Chronic Abdominal Pain

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Drs Collins and Thomas did not disclose any financial relationships relevant to this article.

Objectives

After completing this article, readers should be able to:

1. Define chronic abdominal pain (CAP).
2. Differentiate between functional and nonfunctional CAP.
3. Describe the symptom-based subtypes of CAP based on the Rome III criteria.
4. Diagnose and treat each subtype defined by the Rome III criteria.
5. Determine when referral to a pediatric subspecialist is necessary.

Introduction

Chronic abdominal pain (CAP) is a frequent childhood complaint encountered by primary care physicians as well as by pediatric and surgical subspecialists. The exact prevalence of CAP is unknown, although the literature reports that 13% of middle school children and 17% of high school children experience weekly abdominal pain and that this complaint accounts for 2% to 4% of all pediatric office visits. The economic cost related to CAP in children also is unknown, but it is likely to be substantial, given that expenses associated with irritable bowel syndrome (IBS) in adults (prevalence, 11% to 14%) have been estimated to be $8 to $30 billion per year.

First introduced into the literature by Apley and Naish in 1958, the term CAP, also previously called "recurrent abdominal pain" or "RAP," was used to describe children who experienced at least three bouts of pain severe enough to affect daily activities over a period of at least 3 months. Throughout the last 5 decades, however, CAP has changed definitions several times, most recently being used to describe all children who have abdominal pain for which a specific cause cannot be identified.

We now understand that CAP is not a specific diagnosis, but rather a description of a heterogeneous group of patients who have a variety of symptoms. In children, CAP usually is functional; that is, no readily identifiable physiologic, structural, or biochemical abnormalities are present. In 1997, a pediatric workshop was held in Rome, Italy, to standardize the diagnostic criteria for childhood functional gastrointestinal disorders (FGID), including CAP. Based on evidence that children displayed patterns of symptoms similar to those previously described in adults, the Rome II criteria were created. These criteria represent a symptom-based classification of functional disorders associated with abdominal pain that includes the subtypes functional dyspepsia, IBS, abdominal migraine, and functional abdominal pain (FAP). In 2006, these original criteria were revised and updated to the Rome III criteria (Table 1), which is used as the basis for this review.

It is important to emphasize that there are children who have many of the symptoms and signs of CAP in whom distinct physiologic, structural, or biochemical abnormalities are found (eg, inflammatory bowel disease [IBD], peptic ulcer disease, cholelithiasis, and recurrent pancreatitis). The presence of any "red flag" symptoms or signs (Table 2) or abnormal and unexplainable physical findings suggests a higher likelihood of organic pathology and requires additional evaluation. This article does not address this subset of patients, rather focusing on the pathogenesis, recognition, evaluation, and management of functional CAP disorders.

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Table 1. Rome III Criteria for Functional Bowel Disorders Associated with Abdominal Pain or Discomfort in Children

Functional Dyspepsia

All of the following must be present at least once per week for at least 2 months before diagnosis:
1. Persistent or recurrent pain or discomfort centered in the upper abdomen (above the umbilicus)
2. Pain not relieved by defecation or associated with the onset of a change in stool frequency or stool form (ie, not irritable bowel syndrome)
3. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the symptoms

Irritable Bowel Syndrome

All of the following must be present at least once per week for at least 2 months before diagnosis:
1. Abdominal discomfort (an uncomfortable sensation not described as pain) or pain associated with *two or more* of the following at least 25% of the time:
   - Improved with defecation
   - Onset associated with a change in frequency of stool
   - Onset associated with a change in form (appearance) of stool
2. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the symptoms

Childhood Functional Abdominal Pain

All of the following must be present at least once per week for at least 2 months before diagnosis:
1. Episodic or continuous abdominal pain
2. Insufficient criteria for other functional gastrointestinal disorders
3. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the symptoms

Childhood Functional Abdominal Pain Syndrome must include childhood functional abdominal pain at least 25% of the time and one *or more* of the following:
1. Some loss of daily activity
2. Additional somatic symptoms such as headache, limb pain, or difficulty sleeping

