial, parents and children participated in 3 brief weekly sessions that focused on relaxation training, addressing inappropriate thoughts about symptoms, and working with parents to modify the family's responses to child illness behaviors (social learning). (10)(37)

Hypnotherapy is effective for abdominal pain. In a randomized, controlled trial of 52 children, pain intensity, frequency, and somatization were reduced after treatment and persisted after 5 years, indicating long-term benefit. (9)(38) Self-hypnosis through audiotapes was effective and is a readily available, cost-effective technique. (39)

There is weak evidence to recommend complementary and alternative interventions such as acupuncture or yoga for abdominal pain.

Abdominal Migraine

Abdominal migraine is 1 of 3 paroxysmal brain/gut disorders, along with cyclic vomiting syndrome and migraine headaches. Paroxysmal brain/gut disorders are named by the dominant symptom: abdominal pain, vomiting, or headache. Abdominal migraine accounts for about 0.5% of abdominal pain patients in a pediatric gastroenterology clinic, making it the least common of the pain-associated FGIDs. A most important aspect of abdominal migraine is recognizing the symptom-based criteria to make a proper diagnosis. Often children with abdominal migraine visit emergency departments, are evaluated for acute abdomen, and receive no diagnosis and no relief from pain because emergency department clinicians do not want to mask symptoms. The child suffers needlessly. In the author's opinion, a diagnosis of acute abdominal migraine frees the clinician to titrate narcotics to restful sleep, with repeat doses as needed until the episode passes. After the episode is over, future episodes are usually prevented with amitriptyline 1 mg/kg per day.

DRUG TREATMENT FOR FUNCTIONAL DYSPESIA (TABLE 3)

There are no FDA-approved drugs for children with functional dyspepsia. Cyproheptadine is commonly used for dyspepsia in children. (40) In another trial, cyproheptadine reduced the episodes and severity of functional abdominal pain. (41)

There are no prospective randomized treatment trials for pediatric functional dyspepsia. Extrapolation from adult data suggests that acid blockade with histamine receptor

antagonists and proton pump inhibitors can be offered to older children and adolescents for pain-predominant symptoms. (42) If cure of functional dyspepsia is defined as complete symptomatic relief after 4 weeks of treatment, omeprazole is superior to ranitidine, famotidine, and cimetidine. (43) Although convincing data are lacking in children, low-dose tricyclic antidepressant therapy with agents such as amitriptyline and imipramine is often considered in difficult cases.

A recent trial in adults showed amitriptyline to be superior to placebo and citalopram in the epigastric pain subtype but not the postprandial distress subtype. (44) Extrapolating these data to pediatrics might be risky, but one approach might be to treat epigastric pain with amitriptyline and postprandial distress with another drug. Two drugs that improve gastric receptive relaxation and treat nausea and early satiety are buspirone and mirtazapine. Buspirone, an anxiolytic, requires multiple dosing daily but has no black box warning about suicide. (45) Mirtazapine, an antidepressant, requires only a single bedtime dose and facilitates restful sleep in addition to treating postprandial distress, anxiety, panic, and depression. (46) For chronic daily or constant nausea, mirtazapine is superior to antiemetics such as promethazine or ondansetron.

TREATMENT FOR IRRITABLE BOWEL SYNDROME

The Low FODMAP Diet

The FODMAPs include fructose (fruits, honey, high-fructose corn syrup), lactose (dairy), fructans (wheat, garlic,

