How to approach a child with recurrent abdominal pain?

Alexandra Papadopoulou
Athens Interconnected Children’s Hospitals «AGIA SOFIA» and “P & A KYRIAKOU”
Diagnostic criteria for RAP

At least three episodes of abdominal pain within 3 months, with pain severe enough to interfere with normal functioning

Apley, Arch Dis Childh 1958;33:165

>90% of no organic cause

Age of onset of pain in 115 children with RAP out of 1,000 school children

Differential diagnosis in infants

- Colics
- Infection
- Food Allergy
- GERD
- Pyloric stenosis (2-10 weeks)
- Constipation/dyschezia
Differential diagnosis in toddlers

- Toddler’s diarrhea
- Lactose/fructose malabsorption
- Constipation
- Coeliac disease, cystic fibrosis
- Eosinophilic disorders,
- Infection
Differential diagnosis in children

- Functional abdominal pain
- Lactose/fructose malabsorption
- Infection
- Peptic ulcer disease
- Hepatic, biliary or pancreatic disease
- Coeliac disease, eosinophilic disorders, cystic fibrosis
- Inflammatory bowel disease
- Eosinophilic gastroenteritis
- Other causes (immunodeficiency, Shönlein Henoch purpura)
History to be obtained at the initial visit for children with chronic abdominal pain

<table>
<thead>
<tr>
<th>Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset and course of pain</td>
</tr>
<tr>
<td>Timing, location, character, radiation of pain</td>
</tr>
<tr>
<td>Severity of pain reported by child and parent. Assessed by a pain rating scale of 1 to 10 or, with a young child, using rating scale with faces graded from smile to tears.</td>
</tr>
<tr>
<td>Disruption of sleep</td>
</tr>
<tr>
<td>When in pain, how does the child or adolescent show it?</td>
</tr>
<tr>
<td>When child or adolescent is in pain, how does the family respond? What do they do about the pain?</td>
</tr>
<tr>
<td>Previous medical care and laboratory tests for the pain evaluation</td>
</tr>
</tbody>
</table>

**Aggravating and relieving factors**

Aggravating or relieving factors, including medications

**Associated symptoms**

Associated symptoms, including weight loss, reduced appetite, nausea, intestinal gas, diarrhea, and meals or specific foods (milk products)

Any respiratory symptoms, such as chronic cough, wheezing, hoarse voice
<table>
<thead>
<tr>
<th>Past history</th>
</tr>
</thead>
<tbody>
<tr>
<td>History of trauma or past surgeries</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Family history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family history for gastrointestinal diagnoses, chronic pain disorders, or any other chronic illness</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Habits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary history, any evidence of low-fiber diet</td>
</tr>
<tr>
<td>Restrictive eating behavior/desire to lose weight</td>
</tr>
<tr>
<td>Purging behavior/self-induced vomiting</td>
</tr>
<tr>
<td>Frequency of bowel movements, history of being &quot;too busy&quot; to evacuate completely, encopresis</td>
</tr>
<tr>
<td>Recent excessive exercise</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Review of systems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dates of three last menstrual periods, relationship of pain with menses</td>
</tr>
<tr>
<td>History of sexual activity and contraception</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Psychosocial history</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disruption of normal activities, including school attendance/sports, by the pain</td>
</tr>
<tr>
<td>Any known stressors for the child and adolescent</td>
</tr>
<tr>
<td>Close relationship with any ill family members. Does the family member reside in the patient's home?</td>
</tr>
<tr>
<td>When stressed, how does the child or adolescent show it?</td>
</tr>
</tbody>
</table>
Wong-Baker FACES Pain Rating Scale

0
NO HURT

1
HURTS LITTLE BIT

2
HURTS LITTLE MORE

3
HURTS EVEN MORE

4
HURTS WHOLE LOT

5
HURTS WORST

0-10 Numeric Pain Intensity Scale

No Pain
Mild Pain
Moderate Pain
Severe Pain
Worst Possible

Abdominal pain: Warning symptoms and signs!

