'The evaluation and management of recurrent abdominal pain in childhood'

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Abstract

Recurrent abdominal pain (RAP) is a common complaint in children. Previously considered a single entity, RAP is now used as a descriptive term and sub-classified in the recently published Rome IV criteria, into four functional abdominal pain disorders (FAPD), including functional dyspepsia and irritable bowel syndrome. All share common pathogenic mechanisms of visceral hypersensitivity and central hypervigilance, resulting from disruption of the microbiota-gut-brain axis and abnormal enteric neuro-immune interactions. Although FAPDs are benign in nature, the persistence of symptoms and effects on everyday life can have significant secondary effects including psychosocial morbidity. The diagnosis of FAPDs is based on careful history and examination looking for 'alarm signs', although limited battery of laboratory investigations to screen for organic disease may be of value. The management of FAPDs should be multidisciplinary and based on the bio-psychosocial model of care with careful education and engagement of patients/parents. There is currently little evidence to support the routine use of pharmacotherapy, probiotics or diet and a significant placebo effect should be considered when assessing treatment effect. Hypnotherapy has been shown to be effective therapy. Approximately 50% of FAPDs cases will achieve resolution, especially those that have engaged with the appropriate model of management.

Key words: Children, Recurrent abdominal pain, Functional abdominal pain disorders, microbiota-gut-brain axis, irritable bowel syndrome

'The Evaluation And Management Of Recurrent Abdominal Pain In Childhood'

□ How common? UK and Worldwide

''Recurrent abdominal pain'' (RAP) is a common complaint in children and accounts for 2% to 4% of all paediatric clinic visits. In their seminal work with Bristol school children in the late 1950s two UK paediatricians, Apley and Naish found that approximately 10% of the children were reporting RAP. This ballpark figure of prevalence still stands to this day and appears to be similar across other countries worldwide.

□ Definition

In the past RAP in children was considered to be a single clinical entity. In their study Apley and Naish defined RAP on the basis of four main criteria namely: 1) ≥3 episodes of abdominal pain; 2) pain sufficiently severe to affect the child's activities; 3) episodes recurring over a period of ≥3 months; and 4) no known organic cause. Better classification of symptom profiles along with clinical and laboratory evaluations in more recent years, however, suggest that FGIDs is more complex, and includes conditions with both organic and functional etiologies.

Several terms have been used interchangeably with FGIDs including "non-organic abdominal pain", "psychogenic abdominal pain", and "functional abdominal pain", causing confusion. The challenge in conditions of "chronic abdominal pain" has not only been to differentiate between organic and so-called functional etiologies but also to understand whether the many presentations of pain and its associations constitute a single phenotype. In the late 1990s an international initiative (The Rome Foundation) established the Rome criteria for Functional Gastrointestinal Disorders (FGIDs), aiming to improve the diagnosis and classification of these conditions. In May 2016 the latest revision of these criteria was released (Rome IV criteria). Abdominal pain-related functional gastrointestinal disorders/AP-FGIDs (Rome III), which essentially relate to RAP in children, have now been renamed as Functional Abdominal Pain Disorders (FAPDs). FAPDs have been further sub-classified into a number of disorders, namely abdominal migraine, functional dyspepsia, irritable bowel syndrome, and functional abdominal pain- 'not otherwise specified'. Each constitutes a variable combination of symptoms but with considerable overlap between the entities. By definition the disorders are not secondary to any identifiable organic condition, but may coexist with other medical conditions. For the remainder of the chapter the term 'FAPD' will be used to denote all references to the original term of RAP and subsequent terminologies for RAP from Rome criteria pre-Rome IV.

□ Epidemiology

FAPDs have a reported prevalence in western countries of between 0.3-19% in the paediatric population with peaks at age 4-6 years (slightly more prevalent in boys) and in early adolescence (more prevalent in girls). In a 2015 meta-analysis of 58 studies that included 196,472 children from all around the world, the pooled prevalence of FAPDs was 13.5%.

□

Pathology, pathogenesis and applied physiology

The two final common mechanisms involved in the pathogenesis of FAPDs, are (i) visceral hypersensitivity and (ii) central hypervigilance. In simplest terms they respectively represent a lowered threshold of sensitivity to stimuli in the bowel and altered processing of 'pain' sensations coming into the brain from sensory fibres in the GI tract.