Abdominal Migraine

All of the following must have occurred two or more times in the preceding 12 months before diagnosis:
1. Paroxysmal episodes of intense, acute periumbilical pain that lasts for 1 hour or more
2. Intervening periods of usual health lasting weeks to months
3. Pain interfering with normal activities
4. Pain associated with *two or more* of the following:
   - Anorexia
   - Nausea
   - Vomiting
   - Headache
   - Photophobia
   - Pallor
5. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process considered to explain the symptoms

Pathogenesis of Functional CAP Disorders

Several potential mechanisms are believed to be responsible for the development of abdominal pain in functional gastrointestinal (GI) disorders, many of which are not understood completely. In the past, what has made the pathogenesis of these disorders so difficult to delineate is that symptoms vary greatly among individuals as well as over time in the same individual. The evolution of the biopsychosocial approach to understanding the pathogenesis of CAP has reshaped the approach to diagnosis and management. (1) This model takes into account not only the biologic causes of pain but also the psychological and social factors, suggesting that altered intestinal motility and heightened sensation in the GI tract are modulated by input from the central nervous system. Moreover, both aberrant gut motility and sensation are influenced by genetics, personal experience, and cultural environment. (1)(2) The Figure summarizes a biopsychosocial approach to the pathophysiologic

Table 2. "Red Flag" Signs and Symptoms Suggestive of Organic Diseases

- Weight loss
- Unexplained fevers
- Pain radiating to the back
- Bilious emesis
- Hematemesis
- Hematochezia/melena
- Chronic diarrhea (lasting >2 wk and >20 mL/kg per day)
- Gastrointestinal blood loss
- Oral ulcers
- Dysphagia
- Unexplained rashes
- Nocturnal symptoms
- Arthritis
- Anemia/pallor
- Delayed puberty
- Deceleration of linear growth velocity
- Family history of inflammatory bowel disease

mechanisms that lead to many of the symptoms associated with CAP conditions.

Abnormal Motility

Altered GI motility has been documented in adults who have IBS for several decades and has been shown to occur in children who have FAP. Pineiro-Carrero and colleagues (3) found that children who had recurrent FAP had more frequent interdigestive migrating motor complexes (electrochemical waves of activity seen throughout the gut during fasting periods), but they were of shorter duration and propagated more slowly caudally down the intestine. Affected patients also had higher duodenal peristaltic pressure contractions that were associated with pain. (3) Several studies also have demonstrated that heightened emotional states, particularly stress and anxiety, further disrupt intestinal motility, leading to increased symptoms. (2)

Abnormal Visceral Perception

Abnormalities in visceral sensation have been found in adults who have IBS and now are believed to be a primary reason for pain in children who have functional CAP disorders. The hypothesis is that symptoms are due to changes in the "brain-gut" axis that links the central and enteric nervous systems. (1) Sensations from the GI tract are transmitted through both vagal and spinal afferent pathways. Alterations in gut wall sensory receptors, sensory transmissions in the peripheral or central nervous systems, cortical perceptions, and pain memories can contribute to an increased sensitivity to visceral stimulation, a state termed "visceral hyperalgesia." (1)(4)

Psychological Factors

Psychological symptoms are very common in patients who have functional CAP disorders. Compelling evidence suggests that psychological stress can alter GI motor function. (2) In addition, several investigators have demonstrated not only higher levels of stress in children who have CAP compared with other healthy children, but a significantly stronger relationship between daily stressors and somatic complaints for these patients than for healthy children. Considerable evidence also indicates that patients who have CAP have more anxiety and depression than do community controls.

In addition to these mechanisms, recent research suggests that other important factors contribute to the pathogenesis of CAP. For example, it long has been suspected that infectious gastroenteritis can induce symptoms of IBS. More recently, results of animal studies have indicated that this effect may occur because the initial acute inflammation from the infection leads to persistent changes in neuromuscular function of the gut, similar to the changes seen in humans who have IBS. (5) Additional support for the role of inflammatory dysregulation of the gut in IBS comes from the finding that intestinal biopsies of IBS patients have increased numbers of mast cells. Evidence now is emerging that the number of mast cells in close proximity to nerves and the severity and frequency of abdominal pain are correlated. (6)

Abnormal serotonergic mechanisms also may play a role in IBS. Not only have plasma serotonin (5-HT) concentrations been shown to be elevated in adults who have IBS, but the intestinal mucosal content of the 5-HT reuptake protein SERT was reduced in this population of patients. Differences in SERT function also appear to influence the response to therapy for IBS. (6)

Lastly, small intestinal bacteria overgrowth (SIBO) has been reported in 78% to 84% of adults who have IBS, regardless of their abdominal symptoms, compared with 20% in healthy controls. (7) Moreover, a significant reduction in both GI and extraintestinal symptoms in adults who have IBS and SIBO has been reported when bacterial eradication is successful. The roles of postinfectious IBS, inflammatory dysregulation, serotonin, and SIBO in children who have CAP have not been delineated.

