AMERICAN ACADEMY OF PEDIATRICS

NORTH AMERICAN SOCIETY FOR PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION

TECHNICAL REPORT

Subcommittee on Chronic Abdominal Pain

Chronic Abdominal Pain in Children

ABSTRACT. Chronic abdominal pain, defined as long-lasting intermittent or constant abdominal pain, is a common pediatric problem encountered by primary care physicians, medical subspecialists, and surgical specialists. Chronic abdominal pain in children is usually functional, that is, without objective evidence of an underlying organic disorder. The Subcommittee on Chronic Abdominal Pain of the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition has prepared this report based on a comprehensive, systematic review and rating of the medical literature. This report accompanies a clinical report based on the literature review and expert opinion.

The subcommittee examined the diagnostic and therapeutic value of a medical and psychological history, diagnostic tests, and pharmacologic and behavioral therapy. The presence of alarm symptoms or signs (such as weight loss, gastrointestinal bleeding, persistent fever, chronic severe diarrhea, and significant vomiting) is associated with a higher prevalence of organic disease. There was insufficient evidence to state that the nature of the abdominal pain or the presence of associated symptoms (such as anorexia, nausea, headache, and joint pain) can discriminate between functional and organic disorders. Although children with chronic abdominal pain and their parents are more often anxious or depressed, the presence of anxiety, depression, behavior problems, or recent negative life events does not distinguish between functional and organic abdominal pain. Most children who are brought to the primary care physician's office for chronic abdominal pain are unlikely to require diagnostic testing. Pediatric studies of therapeutic interventions were examined and found to be limited or inconclusive. *Pediatrics* **2005;115:e370–e381. URL: www.pediatrics.org/cgi/doi/10.1542/peds.2004-2523;** ***abdominal pain, functional bowel disorders, irritable bowel syndrome, dyspepsia, stress, anxiety, depression.***

ABBREVIATIONS. IBS, irritable bowel syndrome; RCT, randomized, controlled trial.

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INTRODUCTION

The exact prevalence of chronic abdominal pain in children is not known. It seems to account for 2% to 4% of all pediatric office visits.[1] One study suggested that 13% of middle-school students and 17% of high-school students experience weekly abdominal pain.[2] In the latter study, it was also noted that approximately 8% of all students had seen a physician for evaluation of abdominal pain in the previous year. Quality of life in adult patients with chronic abdominal pain is substantially poorer than that of the general population.[3] The economic cost related to this condition in children is not known but is likely to be substantial, considering that expenses associated with irritable bowel syndrome (IBS) in adults have been estimated to be $8 billion to $30 billion per year.[4–6] The long-term outcome of this condition has not been determined, but preliminary data indicate that young adults with a history of recurrent abdominal pain that began in childhood who are treated by a subspecialist are significantly more likely than their peers without recurrent abdominal pain to have lifelong psychiatric problems and migraine headaches.[7] Despite the high prevalence and effects of this condition, no evidence-based guidelines for its evaluation and treatment exist.

With this background in mind, the American Academy of Pediatrics and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition established a subcommittee charged with developing evidence-based guidelines for the evaluation and treatment of chronic abdominal pain in children. A major problem in reviewing the literature arose in defining criteria for recurrent or chronic abdominal pain. For many years, the term "recurrent abdominal pain" has been used to describe all cases without an organic etiology. It was first introduced in the pediatric literature by Apley and Naish[8] in the late 1950s, an era in which some organic gastrointestinal disorders had not been fully appreciated. Children were considered to have recurrent abdominal pain if they had experienced at least 3 bouts of pain, severe enough to affect activities, over a period of at least 3 months. This definition had initially constituted the entry criteria for their descriptive studies, but recurrent abdominal pain later became a term used clinically to describe

all children with abdominal pain without an organic etiology. It is now agreed that recurrent abdominal pain is a description, not a diagnosis. Recurrent abdominal pain, as a case definition, includes children with a variety of functional gastrointestinal disorders causing abdominal pain, such as nonulcer dyspepsia, IBS, or abdominal migraine. It also may include children with organic disease (see questions 2–6 later in this report). In this article we avoid use of the term "recurrent abdominal pain" whenever possible to lessen the confusion that the term engenders. Table 1 summarizes terms currently used to describe long-lasting constant or intermittent childhood abdominal pain.

The preponderance of the available pediatric literature on this subject is still based on the Apley and Naish criteria.[8] Thus, evidence was sought in articles that were selected based on the presence of Apley and Naish criteria as entry criteria unless the subcommittee felt that other strong qualities (for example, large epidemiologic study or double-blind, randomized, controlled trial [RCT]) justified their evaluation and inclusion as part of the evidence, which meant that some articles including children with abdominal pain of <3 months' duration were excluded from consideration.

After a careful evaluation of the published literature, no evidence-based procedural algorithm could be produced; instead, questions of interest to clinicians were posed and clinical guidance was generated linked to the standard clinical approach of history, physical examination, diagnostic testing, and treatment. This article is organized in 3 parts: (1) the methodology used to review the evidence and generate the statements is described; (2) questions are answered regarding subgroups of disorders, the role of diagnostic evaluation (history, laboratory tests, radiologic and invasive techniques, and psychosocial evaluation), and the efficacy of pharmacologic, behavioral, and surgical interventions; and (3) a summary of the quality of the evidence is provided (Appendix 1).

TABLE 2. Literature-Search Strategy

Search Terms	No. of Articles Returned
([("abdominal pain"[MeSH terms] OR abdominal pain[text word]) AND notpubref[sb]] AND "child"[MeSH terms])	6662
([([(chronic[all fields] OR recurrent[all fields]) OR functional[all fields]] AND ("abdominal pain"[MeSH terms] OR abdominal pain[text word])) AND notpubref[sb]] AND "child"[MeSH terms]))	1498
Clinical queries	
AND therapy/sensitivity	232
AND diagnosis/sensitivity	932

MeSH indicates medical subject heading (PubMed's controlled vocabulary); notpubref[sb] limits the search to the biomedical literature.

