

Adult Outcomes of Pediatric Recurrent Abdominal Pain: Do They Just Grow Out of It?

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ABSTRACT. *Objective.* To determine whether medically unexplained recurrent abdominal pain (RAP) in childhood predicts abdominal pain, irritable bowel syndrome (IBS), other somatic complaints, and psychiatric symptoms and disorders in young adulthood.

Methods. A sample of 28 young adults evaluated for RAP between the ages of 6 and 17 years were compared with 28 individually matched former childhood participants in a study of tonsillectomy and adenoidectomy. RAP caseness was established by structured retrospective chart review requiring agreement by 2 independent reviewers. Standardized assessments of abdominal pain, IBS, other somatic symptoms, psychopathology, perceived health, and history of maltreatment were performed an average of 11.1 years after the index visit.

Results. Former RAP patients were significantly more likely than controls to endorse anxiety symptoms and disorders, hypochondriacal beliefs, greater perceived susceptibility to physical impairment, poorer social functioning, current treatment with psychoactive medication, and generalized anxiety in first degree relatives. There were trends suggesting associations between childhood RAP and lifetime psychiatric disorder, depression, migraine, and family history of depression, but group differences on abdominal pain, IBS, other somatic symptoms, and history of maltreatment were not statistically significant.

Conclusions. There is a strong and relatively specific association between childhood RAP and anxiety in young adulthood. Affected children may be at special risk to perceive physical symptoms as threatening, and should be evaluated for psychiatric disorder on initial presentation. *Pediatrics* 2001;108(1). URL: <http://www.pediatrics.org/cgi/content/full/108/1/e1>; *abdominal pain, anxiety, depression, colonic diseases, functional.*

ABBREVIATIONS. RAP, recurrent abdominal pain; FGD, functional gastrointestinal disorder; IBS, irritable bowel syndrome; DSM, Diagnostic and Statistical Manual of Mental Disorders; SCID-NP, Structured Clinical Interview for DSM-IV, Non-patient Version; BSI, brief symptom inventory; NS, not significant.

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Recurrent abdominal pain (RAP) has been most consistently defined in the pediatric literature as at least 3 episodes of abdominal pain occurring during a period of at least 3 months that are severe enough to affect the activities of the child.^{1,2} RAP is common, affecting between 7% to 25% of school-aged children and adolescents,^{1,3-11} and may be responsible for 2% to 4% of pediatric office visits.¹² RAP becomes more prevalent with increasing age into adolescence^{1,5,7,10} and is more common in girls,^{4,13} with an equal gender ratio in early childhood,^{11,14} but greater female symptom reporting in late childhood and adolescence.^{1,9,10} Specific structural, infectious, inflammatory, or laboratory abnormalities are unusual in RAP, particularly in the absence of "red flags" such as weight loss, gastrointestinal bleeding, pain awakening the child at night, systemic symptoms such as fever, or laboratory evidence of anemia or inflammation.¹⁵

Medically unexplained RAP is often considered to be a functional gastrointestinal disorder (FGD), a condition defined as a variable combination of chronic or recurrent gastrointestinal symptoms in the absence of explanatory structural or biochemical abnormalities.¹⁶ Irritable bowel syndrome (IBS) is a FGD characterized by recurrent abdominal pain or discomfort occurring over a 3-month period, where the symptoms are relieved by defecation and/or are associated with changes in stool frequency or consistency.¹⁷ Although available research is limited, there is some evidence that many children and adolescents with RAP will also meet criteria for IBS¹⁸ or other FGDs, such as functional dyspepsia, where the abdominal discomfort is centered in the upper abdomen and unrelated to bowel function.¹⁷

RAP has been consistently associated with comorbid symptoms of anxiety and depression in both clinical¹⁹⁻²² and community samples,^{7,11,23} as well as with other painful somatic symptoms such as headache,^{1,4,7,10,14,20,21} including migraine.^{3,8,9} RAP has also been associated with functional impairment, particularly school absenteeism,^{7,19-22} and with greater risk for potentially dangerous and unnecessary medical investigations and procedures.²⁴ Maltreatment has been associated with functional abdominal pain in childhood²⁵ and adulthood.²⁶