Visceral hypersensitivity

Visceral pain receptors (nociceptors) on afferent nerves of the inherent nervous system of the GI tract (called the enteric nervous system or ENS) respond to several stimuli, i.e. mechanical (contraction, distension etc.) and chemical (substance P, bradykinin, serotonin, histamine etc.) released in response to ischaemia or inflammation. Signals from stimulated afferent nerves pass up nerve processes and through or near paravertebral ganglia on their way to the spinal cord. From here messages pass up to the brain for processing (e.g. location, context etc.) and via reflex pathways to autonomic ganglion cells, which influence secretory and motor functions. In children with FAPDs, both types of afferent neurons (i.e. those that respond to low-pressure stimuli (nociceptors) and to high-pressure stimuli) become sensitized and show altered patterns of excitation evoked at lower thresholds. In children suffering from Irritable Bowel Syndrome (IBS) this can be shown by rectal barostat studies by reports of discomfort at lower rectal distention pressures compared to control patients.

Central hypervigilance

The co-ordination of gut functions with overall body homeostasis requires continuous communication between the CNS and the GI tract. The processing of visceral pain signals is also performed by the CNS and provides contextual information and determining appropriate responses. Evidence suggests that altered central processing underlies FAPDs, by influencing the perception of pain in these individuals (hyperalgesia). Studies with functional brain MRI suggests that in adults with FAPD there appears to be increased metabolic activity in cortical areas that are concerned with the processing of pain.

Overall, the enhanced responsiveness described above results not only in heightened pain sensation and awareness but also in dysregulation of gut epithelial (i.e. immune, permeability) and neuromuscular function, which in turn produce characteristic symptoms of FAPDs e.g. irritable bowel syndrome symptoms.

Although, both these states appear to involve alterations in the function of neural pathways or processing areas, these seem to occur as a result of insults to components of the so-called gut-brain-microbiota axis as well as neuro-immune interactions within the gut itself. The relatively recent recognition of the gut-brain-microbiota axis, a complex cross-talk between these elements, has heralded not only a better understanding of the pathogenesis of FAPD in children including the potential of 'early life programming' but has also given us insights into the pathogenesis of a whole spectrum of human diseases. A plethora of factors e.g. genetic (e.g. family history of IBS), early life events (e.g. pyloric stenosis, gastroschisis/ gastric surgery and nasogastric tube suction), environmental triggers (e.g. cow's milk protein allergy, post-enteritis syndrome), gastrointestinal factors (e.g. inflammation/ infections, trauma, early exposure to antibiotics/ altered gut microbiome) as well as psychosocial triggers (e.g. abuse, stress, anxiety), may contribute in the complex uncharted pathways that interact and ultimately alter the 'gut microbiome-brain-CNS-immune' axis and the perception of pain.