TABLE 3. Drug Treatment for Functional Dyspepsia

FUNCTIONAL DISORDER	DRUGS	DOSE	MEDICATION CLASS	DURATION OF TREATMENT	ADVERSE EFFECTS	COMMENTS
Functional Dyspepsia	<i>Epigastric pain:</i> Amitriptyline	10-50 mg qhs	Tricyclic antidepressant	Until the pain goes away plus 6 months	Constipation, sedation; nightmares if patient misses a dose	Start at 10 mg and increase by 10 mg/wk until pain resolves or 50 mg
	<i>Postprandial distress:</i> Cyproheptadine	0.25-0.5 mg/kg per day divided bid or tid	Histamine-1 and serotonin-1 antagonist	Until the discomfort goes away plus 6 months	Fatigue, dizziness, weight gain	Increased appetite in about 50% of children lasts about 3 weeks
Irritable Bowel Syndrome	<i>d-IBS:</i> Amitriptyline	10-50 mg qhs	Tricyclic antidepressant	Until the pain goes away plus 6 months	Constipation, sedation, nightmares if patient misses a dose	ECG unnecessary in individuals with no heart disease
	Alosetron	0.5-1 mg qd or bid	Serotonin-3 receptor antagonist	Indefinite	Constipation	Very effective; expensive
	<i>c-IBS:</i> Imipramine	10-50 mg qhs	Tricyclic antidepressant	Until the pain goes away plus 6 months	Sedation	Imipramine is less constipating and sedating than amitriptyline
	Lubiprostone	8-24 µg qd or bid	Chloride channel activator	Indefinite	Diarrhea, nausea	Expensive

bid=twice daily, *c-IBS*=constipation-predominant irritable bowel syndrome, *d-IBS*=diarrhea-predominant irritable bowel syndrome, *ECG*=electrocardiography, *qd*=daily, *qhs*=every bedtime, *tid*=thrice daily



Figure 3. Preteens and teens with functional symptoms associated with disability fall into a gap between conventional medicine and conventional mental health. They require a clinician who understands functional symptoms and a rehabilitation approach to treatment.

onion, inulin), galactans (legumes such as beans, lentils, soybeans), and polyols (sweeteners containing isomalt, mannitol, sorbitol, xylitol, stone fruits such as avocados, apricots, cherries, nectarines, peaches, plums). FODMAPs may not be digested or absorbed well and could be fermented by bacteria in the intestinal tract when eaten in excess. Typical IBS symptoms of diarrhea, constipation, gas, and bloating may improve with a low FODMAP diet. (47) A low FODMAP diet is best initiated in consultation with a dietitian to assure that the diet meets the child's nutritional needs.

Medical Foods

Two medical foods are on the market to treat IBS. IBGast is peppermint oil in an enteric-coated capsule. In one pediatric randomized, controlled trial, peppermint oil was effective

for treating IBS. (48) Dosing is 1 capsule for symptoms 1 to 3 times daily. Bovine serum immunoglobulin taken twice daily was effective for diarrhea-predominant IBS (d-IBS) in adults. (49)

Drugs (Table 3)

There are no FDA-approved drugs for treatment of children with IBS. Randomized clinical trials are missing for most drugs used for childhood IBS. For example, despite their routine use by clinicians, there is no evidence that acid suppression with histamine-2 receptor antagonists or proton pump inhibitors is helpful in IBS.

Tricyclic antidepressants are effective treatment for IBS in adults, (50) but 2 randomized, controlled trials in children were unsatisfying because placebo-treated children did as well as amitriptyline-treated children. (51)(52) However, amitriptyline dosing in the pediatric trials may have been too low to achieve a response. Amitriptyline and, to a lesser extent, imipramine are sedating and constipating. If the patient has abdominal pain, diarrhea, and insomnia, a tricyclic antidepressant may be a good choice (Table 3).

In children with d-IBS who are unable or unwilling to take amitriptyline because of concerns about cardiac arrhythmias, seizures, or mood effects, the serotonin-3 receptor antagonist alosetron is effective. Clonidine may be a good choice for d-IBS and disordered sleep.

There are several alternatives for children with c-IBS. A clinician might choose to treat the constipation with polyethylene glycol titrated to soft stools together with a

