

# Review article: the functional abdominal pain syndrome

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## Publication data

Submitted 30 July 2010  
First decision 25 August 2010  
Resubmitted 7 December 2010  
Accepted 8 December 2010

*This commissioned review article was subject to full peer-review.*

## SUMMARY

### Background

Functional abdominal pain syndrome (FAPS) is a debilitating disorder with constant or nearly constant abdominal pain, present for at least 6 months and loss of daily functioning.

### Aim

To review the epidemiology, pathophysiology and treatment of FAPS.

### Methods

A literature review using the keywords: functional abdominal pain, chronic abdominal pain, irritable bowel syndrome and functional gastrointestinal disorders.

### Results

No epidemiological studies have focused specifically on FAPS. Estimates of prevalence range from 0.5% to 1.7% and tend to show a female predominance. FAPS pathophysiology appears unique in that the pain is caused primarily by amplified central perception of normal visceral input, rather than by enhanced peripheral stimulation from abdominal viscera. The diagnosis of FAPS is symptom-based in accordance with the Rome III diagnostic criteria. These criteria are geared to identify patients with severe symptoms as they require constant or nearly constant abdominal pain with loss of daily function and are differentiated from IBS based on their non-association with changes in bowel habit, eating or other gut-related events. As cure is not feasible, the aims of treatment are reduced suffering and improved quality of life. Treatment is based on a biopsychosocial approach with a therapeutic patient–physician partnership at its base. Therapeutic options include central nonpharmacological and pharmacological modalities and peripheral modalities. These can be combined to produce an augmentation effect.

### Conclusion

Although few studies have assessed functional abdominal pain syndrome or its treatment specifically, the treatment strategies outlined in this paper appear to be effective.

*Aliment Pharmacol Ther*

## INTRODUCTION

Functional abdominal pain syndrome (FAPS) is one of the functional gastrointestinal disorders (FGIDs) defined by the Rome working teams.<sup>1</sup> It can be a debilitating disorder characterised by constant, nearly constant, or frequently recurring abdominal pain that has been present for at least 6 months with some loss of daily functioning.<sup>2</sup> As with the other FGIDs, there is no evidence for a structural disease that causes the symptoms.

Functional abdominal pain syndrome is the only functional GI disorder that stands alone in the Rome diagnostic classification system.<sup>1</sup> Its pathophysiology appears unique in that the pain is caused, almost completely, by amplified central perception of normal visceral input, rather than by enhanced peripheral stimulation from the viscera or other organs (e.g. gynaecological).

This clinical feature often occurs as gastrointestinal disorders become more chronic, and the pain experienced (in cortical centres) is influenced increasingly by central nervous system (CNS) input as modulated by psychosocial variables. In fact, with FAPS, there may be little or no gastrointestinal disturbance: in effect, there is an 'abnormal perception of normal gut function'. Therefore, while the pain is experienced in (and attributed to) the abdomen, the nature and magnitude of the pain are regulated primarily by cognitive and emotional centres. Recognising this concept is central to understanding FAPS in terms of clinical manifestations, pathophysiology, diagnosis and treatment. For this disorder in particular, a biopsychosocial approach is needed to understand and treat this entity of chronic gastrointestinal pain.<sup>3</sup>

Patients with FAPS are similar in many respects to patients with severe IBS.<sup>4</sup> Mild-to-moderate IBS has a greater peripheral (visceral) contribution than severe IBS, with less psychopathology and lower rates of association with other somatic symptoms and syndromes. In contrast, severe IBS shows increasing central nervous system dysfunction with greater modulation by psychosocial factors and higher rates of psychopathology with associated somatic symptoms and syndromes.

As there is a dearth of literature on FAPS, in many respects, severe painful IBS with psychosocial disturbances can be considered as a surrogate condition that represents FAPS. Many of the assumptions relating to the epidemiology, pathophysiology and treatment of FAPS are based on research into severe, painful IBS. Thus, the aim of the present study was to conduct an updated review of the epidemiology, pathophysiology and treatment of FAPS through a literature review using the keywords: functional

abdominal pain, chronic abdominal pain, irritable bowel syndrome and functional gastrointestinal disorders.