Associated symptoms
- Vomiting
- Diarrhea
- Fever
- Weight loss/failure to thrive
- Family history of IBD

Associated signs
- Failure to thrive
- Skin colour (pallor, jaundice)
- Oral pathology
- Perianal pathology
Physical examination

- **Abdominal examination**
  - gas, faeces

- **Rectal examination**
  - position of the anus
  - perianal faeces, erythema
  - haemorrhoids, fissures, scars
The further the pain is localized from the umbilicus, the less the probability that the cause of the pain is not due to an organic disease.
Recurrent retrosternal pain
Recurrent retrosternal pain: recommendations

In children above the age of 8 yrs
- Lifestyle changes with 4 week PPI trial
- If symptoms improve, continue PPI
- If symptoms persist, refer the patient to a paediatric Gastroenterologist for endoscopy

Espghan and Naspghan Guidelines, JPGN 2009
Infant irritability and omeprazole therapy

- Double-blind placebo controlled crossover trial
- 64 infants with microscopic esophagitis or positive esophageal pH study
- Age: 3-12 months

- Treatment group decreased Reflux Index from 9.9 to 1.0%
- Cry/fuss time decreased in both groups over 4 wks (267 min/24hr to 188 min/24hr)
- No difference between Rx and placebo groups

Clinical predictors of pathological gastro-oesophageal reflux in infants with persistent distress

Ralf G Heine,1,4,5 Brigid Jordan,2 Lionel Lubitz,3 Michele Meehan3 and Anthony G Catto-Smith1,4,5

Only predictors of pathologic GER were frequent regurgitation and feeding difficulties

Irritability and discomfort after feeds: is this Sandifer syndrome?
Pediatric Gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society of Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society of Pediatric Gastroenterology, Hepatology, and Nutrition

Co-Chairs: *Yvan Vandenplas and †Colin D. Rudolph
Committee Members: ‡Carlo Di Lorenzo, §Eric Hassall, ||Gregory Liptak,
* Lynnette Mazur, #Judith Sondheimer, **Annamaria Staiano, ††Michael Thomson,
‡‡Gigi Veereman-Wauters, and §§Tobias G. Wenzl

In the infant or child with reflux esophagitis, initial treatment consists of lifestyle changes and PPI therapy. In most cases, efficacy of therapy can be monitored by the degree of symptom relief.
Recurrent abdominal pain:
Does H. pylori cause RAP?

1233 children with H. Pylori Infection, who underwent EGD because of abdominal pain

Peptic ulcer disease was reported in:
- 3.5% in children < 6 yrs
- 4.6% in children 6-12 yrs
- 10.4% in children >12 yrs


RECOMMENDATION: NO TEST FOR H. PYLORI CHILDREN WITH RAP
Recurrent abdominal pain

Lactose malabsorption

Symptoms: Diarrhea, bloating, abdominal pain after ingestion of milk and/or dairy products.

Diagnosis: H2-Breath test with lactose (2g/kg, max. 50g).

Treatment: Dietary modification (limit lactose containing products; use lactose free milk; adjust the type, amount and timing of lactose containing products according to tolerance).
Recurrent abdominal pain

Fructose malabsorption

**Symptoms:** Diarrhea, bloating, abdominal pain after ingestion of fruit juices (>15 ml/Kg/d) or fruits.

**Diagnosis:** H2-Breath test with fructose (1g/kg, max. 25g). Sucrose test (2g/kg, max. 50 g) with equal amounts of fructose mostly normal.

**Treatment:** Dietary modification (avoidance of pear- and apple juice).

**Please, remember:** Glucose (starch, sucrose) enhances, sorbitol inhibits fructose absorption.
Recurrent abdominal pain

Crohn’s disease

Symptoms at diagnosis

- Recurrent abdominal pain: 80 - 90%
- Failure to thrive, malnutrition: 70 - 80%
- Diarrhea: 65 - 75%
- Anorexia: 50 - 60%
- Fever: 50 - 70%
- Growth failure, delayed puberty: 60 / 20%
- Anal fissure, tag, abscess: 20 - 25%
- Recurrent aphthous ulcers: 20 - 25%
- Clubbing: 20%
- Joint pain: 20%

Please remember:
Elevated ESR in 90 % of patients
Recurrent abdominal pain
Constipation or dyschezia or normal

Stool consistency matters

A: watery

C: formed

B: soft

D: hard
Constipation or dyschezia or normal

Retrospective chart review according to Rome criteria in **infants** presented to Pediatric GI-Clinic 2001-2007

Age at onset of symptoms

Recurrent abdominal pain
Work up of a child with recurrent abdominal pain

- Complete blood count
- ESR
- Blood chemistry (ALT, gGT, bilirubin, lipase)
- Urine analysis
- Stool: blood, leucocytes, ova & parasites
- Lactose/fructose restriction for 2 wks or H2 breath tests

- Abdominal ultrasound ??
  - Sonography rarely discovers organic disease in children >3 years of age, which has not been suspected by history, physical or lab.
  - Role for reassurance is not clear.
  - “Abnormal” findings of minimal or no clinical significance may generate anxiety and costs.