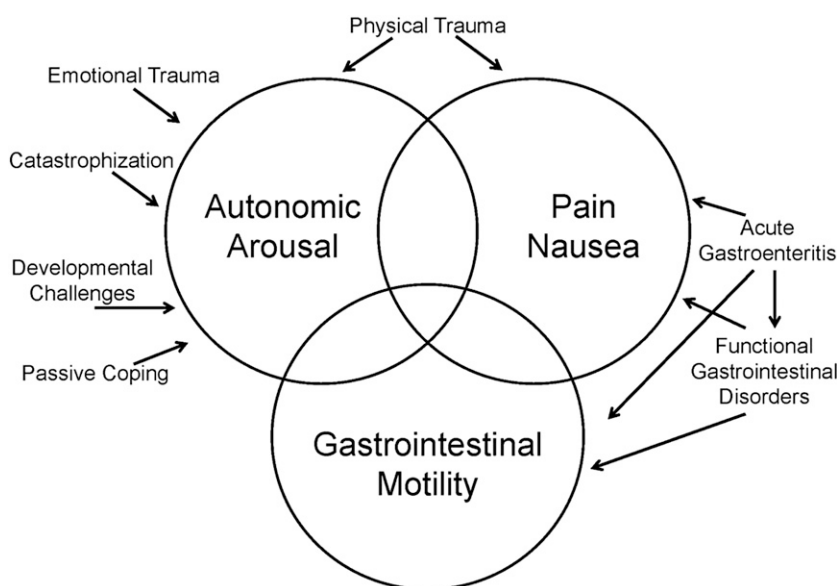


Figure 4. Pathogenesis of pain-associated disability syndrome (PADS). PADS may be triggered by factors causing autonomic arousal in a preteen or teen with a functional gastrointestinal disorder. From Hyman PE, Bursch B, Sood M, Schwankovsky L, Cocjin J, Zeltzer LK. Visceral pain-associated disability syndrome: a descriptive analysis. *J Pediatr Gastroenterol Nutr.* 2002;35(5):663-8. Reprinted with permission from Wolters Kluwer Health.

tricyclic antidepressant or serotonin reuptake inhibitor for pain. Lubiprostone binds to small intestinal epithelium, activating chloride channels to facilitate secretion of chloride and water. Lubiprostone is approved by the FDA for c-IBS and functional constipation in women, but there are scant data in children. (53) Adherence may be better with 1 or 2 tablets of 24- μ g lubiprostone per day compared to asking a teenager to mix and drink polyethylene glycol. Lubiprostone should be taken with food to reduce the chances of nausea.

WHEN TO SEE A SPECIALIST

Children should be referred to a pediatric gastroenterologist for further testing and/or treatment in the event of:

- Treatment failure
- Prolonged school absence
- Presence of alarm features
- Abnormal laboratory test results (including abnormal celiac tests)

DISABILITY ASSOCIATED WITH FUNCTIONAL ABDOMINAL PAIN

Children with abdominal pain may miss school. Caregivers should understand that staying home from school is considered a disability in the same way that staying home from work is considered a disability for adults. The more missed school, the more difficult it is to return. Staying home leads to greater disability, increased focus

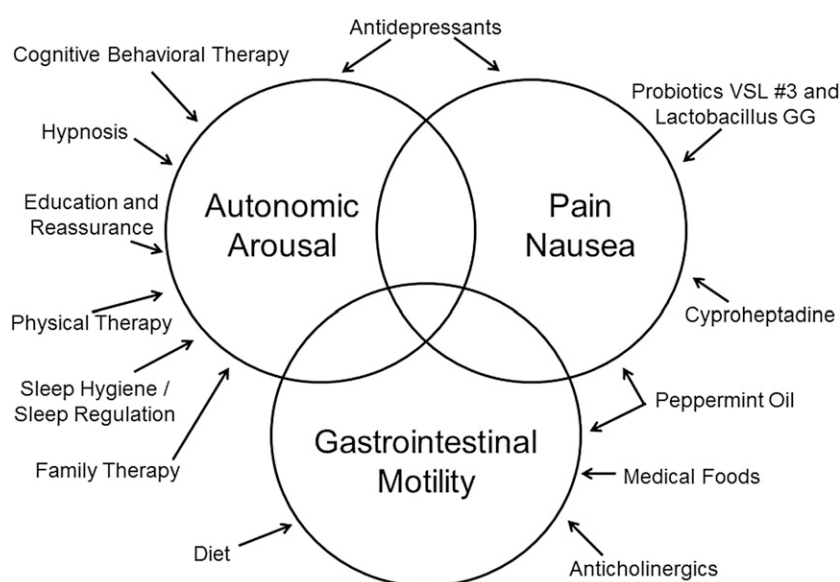
on pain, and fewer opportunities for distraction and social interaction. In addition, children who stay at home for long periods of time may become physically deconditioned and less secure in their ability to interact with their peers. Children who stay at home sometimes adopt a sick role that makes rehabilitation difficult.