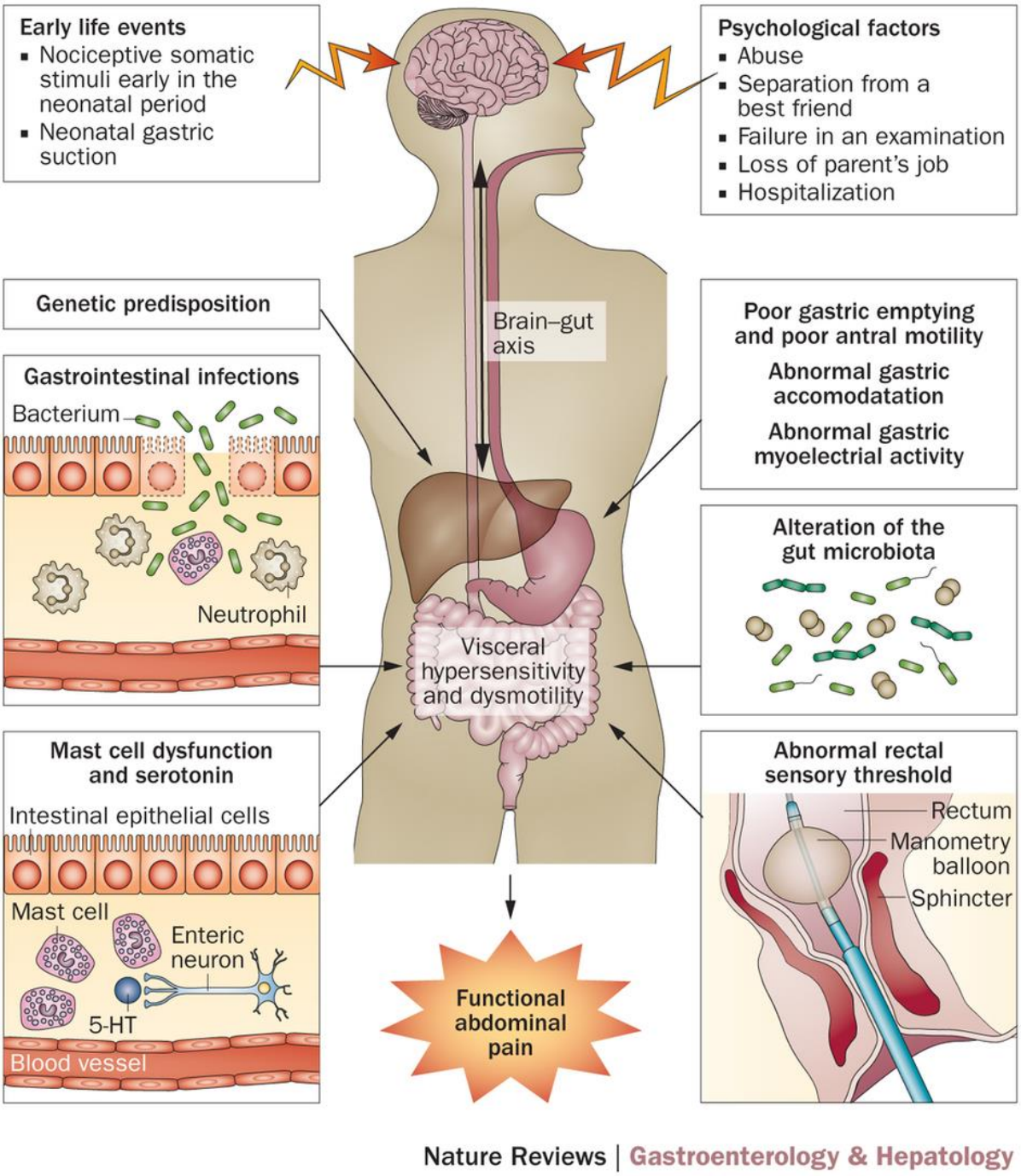

Figure 1. Several risk factors are associated with changes in visceral hypersensitivity and motility and contribute to the development of functional abdominal pain. Abbreviations: 5-HT, 5-hydroxytryptamine; FGID, functional gastrointestinal disorder (Reproduced with permission from Korterink J et al *Nature Reviews Gastroenterology & Hepatology* **12**, 159–171, 2015)

□ **Course of the disease**

As mentioned before, the term FAPD embodies a spectrum of conditions under the umbrella of abdominal pain-related functional GI disorders. Each may vary in course and severity, and have different presentations in different age groups. In the majority of patients, no organic cause is identified. FAPDs usually develop gradually and are benign in nature, but the persistence of symptoms and their effects on everyday life, cause significant secondary

distress and ultimately psychosocial dysfunction to patients and their families. Long-term follow-up of children with FAPD reveals that approximately 50% of them will eventually progress to complete resolution of their symptoms. In those that do not recover persistence of symptoms and ultimately progression to psychological and psychiatric disorders is a concern.

□ Diagnosis

Given that in the majority of cases no significant pathology can be identified, even on extensive and often interventional investigation, diagnosis of FAPD is dependent on careful history and examination. The Rome Foundation has taken on the challenge of establishing symptom-based diagnostic criteria for FGIDs because of a current lack of diagnostic biologic markers. The Rome III, and most recently the Rome IV criteria are largely based on findings from published literature and suggest that FGIDs should be considered as a positive diagnosis and not one of exclusion.

The Rome IV criteria for the four subgroups of abdominal pain-related FGIDs are summarized below. They are further divided, on the basis of differences in symptoms, into two age groups; one for the functional disorders of the infant/toddler (up to 4 years old) and one for the disorders of the child/adolescent. For both of the sub- groups the criteria are similar, varying in regards to the duration of symptoms and/ or structural or biochemical and behavioral differences in between the two age groups.