METHODOLOGY

The guideline-development process of Woolf[9] was used with a subcommittee of experts and community physicians guiding the work of the methodologist (H.P.L.) to assemble the evidence, reviewing the results of the methodologist and using the nominal group technique[10] to arrive at conclusions based on the evidence.

After initial discussions, 15 questions were defined and collapsed into the 8 questions in this review. An initial search (see Table 2) was performed on PubMed (www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=PubMed) on October 27, 2000, searching for "abdominal pain" in the broadest possible way but limited to pediatric studies; 1498 titles were retrieved. The search was repeated on June 19, 2002, providing another 158 references, for a total of 1656.

In the review process, the following were exclusion criteria: non-English, nonpediatric, nonrecurrent/nonfunctional/nonchronic abdominal pain, small study (sample size ≤5), no original data, letter to the editor, study on *Helicobacter pylori*, and study subjects not baseline-healthy (eg, patients with sickle cell disease). The studies regarding *H pylori* were excluded because the literature regarding *H pylori* had been reviewed recently by a North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition committee and a practice guideline had been published.[11] All titles were reviewed by a single reader (H.P.L.); 10% of the excluded articles were reviewed by 2 committee members (C.D.L. and R.B.C.), with 100% agreement regarding exclusion criteria. Of nonrejected titles, abstracts were read by a single reader (H.P.L.), and additional exclusions were made. Articles

TABLE 1. Currently Used Definitions to Describe Childhood Abdominal Pain

Recurrent abdominal pain as defined by Apley and Naish8	≥3 episodes of abdominal pain, over a period of ≥3 mo, severe enough to affect activities
RAP	A common abbreviation for recurrent abdominal pain that has been used in the literature to depict recurrent abdominal pain as defined by Apley and Naish; many physicians incorrectly use this term to imply functional abdominal pain
Chronic abdominal pain	Abdominal pain with a minimum duration of 3 mo; some clinicians believe that pain lasting >1–2 mo is chronic
Rome II criteria for abdominal pain	Abdominal pain for at least 12 wk, which need not be consecutive, in the preceding 12 mo; these criteria apply to IBS, functional dyspepsia, and functional abdominal pain
Functional abdominal pain	Abdominal pain that occurs in the absence of anatomic abnormality, inflammation, or tissue damage
Nonorganic abdominal pain	A term that is often used interchangeably with functional abdominal pain
Psychogenic abdominal pain	A term that is often used interchangeably with functional abdominal pain

TABLE 3. Articles and Studies Processed in the Review

Reason	Title	Abstract	Article	Total
Non-CAP	688	114	55	857
Sample size ≤5	143	32	33	208
Non-English	164	16	0	180
No original data	35	51	69	155
Nonpediatric	32	86	20	138
Nonbaseline normal	16	5	1	22
Case series	0	0	62	60
Duplicates other study	0	0	2	2
Total*	1078	304	242	1562*
Remaining articles				94
Methodology reviewed				94
Article detailed data review				64
Study detailed review				83

CAP indicates chronic abdominal pain. Non-CAP includes articles on *Helicobacter* and abdominal pain.
* These totals reflect the following overlaps: 45 rejected as abstracts and titles; 9 articles rejected as abstracts and articles; 7 rejected as titles and articles; and 1 rejected as abstract, title, and article.

were read by at least 2 readers (medical student and H.P.L.). Ten articles were abstracted in parallel, with similar results, demonstrating a reliable procedure. Data were abstracted regarding the study as a whole, design and quality, patient groups, and outcomes and their values. Efforts were made to standardize the vocabulary used in recording the methodology and results, resulting in a controlled vocabulary of 1262 terms. After review, 94 articles were included in the evidence review.

The definitions of the study designs were as follows: uncontrolled experiment, an unspecified group of participants received intervention and follow-up data were provided; case-series cross section, data were provided on a single group of participants; case-series follow-up, baseline and follow-up data were provided on a single group of participants; cohort cross section, a single group of participants was divided into 2 or more groups on the basis of a specified feature (eg, history or laboratory tests) and described; cohort follow-up, baseline and follow-up data were provided on a single group of participants who were divided into 2 or more groups; case control, 2 or more groups were assembled and retrospective or current data are provided; and RCT, participants were randomly assigned to intervention, and follow-up data are provided. Because the questions were all comparative, only studies with 2 arms or more were included in this review (thereby excluding case series).

Table 3 shows the type of articles and studies as processed in the review. Most articles were rejected on the basis of title review. Some articles were rejected at more than 1 point in the process, as indicated by the overlaps. Ninety-four articles were left for review. Sixty-four articles had full data investigation, which included separating articles into 1 or more studies in case there was, for example, a baseline case-control study with a cohort follow-up; hence, the 64 articles translated into 83 studies.

An article might have more than 1 study in it if, for instance, there was an initial cohort cross-section with a subsequent cohort follow-up reported in the same article. Of the 83 studies for which methodology was reviewed, 46 were case control, 20 were cohort cross section, 10 were cohort follow-up, and 7 were RCTs. A recent systematic review of treatments in recurrent abdominal pain identified the same RCTs,[12] providing validation for our approach.

Data abstracted for each study as a whole included study city; study country; single or multiple site; site type (community, physician office, academic pediatric setting, gastroenterologist office); funding source; age range, mean, and SD; sample size; number of groups; number of outcomes; and number of time points.

A methodology review was performed for each study, based on the Newcastle-Ottawa Scale for assessing the quality of nonrandomized studies in meta-analyses.[13] Inclusion and exclusion criteria were noted by using the controlled vocabulary. The evidence was characterized in terms of outcome type (based on the controlled vocabulary), outcome name (specific to this study), outcome units (for continuous outcomes), outcome time point (baseline or later), method (how outcome was assessed), sample size at outset, and sample size at termination (a difference from sample size at outset indicated loss to follow-up). Data for continuous outcomes (in which a quantity was measured within a participant) were usually characterized by the mean and SD. For categorical data (in which participants were counted once), the category was labeled by using the controlled vocabulary, test statistic name, *P* value (and comments), and data source (page/figure/table).