It also is important to recognize that individual mech-

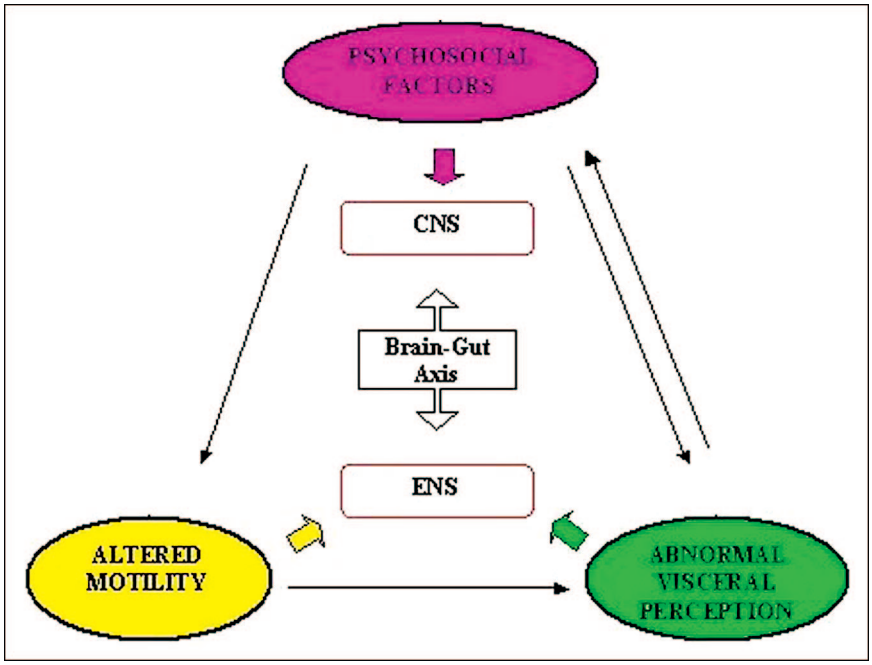

Figure. A biopsychosocial approach to understanding the development of chronic abdominal pain. Physiologic, psychosocial, and perceptual events cause alterations in the "brain-gut" axis that links the central (CNS) and enteric nervous systems (ENS).

anisms are not mutually exclusive and that more than one may be operating in a single patient. Understanding these mechanisms and identifying which apply to an individual patient should provide the basis for optimizing timely diagnosis and management of these disorders.

Diagnosis and Treatment of Functional CAP Disorders

Because CAP encompasses a heterogeneous group of patients, diagnosing the condition often is difficult. Unfortunately, there is no specific diagnostic marker. Although children who have functional CAP most commonly describe inconsistent, nonspecific localization of their pain, they also can present with more localized and specific pain. In fact, the literature reports that frequency, location, and timing of abdominal pain alone do not help distinguish organic from functional pain. Children who have recurrent abdominal pain are more likely than children who have no such pain to have anorexia, nausea, episodic vomiting, constipation, diarrhea, headaches, arthralgias, or eye problems. However, none of these manifestations alone has been reported to differentiate selectively between organic and functional pain. (8)

The Rome III criteria (Table 1) not only provide the clinician with an organized approach to the diagnosis of CAP and its different subtypes, but the classification also can help in the management of the condition.

Functional Dyspepsia

Dyspepsia is defined as persistent or recurrent pain or discomfort centered in the upper abdomen. Functional dyspepsia can have two presentation types, ulcer-like and dysmotility-like, but often the two overlap considerably, and the Rome III criteria do not distinguish between them. In ulcer-like dyspepsia, children experience upper abdominal pain as the dominant complaint, and it often is relieved by food or antacid therapy. In dysmotility-like dyspepsia, pain is not the dominant symptom; rather, the primary complaints are nausea, early satiety, postprandial fullness, retching, vomiting, and a sense of bloating.