## EPIDEMIOLOGY

No epidemiological studies have focused specifically on FAPS and only a few studies on the epidemiology of FGIDs have differentiated between FAPS and IBS enough to provide a clear picture of its epidemiological characteristics. An early epidemiological US Householder study by Drossman *et al.*,<sup>5</sup> using Rome I diagnostic criteria, reported a national estimated prevalence of 1.7%. A Canadian study, using Rome II criteria, reported a prevalence of 0.5%.<sup>6</sup> The Rome II criteria are generally considered more restrictive than the Rome I criteria,<sup>7-9</sup> which may explain the difference, at least in part, between these studies. Furthermore, these data may be overestimates as these survey questionnaires do not incorporate all the criteria for FAPS, such as the loss of daily function associated with the pain.

Thus, in a study of a representative sample of the adult Israeli Jewish population, the prevalence of FAPS was only 0.1%, but FAPS together with unspecified functional abdominal pain was 0.8%.<sup>8</sup> The gender distribution of FAPS is also not clear. The US study reported a 1.5:1 female/male ratio,<sup>5</sup> whereas the Canadian study did not find a gender difference.<sup>6</sup> In the Israeli study, almost all respondents with FAPS or unspecified functional abdominal pain were women. While it seems reasonable to assume that FAPS, like IBS and many other chronic pain syndromes, is more prevalent among women, the data are not available to substantiate this assumption.

Functional abdominal pain syndrome patients have a high utilisation rate for healthcare services including physician visits, endoscopic procedures and abdominal/pelvic surgery.<sup>5, 6, 10</sup> They also have higher rates of work absenteeism.<sup>5</sup> In terms of health care use, FAPS may be similar to severe IBS.<sup>4</sup>

## PATHOPHYSIOLOGY

Few pathophysiological studies have been conducted specifically on patients with FAPS and hence little data are available. For this reason, the following sections are based primarily on data derived from studies on patients with severe IBS. The assumptions underlying this strategy were cited in the introduction above.

Chronic pain is a multidimensional (sensory, emotional, cognitive) experience, best explained by abnormalities in neurophysiological function at the afferent, spinal and CNS levels.<sup>11</sup>

In most functional disorders, such as IBS, there is abnormal or enhanced peripheral input from the gut, which may be related to food, early life experiences, stress, gut mucosal inflammation, menses, previous surgery and acute gastrointestinal infection. The volume of this input is 'turned-up' by central mechanisms in the spinal cord and brain, which are modulated and reinforced by genetic and psychosocial factors. This leads to central hypersensitivity and hypervigilance, which are at the core of the patient's experience of pain. Theoretically, the lower threshold for pain sensitivity in IBS could involve intramural mechanoreceptors, neurotransmission at synapses in the spinal cord, abnormal processing of sensory information in the brain, or a combination of these.<sup>12</sup> In fact, two alternative scenarios could explain the perception of pain. In one, mechanosensitive primary gut afferents react to various stimuli by transmitting at elevated firing frequencies, which is interpreted centrally as nociception. In the other, normally functioning afferents transmit accurate information, which is misinterpreted in processing centres of the spinal cord and the brain to evoke pain perception.<sup>12</sup> The first scenario reflects the peripheral component of pain perception, while the second reflects the central component.

Dorn *et al.*<sup>13</sup> used sensory decision theory analysis to differentiate between physiological and psychological components of pain thresholds in IBS patients. They found that the increased colonic sensitivity in IBS is more influenced by a psychological tendency to report pain (central component) than neurosensory sensitivity (peripheral, physiological component). This suggests that even for IBS, there is good evidence for central dysregulation of visceral afferent input. The impaired homeostatic inhibition of pain (disinhibition) may relate to reduced serotonin, norepinephrine, endorphin and other neuropeptide activity via the medial CNS circuitry to the dorsal horn.<sup>14</sup> While IBS does have a peripheral component, the central component becomes more prominent as disease severity increases.