Figure 1 summarizes the geographic distribution of the studies for which the country was provided. Of 89 articles for which data were provided, 62 (70%) were performed at a single site, 30 (34%) were based on research at an academic pediatric center, 27 (31%) were performed at a gastroenterology clinic, 17 (19%) were performed at the community level, and 9 (10%) were performed at general pediatric offices.

We calculated a quality score for each study as the ratio of quality items attained to the total number of items. The average, SD, and confidence intervals are given for each design in Table 4. Although the quality scores seem to increase for the more preferred designs, the confidence intervals all overlap.

Evidence tables for each of the 8 questions were generated across studies and grouped according to arm type, method, or outcome, as pertinent to the question. There were 685 outcomes across the studies, categorized as history outcomes (550 [80%]), tissue/physiologic outcomes (115 [17%]), physical examination outcomes (15 [2%]), and use of medications (5 [1%]). Among the 685 outcomes, 161 of the *P* values (23%) were not statistically significant, and an additional 316 (46%) were not provided by investigators. Each subcommittee member took responsibility for 1 or more questions. Each reviewed the evidence tables and the

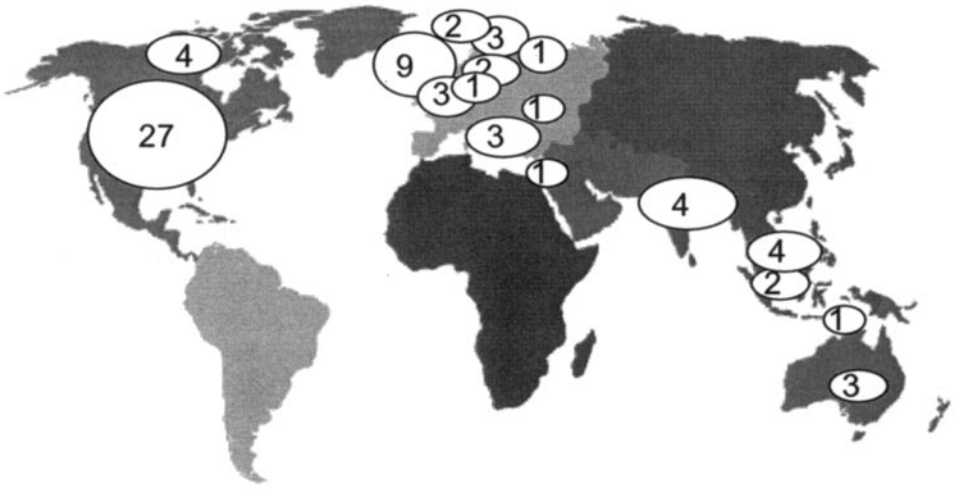

Fig 1. Geographic distribution of articles. Map courtesy of www.worldatlas.com.

TABLE 4. Quality Scores by Design

	No. of Studies	Average Score, %	SD, %	Confidence Interval, %
RCT	7	70	15	(58–82)
Cohort follow-up	9	64	21	(50–78)
Cohort cross section	18	58	18	(50–67)
Case control	46	53	26	(45–60)

TABLE 5. Rating of Evidence Quality

Level	Criteria
A	Well-designed RCTs or diagnostic studies on relevant populations: ≥2 studies that compared the test with a criterion standard in an independent, blind manner in an unselected population of children similar to those addressed in the report
B	RCTs or diagnostic studies with minor limitations and overwhelmingly consistent evidence from observational studies: a single study that compared the test with a criterion standard in an independent, blind manner in an unselected population of children similar to those addressed in the report
C	Observational studies (case-control and cohort design)
D	Expert opinion, case reports, reasoning from first principles

primary articles and generated a summary of the research. The scale for rating evidence is given in Table 5.

The reviews were discussed by the subcommittee, and the nominal group technique[10] was used to achieve consensus.

QUESTIONS

Question 1: Is there evidence that children with chronic abdominal pain have symptom patterns that can be categorized as functional dyspepsia, IBS, or abdominal migraine?

There is limited but credible evidence of the existence of functional dyspepsia, IBS, and abdominal migraine in children (evidence quality C).

Although often discussed as a homogeneous group of patients, there are different phenotypic manifestations of functional abdominal pain. The wide variety of descriptive terms applied to these patients' symptoms, including irritable bowel of childhood, spastic colon of childhood, nonorganic recurrent abdominal pain, and psychogenic recurrent abdominal pain, reflects both the heterogeneity of the group and the limited understanding of the pathogenesis of symptoms.

The sensitivity and specificity of the Apley and Naish criteria have been questioned, and some investigators have proposed the "Rome" criteria,[14] which suggest that many children and adolescents with recurrent or chronic abdominal pain manifest symptom clusters that facilitate the diagnosis of disorders on the basis of symptoms alone. In 1999, a group of investigators (Rome II committee) was charged with identifying and then developing diagnostic criteria for childhood functional disorders including recurrent abdominal pain. They developed a symptom-based classification of functional disorders

TABLE 6. Rome II Criteria for Functional Bowel Disorders Associated With Abdominal Pain or Discomfort in Children[14]

Functional dyspepsia: in children mature enough to provide an accurate pain history (at least 12 wk, which need not be consecutive) within the preceding 12 mo of:
- Persistent or recurrent pain or discomfort centered in the upper abdomen (above the umbilicus); and
- No evidence (including upper endoscopy) that organic disease is likely to explain the symptoms; and
- No evidence that dyspepsia is exclusively relieved by defecation or associated with the onset of a change in stool frequency or stool form

IBS: in children old enough to provide an accurate pain history (at least 12 wk, which need not be consecutive) in the preceding 12 mo of:
- Abdominal discomfort or pain that has 2 of the following 3 features:
  - Relieved with defecation
  - Onset associated with a change in frequency of stool
  - Onset associated with a change in form (appearance) of stool
  - and
- There are no structural or metabolic abnormalities to explain the symptoms
- The following symptoms also support a diagnosis of IBS:
  - Abnormal stool frequency defined as >3 bowel movements per day or <3 bowel movements per week
  - Abnormal stool form (lumpy/hard or loose/watery)
  - Abnormal stool passage (straining, urgency, or feeling of incomplete evacuation)
  - Passage of mucus with stool
  - Bloating or feeling of abdominal distention

