

Functional Abdominal Pain in Children

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Program Audience

Primary care physicians.

Educational Needs Addressed

Recurrent abdominal pain is highly prevalent in childhood. Between 10% and 25% of school-aged children and adolescents complain of recurrent abdominal pain of sufficient severity to interfere with daily activities, accounting for significant school absenteeism, impaired quality of life, and parental frustration. The majority of these children have “functional” symptoms, in which there is no demonstrable disease. Diagnosis and treatment of children with functional abdominal pain can be challenging for the clinician. Symptom-based criteria are available to aid the clinician in making a positive diagnosis.

Educational Objectives

After participating in this CME activity, primary care physicians should be able to

1. Identify the pediatric functional gastrointestinal disorders (FGIDs) associated with abdominal pain and describe their diagnostic criteria
2. Understand the pathophysiology of FGIDs
3. Describe components of a successful therapeutic approach, including the role of diet, probiotics, behavioral modification, and pharmacotherapy
4. Describe the long-term prognosis for FGIDs

for significant school loss, impaired quality of life, and parental frustration [1–3]. It continues to be misunderstood by both the medical and lay communities, often leading to underevaluation or overevaluation of symptoms.

The terms “recurrent abdominal pain” and “chronic abdominal pain” are often used interchangeably. Recurrent implies occurring more than once, and for most clinicians a minimum of 3 separate episodes are required for a symptom to be considered recurrent. Chronic implies persisting over a specific time period. In the original description of recurrent abdominal pain of childhood by Apley and Naish [4], a minimum duration of 3 months was required, but more recently an expert consensus group lowered the minimum duration to 2 months [5]. The severity of pain can be variable, ranging from bothersome to severe, and variably affects the ability of the child to conduct age-appropriate activities.

Although the term recurrent abdominal pain was used as an endpoint in the past (ie, a final diagnosis), it is more appropriately used as a description. There are many disorders that can be associated with recurrent or chronic abdominal pain; however, the majority of children suffer from “functional” symptoms, defined as symptoms that occur in the absence of inflammation, tissue damage, or anatomic abnormality [5,6]. In 2005, a committee of experts from the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition suggested that the term “recurrent abdominal pain” be retired and the term “functional abdominal pain” be used to describe the condition [7]. In this article, we will use the term “functional abdominal pain” in discussing children with recurrent or chronic abdominal pain in whom there is no obvious disease as described above. Functional abdominal pain disorders are associated with end-organ visceral hyperalgesia and increased perception of discomfort. Older terminology that described these children as having “non-organic” abdominal pain reflected a lack of understanding of the pathophysiology of the complaints.

This case-based review will illustrate our current

Recurrent abdominal pain is one of the most common presenting complaints to primary care providers and pediatric gastroenterologists. It affects up to 10% to 25% of school-aged children and adolescents and accounts

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understanding of functional abdominal pain in children with an emphasis on diagnosis and treatment.

CASE STUDY

Initial Presentation



A 13-year-old girl presents to her primary care provider with a 3-month history of abdominal pain.

History

Several mornings each week, the patient awakens with epigastric and periumbilical discomfort and has little appetite for breakfast. Eating makes her pain worse and she occasionally develops increasing nausea and urgency to defecate. The patient usually stools 1 to 3 times per day, with the stools ranging from hard to loose. She often perceives a sense of incomplete evacuation. Mucus has been noted with the stool but not blood. Her abdominal pain does not awaken her from sleep. She has lost 2 lb since her last visit 6 months ago. The patient complains of being tired and has frequent headaches. During the weekends when she can sleep later, her symptoms are not as severe. She began menarche 4 months ago and her menses are irregular. The remainder of her review of systems is noncontributory.

The patient is in 8th grade and is an A student. She is active in sports and plays the oboe in a local youth symphony. She missed 3 days of school because of her gastrointestinal symptoms. Her mother has a history of irritable bowel syndrome.

Physical Examination

On physical examination, the patient is a healthy-appearing adolescent whose weight and height are at the 50th percentile for age. There are no rashes or clubbing. Her heart and lungs are normal. Her abdomen is soft but mildly tender throughout. There is no organomegaly. There is no perirectal disease, and the soft stool in her rectum is free of occult blood.

Laboratory evaluation reveals a normal complete blood count, erythrocyte sedimentation rate, serum aminotransferases, and negative anti-tissue transglutaminase IgA. Urinalysis is unremarkable.

- **What is the initial approach to evaluating a child with recurrent abdominal pain?**

The initial goal of most physicians evaluating a child with recurrent abdominal pain is to exclude any serious disease. It is important to interview adolescent patients both with and without a parent present. Teenagers may have information to disclose that they do not want their parent to hear; disclosure might be facilitated if the parents leaves the examining room.

Table 1. “Red Flag” or Alarm Features in Children with Recurrent Abdominal Pain

Nocturnal pain
Nocturnal diarrhea
Persistent right lower quadrant pain
Perirectal disease
Blood in the stool
Fever
Arthritis
Weight loss
Persistent vomiting
Dysphagia
Growth delay
Delayed puberty
Family history of inflammatory bowel disease, celiac disease, peptic ulcer disease

A search for “red flags” is performed in completing the history and physical examination (Table 1). Finding a red flag prompts further diagnostic steps toward a specific diagnosis, such as upper gastrointestinal endoscopy when ulcer is suspected, ultrasound to detect gallstones, or colonoscopy for inflammatory bowel disease. Most children with recurrent abdominal pain will have no red flags in their history. However, because of the duration of symptoms, many will have some laboratory investigation, including a complete blood count, erythrocyte sedimentation rate, biochemical profile, urinalysis, and more recently a serologic panel to screen for celiac disease. The presence of bloating, gassiness, or diarrhea in some patients can lead to breath hydrogen testing for lactose malabsorption.