We recently reported that significantly more women undergoing elective gynaecological surgery for nonpain related gynaecological conditions reported abdominal pain 3 and 12 months after surgery than nonsurgical controls.<sup>15</sup> No surgery-related or other physiological variables predicted the development of this abdominal pain. The only presurgery variables that predicted this development were psychosocial ones. Although these women were not diagnosed with FAPS, the results of the study imply that their new-onset abdominal pain was associated, much as in FAPS, with central registration and

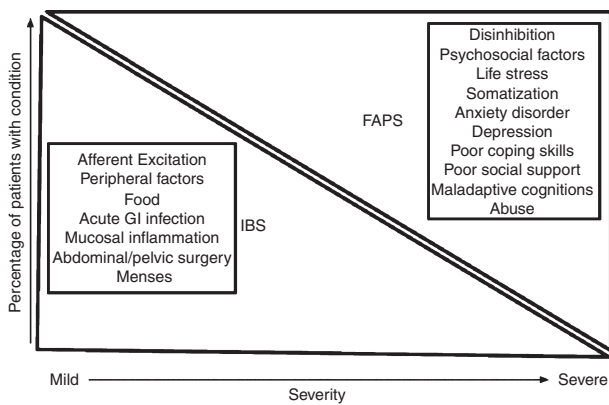
amplification of the afferent signal (via cognitive and emotional input), more than with peripheral causes.

Brain imaging studies have demonstrated an association between sexual abuse and disinhibition of afferent pain signals that was modulated by changes in psychological distress. In one study, patients with abuse history and IBS had greater activation of the cingulate cortex than those with IBS only, abuse only, or neither, and notably this activation correlated strongly with patient reports of pain to rectal distension.<sup>16</sup>

In another brain imaging study, at the time a young woman, who had suffered childhood and adult sexual abuse, manifested increased psychological distress, the investigators found activation of the cingulate cortex leading to decreased inhibition of afferent sensory signals generated by rectal distension.<sup>17</sup> In contrast, after successful psychological treatment, there was less activation of this brain centre and reduced sensitivity to peripheral pain.

Although FAPS patients may be similar to patients with severe IBS, in contrast to IBS where the majority of patients have mild-to-moderate disorders with a considerable degree of peripheral input, FAPS patients are all at the severe end of the spectrum with predominantly central pathophysiology (Figure 1). Compared with IBS, the dominant mechanism for altered pain regulation in FAPS relates, to a much greater degree, to impaired inhibition and possibly even facilitated amplification of normal regulatory afferent input via altered central 'gate control' mechanisms (originating in the prefrontal and cingulate cortex and other limbic structures).<sup>18</sup> Support for this mechanism comes from a recent physiological study that compared small groups of adults with IBS and FAPS. The investigators found that IBS patients were hypersensitive to rectal balloon distention with lowered rectal thresholds, whereas FAPS patients had normal perceptual thresholds to the same stimulation.<sup>14</sup> Thus, the pain reported by the FAPS patients could not be attributed to a peripheral mechanism such as visceral hypersensitivity.

These purported differences in pathophysiology may not translate to a clear-cut, obvious differentiation between FAPS and severe IBS in the clinic. Clinicians experienced in the FGIDs probably find this distinction easier to make than primary care physicians. They recognise the chronicity of pain that is not related to bowel habit, eating or other gut related activity, although this is incomplete. Thus, the distinction between IBS, or other FGIDs, and FAPS may exist on a continuum. While the Rome criteria for FAPS require exclusion of IBS,



**Figure 1** | A conceptual model showing IBS and FAPS symptom severity as a function of the interaction between peripheral sensory initiating factors and central processing variables (psychosocial variables). Impaired central processing of the afferent signals leads to disinhibition and more severe symptoms. It is modulated by the presence of psychosocial co-morbidity. The y-axis represents the percentage of patients with each (central or peripheral) contribution. The opposing triangle shapes demonstrate that most IBS patients have mild or moderate symptoms and more peripheral (visceral) activity with a minority having more severe symptoms (and increasingly impaired central processing), while most FAPS patients have more severe symptoms with a major component of impaired central processing and psychosocial modulation.

clinicians may at times entertain both diagnoses. The following section presents and discusses the diagnostic criteria and work-up that can help in making the diagnosis of FAPS.