Implications of pediatric RAP across the lifespan are not well understood. Early follow-up studies reported persistence of recurrent abdominal pain into

adulthood for one third to one half of affected children,^{24,27,28} but are limited by the lack of standardized assessments and formal diagnostic criteria, and none used any formal assessment of psychopathology. In more recent studies using standardized assessments and control groups, former RAP patients reported significantly greater abdominal pain, other somatic symptoms, functional impairment, health service use, and internalizing psychiatric symptoms in comparison to controls at 5-year follow-up, and females with a history of RAP were significantly more likely to meet diagnostic criteria for IBS.^{29,30} A large, population-based cohort study of adults born in 1946 in the United Kingdom compared the 2% of the sample who consistently reported medically unexplained abdominal pain at ages 7, 11, and 15 years with study participants without a history of chronic abdominal pain on the basis of standardized assessments when participants were 36 years old. Persistent abdominal pain in childhood was significantly associated with an increased risk of psychiatric disorder in adulthood, but not with abdominal pain or headache once psychiatric disorder was controlled for in the regression.³¹

In this study, young adults with a history of RAP in childhood were compared with adults with a history of nongastrointestinal pediatric illness. We hypothesized that adults with a history of pediatric RAP would be significantly more likely to report: 1) a personal and family history of psychiatric symptoms and disorders; 2) a personal and family history of recurrent abdominal pain, IBS, and other somatic symptoms and disorders; 3) greater subjective sensitivity to bodily sensations and illness worry; 4) higher health and mental health service use; and 5) a history of maltreatment in childhood.

METHODS

Case Identification and Recruitment

The Human Rights Committee of the Children's Hospital of Pittsburgh granted study approval. Potential RAP patients were identified from records of the pediatric gastroenterology section and a group of academic general pediatricians at the Children's Hospital of Pittsburgh. Both groups had organized records by presenting complaints and diagnostic categories in the 1980s, including medically unexplained abdominal pain. Charts of children between the ages of 6 and 17 years at the time of the index visit with a birth date of 1979 or earlier with presumably medically unexplained abdominal pain were reviewed independently by the principal investigator (J.V.C.) and a pediatric gastroenterologist (C.D.L.) using a chart review instrument developed for the study. At least 3 episodes of medically unexplained abdominal pain occurring during a period of at least 3 months that were severe enough to affect the activities of the child were necessary for inclusion. Criteria for exclusion included: abdominal pain with atypical features, symptoms, or findings suggestive of physical disease (eg, abnormal physical examination or laboratory findings, persistent vomiting, gastrointestinal bleeding, constitutional symptoms such as fever or weight loss); acute or chronic physical disease; and development disability. There were 133 charts reviewed, with reviewers both agreeing that 49 cases met study criteria for RAP.

An introductory letter and consent form were sent to the most recent address, followed by an effort to contact the potential participant by telephone approximately 1 week later. If the initial letter was returned and/or available telephone numbers incorrect, efforts were made to track the patient by directory assistance or via social security numbers from the records. Initial contact was established with 34 potential RAP participants (contact rate 69%),

with only 4 (all male) declining to participate (refusal rate: 12%). Two RAP participants withdrew from the study, leaving 28 consenting RAP participants. Controls were former participants in a study of tonsillectomy and adenoidectomy in childhood, conducted by Dr Jack Paradise and colleagues, who were matched to consenting RAP patients from an existing computerized database. An effort was made to identify at least 3 potential controls for each consenting RAP participant given the difficulty of tracking, and a procedure identical to that used to find and recruit potential RAP patients was then used. From an initial list of 83 potential controls, initial mailings were sent to 63 and contact was established with 34 (contact rate: 54%). Of these, 28 agreed to participate, 3 declined (all male; refusal rate: 9%), 2 were deceased, and 1 was not eligible to participate because of a history of childhood RAP.

Participants were mailed questionnaires with a stamped, self-addressed return envelope after informed consent was obtained. A single experienced psychiatric interviewer who was blind to participant status subsequently conducted a telephone interview. Psychiatric assessments were conducted first and participants were advised to avoid volunteering their participant status or any unsolicited medical history. The interviewer was not aware of the nature of the control group, and was advised that complaints of gastrointestinal symptoms in adulthood were common and not necessarily indicative of childhood RAP. Psychiatric interviews were reviewed with the principal investigator (J.V.C.) without the interviewer identifying the participant by name or study number. Participants who completed the study received payment of \$50 in consideration of their efforts.