While the presence of abnormal laboratory evaluation is important, the absence of abnormal laboratory tests does not always exclude disease. A recent study of nearly 1000 newly diagnosed children with inflammatory bowel disease revealed that nearly 20% had a normal laboratory evaluation at presentation [8]. Nonetheless, in the absence of red flag historical and physical examination findings and with a normal laboratory evaluation, the likelihood of a functional disorder is high.

- **What pediatric functional gastrointestinal disorders are associated with abdominal pain?**

Table 2 lists the pediatric functional gastrointestinal disorders (FGIDs) that are associated with abdominal pain. Working definitions of these disorders have largely come from the Rome Committee, a group of key thought leaders in the

Table 2. Pediatric Functional Gastrointestinal Disorders Associated with Recurrent or Chronic Abdominal Pain

Irritable bowel syndrome
Functional dyspepsia
Abdominal migraine
Functional abdominal pain
Functional abdominal pain syndrome

field of FGIDs who have developed symptom-based criteria for these conditions [5]. These definitions are derived from both empirical evidence and expert opinion. They are meant to aid the clinician in making a positive diagnosis of a FGID based on a symptom complex rather than making the FGID a diagnosis of exclusion after performing an extensive battery of tests to “rule out” disease.

A brief review of the FGIDs associated with abdominal pain is important in evaluating the symptoms of this 13-year-old girl. In all the FGIDs, there is no obvious inflammatory, anatomic, metabolic, or neoplastic cause of symptoms. Symptoms must be present for at least 2 months to meet Rome III criteria.

Irritable Bowel Syndrome

Irritable bowel syndrome is defined by the presence of abdominal pain or discomfort that is associated with 2 or more of the following at least 25% of the time: improvement with defecation or onset associated with a change in the frequency of the stool or in the form of the stool. Patients fall into 1 of 3 categories: diarrhea-predominant, constipation-predominant, or alternating diarrhea/constipation. There is frequently postprandial fecal urgency and some patients relate copious mucus in their stool. Symptoms consistent with irritable bowel syndrome are seen in up to 6% to 14% of middle school and high school students in the United States [2], and irritable bowel syndrome is among the most common disorders diagnosed in pediatric gastroenterology referral practices [9]. Symptoms occasionally arise following an intercurrent viral illness or bacterial gastroenteritis [10].

Functional Dyspepsia

Functional dyspepsia is defined by the presence of persistent or recurrent pain or discomfort centered in the upper abdomen (above the umbilicus) that is not relieved by defecation or associated with a change in stool frequency or form. In some children, pain is the most common complaint while in others nausea, bloating, early satiety, or simply an uncomfortable abdominal feeling is noted. Symptoms occasionally arise following an intercurrent viral illness [11]. Although inflammatory conditions such as gastroesophageal reflux disease, allergy, *Helicobacter pylori* infection, and Crohn's dis-

ease can cause dyspepsia in children, the majority of children with dyspepsia have no demonstrable disease process [12].

Abdominal Migraine

Abdominal migraine is defined by paroxysmal episodes of intense, acute periumbilical pain that lasts for at least 1 hour and is associated with at least 2 of the following: anorexia, nausea, vomiting, headache, photophobia, or pallor. It is further characterized by the absence of abdominal pain between discrete episodes. Attacks may occur at any time of the day, although most commonly they can awaken the child from sleep or begin shortly after awakening. There is frequently a family history of migraine headaches and an increased likelihood of the child previously complaining of motion sickness. As the attack ends, the child often becomes lethargic and sleepy; the attack typically remits after sleep. Because of the severity of the attacks and their intermittent and paroxysmal nature, other causes of similar pain are often sought, such as obstructive uropathy (ureteropelvic junction obstruction), renal stones, intestinal malrotation, intussusception, biliary tract disease, and recurrent pancreatitis. More rare causes such as familial Mediterranean fever and porphyria can also be considered.

Functional Abdominal Pain and Functional Abdominal Pain Syndrome

Functional abdominal pain is defined as episodic or continuous abdominal pain in the absence of sufficient criteria to define other FGIDs that are associated with abdominal pain. When a child also has some loss of daily functioning or additional somatic symptoms such as headache, limb pain, or difficulty sleeping the child is considered to have functional abdominal pain syndrome.

The 13-year-old case patient has features of both functional dyspepsia and irritable bowel syndrome. An overlap of symptoms is common, with up to 30% of children with irritable bowel syndrome also noting symptoms consistent with functional dyspepsia [9].

• What pathophysiologic mechanisms are important in FGIDs?