### DIAGNOSTIC CRITERIA AND WORK-UP

The diagnostic criteria for FAPS appear in Table 1. The Rome III criteria are geared to patients with more severe symptoms by definition in that they require constant or nearly constant abdominal pain with loss of daily function (work/school absenteeism, limitations in family and social activities).

The authors of this review recently published a clinical diagnostic algorithm for FAPS (Figure 2).<sup>19</sup> The following discussion presents the essentials of that diagnostic process. The physician should elicit specific characteristics of the pain, especially associations with bowel movements, eating and the menstrual cycle. If the abdominal pain is associated with bowel movements (change in frequency or consistency, relief upon defecation), IBS should be considered.<sup>20</sup> In patients with epigastric or

**Table 1** | Rome III diagnostic criteria\* for FAPS

Must include all of the following

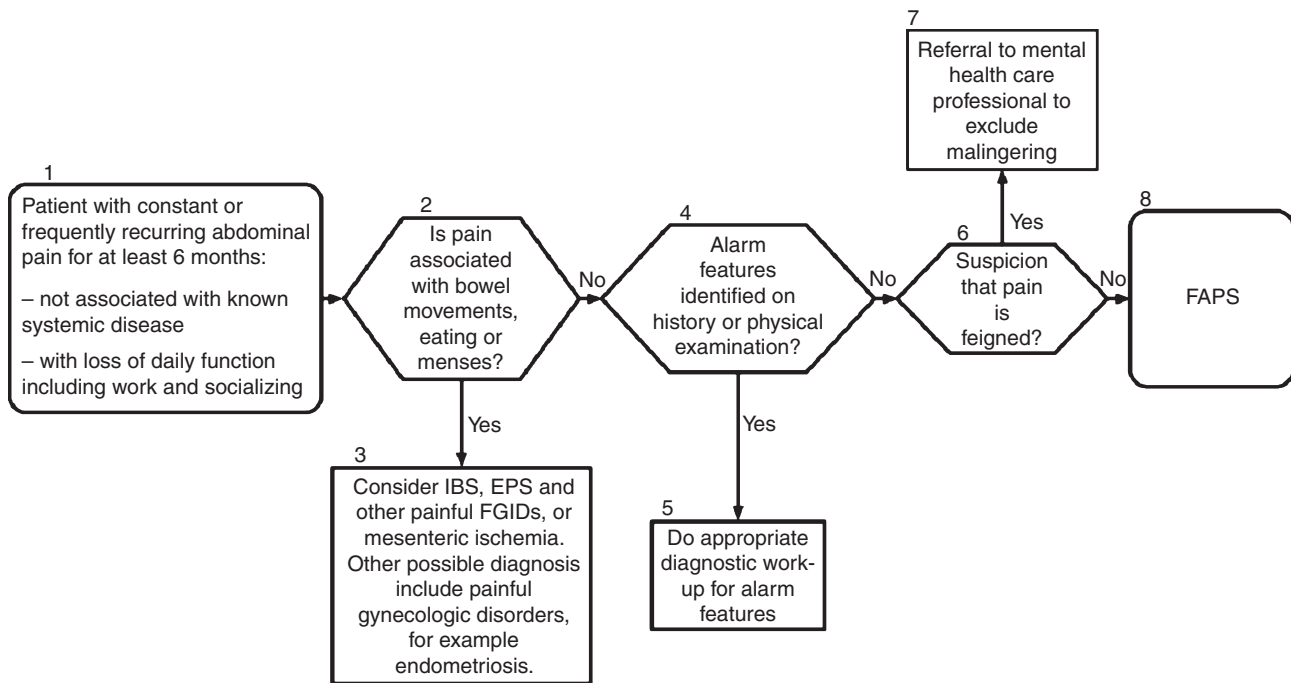
1. Continuous or nearly continuous abdominal pain
2. No or only occasional relationship of pain with physiological events (e.g. eating, defecation, or menses)
3. Some loss of daily functioning
4. The pain is not feigned (e.g. malingering)
5. Insufficient symptoms to meet criteria for another functional gastrointestinal disorder that would explain the pain