The FAPDs for the child/adolescent group are divided into four sub-groups;

(i) *Functional dyspepsia (FD):* when 1 or more of the following symptoms occur (postprandial fullness, early satiety, epigastric pain or burning sensation not related with defaecation), for at least 4 days per month, and for a period of ≥2 months prior to diagnosis, and the symptoms cannot be fully explained by other medical condition. FD incorporates 2 subtypes; a. Postprandial distress syndrome (i.e. fullness or early satiety, with or without upper abdominal bloating, nausea or excessive belching) and b. Epigastric pain syndrome (severe pain or burning sensation localised in the epigastrium or to abdominal/ chest regions that is not relieved by defaecation, and may be accompanied by a burning quality of pain of non-retrosternal nature, or pain induced or relieved by eating, but may occur while fasting)

(ii) *Abdominal migraine (AM):* when there are paroxysms of intense and acute periumbilical, midline or diffuse abdominal pain, (with duration ≥1 hour) that can affect the child's normal activities and are associated with ≥2 of the following symptoms: anorexia, nausea, vomiting, headaches, photophobia and pallor. These episodes of pain are separated from each other by weeks to months, present with a stereotypical pattern individually, the primary symptom is abdominal pain, and the symptoms cannot be explained by other medical condition. The aforementioned criteria must be present at least twice, in a period of ≥6 months prior to diagnosis;

(iii) *Irritable Bowel Syndrome (IBS):* when there is abdominal pain, for at least 4 days per month, associated with ≥1 of the following: related to defaecation, alterations in stool frequency, and/ or the appearance of stool, and when the abdominal pain in children with constipation does not resolve with the resolution of the constipation (in contrast to children in whom the pain resolves, which fulfil the diagnosis of functional constipation, not IBS). The aforementioned criteria need to be present for ≥2 months prior to diagnosis.

(iv) *Functional abdominal pain- Not Otherwise Specified (FAP-NOS):* when episodes of recurrent or continuous abdominal pain occur, not solely during physiologic

events (e.g. eating, menses), and there are insufficient criteria for diagnosing IBS, FD or AM, nor any other medical condition can explain these symptoms, for at least 4 times per month during a period of ≥2 months prior to the diagnosis,
This category most closely resembles, but is not a substitute for, the classically defined recurrent abdominal pain of childhood.

□ **History and physical examination**

This provides the cornerstone for diagnosis. The clinician needs to filter out the clinical findings that could suggest specific organic disease using both diagnostic clues as well as the presence of 'alarm signs' and/or symptoms. In the absence of these, attention should be given to the site, characteristics and associations of the pain in an effort to understand whether the pain falls into one of the FAPD sub-groups. History taking in patients should focus on, amongst others, family history (IBS, Coeliac disease, IBD) and early life events (e.g. irritability and disorders such as reflux and constipation in early life, antibiotic usage, gastric surgery, allergy, gastrointestinal infections etc.), as these factors are possibly associated to the pathophysiology of FAPDs, (Figure 1) and this information will help explain the diagnosis and determine management options.

History: Organic disorders are associated with abnormalities in physiology, structure or homeostasis, and are more likely to be found in children with 'alarm' findings. Clinicians will often rely on the presence or absence of 'alarm signs', e.g. associated weight loss, severe or significant symptoms, to decide whether patients are likely to have an organic or functional disorder. The history should also explore the possibility of abuse given clear associations with FAPDs. The 'alarm signs' are summarized in Table 1. Interestingly, symptoms such as the presence of nocturnal symptoms (i.e. pain that awakens the child) appear less discriminating when compared to children with inflammatory bowel disease. The identification of these 'alarm' features in clinical examination should guide the clinician to consider and ultimately exclude organic disease.

Examination: During the physical examination general appearance, health and level of comfort (as a severity index) should be assessed. Growth parameters, including weight and height (percentiles) and growth velocity are part of the initial evaluation. Blood pressure should be always checked, as hypertension may indicate disease. Perianal and rectal examination is also indicated as part of the first review (i.e. perianal fistulas, deep fissures and skin tags for suspected Crohn's disease; faecal masses, rectal stretching, superficial fissures for constipation) and may also indicate abuse.