The prevalence of functional dyspepsia in children varies between 3.5% and 27%, depending on the patient's sex and country of origin. Based on a Rome II criteria diagnosis, the prevalence was 0.3% among children in Italy and between 12.5% and 15.9% among children 4 to 18 years of age in North America. (9) The reason for this difference is not known.

The approach to a child who has persistent dyspeptic symptoms begins by obtaining a detailed history, including dietary, growth, and psychosocial factors; plotting a serial growth chart; and performing a physical examination. A history suggesting functional dyspepsia must include persistent or recurrent pain or discomfort centered above the umbilicus that is not relieved by defecation or associated with a change in stool frequency or form. The pain must be present at least once a week for at least 2 months. The clinician should ask about a recent history of acute gastroenteritis because some children present with dyspeptic symptoms caused by gastroparesis after a viral illness, even after the acute viral symptoms have resolved.

The clinician also must inquire about specific "red flag" signs and symptoms that may be found in those who have dyspepsia but that suggest organic disease, including pain radiating to the back, persistent bilious or bloody emesis, dysphagia, hematochezia or melena, weight loss, nighttime symptoms, fevers, or anemia. If

any of these manifestations is present, additional investigation and possible endoscopy are warranted because the patient may have a peptic ulcer, recurrent pancreatitis, hepatobiliary disease, or other abnormalities.

Routine testing for *Helicobacter pylori* in children who have functional dyspepsia remains controversial. Specific demographic factors, including low socioeconomic status, family crowding, emigration from developing countries, and a family history of *H pylori*, should raise the suspicion of infection with this organism. (1) However, the coexistence of abdominal pain and an abnormal test for *H pylori* infection does not necessarily indicate a causal relationship between the two. In fact, children who have *H pylori* are not more likely to have CAP than are children who have no *H pylori*. (10)

For a child who has no signs or symptoms suggesting organic disease and who has normal physical findings and normal growth, reassurance and symptomatic relief may be all that is necessary. Medications that can cause or exacerbate dyspeptic symptoms, such as ibuprofen or aspirin, should be stopped when possible. For those who have ulcer-like dyspepsia, specific foods that aggravate symptoms, such as caffeine or spicy, citrus, fried, and fatty foods as well as carbonated beverages, should be avoided. Smaller, more frequent meals can be suggested to those who experience early satiety. Psychosocial factors that may be contributing to the severity of the patient's symptoms also should be addressed at the initial visit.

Pharmacologic treatment of functional dyspepsia is directed toward providing symptomatic relief. Histamine 2-histamine receptor antagonists or gastric proton pump inhibitors can be used for pain-predominant symptoms and prokinetics (metoclopramide and erythromycin) for symptoms of nausea, bloating, postprandial fullness, and early satiety. A trial of low doses of tricyclic antidepressants such as imipramine and amitriptyline (0.2 to 0.4 mg/kg per day) administered at bedtime also can be offered. These agents are believed to work by reducing neuropathic pain. (1) No controlled data are available on the use of the tricyclic antidepressants for the treatment of functional dyspepsia in children. However, several reviews of the pharmacologic approaches to nonulcer dyspepsia in adults support the use of these medications. Upper endoscopy can be considered if the need for acid suppression therapy is prolonged or recurrent or if "red flag" signs or symptoms are present.

IBS

IBS is characterized by the presence of abdominal pain associated with two or more of the following symptoms at least 25% of the time: relief by defecation, a variable stool pattern, or a sense of incomplete evacuation or abdominal distention. Subtypes of adult IBS include diarrhea-predominant, constipation-predominant, and variable defecation pattern. (3) Although these subtypes have not been formally validated in children, similar patterns have been observed.