Pain-associated disability syndrome (PADS) is defined as a preteen or teen with at least 2 months of abdominal pain or other symptom such as nausea that is unresponsive to acute management strategies. (54) Doctors do many tests but find no disease, yet symptoms interfere with the patient's routine activities, such as attending school, eating, and sleeping. The symptoms and disability are out of proportion to the clinicians' findings. Physicians sometimes admit that they find nothing wrong and refer families to mental health professionals. Mental health professionals usually find no overt psychopathology during the first interview because the patient converts emotional distress into physical symptoms and denies symptoms of a mood disorder. PADS patients fall into a gap between conventional medicine and conventional mental health (Fig 3).

PADS appears to be a downward spiral of disability and pain that has 3 continuously interacting features: abnormalities in gastrointestinal motility, abnormalities in sensory experience such as pain and nausea, and dysregulation in the autonomic nervous system (Fig 4).

Every PADS patient meets diagnostic criteria for 1 or more FGIDs that are diagnosed with symptom-based criteria. FGIDs, which occur in approximately 25% of the

Figure 5. Multidisciplinary biopsychosocial rehabilitation model for treating disability associated with functional gastrointestinal disorders. From Hyman PE, Bursch B, Sood M, Schwankovsky L, Cocjin J, Zeltzer LK. Visceral pain-associated disability syndrome: a descriptive analysis. *J Pediatr Gastroenterol Nutr.* 2002;35(5):663-8. Reprinted with permission from Wolters Kluwer Health.



population, are associated with minor abnormalities in gastrointestinal motility and sensation, but nearly all affected patients cope with such disorders without becoming disabled. In PADS, a developmental, family, or mental health problem causes sustained autonomic arousal. The intensity of symptoms and the degree of disability are proportional to the severity of emotional distress. PADS severity is inversely correlated with an individual's assessment of his or her own academic or social competence. PADS patients often feel helpless.

Catastrophization, the belief that symptoms can only worsen and the patient is helpless, further activates autonomic arousal. Similarly, an external locus of control, the belief that the suffering can be reduced only from outside sources, interferes with coping and amplifies arousal. Treatment for teens with PADS encompasses a shift away from the medical model, in which a doctor does something to cure a passive patient, to a rehabilitation model, in which clinicians teach the child the necessary skills to return to a normal lifestyle.

Treatment includes physical therapy, psychotherapy, and drugs to treat coexisting mental health issues and sleep disruptions (Fig 5). Psychotherapy and hypnosis have the advantage of effects that last long after the treatment period compared to drug effects that last only as long as treatment continues. Drugs have the advantage of not requiring a psychotherapist. However, strong evidence for drug efficacy in children with pain related to FGIDs is missing. Treatment requires a multidisciplinary biopsychosocial team approach that must include the family. When the child or family does not accept the diagnosis or challenges the treatment, management fails. When the child, family, and team of professionals are in step, treatment succeeds.

Summary

- On the basis of strong research evidence, most chronic and recurrent abdominal pain in children and adolescents is functional, meaning that symptoms are not feigned, but there is no easily detected disease.
- Symptom-based diagnostic criteria facilitate rapid diagnosis for most children and adolescents with functional abdominal pain. For most children who meet diagnostic criteria for a functional disorder and have no warning signs for disease (weight loss, fevers, blood in stool), no testing is necessary or desirable.
- On the basis of strong epidemiologic evidence, irritable bowel syndrome (IBS), defined by chronic or recurrent abdominal pain associated with diarrhea or constipation or alternating diarrhea and constipation, is the most common of the functional gastrointestinal disorders.
- Because of the very few prospective randomized, controlled trials in children, there is no generally accepted safe and effective treatment for IBS in this population. On the basis of strong research evidence, treatments for IBS in adults include tricyclic antidepressants and cognitive behavioral therapy.
- On the basis of strong research evidence, the placebo response rate in functional abdominal pain is approximately 40%; this response rate ensures that any treatment works some of the time.
- On the basis of some research evidence and consensus, disability from a functional disorder is proportional to comorbid psychological distress from a mental health disorder or learning disability.
- On the basis of primarily consensus, due to lack of prospective studies, treatment for those disabled by functional abdominal pain requires shifting from an acute medical to a rehabilitation model and involves a team approach that includes cognitive behavioral therapy, medication to regulate sleep and reduce autonomic arousal, and physical therapy. Refusal to engage with mental health treatment is associated with treatment failure.