Functional abdominal pain: at least 12 wk of:
- Nearly continuous abdominal pain in a school-aged child or adolescent;
- No, or only occasional, relation of pain with physiologic events (eg, eating, menses, or defecation);
- Some loss of daily functioning;
- Pain that is not feigned (eg, malingering); and
- Insufficient criteria for other functional gastrointestinal disorders that would explain the abdominal pain

Abdominal migraine: in the preceding 12 mo:
- Three or more paroxysmal episodes of intense, acute midline, abdominal pain lasting 2 h to several days, with intervening symptom-free intervals lasting weeks to months;
- Evidence of absence of metabolic, gastrointestinal, and central nervous system structural or biochemical diseases is absent; and
- Two of the following features:
  - Headache during episodes
  - Photophobia during episodes
  - Family history of migraines
  - Headache confined to 1 side only
  - An aura or warning period consisting of visual disturbances, sensory symptoms, or motor abnormalities

associated with abdominal pain (Table 6). The goal for these criteria was to decrease cost and suffering for the patients by encouraging a defined-criteria diagnosis of the disorder rather than one obtained after excluding organic diseases. The group felt that the classic Apley and Naish criteria of recurrent abdominal pain were too general and failed to recognize that recurrent abdominal pain was not a final diagnosis. It was also apparent to the group that children and adolescents often displayed a symptom complex similar to previously described functional disorders in adults, such as IBS and functional dyspepsia. Clinical experience also suggested that a symptom complex called abdominal migraine existed.

A prospective study of 257 children 5 years of age or older presenting with abdominal pain or discomfort, nausea, or vomiting for 1 month or more identified 127 subjects meeting the Rome II criteria for dyspepsia (before evaluation for disease).[15] Symptoms were ulcer-like in 26% and dyspepsia-like in 15% of the subjects. Fifty six of these subjects underwent esophagogastroduodenoscopy, and 35 were found to have no evidence of disease. These 35 subjects were believed to fulfill strict criteria for functional dyspepsia. Symptoms of IBS were present in approximately one fourth of the patients with functional dyspepsia.

Questionnaires administered during a population-based study of middle- and high-school students revealed a symptom complex consistent with IBS in 6% of middle-school students and 14% of high-school students.[2] None of these subjects were tested for organic disease. A prospective study of 227 children 5 years of age or older referred to a pediatric gastroenterology clinic for evaluation of chronic abdominal pain showed that 117 had symptoms consistent with IBS.[16] Diagnostic testing failed to reveal underlying disease. Concomitant upper abdominal discomfort or nausea was present in one third of these subjects.

A well-designed and implemented epidemiologic study[17] of a general population demonstrated an increased prevalence of a lifetime maternal history of migraine in children with recurrent abdominal pain, migraine headache, and abdominal migraine. Abdominal migraine was defined as recurrent abdominal pain associated with nausea and/or vomiting of sufficient severity to stop normal activity plus 3 of the following: pallor, fever, limb pain, dizziness, or headache. Among study patients, 2.4% had abdominal migraine. Children with abdominal migraine were 2.6 times more likely to have a maternal history of migraine. Another prospective cross-sectional questionnaire study[18] of a large random sample of school children 5 to 15 years old compared children with migraine headaches and children with abdominal migraine. Abdominal migraine was defined as (1) pain severe enough to interfere with normal daily activities; (2) pain dull or colicky in nature; (3) periumbilical or poorly localized pain; (4) any 2 of anorexia, nausea, vomiting, or pallor; (5) attacks lasting for at least 1 hour; and (6) complete resolution of symptoms between attacks. Approximately 4.1% had abdominal migraine. Children with migraine headaches were twice as likely to have abdominal migraine, and children with abdominal migraine were twice as likely to have migraine headaches as the general population.

Question 2: What is the predictive value of history items?

There are no studies of unselected patients showing that pain frequency, severity, location, or effects on lifestyle are able to distinguish between functional and organic disorders (evidence quality C).

Children with recurrent abdominal pain are more likely than children without recurrent abdominal pain to have headache, joint pain, anorexia, vomiting, nausea, excessive gas, and altered bowel symptoms. There are insufficient data to determine if the presence of associated symptoms can help the physician distinguish between functional and organic disorders (evidence quality C).

The presence of alarm symptoms or signs suggests a higher pretest probability or prevalence of organic disease and may justify the performance of diagnostic tests. Alarm symptoms or signs include but are not limited to involuntary weight loss, deceleration of linear growth, gastrointestinal blood loss, significant vomiting, chronic severe diarrhea, persistent right upper or right lower quadrant pain, unexplained fever, and family history of inflammatory bowel disease (evidence quality D).

Functional abdominal pain lacks a diagnostic marker. Because no prospective studies on natural history or incidence compare the history of children with and without recurrent episodes of abdominal pain, it cannot be stated that duration of pain itself supports a diagnosis of functional pain. The committee was able to identify 25 peer-reviewed studies of patients with chronic abdominal pain of >3 months' duration in which symptom description was included in the results and patient-selection criteria were most likely to exclude author bias (survey, questionnaire, or consecutive patients prospectively or retrospectively enrolled for study).[2,8,19–41] One quarter of these studies were performed in North America, one quarter were performed in the Far East, and half were performed in Europe. The available studies provide evidence that frequency, severity, location, and timing (postprandial, waking during night) of abdominal pain do not help distinguish between organic and functional abdominal pain. Children with recurrent episodes of abdominal pain are more likely than children without abdominal pain or children with behavior disorders to have anorexia, nausea, episodic vomiting, constipation, diarrhea, headache, arthralgia, or eye problems. Yet, none of these associated symptoms have been reported to help distinguish between organic and functional abdominal pain. Younger age of onset of pain and inability to attend school because of pain were associated with a decision to consult a physician.[37]

Physical examination of children with recurrent or chronic abdominal pain has been described rarely. The presence of tenderness on abdominal palpation has been reported to be characteristic of children with recurrent episodes of abdominal pain without

evidence of organic disease when compared with control children.[28]

Question 3: What is the predictive value of laboratory tests?