Abnormalities in brain–gut communication and regulation of the enteric nervous system (ENS) are thought to contribute to the pathophysiology of FGIDs. The early neonatal period is a time in which nociceptive circuits are formed. These circuits normally require use-dependent activity for appropriate development. Animal models have demonstrated a critical period during development in which the spinal cord is vulnerable to permanent structural and functional alterations

in pain pathways, including those that communicate with the gastrointestinal system [13]. Exposure to chronic antibiotic use, bacterial infections, or food allergy may all play a role at the cellular level in inducing microscopic inflammation and immunologic dysregulation that eventually sensitizes nociceptive pathways. If these events occur early in childhood, they can lead to neuroplasticity of the ENS and development of symptoms later in adolescence caused by alterations in local reflex activity or via altered neural processing along the brain–gut axis [14].

While multiple mechanisms have been proposed at a molecular level to contribute to FGIDs, the final common pathway often includes visceral hypersensitivity and abnormal central processing of nociceptive input from the gut [15–18]. Age, gender, culture, societal expectations, concomitant conditions, and past life experiences all contribute to the patient experience or “illness.”

Serotonin

Serotonin is an important gastrointestinal signaling molecule that activates intrinsic and extrinsic primary afferent neurons initiating peristaltic and secretory pathways as well as mediating sensation [19]. In irritable bowel syndrome considerable attention has been paid to serotonin metabolism at gut afferent (sensory) neurons. Serotonergic signaling in intestinal mucosa and the ENS is partly regulated by the transmembrane serotonin transporter, SERT [15]. Polymorphisms in serotonin receptors may be important in the pathogenesis of FGIDs [20]. One of the body’s primary mechanisms for regulating availability of serotonin within the extracellular space is the SERT system [21]. The amount of serotonin reuptake that occurs from the extracellular space is genetically determined and is based on whether there are long, short, or heterozygous polymorphisms in the promoter for synthesis of SERT. Homozygosity for the short variant and presence of the heterozygous variant result in less transcript, less protein expression, and less reuptake of serotonin. SERT activity is an important factor influencing serotonin availability at postsynaptic receptors. Previous intestinal inflammation, bacterial overgrowth in the small bowel, and dysregulation of intestinal immunity have also been postulated to be important in the pathogenesis of visceral hypersensitivity [16,22,23].

Gastric Motor Dysfunction

Gastric motor and/or myoelectric abnormalities have been shown in up to 77% of pediatric patients with functional dyspepsia [24]. Gastric accommodation is a reflex adaptation of the proximal stomach to relax to accommodate food and can be studied with either a gastric barostat or with specialized scintigraphy [25]. This normal reflex is mediated by the vago-vagal pathway and can be induced by many factors,

such as eating, and results in reduction of tone and provides a reservoir for a meal. This relaxation allows ingestion of a considerable volume load without a significant rise of intragastric pressure or induction of upper gastrointestinal symptoms such as distension, bloating, early satiety, or vomiting [26]. Multiple studies have shown that impaired gastric accommodation has been associated with upper gastrointestinal symptoms including early satiety, bloating, epigastric pain, weight loss, and nausea [27]. Gastric accommodation is normal in patients with functional dyspepsia during fasting but is impaired in approximately one third of patients after a meal [28].

Visceral Hypersensitivity

As noted previously, functional abdominal pain disorders may be associated with visceral hyperalgesia, a decreased threshold for pain in response to changes in intraluminal pressure. Mucosal inflammatory processes attributable to infections, allergies, or primary inflammatory diseases may cause sensitization of afferent nerves and have been associated with the onset of visceral hyperalgesia. There is also an increasing body of evidence in adults suggesting that an abnormal central processing of afferent signals at the level of the central nervous system may play a role in the pathophysiology of this condition [29].

Visceral hypersensitivity has been demonstrated by barostat studies in the pediatric population in a variety of conditions including functional dyspepsia, functional abdominal pain, and irritable bowel syndrome [17,30]. Approximately 30% of patients with functional dyspepsia have gastric hypersensitivity to distension in the fundus and the antrum [31]. Antral hypersensitivity can be exacerbated by impaired gastric accommodation that can lead to rapid emptying with resultant quickened antral distension. Delayed gastric emptying has been shown in up to 68% of children with functional dyspepsia compared with a 60% prevalence among adults [32]. Forty percent of children with functional dyspepsia have slow small bowel transit time and an increased likelihood of reporting bloating and abdominal pain [33].

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- **What is the therapeutic approach to the child with functional abdominal pain?**
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The foundation of a successful therapeutic approach is a strategy in which the clinician educates both the child and family about the common occurrence of functional abdominal pain, its proposed pathogenesis, and most importantly, that while uncomfortable it does not pose a significant risk. Using the Rome III criteria for a symptom-based diagnosis will facilitate

categorization of the pain as legitimate and not imagined. The confirmation of diagnosis is what most families and patients are seeking when they consult multiple physicians for persistent symptoms. A successful strategy will also couple education with an effective physician-patient-family relationship where allocation of sufficient consultative time and availability for the patient to follow-up is encouraged if doubt or if misconceptions still persist. It is during this critical time of making a positive diagnosis and education that patient and family expectations can be set. A therapeutic plan is then developed with a focus on managing symptoms rather than curing a "disease" [34]. Given the premise that some cases of FGIDs may result from visceral hyperalgesia following bowel inflammation (eg, infections, allergy), this concept of hyper-sensitivity is an important educational tool. The concept of visceral hyperalgesia may be explained to patients and family members by comparing sensation following a burn. The skin may remain sensitive for prolonged periods and perceive stimuli as noxious even if they are not uncomfortable (such as contact with clothing).