Sample Characteristics (Table 1)

Twenty-eight RAP participants (21 females, 7 males) were successfully recruited. Mean age was 12.6 years (standard deviation [SD]: 2.4) at the index visit and 23.7 years (SD: 3.1) at the time of assessment, an average of 11.1 years (SD: 2.7) later. One participant was black and the remainder white. Twenty-eight comparison participants individually matched for age, gender, race, and parental occupation at the index pediatric visit were identified, tracked, and successfully recruited by an analogous procedure. The groups did not differ in current marital, employment, or educational status. One RAP participant failed to return completed questionnaires, but all participants completed the telephone interview, leaving 27 and 28 patient-control pairs available for analysis of questionnaire and interview based data, respectively.

Measures

- The RAP Chart Review Instrument was developed for this study. Examination of case notes seems to be a reliable method of determining whether symptoms may be considered medically unexplained by other physicians.³² Four criteria had to be met to be classified a RAP case (ie, >3 episodes of abdominal pain with functional impairment; unremarkable physical examination; unremarkable diagnostic investigations; absence of features suggesting physical disease). Of the 133 charts reviewed, reviewers independently agreed that 37 cases met study criteria and 71 did not. Reliability was good ($\kappa = 0.76$). After joint review of the 25 charts where reviewers had initially disagreed, 12 cases met RAP case criteria by consensus (overall agreement: 81%).
- Structured Clinical Interview for *Diagnostic and Statistical Manual of Mental Disorders-Fourth Edition (DSM-IV)*, Non-Patient Version (SCID-NP) is a standardized clinical research interview for psychiatric disorders³³ based on *DSM-IV*³⁴ criteria.

TABLE 1. Demographics

| | Cases (n = 28) | Controls (n = 28) |
|---------------------------------|-------------------|----------------------|
| Sex (% female) | 75.0 | 75.0 |
| Race (% white) | 96.4 | 96.4 |
| Age (mean [standard deviation]) | 23.7 (3.1) | 23.8 (3.0) |
| Marital status (% single) | 72.0 | 76.0 |
| Employment status (% employed) | 80.0 | 80.0 |
| Education (% college graduate) | 28.0 | 24.0 |

- Brief Symptom Inventory (BSI) is a 53-item, psychometrically sound measure of psychiatric distress in adults, generating 3 global indices and 9 primary symptom dimensions, including somatization, anxiety, and depression.³⁵
- Somatosensory Amplification Scale is a brief, easily completed 10-item scale that measures individual sensitivity to various unpleasant but nonpathological bodily and environmental sensations, and correlates with hypochondriacal attitudes.³⁶
- The Illness Attitude Scale is a 28-item instrument designed to measure attitudes, fears, and beliefs associated with hypochondriasis and abnormal illness behavior with good stability and known-groups validity.³⁷
- The Supplemental Interview for Forms of "Affective Spectrum Disorder" is a standardized interview using the SCID format that was modified to diagnose IBS, migraine, chronic fatigue syndrome, and fibromyalgia.³⁸
- The Bowel Disease Questionnaire is a reliable, self-report measure of gastrointestinal and physical symptoms.³⁹
- The MOS 36-Item Short-Form Health Survey (SF-36) is a standardized, self-report questionnaire with acceptable psychometric properties that assesses physical function, social function, pain, psychological well-being, impairment attributable to emotional problems, energy, and general health perceptions.⁴⁰
- Health and Mental Health Service Use was assessed retrospectively over the previous 6 months using a set of questions developed for this study.
- Child Maltreatment History Self-Report is a questionnaire used to assess history of childhood physical and sexual maltreatment in the Ontario Health Supplement.⁴¹
- Family Informant Schedule and Criteria (revised for *DSM-IV*; FISC-IV) is an interview assessment of family history of psychiatric disorders updated to be compatible with *DSM-IV*.⁴² The interview was modified to include a supplement assessing for family history of IBS, migraine, chronic fatigue syndrome, fibromyalgia, somatization disorder, hypochondriasis, and other somatoform disorder. Proband was asked to provide information about all first-degree relatives.

Data Analysis

Patients and controls were matched based on race, sex, age, and parental occupation. Pair-wise analyses were performed for all outcomes. Data were examined for normality using the Shapiro and Wilks *W* statistic.⁴³ RAP patients and controls were compared using paired *t* tests and McNemar's test for agreement. For significantly non-normal distributions, Wilcoxon Sign Rank tests were used. In the case of zero cells, the binomial test was performed to compare proportions. Differences between patients and controls at the *P* = .05 level were considered statistically significant, with trends in the data being reported for items where the effect size was 0.4 or greater.