If alarm signs are present, there is a range of potential conditions that could be present. The most frequently encountered are listed below in Table 2.

Table 1. 'Alarm signs' that may suggest the presence of an underlying organic pathology for recurrent abdominal pain in children

FROM HISTORY

1. Onset of symptoms <5 years of age
2. Presence of constitutional/ systemic symptoms (i.e. unexplained fever, involuntary weight loss)
3. Gastrointestinal bleeding (melaena, black, tarry stools)
4. Dysphagia or painful swallowing (odynophagia)
5. Significant, persistent vomiting (bilious, protracted, projectile)
6. Persistent right upper or right lower abdominal quadrant pain
7. Presence of referred pain (back, shoulders, extremities)
8. Chronic severe diarrhoea (>3 watery stools/ day, for > 2 weeks)
9. Nocturnal diarrhoea
10. Urinary symptoms (dysuria, haematuria, change in bladder function etc.)
11. Family history of inflammatory bowel disease, coeliac or peptic ulcer disease
12. History of abuse (difficult social/family circumstances)

FROM PHYSICAL EXAMINATION

1. Faltering growth, delayed puberty
2. Hepatomegaly, splenomegaly
3. Jaundice
4. Signs of perianal disease (tags, fissures, fistulas)
5. Skin changes (rash, eczema), oral apthous ulcerations
6. Localized R upper or R lower or L lower quadrant abdominal pain
7. Arthritis

FROM FIRST LINE TESTS

1. Anaemia, neutropenia or thrombocytopenia
2. Hypoalbuminemia
3. Elevated inflammatory markers (white blood cell count, erythrocyte sedimentation rate, C-reactive protein)
4. Guaiac positive stool
5. Coeliac screen positive

□ **Investigations**

If a diagnosis of an FAPD is suspected the setting of the consultation (i.e. primary, secondary, tertiary, inpatient or outpatient) should have little bearing on the clinical pathway. In theory, the diagnosis should be made on careful clinical assessment without additional diagnostic testing in children and adolescents with FAPDs in the absence of alarm symptoms and examination findings. In several observational and prospective studies, as well as systematic reviews, the value of diagnostic investigations was only noted in those with alarm findings. In practice, this clarity is difficult to achieve especially in the context of vague symptoms and signs as well as highly anxious patients and families concerned about severe disease.

It has been proposed that a limited number of laboratory tests may be indicated as part of first line evaluation, for children with likely FAPDs. These tests, however, should not be performed to facilitate the acceptance of the diagnosis for the patient and the family, but as a screening tool for underlying conditions with subtle 'alarm findings' that may be missed in the

initial diagnosis. A 2005 systematic review found very little evidence to suggest that ultrasonography, endoscopy, or oesophageal pH monitoring increases the yield of organic disease in the absence of 'alarm findings'. Extensive investigations within a hospital setting not only carry significant financial cost they rarely change the course of the management and may lead to more unnecessary testing increasing the patient's/ family's anxiety and uncertainty regarding the diagnosis.

A 6-year prospective cohort study from Italy, published in 2014, studied a total of 782 children with symptoms of FAPDs classified according to the Rome III criteria. Upon screening for coeliac disease 4.4% of the IBS subgroup were found to be positive for CD, suggesting a 4 times higher risk for this condition.

Faecal calprotectin has evolved as a useful screening test for inflammatory bowel disease. Although it has been associated with IBS in some studies the relationship or mechanism is not clear. In healthy infants and young children the upper limit of normal is not clear and likely to be higher leading to the possibility of false-positive results.

Part of the challenge of investigations is elucidating whether abnormal results confirm a cause for a symptom and this seems to be true for the role of *Helicobacter Pylori* in RAP. In a 2010 meta-analysis of five studies, the prevalence of *H. pylori* was the same amongst children with and without chronic abdominal pain (approximately 30- 40%) suggesting that presence and therefore abnormal testing (breath test, stool) may not be causally related to the pain. There is little evidence to support the routine screening for *Helicobacter Pylori* in children with FAPDs.