Currently, therapy for FGIDs can be divided into 2 main categories: those directed to treat the predominant symptom (or end-organ therapy) and treatment aimed at cognitive retraining with a focus on providing patients with adequate tools for modifying symptom perception. Often an approach utilizing both strategies is needed to reach a successful outcome in moderate to severe cases of FGIDs. Patients with mild symptoms may only need education and possibly diet modification if an offending food trigger can be found. Reviews of the literature on treatment have been previously published [6,35].

Diet

The role of diet continues to be controversial and will vary in response to the patient's particular FGID. Avoidance of foods that aggravate symptoms (caffeine, spicy foods, fatty foods) is recommended in functional dyspepsia [36]. Nonsteroidal anti-inflammatory medications are noted by some to increase symptoms. Provision of adequate dietary fiber should be included in the first-line treatment for constipation-predominant irritable bowel syndrome [37]. Sorbitol and high fructose corn syrup can cause symptoms mimicking those of irritable bowel syndrome and large amounts should be avoided [38].

Peppermint oil has been used to treat irritable bowel syndrome. In a recent 4-week, double-blind, randomized clinical trial of patients with irritable bowel syndrome, peppermint oil was found to significantly reduce abdominal pain complaints [39]. This beneficial effect may be due to intestinal smooth muscle relaxation by preventing calcium entry into intestinal smooth muscle cells.

Ginger (rhizome of *Zingiber officinale*) has been widely used for centuries in gastrointestinal disorders, particularly dyspepsia, but its precise mechanism of action has yet to be elucidated. Ginger extract contains a cholinergic, spasmogenic component evident in stomach fundus preparations, which may provide a sound mechanistic insight for the prokinetic action of ginger [40]. Ginger rhizome extract (2 × 100 mg) was studied on fasting and postprandial gastroduodenal motility in 12 healthy volunteers [41]. The results showed that interdigestive antral motility was significantly increased by ginger and that the study participants also had a significantly increased gastric motor response to a test meal.

Probiotics

The putative interaction between host gut flora and mucosal inflammation in irritable bowel syndrome [22,42] has prompted use of probiotic therapy. Probiotics containing specific strains of *Bifidobacterium* and *Lactobacillus* have shown the most promise in adult patients with irritable bowel syndrome [43]. However, *Lactobacillus* GG was no better than placebo in relieving abdominal pain in adolescents with irritable bowel syndrome, although it did reduce perceived abdominal distention [44]. In another trial, *Lactobacillus* GG was superior to placebo in reducing the frequency but not severity of pain in irritable bowel syndrome; however, it was not helpful in functional dyspepsia or functional abdominal pain [45].

Behavioral Modification

Techniques to reduce physiologic arousal associated with chronic abdominal pain can alleviate symptoms in patients with FGIDs. There have been well-documented and well-designed studies both in adults and adolescents using several techniques such as cognitive behavioral therapy, guided imagery and hypnosis, and yoga [46–51]. Parental attention to pain as compared with distraction has been shown to increase a child's subjective discomfort [52]. Parents must maintain a sympathetic attitude that acknowledges the presence of pain but encourage continued activities and school attendance to the greatest degree possible. It is important to point out that young children are highly suggestible to parental clues, and parents should refrain from questioning the child about the pain if the child is not complaining. This has been recently highlighted in work by Walker and colleagues [53] investigating the effects of parental attention versus distraction on abdominal discomfort in children.

Cognitive behavioral therapy teaches the patient coping skills by refraining or modifying maladaptive thoughts such as helplessness. Studies have demonstrated effectiveness both when administered to the patient and utilized as a family intervention [49]. In addition, when cognitive

behavioral therapy is used in combination with standard care, it appears to be more beneficial [48]. Guided imagery is a form of relaxed, focused concentration similar to hypnosis. Guided imagery not only produces distraction from gut pain but enhances relaxation. One study revealed that guided imagery was effective in patients with treatment-refractory abdominal pain with improvement lasting up to 1 year and a significant increase in quality of life [49].

Gut-Directed Hypnotherapy

Gut-directed hypnotherapy has been shown to be highly effective in the treatment of adults with irritable bowel syndrome [54]. A recent randomized controlled trial of hypnotherapy in children with at least 1 year of recurrent abdominal pain or irritable bowel syndrome demonstrated superiority to standard medical therapy [55]. Durability of improvement with hypnotherapy was demonstrated, with 85% of the hypnotherapy group remaining improved at 1 year following therapy compared with only 25% of those who received standard medical therapy. Since this was a small study utilizing 1 highly trained hypnotherapist, it is not known whether these results will be applicable to a larger population using hypnotherapists with variable skills.

Pharmacotherapy

The treatment of pain-associated FGIDs is directed toward symptom improvement and restoration of good quality of life. Current therapies do not “cure” FGIDs. Nonetheless, many therapies from placebo to drugs to psychological intervention can be associated with symptom improvement. Indeed, clinical trials have demonstrated the high efficacy of placebo in many FGIDs [56]. Given the heterogeneity of patients with FGIDs and the likely many contributing factors to symptom development and severity, it is unlikely that any single therapy will be effective for all patients.