There is no evidence to evaluate the predictive value of blood tests (evidence quality D).

There is no evidence to determine the predictive value of blood tests in the face of alarm signals (evidence quality D).

Because researchers have used results of laboratory testing as inclusion or exclusion criteria for functional abdominal pain, there are no studies that have evaluated the usefulness of common laboratory tests (complete blood cell count, erythrocyte sedimentation rate, comprehensive metabolic panel, urinalysis, stool parasite analysis) to distinguish between organic and functional abdominal pain. Investigations of specific biological markers have described significant differences between patients with recurrent episodes of abdominal pain and control subjects (such as increased plasma cholecystokinin concentrations and decreased plasma oxytocin and cortisol concentrations in children with pain).[29,42] However, the number of patients in these studies is small, and the value of such measurements to clinical practice remains to be determined. The coexistence of abdominal pain and an abnormal test result for a common gastrointestinal disorder such as lactose malabsorption or *H pylori* infection does not necessarily indicate a causal relationship between the 2. Treatment of lactose malabsorption often does not result in resolution of abdominal pain, and children with *H pylori* infection are not more likely to have abdominal pain than children without *H pylori*. Children with lactose malabsorption may have a phenotype overlapping with diarrhea-predominant IBS.

Question 4: What are the predictive values of other diagnostic tests?

There is no evidence to suggest that the use of ultrasonographic examination of the abdomen and pelvis in the absence of alarm symptoms has a significant yield of organic disease (evidence quality C).

There is little evidence to suggest that the use of endoscopy and biopsy in the absence of alarm symptoms has a significant yield of organic disease (evidence quality C).

There is insufficient evidence to suggest that the use of esophageal pH monitoring in the absence of alarm symptoms has a significant yield of organic disease (evidence quality C).

Ultrasonographic examination of the abdomen and pelvis is a painless, noninvasive, and inexpensive test that can detect abnormalities of the kidneys, gallbladder, liver, pancreas, appendix, intestines, ovaries, and uterus. When abdominal and pelvic ultrasonography has been performed in children with recurrent episodes of abdominal pain without alarm symptoms, abnormalities have been found in fewer than 1%.[43] Abnormalities detected on ultrasonography may not be causally related to the patient's abdominal pain. When atypical symptoms are present, such as jaundice, urinary symptoms, back or flank pain, vomiting, or abnormal findings on physical examination, an abdominal and pelvic ultrasonography is more likely to detect an abnormality (approximately 10%).

Endoscopy and biopsy of the esophagus, stomach, and duodenum, an invasive and expensive procedure, can detect esophagitis, gastritis, duodenitis, and ulceration. Esophageal pH monitoring, also an invasive and expensive test, measures the frequency and duration of exposure of the esophagus to gastric acid as a means of diagnosing gastroesophageal reflux. Studies of endoscopy, biopsy, and/or esophageal pH monitoring performed in children with recurrent abdominal pain have demonstrated abnormalities in 25% to 56%, but reports have been limited by small sample size, sample bias, variability of findings, and questionable specificity and generalizability.[40,44–46] Endoscopic or histopathologic abnormalities such as esophagitis, gastritis, or duodenitis do not predict the prognosis, which is generally favorable in children with recurrent abdominal pain, including those with dyspepsia.[15]

Question 5: What is the diagnostic value of the psychosocial history?

The literature was reviewed with respect to 3 domains of psychosocial history: life-event stress, child emotional/behavioral symptoms, and family functioning.

Life-Event Stress

There is a small amount of evidence suggesting that the presence of recent negative life events is not useful in distinguishing between functional abdominal pain and abdominal pain of other causes (evidence quality B). There is limited evidence suggesting that daily stressors are associated with the occurrence of pain episodes and that higher levels of negative life events are associated with increased likelihood of symptom persistence (evidence quality C). There is no evidence on whether life stress influences symptom severity, course, or response to treatment (evidence quality D).

Studies including comparison groups of other patients are relevant in assessing the value of the psychosocial history in the differential diagnosis of chronic abdominal pain. One study[47] compared 30 pediatric patients with recurrent episodes of abdominal pain with 30 patients referred for acute minor illness or injury. Life-event change in the previous year did not differ significantly between the 2 groups. Another study found no difference between patients with recurrent abdominal pain and patients with minor organic disease (eg, gastritis, esophagitis) on measures of patients' personal life events or mothers' reports of family life events.[48] No studies have found that the presence of life-event stress significantly differentiates patients with functional abdominal pain from other patient groups.

Nonetheless, several investigations have reported higher levels of life stress in children with chronic abdominal pain compared with children without abdominal pain. Two studies compared pediatric patients with abdominal pain with healthy school children and found significantly higher levels of life-event stress in patients with pain.[23,49] A diary study

found that patients with recurrent episodes of abdominal pain reported significantly more daily stressors than healthy school children; moreover, the relation between daily stressors and somatic complaints was significantly stronger for patients with abdominal pain than for healthy school children.[41] Thus, although there is no evidence that life stress helps distinguish between patients with functional abdominal pain and patients with organic disease, children with functional abdominal pain may experience stressors that warrant attention. Additional research is needed to evaluate whether these stressors contribute to symptom severity, course, or response to treatment.

Emotional/Behavioral Symptoms

There is evidence suggesting that the presence of anxiety, depression, or behavior problems is not useful in distinguishing between functional abdominal pain and abdominal pain of other causes (evidence quality B). There is evidence that patients with recurrent abdominal pain have more symptoms of anxiety and depression (internalizing emotional symptoms) than do healthy community controls (evidence quality B). In contrast, there is evidence that children with recurrent abdominal pain do not have higher levels of conduct disorder and oppositional behavior (externalizing emotional symptoms) compared with healthy community controls (evidence quality B). There are no data on whether emotional/behavioral symptoms predict symptom severity, course, or response to treatment (evidence quality D). There is evidence suggesting that children with recurrent abdominal pain are at risk of later emotional symptoms and psychiatric disorders (evidence quality B).

