

## Recurrent Abdominal Pain in Childhood: The Functional Element

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Many children report chronic abdominal pain that is severe and disruptive to normal lifestyle and schooling. Assessment and management depends on indentifying those with underlying organic disease, such as chronic infection, celiac disease or inflammatory bowel disease, but avoiding unnecessary invasive investigations. In those with a functional gut disorder, the aim of therapy is reassurance, a return to normal activity and symptom control. We address the evidence for the use of investigative and management strategies in situations where recurrent abdominal pain is likely to be a functional disorder. Epidemiological studies of European and American populations show that organic causes are uncommon, and that chronic abdominal pain is a risk factor for functional gut disorders in adulthood. There is a paucity of high quality therapeutic trials, none showing conclusive evidence of benefit. Psychological interventions, such as cognitive behavioral and family therapy are effective, reducing symptoms and improving school attendance. Asian studies suggest gastrointestinal infection, such as giardiasis, are common causes of recurrent abdominal pain, but that functional abdominal pain is also prevalent.

**Key words:** *Abdominal pain, Functional, Recurrent.*

**R**ecurrent abdominal pain (RAP) is a presenting feature of many diseases. However, RAP is also a common childhood experience, and most often this is in the absence of significant organic pathology(1-5). It is commonly a cause of significant anxiety for carers, with both a fear of serious disease and a feeling of helplessness in their inability to relieve pain(6). It is this dichotomy that presents the physician with a difficult task; to reassure the majority of families without subjecting the child to extensive unnecessary medical investigations, while ensuring that significant pathologies are not missed.

### CLASSIFICATION

Recurrent abdominal pain is a symptom, not a diagnosis. The seminal work of Apley and Naish, who studied 1000 school children in Bristol, England, used a pragmatic definition of 3 episodes over 3 months, severe enough to affect daily activity to define recurrent abdominal pain (RAP)(1). In

previous clinical practice, RAP was adopted as a diagnostic label in children that presented with longstanding abdominal pain in whom no pathology to explain the symptoms was found. This reflected a previous lack of well defined diagnostic labels for functional gut disorders. The Rome Foundation addressed this in their Rome II consensus statements on the criteria for functional gut disorders, which included definitions for pediatric disorders(7). The updated statement, Rome III, has two pediatric categories divided by age, and includes abdominal pain of greater than 8 weeks duration as part of the definition of several of the functional gut disorders(8,9).

### EPIDEMIOLOGY

European and American community based epidemiological studies have found prevalence rates of RAP varying between 0.5% and 19%(3-8). Apley and Naish found that the incidence of detectable pathology in RAP was only 8%(1). This reflected the

era in which the study was done, when endoscopy and many other current investigations were not available. More recent studies, with analysis of the results of investigations in selected cohorts, have found rates of pathology in up to 30% in a tertiary referral setting(2-4). In the present day Western setting, irritable bowel syndrome is the commonest cause of functional RAP in children, accounting for 52% of cases(3,4).

The diagnosis of RAP may differ in developing countries compared to Western Nations, as infective causes are more prevalent and inflammatory bowel disease is less common(9-13). Cohort studies from India and Pakistan suggest that RAP is most likely to have an organic cause (up to 82% of cases), with giardiasis being the most common underlying condition(14,15). However, another Indian cohort and a Sri Lankan cohort showed that non-organic RAP is more prevalent (74% and 76%, respectively)(16,17). In Malaysia, both urban and rural population-based cohorts had a similar prevalence of RAP at 9.6% and 11%, respectively (18,19).

#### **PATHOPHYSIOLOGY**

In adults, functional bowel disorders have been subject to many studies examining underlying pathophysiological mechanisms. Familial clustering in IBS may reflect genetic rather than social factors(20). Recent interest has focussed on immune, neuronal and genetic factors underlying the development of IBS. Evidence of subtle immune dysregulation includes abnormal pro-inflammatory (Th1-type) cytokine profiles in peripheral lymphocytes, and quantitative differences in the T-lymphocytes within the mucosa(21,22). The neurotransmitter serotonin, predominantly found in the enterochromaffin cells, and its receptor is depleted in the rectal mucosa in IBS(23). Recent data has implicated genetic variants affecting the serotonin receptor gene expression in IBS(24).

#### **ASSESSMENT**

The evaluation of the child with abdominal pain is directed primarily to determine the likelihood of serious pathology and to direct investigations appropriately. The key to this is a thorough multisystem review of symptoms and examination.

There are several “red flag” symptoms and signs to alert the clinician to those at potentially higher risk of significant pathology(25). These include presence of involuntary weight loss, reduced growth, significant vomiting, chronic severe diarrhea, bleeding per-rectum, hematemesis, unexplained fever and a family history of IBD.