ABDOMINAL ULTRASOUND NOT OBLIGATORY IN CHILDREN WITH RAP
Recurrent abdominal pain in 44 children admitted to Children’s hospital

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>No organic findings</td>
<td>24</td>
<td>55%</td>
</tr>
<tr>
<td>Constipation</td>
<td>7</td>
<td>16%</td>
</tr>
<tr>
<td>Gastroesophageal reflux disease</td>
<td>10</td>
<td>22%</td>
</tr>
<tr>
<td>Lactose intolerance</td>
<td>2</td>
<td>5%</td>
</tr>
<tr>
<td>Nodular gastritis</td>
<td>1</td>
<td>2%</td>
</tr>
</tbody>
</table>


No organic cause in 54% of patients with FAP followed by GPs
THE PEDIATRIC ROME CRITERIA

1997
First consensus conference for definition of FGIDs in childhood

1999
The pediatric Rome II Criteria are published
Gut 1999; 45 (Suppl II):II60-II68

2006
The pediatric Rome III Criteria are updated
Gastroenterology 2006; 130: 1527-37
ROM III criteria
Childhood functional gastrointestinal disorders

- Vomiting and aerophagia
- Adolescent rumination syndrome
- Cyclic vomiting syndrome
- Aerophagia

- Functional dyspepsia
- Irritable bowel syndrome
- Abdominal migraine
- Childhood functional abdominal pain
- Childhood Functional abdominal pain syndrome

www.romecriteria.org
H2d1. Diagnostic Criteria* for Childhood Functional Abdominal Pain Syndrome

Must include childhood functional abdominal pain at least 25% of the time and 1 or more of the following:

1. Some loss of daily functioning
2. Additional somatic symptoms such as headache, limb pain, or difficulty sleeping

*Criteria fulfilled at least once per week for at least 2 months before diagnosis
H2c. Diagnostic Criteria* for Abdominal Migraine

Must include all of the following:

1. Paroxysmal episodes of intense, acute periumbilical pain that lasts for 1 hour or more
2. Intervening periods of usual health lasting weeks to months
3. The pain interferes with normal activities
4. The pain is associated with 2 or more of the following:
   a. Anorexia
   b. Nausea
   c. Vomiting
   d. Headache
   e. Photophobia
   f. Pallor
5. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process considered that explains the subject’s symptoms

*Criteria fulfilled 2 or more times in the preceding 12 months
H2a. Diagnostic Criteria* for Functional Dyspepsia

Must include all of the following:

1. Persistent or recurrent pain or discomfort centered in the upper abdomen (above the umbilicus)
2. Not relieved by defecation or associated with the onset of a change in stool frequency or stool form (ie, not IBS)
3. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject’s symptoms

*Criteria fulfilled at least once per week for at least 2 months before diagnosis
H2b. Diagnostic Criteria* for Irritable Bowel Syndrome

Must include all of the following:

1. Abdominal discomfort (an uncomfortable sensation not described as pain) or pain associated with 2 or more of the following at least 25% of the time:
   a. Improved with defecation
   b. Onset associated with a change in frequency of stool
   c. Onset associated with a change in form (appearance) of stool

2. No evidence of an inflammatory, anatomic, metabolic, or neoplastic process that explains the subject’s symptoms

*Criteria fulfilled at least once per week for at least 2 months before diagnosis
Post gastroenteritis functional GI disorders
N=88 patients

Salmonella (54%), Campylobacter (32%), and Shigella (14%)

Saps M, J Pediatr 2008
Mechanisms of post-infectious FAP and IBS
Increased activation of visceral stimuli in the brain

Yuan et al. 2003
Symposium on Brain-Gut Axis in Gastrointestinal Protection & Damage
September 15, 2001
Medical Faculty, Jagiellonian University
52 St. Anne Street
Cracow, Poland

2001: A Brain-Gut Axis
Child over protection
Impact of parent attention vs distraction on symptom complaints by children with and without FAP
L.S. Walker et al Pain 2006;122:43-52

- Water load symptom provocation test in 104 FAP & 119 well children, 8-15 y
- Parents randomized: distraction, no intervention, attention
- Outcome: children's GI symptoms and complaints parents' & children's perception of interaction
Impact of parent attention vs distraction on symptom complaints by children with and without FAP

L.S. Walker et al Pain 2006;122:43-52

- Effect of attention was 2.5 higher in children with pain compared to children without (higher in females)
- Distraction had a better effect in children without pain than in those with
- Both, children with pain and children without rated distraction better than attention.
- In contrast, parents of children with pain considered distraction as inappropriate response to pain
Pharmacological interventions for RAP and IBS in childhood

- Bulking agents
- Laxatives
- Prokinetics
- Antispasmodics
- Antibiotics
- 5-HT₃ antagonists
- 5-HT₄ agonists
- Antidepressants

Pharmacological interventions for RAP and IBS in childhood

- Weak evidence of benefit on medication in children with functional abdominal pain
- Little reason for their use outside of clinical trials
- FAP is a fluctuating condition and any "response" may reflect the natural history of the condition or a placebo effect rather than drug efficacy

Dietary interventions for RAP and IBS in childhood

There is a lack of high quality evidence on the effectiveness of dietary interventions.