Several studies have used standardized measures to assess emotional/behavioral symptoms in patients with chronic abdominal pain and other patient groups. In a study comparing 30 patients with abdominal pain with 30 patients with acute minor illness or injury, no significant differences were found between the patient groups when depression was assessed by interview or a child self-report measure.[47] Another study comparing 19 patients with functional abdominal pain with 19 patients with an organic etiology of abdominal pain found no significant differences between the groups on the Child Behavior Checklist completed by the mother or on the Rutter B2 Behavioral Scale completed by the teacher.[50] Similarly, no significant differences were found between patients with and without organic findings in 2 studies that included pediatric patients whose abdominal pain ranged in duration from 1 month to several years.[48,51] Thus, no studies have found a significant difference between patients with abdominal pain that is functional or organic in etiology with respect to emotional/behavioral symptoms.

Considerable evidence suggests that patients with chronic abdominal pain have more symptoms of anxiety and depression than do community controls. In a study of 31 children with recurrent abdominal pain and 31 matched classroom control children, mothers' reports indicated significantly higher scores for internalizing emotional symptoms (anxiety, depression) in children with abdominal pain.[52] Teachers' reports did not show significant group differences. However, a structured diagnostic interview indicated that 26 of the 31 children with abdominal pain met the criteria for a psychiatric diagnosis. In most cases, these diagnoses were anxiety related. Others also have observed higher levels of anxiety and depression in patients with recurrent episodes of abdominal pain compared with community controls,[48,51] although 1 study found that patients with abdominal pain were within the normal range for anxiety and depression on the basis of published normative data,[53] and another found no difference between patients with abdominal pain and controls on self-report or interview measures of depression.[25] A community-based study of students in middle and high school found that those with IBS-like symptoms had significantly higher scores than their peers without IBS on self-report questionnaire measures of anxiety and depression.[2] In contrast to the positive findings for anxiety and depression, no studies have found significant differences between children with recurrent episodes of abdominal pain and community controls on measures of conduct disorder or oppositional behavior.

Finally, results of 3 studies suggest that children with recurrent abdominal pain may be at risk of later anxiety and depression. A recent study compared 28 young adults evaluated for functional abdominal pain between the ages of 6 and 17 years with 28 matched former childhood participants of a study of tonsillectomy and adenoidectomy (controls).[7] An average of 11 years after the target visit, a structured psychiatric diagnostic interview was administered to identify psychiatric disorders based on *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*[54] criteria. Compared with controls, those with persistent abdominal pain were significantly more likely to meet criteria for a lifetime or current history of anxiety disorder. In another study, children with abdominal pain and controls were identified in data from a national longitudinal birth cohort study.[34] At 36 years of age, participants were administered a semistructured psychiatric interview that generated scores representing thresholds for psychiatric disorder. Persistent abdominal pain in childhood was significantly associated with psychiatric disorder in adulthood. In a prospective study of 31 patients with recurrent abdominal pain and 31 control children, mothers' reports of depressive symptoms and anxiety in their children 5 years after baseline assessment were significantly higher for patients with abdominal pain than for control children.[55]

Family Functioning

There is evidence that parents of patients with recurrent abdominal pain have more symptoms of anxiety, depression, and somatization than do parents of community controls or parents of other pediatric patients (evidence quality C). There is some evidence that families of patients with recurrent abdominal pain do not differ from families of control children or families of patients with acute illness in broad areas of family functioning, such as family cohesion, conflict, and marital satisfaction (evidence quality C).

Two studies used structured diagnostic interviews to assess family history of psychiatric disorders in patients with recurrent episodes of abdominal pain compared with other patient groups. In 1 study, 28 adults with a childhood history of recurrent episodes of abdominal pain were compared with 28 adults who had undergone minor surgery as children (controls).[7] Participants with a history of childhood abdominal pain were significantly more likely than controls to report having a first-degree relative with generalized anxiety disorder, and there was a trend suggesting group differences on family history of major depression. In another study, on the basis of interviews with 20 mothers of children with functional abdominal pain and 20 mothers of children with an organic etiology for abdominal pain, the mean number of psychiatric disorders per relative was found to be significantly higher in the functional-pain group than in the organic-pain group.[56] With respect to particular types of disorders, a significant difference was found only for somatization disorder, with the functional-pain group having a higher proportion of affected relatives. A third study[51] found that, compared with control parents, mothers (but not fathers) of children with recurrent episodes of abdominal pain had significantly higher levels of anxiety, depression, and somatization symptoms. Studies also have reported higher levels of emotional distress in parents of children with recurrent episodes of abdominal pain compared with parents of children without abdominal pain.[24,25,34]

Finally, a few studies have examined broad areas of family functioning. These studies found no difference between patients with abdominal pain and other patient groups or controls on measures of parent marital satisfaction[47,48] or family cohesion and conflict.[48] In 1 study, children with recurrent episodes of abdominal pain reported greater parental encouragement of illness behavior than did children without abdominal pain.[48]

Question 6: What is the effectiveness of pharmacologic treatment?

A thorough review of the literature with a focus on RCTs revealed a paucity of studies examining pharmacologic and dietary interventions. Therefore, definitive statements concerning therapeutic efficacy are quite limited.

There is evidence that treatment for 2 weeks with peppermint oil may provide benefit in children with IBS (evidence quality B).

In a randomized, double-blind, controlled trial, 42 children with IBS were given pH-dependent, enteric-coated peppermint-oil capsules or placebo. After 2 weeks, 75% of those receiving peppermint oil had decreased severity of pain associated with IBS.[57] It was concluded that peppermint oil can be used as a therapeutic agent during the symptomatic phase of IBS. This was a short study of an agent not commonly used in the treatment of IBS. Entry criteria were not well described, other symptoms were not affected, and the safety and palatability of the drug were not described. Despite these shortcomings, the study represents an important proof-of-concept study supporting a beneficial effect of a medication with possible smooth muscle–relaxing properties in children with IBS.

There is inconclusive evidence of the benefit of H_2-receptor antagonists to treat children with dyspepsia (evidence quality B).