The American Academy of Pediatrics technical report concluded that there is insufficient evidence to evaluate the predictive value of blood investigations for organic pathology, even in the presence of alarm signals(25). Also, ultrasonography, pH probe studies and endoscopy have little diagnostic yield in absence of alarm signals. Interestingly, the presence of a detectable gastrointestinal disorder does not always determine the cause of RAP, for example *Helicobacter pylori* infection is as common in children with RAP as those without it(26). Thus, the history and examination should determine the appropriate level of investigation. It is the practice of most hospital pediatricians to at least undertake a set of basic blood investigations including: full blood count with differential, inflammatory markers (eg. C-reactive protein, erythrocyte sedimentation rate) urea and electrolytes, liver function tests and, serological screening for celiac disease. Urinary tract infection should be considered. Further investigations depend on the possible differential diagnosis. In a tertiary hospital setting, the commonest organic causes include gastro-esophageal reflux disease (8.7%), Crohn’s disease (7%), Celiac disease (4%), duodenal ulcer (1%), food allergy (1%) and *Helicobacter pylori* gastritis (8%). If celiac screen (anti-endomysial antibodies) is positive, then a small bowel biopsy is indicated for definitive diagnosis; if inflammatory bowel disease (IBD) is suspected, then upper and lower gastrointestinal endoscopy is indicated(27).

The role of disordered gut motility in RAP is not clear and at present motility studies are appropriate only in a research setting.

#### **MANAGEMENT**

Most cases of RAP do not require any treatment other than reassurance that there is no evidence of underlying organic pathology. In those that have significant persistent symptoms, finding an effective

treatment can be difficult and may need multidisciplinary approach and involve the family.

### **Medications**

There are few well-designed clinical trials examining drug efficacy in functional bowel disorders in children(28). Symptoms of functional dyspepsia responded poorly to acid reduction therapy with a H2-blocker, famotidine 0.5mg/kg twice daily, for at least 2 weeks(29). Anti-spasmodics are often prescribed for pain relief in IBS, on short term trial basis. Of these, only peppermint oil (one or two capsules three times daily) has been found to be effective in reducing symptom severity in children with IBS in a single small randomised-controlled trial(30). Abdominal migraine can be prevented or attacks ameliorated by using a serotonin 2A receptor antagonist, pizotifen 0.25mg twice or three times daily(31).

### **Dietary management**

Food allergy and intolerance is common in small children, and dietary manipulation is often attempted by families prior to seeking advice from health professionals. In practice, however, this is rarely effective, and puts children at risk of nutrient deficiency (eg dairy food exclusion resulting in suboptimal calcium intake). Careful history-taking will usually identify those with food allergies or intolerances. Lactose intolerance is relatively rare in Caucasian populations, but is more common in African and South East Asians in whom levels of lactase in small intestinal mucosa decline after infancy. However, there is little conclusive evidence that RAP is ameliorated by a lactose free diet in either lactase-deficient or lactase-sufficient children(32).

Dietary fiber is often low in the Western diet. Supplementing this has been evaluated in a small randomized, double-blind placebo-controlled trial of 52 children in a primary care setting. More children in fibre-supplemented group (13/26) had fewer episodes of pain than those with placebo (7/26), an effect that reached statistical significance(33).

In recent years, probiotics (foods that include live health-promoting bacteria) and prebiotics (food that

encourage growth of endogenous health-promoting bacteria) have gained popularity. The concept that “healthy bacteria” can redress an imbalance within the gut that causes RAP is an attractive one. However, the small randomized-controlled trials using *Lactobacillus* GG for IBS have shown conflicting results(34,35).

### **Psychological management**

In the biopsychosocial model of functional disorders, non-organic abdominal pain is multifactorial, with contributions from learned-behaviour in response to environmental and social stimuli that interact with the child’s experience of physical illness. This hypothesis is supported by psychological studies showing altered subminimal responsiveness to pain- and stress-related cues(36). Epidemiological studies suggest that maternal anxiety is an important predictor of health-seeking in young children with RAP and it is also associated with RAP and anxiety disorder later in childhood(37). Adolescents with RAP often have maladaptive coping strategies(38,39). Psychological interventions including family therapy and cognitive behavioural therapy are effective in reducing the severity and duration of symptoms and improving school attendance(40,41).

### **PERSONAL PRACTICE**

The key to managing RAP is a detailed history including psychological, family and school history, a thorough physical evaluation, appropriate investigations and building an effective therapeutic relationship with the patient and carers. The likelihood of a functional disorder as the cause should be openly discussed at the first consultation. The concept of “visceral hyperalgesia” is useful to explain pain in the absence of disease(42). This phenomenon can be compared to functional tension headaches, something most adults have experienced. Normal results from initial investigations reinforce that the pain has not arisen from a harmful process. Invasive tests such as endoscopy and pH probe studies are reserved for those with “red flag” symptoms. Trials of medical therapy are best time-limited and with specific measurable outcome criteria to assess their efficacy. Laxatives or anti-motility drugs can be helpful to improve symptoms

when there is associated constipation or diarrhea, respectively. There is no evidence to support blind *H. pylori* eradication therapy(43). Reassurance is central to management, with the caveat that if symptoms change, reassessment is required.

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