\* Criterion fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis.

right upper quadrant pain, the epigastric pain syndrome<sup>21</sup> should be considered and the differential diagnosis should include functional gall-bladder syndrome or sphincter of Oddi syndrome.<sup>22</sup> If the pain is associated with eating, particularly in cases of recent-onset pain in older patients with a history of vascular disease, chronic mesenteric ischaemia should be assessed. Finally, if the pain is associated with menses, gynaecological conditions such as endometriosis or dysfunctional uterine bleeding should be evaluated, in some cases by referral to a gynaecologist.

Patients with FAPS may manifest typical symptom-reporting behaviours,<sup>2</sup> which can provide important clues to the diagnosis. In addition to their contribution to diagnosis, recognising and addressing these behaviours may play a critical role in the establishment of a therapeutic patient–physician relationship as well as in delineation of the treatment plan. These behaviours include verbal and nonverbal expression of pain intensity, reporting symptoms with a sense of urgency, minimising or denying a role for psychosocial factors, requesting additional diagnostic studies, focusing attention on complete recovery, frequently seeking health care, taking limited personal responsibility for self-management and making requests for narcotic analgesics. These behavioural communications are not criteria for the diagnosis, but they are a commonly observed feature of the disorder and provide important information that can help the physician in diagnostic and treatment planning.

All patients should undergo a complete physical examination. Among others, chronic abdominal wall pain should be differentiated from pain of visceral origin. Abdominal wall pain is usually localised and increases with contraction of the abdominal muscles. Carnett’s sign in which pain or tenderness increases with intentional tensing of the abdominal muscles can be elicited



**Figure 2 |** Clinical algorithm for the diagnosis of FAPS (reprinted with permission of the Rome Foundation).

in these cases.<sup>23</sup> However, one should bear in mind that FAPS patients might manifest a positive Carnett's sign that is related to central hypersensitivity with hypervigilance rather than abdominal wall aetiology. In this very specific and unique context, the original Carnett's sign is modified to differentiate visceral from central pain mechanisms rather than to differentiate visceral pain from abdominal wall pain, as originally designed.

Other findings on physical examination that may not be sought or recognised by physicians unfamiliar with syndromes such as FAPS may include the 'closed eyes sign' and the 'stethoscope sign', which can help differentiate FAPS from more acute causes of abdominal pain. In the 'closed eyes sign', patients with FAPS might wince with their eyes closed when the abdomen is palpated. In contrast, patients with an acute abdominal pain episode usually keep their eyes open in anxious anticipation. In the 'stethoscope sign' the physician may use a stethoscope to palpate the abdomen. In patients with acute abdominal pain any contact with the abdomen will increase pain behaviour, whereas in patients with FAPS, this procedure may reduce the behavioural response to pain. The minimal laboratory work-up should include CBC, ESR/CRP and a biochemistry panel (including albumin and liver function tests).

A major objective of the history, physical examination and laboratory tests is to elicit possible alarm features,

which can include abnormal findings on physical examination, unintentional weight loss, family history of abdominal cancer and/or laboratory abnormalities such as anaemia, hypoalbuminemia, abnormal liver function tests, elevated ESR or CRP, and positive faecal occult blood. If alarm features are identified, appropriate tests should be conducted to evaluate for other sources of pain.

In the absence of alarm features, no further diagnostic testing is required if the diagnostic criteria for FAPS are met. Unfortunately, by the time many of these patients have reached a specialist in the field, they have already undergone an extensive investigation, including non-invasive procedures such as abdominal US, abdominal CT, and abdominal MRI, as well as invasive procedures such as capsule videoendoscopy, upper endoscopy, colonoscopy, EUS and ERCP. This testing is not only unnecessary, but it involves risk to the patient, excessive healthcare costs and can reinforce the patient's inclination to think that another diagnosis is being missed, which, together with lack of experience and confidence in the diagnosis on the part of the physician, is often the reason for the extensive testing in the first place.