A double-blind, placebo-controlled trial of famotidine was conducted in 25 children with abdominal pain and dyspepsia.[58] Among the different variables evaluated, only the global evaluation suggested that there was a benefit of famotidine over placebo. Using the quantitative assessment, however, the mean improvement of the score using famotidine versus placebo was not statistically significant. There was also a significant improvement in symptoms during the first treatment period regardless of the medication used. A subset of patients with dyspeptic symptoms demonstrated a significant benefit from the drug. In this study, enrolled children had to meet Apley and Naish criteria and had to have dyspeptic symptoms. The study population was heterogeneous, with some patients having positive *H pylori* titers and others having an abnormal lactose breath hydrogen test. It is the opinion of the subcommittee that H_2-receptor antagonists may be beneficial for children with severe dyspeptic symptoms (including heartburn), but the results were difficult to generalize to children with functional abdominal pain.

There is inconclusive evidence that fiber supplement intake decreases the frequency of pain attacks for patients with recurrent abdominal pain (evidence quality B).

A randomized, double-blind, placebo-controlled study in 52 children with recurrent episodes of abdominal pain recruited from primary care practices[59] demonstrated a statistically significant decrease in pain attacks in children who were given additional fiber, compared with those receiving placebo. The study involved small groups (26 each), and improvement was marginal (7 improved with placebo and 13 with fiber).

There is inconclusive evidence that a lactose-free diet decreases symptoms in children with recurrent abdominal pain (evidence quality B).

In a study of 103 children 6 to 14 years of age with nonlocalized abdominal pain for 4 months, a similar prevalence of lactase deficiency was found in the control and abdominal-pain groups.[60] Thirty-eight patients completed 3 successive 6-week diet trials conducted in a double-blind fashion. The patients then were placed on a 12-month milk-elimination diet. The results suggested that the elimination of lactose did not affect the overall rate of improvement in abdominal pain. In addition, the recovery rate was similar in both lactose absorbers and nonabsorbers, independent of dietary restrictions. This study suggested that lactose intolerance and recurrent abdominal pain are 2 separate entities, and a lactose-free diet has no effect on outcome of abdominal pain in lactose absorbers and nonabsorbers.

There are limited data to suggest that pizotifen is efficacious in the treatment of abdominal migraine (evidence quality B).

Pizotifen is a potent antagonist of the serotonin 2A (5-HT2A) receptor, which is not approved for use in

the United States. A placebo-controlled crossover study used pizotifen for the treatment of 14 children with abdominal migraine.[61] Patients received either pizotifen (0.25 mg, twice daily) or placebo syrup for 2 months, then the alternate treatment for 2 months. While being treated with pizotifen, the study children had fewer days of abdominal pain and lower indices of severity and misery. The medication was well tolerated. These results may not be generalizable to children with milder symptoms. Common adverse effects include drowsiness, dizziness, increased appetite, and weight gain.

Question 7: What is the effectiveness of cognitive-behavioral therapy?

There is evidence that cognitive-behavioral therapy may be useful in improving pain and disability outcome in the short term (evidence quality B).

Two RCTs[62,63] evaluated the efficacy of a cognitive-behavioral program and a cognitive-behavioral family intervention for the treatment of nonspecific abdominal pain. In the first study, results showed that both the experimental and the control groups had decreased levels of pain. However, the treated group improved more quickly, the effects generalized to the school setting, and a larger proportion of subjects were completely pain-free by 3 months' follow-up. In the second study, the children and mothers who were taught coping skills had a higher rate of complete elimination of pain, lower levels of relapse at 6 and 12 months' follow-up, and lower levels of interference with their activities as a result of pain, and parents reported a higher level of satisfaction with the treatment. After controlling for pretreatment levels of pain, children's active self-coping and mothers' caregiving strategies were significant independent predictors of pain behavior after treatment.

Question 8: What is the effectiveness of surgery?

There is no evidence of the possible beneficial role of surgery in the evaluation or management of children with recurrent abdominal pain (evidence quality D).

There are no studies comparing diagnostic or therapeutic surgery with other approaches (evidence quality D).

The literature search identified a study[64] aimed at evaluating the results of diagnostic laparoscopy in children with chronic recurrent abdominal pain. It was a series of 13 children with chronic severe episodes of abdominal pain who were subjected to diagnostic laparoscopy. Extensive laboratory and imaging studies did not contribute to the diagnosis. Laparoscopic findings that identified the cause of abdominal pain were obtained in 12 of 13 patients. Laparoscopic appendectomy was performed in all patients. Follow-up varied from 6 months to 3 years. Abdominal pain resolved in 10 patients. It was concluded that diagnostic laparoscopy is a valuable procedure in the management of children with chronic recurrent abdominal pain. The study patients represented a subgroup of children with very severe symptoms of abdominal pain, all having required hospitalization and multiple imaging studies. Although they all were found to have an organic etiology for their pain, some of the etiologies may actually be debatable as causes of disease (for example, cecal adhesion or fibrosed appendix). Two patients required a second laparoscopy for complications related to the first one. No other study addresses laparoscopy or other procedures as treatments of recurrent abdominal pain.

SUMMARY

Chronic abdominal pain (long-standing intermittent or constant abdominal pain) is common in children and adolescents. In most children, chronic abdominal pain is functional, that is, without objective evidence of an underlying organic disorder. Yet, an important part of the physician's job is to determine which children have an organic disorder. A review of the current evidence, however, indicates that there are no studies showing that pain frequency, severity, location, or effects on lifestyle help to discriminate between functional and organic disorders. Children with chronic abdominal pain are more likely than children without chronic abdominal pain to have headache, joint pain, anorexia, vomiting, nausea, excessive gas, and altered bowel symptoms, but there is insufficient evidence that the presence of the associated symptoms can help the physician discriminate between functional and organic disorders. Although children with chronic abdominal pain and their parents are more often anxious or depressed, the presence of anxiety, depression, behavior problems, or recent negative life events does not seem to be useful in distinguishing between functional and organic abdominal pain.

There is evidence that children with functional abdominal pain can have symptom clusters characterized as functional dyspepsia, IBS, or abdominal migraine as well as isolated abdominal pain. Some patients have features of more than 1 type of functional abdominal pain.