RESULTS

Psychiatric Symptoms and Disorders (Tables 2 and 3)

RAP patients were significantly more likely to meet criteria for a lifetime (46.4% vs 17.9%, *P* = .04) and current (21.4% vs 0%, *P* = .01) history of anxiety disorder. Regarding specific anxiety disorders associated with childhood RAP, a lifetime history of so-

cial phobia was noted in 7 participants (25%), panic disorder in 5 (18%), generalized anxiety disorder in 4 (14%), anxiety disorder not otherwise specified in 4 (14%), obsessive compulsive disorder in 3 (11%), and posttraumatic stress disorder in 3 (11%); the most common current anxiety disorders were generalized anxiety disorder (14%), anxiety disorder not otherwise specified (14%), and social phobia (11%). There were also trends suggesting differences between the groups on probable or definite lifetime history of at least 1 *DSM-IV* categorical psychiatric disorder (82.1% vs 53.6%, *P* = .08) and lifetime history of mood disorder (57.1% vs 28.6%, *P* = .08). RAP patients were also significantly more likely to endorse symptoms of anxiety than controls on the BSI self-report, with significant differences noted on the Anxiety (*P* < .001), Phobic Anxiety (*P* = .04), and Obsessive-Compulsive subscales (*P* = .006), the Positive Symptom Total (*P* = .03), and on the Global Severity Index (*P* = .01), the most sensitive single indicator of overall distress on the BSI.

Somatic Symptoms and Disorders (Tables 2 and 3)

There were trends suggesting that RAP patients were more likely to interrupt activities because of abdominal pain (40% vs 12%, *P* = .07), to report a history of appendectomy (11.1% vs 0%, *P* = .08), and to score higher on the Somatization subscale of the BSI (*P* = .06) than controls. There was also a trend suggesting that RAP patients endorsed a greater mean number of somatic symptoms on the SCID-NP (4.0 vs 2.3, *P* = .12). One third of RAP patients endorsed a history of migraine, over twice as many as controls, with a trend toward statistical significance (35.7% vs 14.3%, *P* = .07), but RAP patients were not significantly more likely to report a history of headache (53.6% vs 42.9%, not significant [NS]), abdominal pain (70.4% vs 44.4%, NS), or recurrent abdominal pain (51.9% vs 25.9%, NS) in the previous year than controls. Although approximately one third of the RAP group met criteria for IBS, patients and controls did not differ significantly on interview measures of IBS (39.3% vs 21.4%, NS), or on self-report measures of IBS (29.6% vs 22.2%, NS) or dyspepsia (33.3% vs. 22.2%, NS). None met criteria for chronic fatigue or fibromyalgia. A somatoform disorder could be diagnosed in 28.6% of RAP patients in comparison to 17.9% of controls, but differences were not significant. Females with RAP did not differ

TABLE 2. Interview Diagnoses (From SCID and Supplemental Interview for Forms of Affective Spectrum Disorder)

| | Cases (<i>n</i> = 28) | | Controls (<i>n</i> = 28) | | Test | <i>P</i> Value |
|---------------------------------|------------------------|------|---------------------------|------|----------|----------------|
| | <i>N</i> | % | <i>n</i> | % | | |
| Lifetime | | | | | | |
| Any psychiatric disorder | 23 | 82.1 | 15 | 53.6 | McN | .08 |
| Any mood disorder | 16 | 57.1 | 8 | 28.6 | McN | .08 |
| Any anxiety disorder | 13 | 46.4 | 5 | 17.9 | McN | .04 |
| Current | | | | | | |
| Any anxiety disorder | 6 | 21.4 | 0 | 0.0 | Binomial | .01 |
| Migraine | 10 | 35.7 | 4 | 14.3 | McN | .07 |
| Mean number of somatic symptoms | 4.0 (3.9) | | 2.3 (1.9) | | WSR | .12 |

McN indicates McNemar; WSR, Wilcoxon Sign Rank.