We would not suggest routine testing for food allergies unless there is a clear history for immediate reactions given the relatively poor predictive value of available tests. If there is a family or personal history of atopy or early onset of eczema a limited trial of allergen exclusion to show remission followed by re-challenge to show relapse (unless there is history or risk of an immediate allergic reaction) could be of value.

A suggested baseline screen could therefore include:

- Full blood count with differential,
- Erythrocyte sedimentation rate,
- C-reactive protein,
- Coeliac serology (including immunoglobulin levels)
- Urinalysis/ urine culture
- Faecal examination for blood, ova and parasites
- Faecal calprotectin

□ **Differential diagnosis**

The differential diagnosis of FAPDs includes conditions listed below in Table 2. Further testing should be guided by the presence of 'alarm signs' and symptoms, and can be performed within the facilities of a ward and under the guidance of the paediatric gastroenterology team.

Table 2. Suggested organic disorders as differential diagnoses of recurrent abdominal pain, when 'alarm signs' present

Gastrointestinal system
Gastroesophageal reflux, peptic ulcer disease
Eosinophillic gastrointestinal disease
Food allergy
Coeliac disease
Foreign body
Inflammatory bowel disease (IBD)
Achalasia
Malrotation, Intussusception
Meckel's diverticulum
Hernias
Tumors (i.e. lymphoma)
Enteric infection (parasitic, bacterial, viral)
Juvenile polyps
Chronic constipation

Pancreatic and hepatobiliary
Cholelithiasis, cholecystitis, choledochal cyst
Chronic hepatitis
Chronic pancreatitis

Respiratory system
Pneumonia

Genitourinary system
Recurrent urinary tract infections, Pyelonephritis/ Cystitis
Nephrolithiasis
Uretero-pelvic junction obstruction
Hematocolpos
Ovarian cyst or mass

Musculoskeletal system
Trauma
Tumors, malignancies

Metabolic
Diabetic ketoacidosis
Adrenal crisis
Storage disease
Porphyria

Other systems
Sickle cell disease
Leukemia
Immune deficiency
Diabetes mellitus
Porphyria
Infectious or other inflammatory process
Familial Mediterranean Fever
Lead poisoning
Intracranial pressure
Vasculitis (e.g. polyarteritis nodosa)

□ **Management**

The management of FAPDs is multifactorial and should be based on the bio-psychosocial model of care. A multidisciplinary approach specifically developed for each child's symptoms and triggers is the cornerstone for treating these conditions. It is clear that management of most cases of FAPDs should occur in primary and secondary care settings and consist of a number of key processes:

A therapeutic relationship: The patient and the family must be given confidence that their concerns are being addressed, acknowledgement that the symptoms of pain are real (caused by visceral hypersensitivity), that a positive diagnosis has been made of a subtype of FAPDs, that this is a common albeit complex entity affecting 10- 20% of children, and finally that the children can be treated most effectively with the help of a bio-psychosocial model of care (Figure 2).

Patient/Parent education: this is most important for therapy success. Parents and patients are educated about the benign clinical course, expectations of the treatment (e.g. improvement of tolerance of pain and not complete resolution in some cases), about avoiding the triggers and psychosocial factors that exacerbate FAPDs, about improving coping skills, and about setting realistic goals for management, as FAPDs can have an intense impact on everyday life. Furthermore, a plan of returning to school constitutes a crucial point, as homeschooling is not indicated, and the return to the previous activities is sought.