The physician also must decide whether to order diagnostic tests and, if so, which tests. The presence of alarm symptoms or signs suggests a higher pretest probability or prevalence of organic disease and may justify the performance of diagnostic tests. Alarm symptoms or signs include but are not limited to weight loss, deceleration of linear growth velocity, significant vomiting, chronic severe diarrhea, evidence of gastrointestinal blood loss, persistent right upper or right lower quadrant pain, unexplained fever, family history of inflammatory bowel disease, or abnormal or unexplained physical findings. The predictive value of blood tests, with or without alarm signals, has not been studied adequately. There is no evidence to suggest that the use of ultrasonographic examination of the abdomen and pelvis in the absence of alarm symptoms has a significant yield of organic disease. There is little evidence to suggest that the use of endoscopy with biopsy or esophageal pH monitoring has a significant yield of organic disease in the absence of alarm symptoms.

There is limited evidence suggesting that daily stressors are associated with the occurrence of pain episodes and that higher levels of negative life events are associated with increased likelihood of symptom persistence. Some evidence suggests that patients

with chronic abdominal pain have more symptoms of anxiety and depression than do community controls and are at greater risk of later emotional symptoms and psychiatric disorders. However, there are no data on whether emotional or behavioral symptoms predict symptom severity, course, or response to treatment. Parents of patients with chronic abdominal pain seem to have more symptoms of anxiety, depression, and somatization than do parents of community controls or parents of other pediatric patients. However, families of children with chronic abdominal pain do not seem to differ from families of children without abdominal pain or families of patients with acute illness in broad areas of family functioning.

There have been few studies of the treatment of chronic abdominal pain in children. There is inconclusive evidence that a lactose-free diet decreases symptoms or that a fiber supplement decreases the frequency of pain attacks. There is inconclusive evidence of the benefit of acid suppression with H_2-receptor antagonists to treat children with dyspepsia. There is evidence that treatment for 2 weeks with peppermint oil may provide benefit in children with IBS. There is also evidence that cognitive-behavioral therapy may be useful in improving pain and disability outcome in the short term.

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APPENDIX 1. Summary of the Quality of the Evidence

Question	Evidence	Quality of Evidence
1	There is limited but credible evidence of the existence of functional dyspepsia, IBS, and abdominal migraine in children.	C
2	There are no studies of unselected patients showing that pain frequency, severity, location, or effects on lifestyle are able to distinguish between functional and organic disorders.	C
2	Children with recurrent abdominal pain are more likely than children without recurrent abdominal pain to have headache, joint pain, anorexia, vomiting, nausea, excessive gas, and altered bowel symptoms. There are insufficient data to determine whether the presence of associated symptoms can help the physician to distinguish between functional and organic disorders.	C
2	The presence of alarm symptoms or signs suggests a higher pretest probability or prevalence of organic disease and may justify the performance of diagnostic tests. Alarm symptoms or signs include but are not limited to involuntary weight loss, deceleration of linear growth, gastrointestinal blood loss, significant vomiting, chronic severe diarrhea, persistent right upper or right lower quadrant pain, unexplained fever, and family history of inflammatory bowel disease.	D
3	There is no evidence to evaluate the predictive value of blood tests.	D
3	There is no evidence to determine the predictive value of blood tests in the face of alarm signals.	D
4	There is no evidence to suggest that the use of ultrasonographic examination of the abdomen and pelvis in the absence of alarm symptoms has a significant yield of organic disease.	C
4	There is little evidence to suggest that the use of endoscopy and biopsy in the absence of alarm symptoms has a significant yield of organic disease.	C
4	There is insufficient evidence to suggest that the use of esophageal pH monitoring in the absence of alarm symptoms has a significant yield of organic disease.	C
5	There is a small amount of evidence suggesting that the presence of recent negative life events is not useful in distinguishing between functional abdominal pain and abdominal pain of other causes.	B
5	There is limited evidence suggesting that daily stressors are associated with the occurrence of pain episodes and that higher levels of negative life events are associated with increased likelihood of symptom persistence.	C
5	There is no evidence on whether life stress influences symptom severity, course, or response to treatment.	D
5	There is evidence suggesting that the presence of anxiety, depression, or behavior problems is not useful in distinguishing between functional abdominal pain and abdominal pain of other causes.	B
5	There is evidence that patients with recurrent abdominal pain have more symptoms of anxiety and depression (internalizing emotional symptoms) than do healthy community controls.	B
5	In contrast, there is evidence that children with recurrent abdominal pain do not have higher levels of conduct disorder and oppositional behavior (externalizing emotional symptoms) compared with healthy community controls.	B
5	There are no data on whether emotional/behavioral symptoms predict symptom severity, course, or response to treatment.	D
5	There is evidence suggesting that children with recurrent abdominal pain are at risk of later emotional symptoms and psychiatric disorders.	B
5	There is evidence that parents of patients with recurrent abdominal pain have more symptoms of anxiety, depression, and somatization than do parents of community controls or parents of other pediatric patients.	C
5	There is some evidence that families of patients with recurrent abdominal pain do not differ from families of community controls or families of patients with acute illness in broad areas of family functioning, such as family cohesion, conflict, and marital satisfaction.	C
6	There is evidence that treatment for 2 wk with peppermint oil may provide benefit in children with IBS.	B
6	There is inconclusive evidence of the benefit of H_2 blockers to treat children with dyspepsia.	B
6	There is inconclusive evidence that fiber supplement intake decreases the frequency of pain attacks for patients with recurrent abdominal pain.	B
6	There is inconclusive evidence that a lactose-free diet decreases symptoms in children with recurrent abdominal pain.	B
6	There are limited data to suggest that pizotifen is efficacious in the treatment of abdominal migraine.	B
7	There is evidence that cognitive-behavioral therapy may be useful in improving pain and disability outcome in the short term.	B
8	There is no evidence of the possible beneficial role of surgery in the evaluation or management of children with recurrent abdominal pain.	D
8	There are no studies comparing diagnostic or therapeutic surgery with other approaches.	D

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