TABLE 3. Self Reports (*n* = 27)

| | Cases (<i>n</i> = 28) | | Controls (<i>n</i> = 28) | | Test | <i>P</i> Value |
|---------------------------------------|------------------------|-------------|---------------------------|-----------|-----------------|----------------|
| | Mean (SD) | Mean (SD) | Mean (SD) | Mean (SD) | | |
| BSI | | | | | | |
| Somatization (<i>n</i> = 26) | 5.3 (5.1) | 2.8 (2.5) | | | <i>t</i> = 1.94 | .06 |
| Obsessive-compulsive (<i>n</i> = 26) | 6.6 (4.3) | 3.4 (3.2) | | | <i>t</i> = 3.00 | .006 |
| Interpersonal sensitivity | 3.5 (2.7) | 2.3 (1.7) | | | <i>t</i> = 1.92 | .07 |
| Anxiety | 6.0 (3.7) | 2.6 (2.3) | | | <i>t</i> = 5.02 | <.001 |
| Phobic anxiety | 1.8 (2.7) | 0.6 (1.0) | | | WSR | .04 |
| Positive symptom total | 24.2 (12.5) | 16.2 (10.4) | | | WSR | .03 |
| Global severity index | 0.8 (0.5) | 0.4 (0.3) | | | <i>t</i> = 2.72 | .01 |
| Illness Attitude Scale | | | | | | |
| Hypochondriacal beliefs | 4.7 (2.6) | 3.5 (1.1) | | | WSR | .03 |
| Thanatophobia | 5.7 (2.4) | 4.5 (2.0) | | | <i>t</i> = 1.85 | .08 |
| Bodily preoccupation | 5.1 (2.0) | 4.2 (1.3) | | | <i>t</i> = 1.71 | .10 |
| Effect of symptoms | 5.9 (2.9) | 4.3 (1.9) | | | WSR | .04 |
| MOS | | | | | | |
| Role-physical | 7.3 (1.1) | 7.9 (0.4) | | | WSR | .04 |
| Social functioning | 6.0 (4.3) | 7.4 (4.1) | | | WSR | .02 |

WSR indicates Wilcoxon Sign Rank.

from controls on menstrual complaints or irregularities.

On the Illness Attitude scale, RAP participants scored significantly higher on the Hypochondriacal Beliefs subscale, reflecting greater concerns about undiagnosed physical disease, and on the Effect of Symptoms subscale, suggesting greater perceived susceptibility to functional impairment by pain and other physical symptoms. There were trends toward significance on the Bodily Preoccupation and Thanatophobia subscales, reflecting hypervigilance to physical sensations and fear of death, respectively. Although the RAP group scored somewhat higher on the Somatosensory Amplification Scale, suggesting greater sensitivity to somatic sensations, the difference was not statistically significant.

Health and Health Service Use (Tables 3 and 4)

Control participants made significantly more physician visits in the previous 6 months than RAP participants (*P* = .003). RAP participants were nevertheless significantly more likely to describe themselves as impaired by physical symptoms and concerns than controls on the MOS 36-Item Short-Form Health Survey, and also rated themselves as doing poorer socially. RAP participants were significantly more likely to report current treatment with psychoactive medication, and although greater use of mental health services was suggested by more than half

of RAP participants endorsing some lifetime history of mental health treatment (59.3% vs 37.0%), differences between the groups were not significant.

History of Maltreatment

Rates of reported maltreatment in childhood were relatively low in both groups. Physical abuse was reported by 18.5% and sexual abuse by 7.4% of RAP participants compared with 3.7% and 7.4% of controls, respectively. Differences were not significant.

Family History (Table 4)

Participants with a history of childhood RAP were significantly more likely to report having a first-degree relative with generalized anxiety disorder, the most common anxiety disorder reported by participants (40.7% vs 11.1%, *P* = .04), and there was a trend suggesting group differences on family history of major depression (44.4% vs 18.5%, *P* = .09). The groups did not differ significantly on family history of IBS, migraine, somatoform disorder, hypochondriasis, alcoholism, substance abuse, or antisocial personality.