Functional dyspepsia is often treated with acid-reducing medications. Cochrane analyses of both H₂-receptor antagonists and proton pump inhibitors as well as expert consensus have suggested superiority compared with placebo, but the numbers needed to treat to establish efficacy were 8 and 9, respectively [57,58]. There are no dose-response data concerning acid-reducing medications for the treatment of functional dyspepsia in children. Prokinetics such as metoclopramide, domperidone, cisapride, tegaserod, and motilin agonists have been used, but consensus on efficacy is lacking; tegaserod and cisapride have been removed from the U.S. market because of safety concerns. The tricyclic antidepressant amitriptyline was found superior to placebo in 1 small study in adults [59].

The treatment of irritable bowel syndrome also lacks consensus. Constipation-predominant subjects have been treated


with fiber, bulking agents, osmotic laxatives, and the 5-HT₄ receptor agonist tegaserod [60]. As previously mentioned, tegaserod has been removed from the market in the United States. Diarrhea-predominant subjects have been treated with loperamide, diphenoxylate, the 5-HT₃ receptor antagonist alosetron, tricyclic antidepressants, and selective serotonin reuptake inhibitors (SSRIs). Alosetron was removed from the market but is now available on a company-controlled basis. In irritable bowel syndrome, therapy should be directed primarily toward pain reduction and improved global well-being. The use of antidepressants in irritable bowel syndrome is based on the premise that these agents alter pain perception by central modulation of input from visceral afferents while potentially also treating comorbid psychological disorders. Tricyclic antidepressants have analgesic qualities and have been well studied. While a systematic review of trials of tricyclic antidepressants for irritable bowel syndrome in adults published in 2002 concluded that their role was not well-established because of methodologic issues [61], a subsequent double-blind placebo controlled trial of desipramine in adults published in 2003 showed significant benefit compared with placebo in the per protocol analysis subgroup (ie, patients who completed treatment protocol) [62]. Side effects that can affect tolerability of tricyclic antidepressants include drowsiness, constipation, and dry mouth. These side effects can be used advantageously when treating patients with irritable bowel syndrome who have diarrhea-predominant symptoms and those who have difficulty falling asleep. A baseline and follow-up electrocardiogram is recommended for patients before starting this class of medications to detect unsuspected instances of long-QT syndrome and to monitor for cardiac side effects such as syncope or palpitations. SSRIs have been studied in small trials suggesting potential benefit of paroxetine [63] and citalopram [64]. It should be noted that the doses of tricyclic antidepressants and SSRIs used to treat FGIDs are often much lower than those used to treat mental health disorders. Pediatric dosing guidelines have not been established.

Nonabsorbable antibiotics have been used to treat irritable bowel syndrome under the premise that small bowel bacterial overgrowth is a contributing factor. Rifaximin, which has activity against gram-positive and gram-negative aerobes and anaerobes, was found to be superior to placebo in a double-blind controlled trial with respect to global symptoms and bloating but not abdominal pain or bowel pattern [65]. These data were from adult participants and there are no prospective data on the use or potential complications of this therapy in children.

- What is the long-term prognosis for FGIDs?

There are limited data on the natural history of FGIDs associated with pain in childhood. Functional abdominal pain is not always a benign condition with a satisfactory outcome. Poor outcome at 1 year following presentation has been associated with lack of parental insight into psychosocial influences on symptoms, refusal to engage in psychological interventions, and parental utilization of multiple consultants [66]. Children with chronic symptoms may become adults with irritable bowel syndrome [67]. Irritable bowel syndrome in adults has been associated with direct and indirect medical expenses up to \$30 billion a year which is comparable to expenditures for asthma, stroke, hypertensive disease, migraine, and arthritis [68]. Long-term psychiatric disorders have been identified in patients suffering from functional abdominal pain in childhood [69]. Children with abdominal pain do not necessarily continue to experience physical symptoms in adulthood but may have an increased risk of adult psychiatric disorders [70]. These long-term concerns underscore the importance of a correct diagnosis in childhood and adolescence with institution of effective therapies such as coping strategies and innovative therapies early in the illness process.

Follow-up

 The patient is initially treated with ranitidine for her nausea and hyoscamine for her cramping. When seen at a follow-up visit 4 weeks later she reports some initial relief but says that at the present time she is feeling poorly each day. Referral for cognitive behavioral therapy is made.

Three months later, the patient is seen by her primary care physician. She states that she is "80%" better and only feels poorly on particularly stressful days.

SUMMARY

Recurrent or chronic abdominal pain in children is a common problem presenting to both primary care and specialist physicians. While most children will have a functional gastrointestinal disorder in which there is no demonstrable disease, significant impairment in quality of life occurs, and demands on medical personnel to find a "cause" and fix the problem are common. Using a symptom-based approach as outlined by the Rome III criteria will facilitate a positive diagnosis based on the patient's history and physical examination. Intervention for these children starts with education about current theories of pathogenesis and is followed by dietary, psychological, and medical therapies as needed. A biopsychosocial approach to these patients will identify previous illness or stressors as precipitating events; assess genetic, cultural, social factors as modifiers of the pain response; and provide psychological tools to cope and facilitate recovery [52].