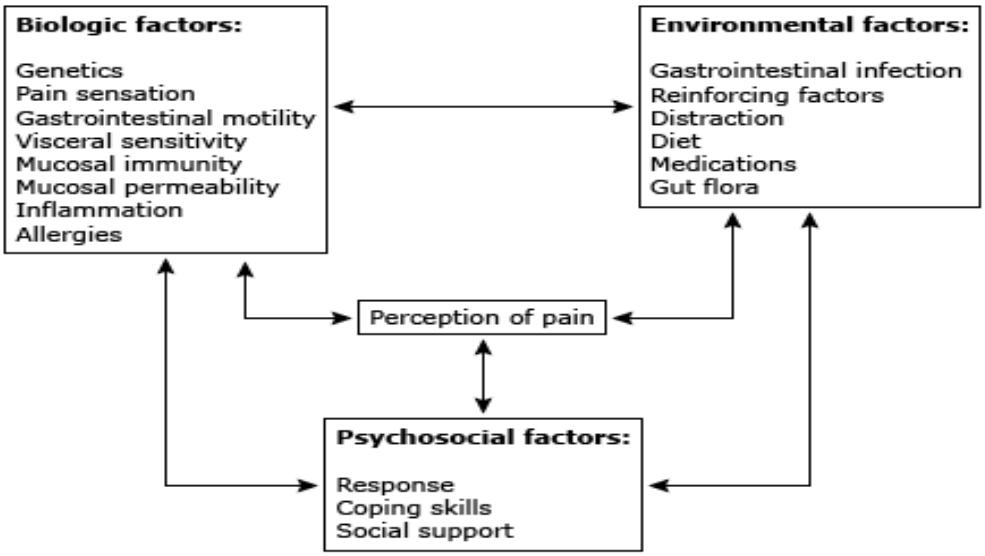

Figure 2: Bio-psychosocial model of abdominal pain (Reproduced with permission from UpToDate @2016)

Pharmacotherapy

A recent systematic review suggested that the evidence for the effectiveness of pharmacological treatments for FAPDs is low. This is further confounded by findings from a number of studies that show a significant placebo effect of up to 50%. The main groups of pharmacotherapeutic agents that have been tested include anti-spasmodics, antidepressants, antihistamines and treatments for gastro-oesophageal reflux and constipation. There are some reports suggesting the benefit from the use of peppermint oil/

antispasmodics but further trials and follow-up data is needed. Anti-depressant agents (SSRIs or tricyclic antidepressants) presumably working through peripheral and/or central modulation of pain pathways also appear to have some benefit but adverse effects have been reported and interpretation of the results are limited due to placebo effect. Beneficial effects of the antihistamine cyproheptadine have been reported, but only in small and retrospective trials. There is little evidence for the use of prokinetics or laxatives. Overall, the routine use of pharmacotherapy for FAPDs is not supported with a need for well-designed RCTs.

Diet

One of the commonest reported triggers for symptoms in FAPDs is food and as a result there is an abundance of dietary interventions and specialized diets promoted for use in FAPDs. It the majority, however, it is not clear whether any improvement relates to a placebo effect, allergy or intolerance secondary to known consequences of ingestion of certain foods (e.g. unabsorbed carbohydrates) occurring in the context of visceral hypersensitivity or altered elements of the microbiota-gut-immune axis at the mucosal level. A 2009 systematic review concluded that there is no high-quality evidence supporting that dietary interventions are effective in the management of childhood FAPDs. Recent data, however, suggests that restriction diets such as low FODMAPs diet may be of benefit in patients with IBS. A small recent trial in children showed some improvement in abdominal pain reporting in children on a low FODMAP diet. More data is needed to conclusively support this, including the long-term safety and nutritional adequacy of such restricted diets. Although studies have suggested some benefit in supplementing diet with fibre, this is not supported by a recent meta-analysis. Although, at present, dietary restrictions for children with FAPDs are therefore not routinely recommended, however, in some cases, a limited 4 or 6-week trial of restriction under expert advice may be tested.

Probiotics

There is a significant body of evidence showing the link between intestinal microbiota and functioning of the gut-brain axis. The use of probiotics has been reported to show encouraging results in certain groups of patients with FAPD. A recent meta-analysis of RCTs looking at the use of probiotics was suggestive of benefit in IBS with the use of *Lactobacillus sp. (GG, reuteri* and VSL#3). More randomized placebo- controlled trials are needed to establish their use in FAPDs and whether specific strains or combinations are of benefit.

Behavior modification and psychological treatment (including hypnotherapy)*:*

Anxiety and stress have long been associated with FAPDs but form only part of the overall bio-psychosocial model of disease. It is now clear that psychosocial interventions can have real beneficial effects upon many elements across the bio-psychosocial model of disease for FAPDs (Figure 2). They can help facilitate the return to normal function, by strengthening coping strategies and avoiding the reinforcement of pain behaviors. Suggestions for behavior modification techniques may be provided by the primary care provider and/ or, if necessary, by a prompt psychotherapy program (e.g. cognitive behavior therapy, biofeedback). Strategies to improve pain tolerance and coping include relaxation techniques, distraction management (conversation, guided imagery etc.), hypnotherapy (incorporates imagined pictures, sound or sensations used to distract attention from pain). Cognitive behavioral therapies combine the psychotherapy approach with education, relaxation and stress management to address behaviours that may generate or maintain symptoms. Of these therapies, hypnotherapy has been shown to be most effective. Compared to standard medical care and supportive treatment in children with IBS or FAP, hypnotherapy significantly reduced symptoms and was able to sustain improvement in the long-term, as shown at follow-up with a mean duration of 4.8 years.