CONCLUSION

This is the first systematic follow-back study of pediatric RAP to use a control group with a history of physical illness in childhood and to use standardized assessment interviews for psychiatric disorder,

TABLE 4. Family History and Medical History

| | Cases (<i>n</i> = 28) | | Controls (<i>n</i> = 28) | | Test | <i>P</i> Value |
|---|------------------------|------|---------------------------|------|----------|----------------|
| | <i>N</i> | % | <i>n</i> | % | | |
| Family History | | | | | | |
| Major depression | 12 | 44.4 | 5 | 18.5 | McN | .09 |
| Generalized anxiety | 11 | 40.7 | 3 | 11.1 | McN | .04 |
| Medical History | | | | | | |
| >1 Physician visits—past year | 14 | 50.0 | 25 | 89.3 | McN | .003 |
| Current psychiatric meds | 4 | 14.3 | 0 | 0.0 | Binomial | .05 |
| History of appendectomy | 3 | 11.1 | 0 | 0.0 | Binomial | .08 |
| Interrupted activities attributable to abdominal pain | 10 | 40.0 | 3 | 12.0 | McN | .07 |

McN indicates McNemar.

IBS, and migraine. A history of childhood RAP seems to be associated with anxiety and anxiety disorders in adulthood, and generalized anxiety is more common in the families of affected children than in those of controls. Differences between RAP patients and controls also approached statistical significance for mood disorder and psychiatric disorder in general, with the percentages reported being quite high by community standards and suggesting that a history of childhood RAP is associated with a heightened risk of both anxiety and depressive disorders in adulthood. Comorbid psychopathology in individuals with IBS has been considered related to health care seeking rather than characteristic of FGD,⁴⁴ although recent data suggest that FGD and psychiatric disorder may be related regardless of treatment seeking status.⁴⁵ The use of a physically ill control group and the finding that controls used significantly more health services in adulthood suggest that there may be a specific association between RAP and anxiety disorder in excess of the risk conferred by physical illness and associated medical help seeking per se.

Although there were trends in the data suggesting that RAP participants were more likely to report common somatic symptoms and migraine, differences between the groups failed to reach statistical significance. The failure to show significant differences in the prevalence of IBS and somatoform disorders between RAP participants and controls was surprising, but consistent with the results of Hotopf and colleagues,³¹ who found persistent pediatric abdominal pain to be associated with an increased risk of psychiatric disorder in adulthood, but not a comparatively heightened risk of abdominal pain or other physical symptoms after controlling for psychiatric disorder. Our results suggest that pediatric RAP is likely a better predictor of emotional disorder than of somatic disorders and FGD in adulthood. Given our small sample size, a meaningful regression analysis addressing whether trends toward greater somatic symptom reporting in the RAP group would fall away once psychiatric disorder was controlled for in the analysis was not feasible. The relatively high rate of migraine in young adults with a history of childhood RAP is nevertheless intriguing given reports that RAP may bear a special association with headache⁵ and migraine^{3,8,9} in childhood, and the consistent association of migraine with anxiety and depression⁴⁶ and with IBS in adults.⁴⁷

The relatively specific association between RAP and anxiety across the lifespan is in keeping with previous studies documenting a strong and consistent association between RAP and anxiety during childhood.^{7,19,20,21} Trait anxiety may correlate positively with the severity, frequency, and duration of pediatric abdominal pain.⁷ Both community- and clinic-based studies of adults with IBS have similarly documented a powerful association between IBS and anxiety disorders,^{45,48} and adults reporting abdominal pain and changes in bowel habits in response to stress report higher levels of trait and state anxiety.⁴⁹ Conversely, children with anxiety disorders commonly report abdominal pain and other somatic symptoms,^{50,51,52} and somatic complaints have been

uniquely related to pediatric anxiety in selected studies.⁵³ Several studies have failed to find significant differences between children with RAP and psychiatric comparison participants on measures of anxiety, although psychiatric groups score higher on measures of disruptive behavior and depression.^{19–21}

Our finding that RAP participants and controls differed primarily on family history of anxiety but not IBS provides additional support for the association between RAP and anxiety. This finding is consistent with the results of a recent family study which found that first degree relatives of adult IBS probands were no more likely to suffer from FGD than those of comparison participants who had undergone cholecystectomy, but were significantly more likely to suffer from anxiety and depressive disorders.⁵⁴ Parents of children with RAP report higher levels of anxiety, depression, and somatic symptoms than those of unaffected controls,^{8,11,19,20,55} with levels of anxiety²⁰ and depression indistinguishable from mothers of psychiatrically referred children.^{19,55} In addition, children of parents with anxiety disorders report more somatic complaints than children of nonanxious parents.⁵⁶