Early studies using adult criteria found that approximately 8% of middle school students and 17% of high school students experienced IBS-type symptoms. According to the pediatric Rome II criteria for FGID, IBS was diagnosed in 22% to 45% of children ages 4 to 18 years who presented to a tertiary care clinic. (9)

Much like functional dyspepsia, the approach to a child who is suspected of having IBS begins with a history and physical examination. Symptoms that support the diagnosis include abnormal stool patterns (four or more stools per week or <2 stools per week), abnormal stool form (lumpy/hard or loose/watery), abnormal stool passage (straining, a feeling of urgency, or a feeling of incomplete evacuation), passage of mucus, bloating, or abdominal distention. (11) For a patient whose clinical picture suggests IBS, any of the following "red flag" signs and symptoms should prompt consideration of other, more serious disorders: nocturnal pain, weight loss, oral ulcers, rash, pallor, rectal bleeding, anemia, fever, arthritis, delayed puberty, short stature, and a family history of IBD. The clinician must ask about adequate water and fiber intake in patients who have constipation and about the excess ingestion of specific sugars such as sorbitol and fructose in children who have diarrhea. It also is essential during the initial visit for the physician to inquire about psychosocial stressors for the patient and in the home. Anxiety, depression, and many other somatic complaints have been reported both in children who have IBS and in their parents. (2)

Questions remain about the role of lactose intolerance in children who have IBS. Lactose intolerance is a common GI disorder that can present similarly to diarrhea-predominant IBS. Although initiation of a lactose-free diet can result in improvement of symptoms in some children, particularly their complaints of bloating, gas, and diarrhea, a positive test result for lactose intolerance does not necessarily indicate a causal relationship between the two. In their study of the association between lactase deficiency and recurrent abdominal pain, Lebenthal and associates (12) found a similar prevalence of lactase deficiency in children who had recurrent abdominal pain and healthy controls. They also found that the long-term elimination of lactose from the diets of children who had recurrent adbominal pain did not affect the

frequency of symptom improvement. These data suggest that lactose intolerance and recurrent abdominal pain are two separate entities.

The goals of treatment for IBS are to provide effective support for the patient and family and to reduce or eliminate symptoms. Providing a confident diagnosis with an explanation of the reasons for pain as well as reassurance that IBS is not life-threatening can be therapeutic. If psychosocial stressors or triggering events for symptoms are identified, these should be addressed at the outset of therapy.

It has been suggested that abdominal migraine, cyclic vomiting syndrome, and migraine headache comprise a continuum of a single disorder. . . .

Dietary modifications also can be used to reduce symptoms. If pain is associated with diarrhea and bloating, patients can be advised to reduce intake of sorbitol (candy, chewing gum, jelly), fructose (fruit juices, corn syrup), and gas-forming vegetables (cabbage, broccoli, beans). For those who have constipation, increasing water and dietary fiber intake may help reduce symptoms.

Drug therapy plays an adjunctive role in the treatment of IBS, and controlled data on therapeutic interventions are limited. For constipation-predominant IBS, osmotic laxatives, stool softener, and lubricants can be offered. Peppermint oil has been shown to provide some benefit in children who have IBS through its smooth muscle-relaxing properties, although the data are limited. (8)(13)

Tricyclic antidepressants such as imipramine and amitriptyline (0.2 to 0.4 mg/kg per day) can be used to decrease pain and diarrhea, possibly through their anticholinergic and central analgesic effects. (1) Although significant data support the efficacy of tricyclic antidepressants in adults who have IBS, reports are only anecdotal of their successful use in children who have CAP. Evidence also is limited that probiotics such as *Lactobacillus* and *Bifidobacterium* sp, either alone or in combination with other medications, may be effective for the treatment of pain, bloating, and flatulence experienced by patients who have IBS.

A large subset of children who have functional CAP and constipation do not meet the criteria for IBS. From our experience, most of these children have fecal retention, which exacerbates their pain. For such children, dietary modification should be the initial treatment. Parents should be encouraged to increase their child's intake of fruits and vegetables and decrease that of fried and fatty food as well as "junk" food and soda. Children also should be advised to drink several glasses of water daily, with a goal of drinking 6 to 8 glasses each day, as recommended by the American Academy of Pediatrics. Stool softeners and osmotic laxatives can be used as adjunctive therapy.