References for this article are at <http://pedsinreview.aappublications.org/content/37/9/377>.

Parent Resources from the AAP at HealthyChildren.org

Chronic and Recurrent Abdominal Pain

- <https://www.healthychildren.org/English/health-issues/conditions/abdominal/Pages/Abdominal-Pain-in-Children.aspx>
- Spanish: <https://www.healthychildren.org/spanish/health-issues/conditions/abdominal/paginas/abdominal-pain-in-children.aspx>
- <https://www.healthychildren.org/English/health-issues/conditions/abdominal/Pages/Abdominal-Pains-in-Infants.aspx> (English only)

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1. A 10-year-old girl is brought by her parents to see you for the first time for evaluation of a 1-year history of abdominal pain that she has been experiencing several times a week. You know that chronic recurrent abdominal pain is common among children across the world. You also know that most such pain is not caused by isolated organic disease, but rather reflects a symptom sparked by a combination of overlapping physical, physiological, mental, and social factors. Which of the following characteristics of the pain will prompt you to initiate an immediate search for an organic explanation?
 - A. Has a consistent periumbilical distribution.
 - B. Is associated with a 10-lb weight loss.
 - C. Occurs primarily upon awakening.
 - D. Occurs primarily upon going to sleep.
 - E. Occurs several times a day, lasting less than 5 minutes for each episode.
2. Over the past 25 years, the uncovering of a better understanding of the pathophysiology of chronic and recurrent abdominal pain has:
 - A. Decreased the need for mental health counseling for the complaint.
 - B. Increased the clinician's ability to use history and physical examination to reliably differentiate one functional disorder from another.
 - C. Increased the need for primary care physicians to refer patients with such pain to gastroenterologists.
 - D. Increased the requirement for sophisticated diagnostic laboratory testing.
 - E. Raised doubt about the role of social stress as a contributing cause.
3. Since starting kindergarten, an 8-year-old boy has had frequent periumbilical pain and nausea in the morning. He occasionally vomits. Which of the following statements would strongly suggest that he suffers from separation anxiety?
 - A. He has postbreakfast fullness, bloating, and belching.
 - B. He feels fine soon after being permitted to stay home from school.
 - C. His symptoms are present both on weekdays and weekends.
 - D. His symptoms are relieved by defecation.
 - E. His symptoms improve at school as the day goes on.
4. A 12-year-old girl has experienced daily periumbilical abdominal pain lasting several hours for the past 2 years. She rarely misses school. She has gained weight normally and experienced normal menarche. She strains to defecate and passes small hard stools every 2 days, after which she experiences some relief from pain but no complete resolution. Treatment with polyethylene glycol has failed to resolve the problem. Her physical examination yields normal results. Based on her history and examination, which of the following is the most likely diagnosis?
 - A. Abdominal migraine.
 - B. Functional constipation.
 - C. Functional dyspepsia.
 - D. Irritable bowel syndrome.
 - E. Postprandial distress syndrome.

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This journal-based CME activity is available through Dec. 31, 2018, however, credit will be recorded in the year in which the learner completes the quiz.

5. The caregivers of children and adolescents diagnosed with functional abdominal pain in your practice ask you about options for treatment and their effectiveness. Assuming that you already have established a therapeutic alliance with patients and families, provided them with assurances that you believe that the pain is real, and offered empathy, education, and reassurance, which of the following proposed treatment options currently promises the best treatment outcome for children and adolescents with functional abdominal pain?
- A. Acupuncture.
 - B. Changes in diet.
 - C. Cognitive behavioral therapy.
 - D. Intensive personal psychotherapy.
 - E. Prescription of U.S. Food and Drug Administration-approved medications.

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Pediatrics in Review 2016;37;377

DOI: 10.1542/pir.2015-0169

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Pediatrics in Review

An Official Journal of the American Academy of Pediatrics

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