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References

1. Miele E, Simeone D, Marino A, et al. Functional gastrointestinal disorders in children: an Italian prospective survey. *Pediatrics* 2004;114:73-8.
2. Hyams JS, Burke G, Davis PM, et al. Abdominal pain and irritable bowel syndrome in adolescents: a community-based study. *J Pediatr* 1996;129:220-6.
3. Youssef NN, Murphy TG, Langseder AL, Rosh JR. Quality of life for children with functional abdominal pain: a comparison study of patients' and parents' perceptions. *Pediatrics* 2006; 117:54-9.
4. Apley J, Naish N. Recurrent abdominal pains: a field survey of 1,000 school children. *Arch Dis Child* 1958;33:165-70.
5. Rasquin A, Di Lorenzo C, Forbes D, et al. Childhood functional gastrointestinal disorders: child/adolescent. *Gastroenterology* 2006;130:1527-37.
6. Di Lorenzo C, Colletti RB, Lehmann HP, et al. Chronic abdominal pain in children: a technical report of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr* 2005;40:249-61.
7. Di Lorenzo C, Colletti RB, Lehmann HP, et al. Chronic abdominal pain in children: a clinical report of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *J Pediatr Gastroenterol Nutr* 2005;40:245-8.
8. Mack DR, Langton C, Markowitz J, et al. Laboratory values for children with newly diagnosed inflammatory bowel disease. *Pediatrics* 2007;119:1113-9.
9. Hyams JS, Treem WR, Justinich CJ, et al. Characterization of symptoms in children with recurrent abdominal pain: resemblance to irritable bowel syndrome. *J Pediatr Gastroenterol Nutr* 1995;20:209-14.
10. Mearin F, Perez-Oliveras M, Perello A, et al. Dyspepsia and irritable bowel syndrome after a *Salmonella* gastroenteritis outbreak: one-year follow-up cohort study. *Gastroenterology* 2005;129:98-104.
11. Sigurdsson L, Flores A, Putnam PE, et al. Postviral gastroparesis: presentation, treatment, and outcome. *J Pediatr* 1997;131: 751-4.
12. Hyams JS, Davis P, Sylvester FA, et al. Dyspepsia in children and adolescents: a prospective study. *J Pediatr Gastroenterol Nutr* 2000;30:413-8.
13. Anand KJ, Coskun V, Thrivikraman KV, et al. Long-term behavioral effects of repetitive pain in neonatal rat pups. *Physiol Behav* 1999;66:627-37.
14. Anand KJ, Runeson B, Jacobson B. Gastric suction at birth associated with long-term risk for functional intestinal disorders in later life. *J Pediatr* 2004;144:449-54.