Abdominal Migraine

Abdominal migraine is a subtype of CAP characterized by acute, incapacitating, noncolicky, periumbilical abdominal pain that lasts for 1 or more hours and is accompanied by at least two of the following: pallor, anorexia, nausea, vomiting, headache, or photophobia. Characteristically, periods of usual health last weeks to months between episodes of pain. Associated features include personal and maternal history of migraine headache. It has been suggested that abdominal migraine, cyclic vomiting syndrome, and migraine headache comprise a continuum of a single disorder and that affected individuals often progress from one clinical entity to another. (14)

Abdominal migraine affects 1% to 4% of children. It is more prevalent in girls than in boys (3:2), with a mean age of onset at 7 years and a peak at 10 to 12 years for both sexes. (14)

When accompanied by a history of migraine headaches, the diagnosis of abdominal migraine is straightforward. In all other cases, however, the diagnosis should remain presumptive and other causes of intermittent severe abdominal pain considered and excluded. Such disorders include obstructive uropathy, intermittent bowel obstruction or volvulus, biliary tract disease, recurrent pancreatitis, familial Mediterranean fever, and metabolic diseases. The diagnosis of abdominal migraine is supported by symptomatic improvement with medications used prophylactically for migraines.

Treatment involves avoidance of potential triggers, including caffeine, nitrite- and amine-containing foods, emotional stress, prolonged fasting, altered sleep patterns, and exposure to flickering or glaring lights. If episodes are frequent, prophylactic therapy can be offered using propranolol, cyproheptadine, or sumatriptan. Data are limited supporting the use of pizotifen, a sero-

tonin receptor antagonist, in children who have this entity. Pizotifen is not available in the United States. (8)

FAP

Some children who have chronic episodic or continuous abdominal pain do not meet the symptom-based criteria for other functional GI disorders. These children are given the diagnosis of FAP. A new classification in the Rome III criteria, termed functional abdominal pain syndrome (FAPS), is used to describe a subgroup of children who have FAP in whom loss of daily functioning or presence of accompanying somatic symptoms forms an important component of their symptom complex.

Using the Rome II criteria, the prevalence of FAP in 4- to 18-year-old patients presenting to gastroenterology clinics has varied from 0% to 7.5%. (11) This low prevalence is not surprising in that the old criteria were restrictive, requiring that the pain be continuous or nearly continuous, there be no association with physiologic events, and there be some impairment in daily activities. With the new Rome III criteria for FAP and its distinction from FAPS, the prevalence of FAP is likely to be significantly higher.

As with all of the other FAP disorders, the approach to the child who is suspected of having FAP or FAPS begins with a history and physical examination, paying close attention for the presence of all the "red flag" signs listed in Table 2. A detailed psychosocial history must be taken because the symptoms of anxiety, depression, and somatization described in children who have recurrent abdominal pain and their parents often apply to children who have FAP and FAPS.

Limited screening for organic disease, including a complete blood count (CBC), an erythrocyte sedimentation rate (ESR) or C-reactive protein measurement, a urinalysis, and a urine culture, may be reasonable. Other tests evaluating liver and kidney function and stool tests for ova and parasites can be considered if the clinician feels they are necessary based on the child's symptoms, degree of functional impairment, and level of parental anxiety.

A biopsychosocial treatment approach is particularly critical for children who have FAP and FAPS. Reassurance and an explanation of the mechanisms for pain involving the "brain-gut" axis should be provided. There also is some evidence that cognitive behavioral therapy is useful in improving pain and disability in children who have nonspecific abdominal pain. (15) As mentioned previously, there are anecdotal reports of the successful use of tricyclic antidepressants in children who have FAP. A more recent open-label trial of the use of the selective serotonin reuptake inhibitor citalopram in children who have recurrent abdominal pain reported that abdominal pain, anxiety, depression, other somatic symptoms, and functional impairment all improved significantly over a 12-week period. (16) These results may foretell a promising new treatment for affected children.

Laboratory, Radiographic, and Endoscopic Testing

Occasionally, the clinician may have difficulty distinguishing between functional and organic CAP. Without the presence of warning signs or symptoms in the history or physical examination, however, common laboratory tests (CBC, ESR, comprehensive metabolic panel, urinalysis, stool culture, parasite analysis) are not likely to be helpful. In addition, when abdominal and pelvic ultrasonography was performed in children who had recurrent abdominal pain but no "red flag" signs or symptoms, imaging abnormalities were found in fewer than 1%. (8)

Studies examining the utility of endoscopy with biopsies and esophageal pH monitoring (both invasive and expensive tests) in children who had apparent functional bowel disorders have demonstrated abnormalities in 25% to 56%. (8) However, these reports were limited by small sample size, sample bias, and variability of findings. Therefore, evidence to support their use in children who have clinical characteristics of functional CAP remain insufficient.