No evidence that fiber supplements or lactose free diets are effective in the management of children with FAP or IBS.

Huertas-Ceballos et al. Cochrane Database of Systematic Reviews 2009
Hypnotherapy
Hypnotherapy in childhood functional abdominal pain

- 27 patients with IBS/FAP vs. 25 controls (medical therapy)
- 6 sessions of 50 min. of gut directed hypnotherapy over 3 months vs. standard medical care.
- Gut-directed Manchester protocol (adapted)
  - general relaxation
  - ego strengthening
  - control of abdominal pain and gut functions

Vlieger AM, Gastroenterology 2007
Hypnotherapy in children with FAP or IBS


P < 0.002
Audio-recorded Guided Imagery Treatment
**Effects of guided imagery treatment on abdominal pain**

N=34 children 6 to 15 years of age

2 month standard medical treatment with or without home-based guided imagery treatment

Dr Gary Huffnagle with Sarah Wernick

The Probiotics REVOLUTION

Breakthrough discoveries to:
- Prevent allergies and asthma
- Fight IBS
- Enhance immune function
- Curb inflammation
Lactobacillus GG for Abdominal Pain

Gawrońska AM et al. Aliment Pharmacol Ther 2007

FAP (n = 47) IBS (n = 37)

Placebo LGG (3x10^9 bid) Placebo LGG (3x10^9 bid)

No effect Improved Asymptomatic

Percentages:
- NS
- P < 0.04

4 week therapy
Lactobacillus Reuteri vs Simethicone in the Treatment of Breastfed Infants with Colic

N=83, 21 – 90 days of age
Duration of crying: 3 hrs/day
Treatment: L. Reuteri or simethicone for 28 days

* p<0.001

Lactobacillus Reuteri for functional abdominal pain in children: a DBRPC trial

- 60 children
- 2×10^8 CFU/day x 4 weeks
- Wong-Baker

P < 0.0001

Pain intensity

0 0.5 1.0 1.5 2.0 2.5

0 4 wks 8 wks

L Reuteri Placebo

Romano et al. J Pediatr Child Health 2010
Lactobacillus Reuteri for functional abdominal pain in children: a DBRPC trial

N=60 children

P <.05

Romano et al. J Pediatr Child Health 2010
L. Rhamnosus GG in childhood IBS and FAP

- RDBC trial
- 140 children with IBS/FAP
- Intestinal permeability test
  - at entry and end of trial
- LGG $3 \times 10^9$ CFU/day for 8 weeks
- Follow-up for 8 weeks
- Primary outcome: overall pain at end of intervention

Francavilla R, J Pediatr 2010
VSL#3 Improves Symptoms in Children with IBS: A Multicenter, DBRP cross-over Study

59 children (5-18 yrs)

Global relief of symptoms

VSL#3
Placebo

Baseline  start  2 wks  4 wks  6 wks

VSL#3
Lactic Acid Bacteria: 450 billion/packet
Streptococcus thermophilus
Bifidobacterium breve
Bifidobacterium longum
Bifidobacterium infantis
Lactobacillus acidophilus
Lactobacillus plantarum
Lactobacillus casei
Lactobacillus bulgaricus

Guandalini S et al. JPGN 2010
VSL#3 Improves Symptoms in Children with IBS: A Multicenter, DBRP cross-over Study

Abdominal pain

- VSL#3
- Placebo

Baseline | start | 2 wks | 4 wks | 6 wks

Guandalini S et al. JPGN 2010
Possible mechanism of action of Lactobacilli strains on visceral pain

- **L. Acidophilus**
  - up-regulate opiate and cannabinoid 2 receptors
  - ↑ pain threshold
  - **Dose related effect**

- **L. Reuteri**
  - inhibites TNF$_\alpha$ and induces IL-8 production
  - ↓ colorectal distension
  - ↓ pain perception

Storr MA, Neurogastroenterol Motil 2008; Storr MA, J Physiol GLP 2009
Functional abdominal pain
What to do:

- Clinical assessment to exclude organic disease
- Avoid extensive examinations; prescription of drugs; needless dietary restrictions
- Reassure patients and parents
- Recommend distraction to reverse environmental reinforcement of pain behavior
- Identify stress factors; consider behavioral therapy