15. Gershon MD. Nerves, reflexes, and the enteric nervous system: pathogenesis of the irritable bowel syndrome. *J Clin Gastroenterol* 2005;39(5 Suppl):S184–93.
16. Barbara G, De Giorgio R, Stanghellini V, et al. New pathophysiological mechanisms in irritable bowel syndrome. *Aliment Pharmacol Ther* 2004;20 Suppl 2:1–9.
17. Hoffman I, Vos R, Tack J. Assessment of gastric sensorimotor function in paediatric patients with unexplained dyspeptic symptoms and poor weight gain. *Neurogastroenterol Motil* 2007;19:173–9.
18. Van Oudenhove L, Vandenbergh J, Geeraerts B, et al. Relationship between anxiety and gastric sensorimotor function in functional dyspepsia. *Psychosom Med* 2007;69:455–63.
19. Gershon MD, Tack J. The serotonin signaling system: from basic understanding to drug development for functional GI disorders. *Gastroenterology* 2007;132:397–414.
20. Camilleri M, Atanasova E, Carlson PJ, et al. Serotonin-transporter polymorphism pharmacogenetics in diarrhoea-predominant irritable bowel syndrome. *Gastroenterology* 2002;123:425–32.
21. Kim DY, Camilleri M. Serotonin: a mediator of the brain-gut connection. *Am J Gastroenterol* 2000;95:2698–709.
22. Gwee KA, Collins SM, Read NW, et al. Increased rectal mucosal expression of interleukin 1beta in recently acquired post-infectious irritable bowel syndrome. *Gut* 2003;52:523–6.
23. Chatterjee S, Park S, Low K, et al. The degree of breath methane production in IBS correlates with the severity of constipation. *Am J Gastroenterol* 2007;102:837–41.
24. Friesen CA, Lin Z, Garola R, et al. Chronic gastritis is not associated with gastric dysrhythmia or delayed solid emptying in children with dyspepsia. *Dig Dis Sci* 2005;50:1012–8.
25. Kim DY, Myung SJ, Camilleri M. Novel testing of human gastric motor and sensory functions: rationale, methods, and potential applications in clinical practice. *Am J Gastroenterol* 2000;95:3365–73.
26. De Schepper HU, Cremonini F, Chitkara D, Camilleri M. Assessment of gastric accommodation: overview and evaluation of current methods. *Neurogastroenterol Motil* 2004;16:275–85.
27. Thumshirn M, Camilleri M, Saslow SB, et al. Gastric accommodation in non-ulcer dyspepsia and the roles of *Helicobacter pylori* infection and vagal function. *Gut* 1999;44:55–64.
28. Karamanolis G, Caenepeel P, Arts J, Tack J. Association of the predominant symptom with clinical characteristics and pathophysiological mechanisms in functional dyspepsia. *Gastroenterology* 2006;130:296–303.
29. Tougas G. The autonomic nervous system in functional bowel disorders. *Gut* 2000;47 Suppl 4:iv78–80.
30. Van Ginkel R, Voskuijl WP, Benninga MA, et al. Alterations in rectal sensitivity and motility in childhood irritable bowel syndrome. *Gastroenterology* 2001;120:31–8.
31. Tack J, Caenepeel P, Corsetti M, Janssens J. Role of tension receptors in dyspeptic patients with hypersensitivity to gastric distention. *Gastroenterology* 2004;127:1058–66.
32. Riezzo G, Chiloiro M, Guerra V, et al. Comparison of gastric electrical activity and gastric emptying in healthy and dyspeptic children. *Dig Dis Sci* 2000;45:517–24.
33. Chitkara DK, Delgado-Aros S, Bredenoord AJ, et al. Functional dyspepsia, upper gastrointestinal symptoms, and transit in children. *J Pediatr* 2003;143:609–13.
34. Drossman DA. Psychosocial sound bites: exercises in the patient-doctor relationship. *Am J Gastroenterol* 1997;92:1418–23.
35. Weydert JA, Ball TM, Davis MF. Systematic review of treatments for recurrent abdominal pain. *Pediatrics* 2003;111:e1–11.
36. Talley NJ. How to manage the difficult-to-treat dyspeptic patient. *Nat Clin Pract Gastroenterol Hepatol* 2007;4:35–42.
37. Zuckerman MJ. The role of fiber in the treatment of irritable bowel syndrome: therapeutic recommendations. *J Clin Gastroenterol* 2006;40:104–8.
38. Skoog SM, Bharucha AE. Dietary fructose and gastrointestinal symptoms: a review. *Am J Gastroenterol* 2004;99:2046–50.
39. Cappello G, Spezzaferro M, Grossi L, et al. Peppermint oil (Mintoil) in the treatment of irritable bowel syndrome: a prospective double blind placebo-controlled randomized trial. *Dig Liver Dis* 2007;39:530–6.
40. Ghayur MN, Gilani AH. Pharmacological basis for the medicinal use of ginger in gastrointestinal disorders. *Dig Dis Sci* 2005;50:1889–97.
41. Micklefield GH, Redeker Y, Meister V, et al. Effects of ginger on gastroduodenal motility. *Int J Clin Pharmacol Ther* 1999;37:341–6.
42. Chadwick VS, Chen W, Shu D, et al. Activation of the mucosal immune system in irritable bowel syndrome. *Gastroenterology* 2002;122:1778–83.
43. O'Mahony L, McCarthy J, Kelly P, et al. *Lactobacillus* and *bifidobacterium* in irritable bowel syndrome: symptom responses and relationship to cytokine profiles. *Gastroenterology* 2005;128:541–51.
44. Bausserman M, Michail S. The use of *Lactobacillus* GG in irritable bowel syndrome in children: a double-blind randomized control trial. *J Pediatr* 2005;147:197–201.
45. Gawronska A, Dziechciarz P, Horvath A, Szajewska H. A randomized double-blind placebo-controlled trial of *Lactobacillus* GG for abdominal pain disorders in children. *Aliment Pharmacol Ther* 2007;25:177–84.
46. Robins PM, Smith SM, Glutting JJ, Bishop CT. A randomized controlled trial of a cognitive-behavioral family intervention for pediatric recurrent abdominal pain. *J Pediatr Psychol* 2005;30:397–408.
47. Sanders MR, Rebetz M, Morrison M, et al. Cognitive-behavioral treatment of recurrent nonspecific abdominal pain in children: an analysis of generalization, maintenance, and side effects. *J Consult Clin Psychol* 1989;57:294–300.
48. Heymann-Monnikes I, Arnold R, Florin I, et al. The combination of medical treatment plus multicomponent behavioral therapy is superior to medical treatment alone in the therapy of irritable bowel syndrome. *Am J Gastroenterol* 2000;95:981–94.
49. Youssef NN, Rosh JR, Loughran M, et al. Treatment of functional abdominal pain in childhood with cognitive behavioral strategies. *J Pediatr Gastroenterol Nutr* 2004;39:192–6.
50. Weydert JA, Shapiro DE, Acra SA, et al. Evaluation of guided imagery as treatment for recurrent abdominal pain in children: a randomized controlled trial. *BMC Pediatr* 2006;6:29.