Contrary to expectations, controls used significantly more health services in adulthood, although RAP participants were more likely to be taking psychoactive medications. Nonetheless, adults with a history of RAP were more likely to suffer from hypochondriacal fears and perceive themselves as susceptible to impairment by physical illness. It has previously been suggested that childhood RAP may be associated with heightened sensitivity to visceral sensations⁵⁷ and a vulnerability to respond to life stress with somatic symptoms.^{2,58} Children with RAP have long been described as temperamentally anxious and inhibited^{1,59} and as more likely to withdraw in novel situations.⁶⁰ Such temperamental characteristics have been associated with a heightened risk for anxiety disorder later in life⁶² and greater vulnerability to activate neural circuits that generate distress responses to potentially threatening or uncertain stimuli.⁶¹ Differences in temperament may also be linked to differences in biobehavioral reactivity.⁶³ Temperamentally anxious children may be more likely to report somatic symptoms than noninhibited peers,⁶⁴ and to perceive novel bodily sensations as threatening in a manner consistent with that described by Barsky and colleagues⁶⁵ in the conceptualization of "somatosensory amplification."

It has been argued that children with RAP likely represent a heterogeneous population from both the physical and psychosocial perspectives.^{57,66} Efforts are now underway to better categorize children with RAP, including the use of a newly developed classification system for pediatric FGDs.¹⁷ Although such efforts deserve empirical study, this diagnostic system has not yet been validated, and its reliability remains unknown. The investigation of physical and psychiatric comorbidity in pediatric RAP may contribute to the identification of relevant subtypes of the disorder, and information regarding differential associations between RAP, anxiety, and other comorbid conditions such as depression or migraine may

provide clues to cause. If the observed comorbidity between RAP and anxiety does not prove artifactual, the relationship may be understood by virtue of a causal model where one disorder essentially causes the other, or by a shared vulnerability model, with the comorbid conditions sharing an underlying risk factor or factors or representing different stages of the same disease or pathophysiologic process.⁶⁷

This study suffers from a number of potential limitations. Like most studies of RAP, this was a referred sample from a specialized care setting. The charts examined may not have been representative of a random sample of referred children with medically unexplained RAP given the possibility of clinician bias when a registry for “functional” abdominal pain was first created. Despite efforts to minimize assessment bias by performing the psychiatric interview before physical health history, it was also difficult to insure blind psychiatric assessment and scoring of interviews in all cases. The sample is predominantly female, perhaps limiting conclusions that can be drawn about males with RAP, as one population-based study identified an association between RAP and anxiety in girls, but not boys.²³ Finally, the rates of psychopathology and somatic symptoms in the comparison group were quite high, perhaps providing an overly rigorous test of study hypotheses. This could be derivative of the small sample size or problems in measurement, but may also reflect a truly increased risk of psychopathology and somatic complaints in our chosen control group. Some participants in the tonsillectomy and adenoidectomy study could have been self-referred, and not all met criteria for surgical intervention, perhaps being added to the pool primarily because of parental concern about illness rather than objective disease. Febrile illness and infections during early childhood have been associated with subsequent anxiety disorders,⁶⁸ and pediatric physical illness has been associated with a heightened risk for psychiatric disorder across development,⁶⁹ with allergic disorders specifically being associated with depression⁷⁰ and behavioral inhibition.⁷¹

Clinicians should nevertheless be reluctant to dismiss medically unexplained RAP as a completely benign condition or a transient reaction to stress, and children with RAP should be carefully evaluated for psychiatric disorder, particularly anxiety. Current referral rates of patients with RAP to mental health professionals seem to be low, possibly reflecting difficulties in recognizing emotional disorder, concerns about cost, sensitivity to stigma, the belief that the disorder will remit on its own, and/or a lack of faith in available mental health professionals and interventions.⁷² Internalizing disorders such as anxiety and depression may be especially difficult for pediatricians to detect, so recognition of more readily identified disorders such as RAP could increase the likelihood of recognition for children with and at risk for emotional disorder. The consistent association of RAP with anxiety suggests that future research examine the nature of the observed comorbidity and whether there are additional risk factors that might predispose individuals with an anxious diathesis to

develop RAP. Given the existence of efficacious psychotherapeutic⁷³ and psychopharmacologic⁷⁴ treatments for pediatric anxiety disorders, it seems relevant to explore whether successful treatments for anxiety might be worthy of investigation in the management of pediatric RAP, as well as whether the early identification and treatment of children with RAP might alter the difficult life trajectory of affected children.

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