□ Complications and disabilities

Poor quality of life (induced by on-going symptoms), poor school attendance, and therefore impact on the patient's education and personal development, may be considered as potential immediate complications of the disease left untreated. Family and personal stress and anxiety disorders, are also included in the potential hurdles and complications of the disease.

□ Prognosis and explanation to patient

Long-term follow-up reveals that FAPDs resolve in the 35-50% of cases with a percentage (25-29%) continuing to experience abdominal pain into adulthood. Those given a clear and thorough explanation of their condition and symptom management appear less likely to enter adulthood with symptoms or show relapse later on in adult life. In a prospective study of 132 children with FAPDs followed in a gastroenterology department, symptoms improved in 85% of patients by two months and improvement was sustained at 1 and 5 years. On the other hand, some studies suggest that children with FAPDs will become adults with irritable bowel syndrome (IBS). A 2013 prospective study from the US which included 322 children with FAPDs followed to young adulthood (mean age 20 years), showed that the lifetime risk of anxiety and depression were 51 and 40% (versus 20 and 16% in controls respectively), revealing a progression to psychiatric disorders in later life.

In a 2005 UK-based retrospective analysis of 23 children with FAPDs with persistence of symptoms 1 year after onset suggested that poor outcome (i.e. persistence of pain, no return to normal activity) was positively associated with non-adherence to the biopsychosocial model of care or psychological services provided, not engaging to patient education and modification techniques, and finally 'consumerism' of healthcare providers, and perpetuating FAPDs in childhood. Therefore, maintaining the therapeutic relationship between the family and the clinician, and engaging with the biopsychosocial model of care, is the mainstay for successfully treating these conditions.

□ Follow up

Children and adolescents with FAPDs require regular follow-up to maintain the therapeutic relationship with the clinician, in order to continue to provide them the education and reassurance needed, as well as to monitor the response to treatment and the development of secondary dysfunction given an often-prolonged course. Ideally, and certainly for the more challenging cases, follow-up should occur within a multi-disciplinary setting.

□ Prevention

There is no evidence that prevention is feasible for FAPDs at the current time. Given growing evidence that early life events and environmental factors are crucial in the pathogenesis of FADPs, it is likely that preventative strategies will be developed in the future. It seems sensible that promoting natural birth and breast feeding, avoiding minimally invasive procedures (e.g. nasogastric suction, minimal GI irritation, surgeries) during the first months of life and restricting use of antibiotics may have a preventative role, especially where there is a positive family history for FAPDs, food allergy or post-infectious syndromes.

Practice Points

- *"Recurrent abdominal pain'' (RAP) is a common complaint in children.*
- *At presentation a careful clinical history and examination looking for red flags should be taken together with, if needed, a focussed battery of tests to exclude an organic cause for RAP or confirm a functional abdominal pain disorder (FAPD).*
- *Where a positive diagnosis of a FAPD is made the disorder should, where possible and using the Rome IV criteria, be classified into one of the 4 sub-types (abdominal migraine, functional dyspepsia, irritable bowel syndrome and functional abdominal pain-not otherwise specified).*
- *A bio-psychosocial model for FAPDs, with consideration of risk factors, should be adopted when thinking about aetiopathogenesis and treatment as well as informing patients and parents.*
- *The management of FAPDs should be multidisciplinary with careful education and engagement of patients/parents.*
- *There is currently little evidence to support the routine use of pharmacotherapy, probiotics or diet and a significant placebo effect should be considered when assessing treatment effect.*
- *Hypnotherapy has been shown to be effective therapy for both short and long-term of FAPDs.*
- *Overall, approximately half of FAPDs cases will achieve resolution, especially where patients and parents have engaged with the appropriate model of management.*

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