Conclusion

Children who have CAP represent a heterogeneous group of patients who have a spectrum of disorders much greater than that presented by Apley and Naish in 1958. Although CAP is functional in most children, an important part of the physician's job is to determine which children have an organic cause for their pain. The presence of "red flag" symptoms or signs (Table 2), including weight loss, deceleration of linear growth velocity, delayed puberty, significant vomiting, chronic severe diarrhea, GI blood loss, unexplained fever, family history of IBD, or abnormal and unexplainable physical findings, suggests a higher likelihood of organic pathology. If any of these findings is present, additional evaluation, including subspecialty referral and endoscopy, should be considered.

The recently developed Rome III symptom-based diagnostic criteria for functional disorders associated with abdominal pain in children can help physicians identify this population of patients better without unnecessary extensive and invasive diagnostic studies. Once

identified, use of the biopsychosocial approach, which not only addresses symptoms, but also a patient's subjective sense of suffering, interpretation of pain, and psychological profile, increases the potential for accurate diagnosis and treatment.

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PIR Quiz

Quiz also available online at www.pedsinreview.org.

1. Which of the following is a *true* statement regarding functional gastrointestinal disorders in children?

   A. All children who are suspected of having functional abdominal pain should undergo radiographic or endoscopic testing to rule out other pathologic diseases.
   B. Children who have chronic functional abdominal pain have less anxiety and depression than do normal controls.
   C. Frequent school absences indicate that abdominal pain is caused by an organic disease rather than by functional pain.
   D. Functional abdominal pain can be distinguished easily from organic abdominal pain by taking a history regarding the location and nature of the pain.
   E. Symptoms may be due to a combination of abnormal intestinal motility and heightened visceral sensation.

2. Which of the following is a "red flag" symptom that would prompt consideration of diagnoses other than functional gastrointestinal disorder?

   A. Constipation.
   B. Lower abdominal pain.
   C. Nausea when anxious.
   D. Occasional diarrhea.
   E. Weight loss.

3. A 9-year-old boy is brought to the clinic because of a 3-month history of intermittent upper epigastric abdominal pain, which occurs several times a week and occasionally wakes him at night. His appetite is normal, and he has not lost weight. He reports "throwing up a little blood" at school last week. His stools have been dark brown and normally formed. His physical examination findings are normal, except for very mild midepigastric tenderness without rebound or guarding. Of the following, the *most* likely diagnosis is:

   A. Abdominal migraine.
   B. Functional dyspepsia.
   C. Hereditary pancreatitis.
   D. Irritable bowel syndrome.
   E. Peptic ulcer disease.

4. You are evaluating a 7-year-old girl for abdominal pain that has been present for 4 months. She complains of the pain one to two afternoons a week and has been sent home from school several times. There is no history of vomiting, fever, or weight loss, and she has one formed stool every day. When asked where she hurts, she points to her abdomen just above her umbilicus. Social history reveals no obvious stressors. Results of her physical examination, including vital signs, growth parameters, and abdominal examination, are within normal limits. Of the following, the *best* management at this time is:

   A. Administration of histamine$_2$-histamine receptor antagonists.
   B. Administration of ibuprofen.
   C. Obtaining complete blood count and abdominal ultrasonography.
   D. Referral to gastroenterology for possible endoscopy.
   E. Strict avoidance of foods containing lactose.

5. A 12-year-old girl comes to the emergency department with a complaint of severe periumbilical abdominal pain for 1 day. She has vomited several times (nonbilious) and complains of constant nausea and a frontal headache, which she rates as being an 8 out of 10. She has had no changes in her urination or stooling pattern and no fever. She reports having had similar episodes five times over the last year, each of which lasted 3 days and resolved. Her mother reports having had headaches, but there is no history of gastrointestinal disease. Physical examination reveals an anxious, well-hydrated girl who is in obvious discomfort. She has normal bowel sounds and vague generalized abdominal tenderness without rebound or guarding. Of the following, the *most* likely diagnosis is:

   A. Abdominal migraine.
   B. Childhood functional abdominal pain syndrome.
   C. Crohn disease.
   D. Irritable bowel syndrome.
   E. Obstructive uropathy.

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