51. Kuttner L, Chambers CT, Hardial J, et al. A randomized trial of yoga for adolescents with irritable bowel syndrome. *Pain Res Manag* 2006;11:217-23.
52. Walker LS, Smith CA, Garber J, Claar RL. Testing a model of pain appraisal and coping in children with chronic abdominal pain. *Health Psychol* 2005;24:364-74.
53. Walker LS, Williams SE, Smith CA, et al. Parent attention versus distraction: impact on symptom complaints by children with and without chronic functional abdominal pain. *Pain* 2006;122:43-52.
54. Gonsalkorale WM, Miller V, Afzal A, Whorwell PJ. Long term benefits of hypnotherapy for irritable bowel syndrome. *Gut* 2003;52:1623-9.
55. Vlieger AM, Menko-Frankenhuis C, Wolfkamp SC, et al. Hypnotherapy for children with functional abdominal pain or irritable bowel syndrome: a randomized controlled trial. *Gastroenterology* 2007;133:1430-6.
56. Pitz M, Cheang M, Bernstein CN. Defining the predictors of the placebo response in irritable bowel syndrome. *Clin Gastroenterol Hepatol* 2005;3:237-47.
57. Moayyedi P, Soo S, Deeks J, et al. Pharmacological interventions for non-ulcer dyspepsia. *Cochrane Database Syst Rev* 2004;(4):CD001960.
58. Talley NJ, Vakil NB, Moayyedi P. American gastroenterological association technical review on the evaluation of dyspepsia. *Gastroenterology* 2005;129:1756-80.
59. Mertz H, Fass R, Kodner A, et al. Effect of amitriptyline on symptoms, sleep, and visceral perception in patients with functional dyspepsia. *Am J Gastroenterol* 1998;93:160-5.
60. Spiller R, Aziz Q, Creed F, et al. Guidelines on the irritable bowel syndrome: mechanisms and practical management. *Gut* 2007;56:1770-98.
61. Brandt LJ, Bjorkman D, Fennerty MB, et al. Systematic review on the management of irritable bowel syndrome in North America. *Am J Gastroenterol* 2002;97(11 Suppl):S7-26.
62. Drossman DA, Toner BB, Whitehead WE, et al. Cognitive-behavioral therapy versus education and desipramine versus placebo for moderate to severe functional bowel disorders. *Gastroenterology* 2003;125:19-31.
63. Tabas G, Beaves M, Wang J, et al. Paroxetine to treat irritable bowel syndrome not responding to high-fiber diet: a double-blind, placebo-controlled trial. *Am J Gastroenterol* 2004;99:914-20.
64. Tack J, Broekaert D, Fischler B, et al. A controlled crossover study of the selective serotonin reuptake inhibitor citalopram in irritable bowel syndrome. *Gut* 2006;55:1095-103.
65. Pimentel M, Park S, Mirocha J, et al. The effect of a nonabsorbed oral antibiotic (rifaximin) on the symptoms of the irritable bowel syndrome: a randomized trial. *Ann Intern Med* 2006;145:557-63.
66. Lindley KJ, Glaser D, Milla PJ. Consumerism in healthcare can be detrimental to child health: lessons from children with functional abdominal pain. *Arch Dis Child* 2005;90:335-7.
67. Howell S, Poulton R, Talley NJ. The natural history of childhood abdominal pain and its association with adult irritable bowel syndrome: birth-cohort study. *Am J Gastroenterol* 2005;100:2071-8.
68. Talley NJ, Gabriel SE, Harmsen WS, et al. Medical costs in community subjects with irritable bowel syndrome. *Gastroenterology* 1995;109:1736-41.
69. Campo JV, Di Lorenzo C, Chiappetta L, et al. Adult outcomes of pediatric recurrent abdominal pain: do they just grow out of it? *Pediatrics* 2001;108:E1.
70. Hotopf M, Carr S, Mayou R, et al. Why do children have chronic abdominal pain, and what happens to them when they grow up? Population based cohort study. *BMJ* 1998;316:1196-200.

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CME EVALUATION: Functional Abdominal Pain in Children

DIRECTIONS: Each of the questions below is followed by several possible answers. Select the ONE lettered answer that is BEST in each case and circle the corresponding letter on the answer sheet.

1. Irritable bowel syndrome is characterized by all of the following features EXCEPT
 - A. Diarrhea
 - B. Constipation
 - C. Abdominal pain
 - D. Bloating
 - E. Weight loss
2. All of the following statements concerning the pathophysiology of functional gastrointestinal disorders (FGIDs) are accurate EXCEPT
 - A. Traumatic events that occur early in life may predispose to FGIDs
 - B. Microscopic inflammation from allergy or infection may sensitize gut nociceptive nerve fibers
 - C. Serotonin down-regulates gut motor and sensory neurons leading to decreased motility and impaired sensation
 - D. Impaired gastric accommodation is seen in some patients with functional dyspepsia following a meal
3. The proper approach to a child with recurrent or chronic abdominal pain should always include
 - A. Endoscopic evaluation of the upper and lower gastrointestinal tract
 - B. A careful medical and social history with particular attention to red flag signs and symptoms and potential predisposing stressful events
 - C. Serologic testing to exclude celiac disease
 - D. Referral to a mental health professional
4. Which of the following is the most appropriate approach for a parent whose child has been diagnosed with functional abdominal pain?
 - A. Daily questioning of the child to assess the severity of pain
 - B. Limitation of activities that are known to precipitate painful episodes
 - C. Reassurance that although the pain is real it is not harmful and that daily functioning needs to be maintained
 - D. Consultation with pain specialists for pharmacologic interventions that decrease pain
5. Side effects of tricyclic antidepressants used to treat FGIDs may include all of the following EXCEPT
 - A. Dry mouth
 - B. Sleepiness
 - C. Diarrhea
 - D. Palpitations
6. Which of the following statements most accurately reflects the natural history of FGIDs associated with abdominal pain?
 - A. By adolescence, most younger children will no longer experience symptoms
 - B. Utilization of psychiatric services is associated with a worse prognosis
 - C. Utilization of multiple medical consultants is associated with a worse prognosis
 - D. Adult psychiatric disorders are very rare in children who had suffered from FGIDs



EVALUATION FORM: Functional Abdominal Pain in Children

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