Thus, if the diagnostic criteria are met and no alarm features are present, the diagnosis of FAPS can be made unless there is suspicion that the pain is feigned. Feigned pain or malingering<sup>24</sup> relates to the intentional

production of false or grossly exaggerated physical (or psychological) symptoms, motivated by external incentives. Feigning is not easy to detect, especially by physicians who lack experience with this entity and therefore it may be appropriate to refer to a mental health professional to confirm suspicion. It should not be presumed unless there is clear evidence for its presence.

**TREATMENT**

Although there is limited evidence-based information from studies specifically designed for the treatment of FAPS, in many ways, the concepts are generic and similar to severe IBS. Therefore, the following discussion is based on IBS and particularly severe IBS studies.

**The patient-physician relationship**

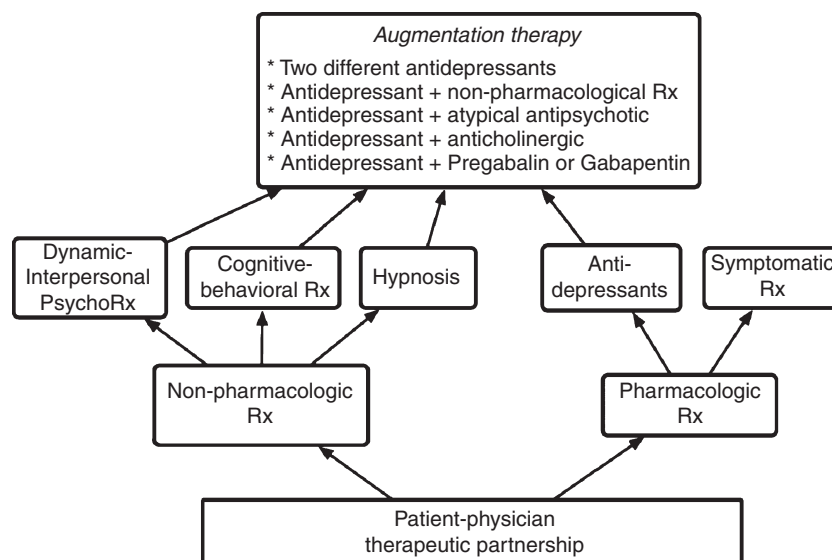
As many physicians are not trained in the biopsychosocial model, they may feel challenged, to say the least, or even uncomfortable in trying to understand and care for patients with functional GI disorders.<sup>25</sup> These patients may be perceived as ‘difficult’, but it is not the patient, but the nature of the condition and the physician’s knowledge and attitudes that make it difficult. This may be related to physicians not being certain of the diagnosis and hence feeling compelled to do more diagnostic studies, or to the fact that the patients do not readily respond to treatments, or to feeling uncertain as to how to treat the patients’ psychosocial co-morbidities including anxiety, depression and somatization. A better understanding of FAPS and a proper treatment approach can readily reduce this sense of difficulty. Furthermore, the

perception of patients with FAPS as being difficult to manage has a deleterious impact on the patient-physician relationship (see treatment below), the cornerstone of successful treatment.

A diagram of the approach to patient management in FAPS can be seen in Figure 3. Notably, the evidence for benefit of some of the treatment modalities is based on experience with severe IBS patients or patients with other painful disorders, rather than on clinical trials with FAPS patients.

In all cases, the patient-physician relationship is the cornerstone of any successful treatment plan. Other therapeutic strategies including medication and psychological therapy are based on this relationship and its implied therapeutic partnership. Care needs to be patient, non-judgemental, and ongoing. Treatment goals have to be clearly defined and agreed upon by the patient and physician. In the absence of cure, the emphasis should be on care, essentially on the reduction of symptoms, and improvement in function and quality of life. Important patient-related and physician-related factors that can affect the patient-physician relationship are listed in Table 2 and some are discussed below.

*Patients’ expectations.* If the patient’s expectations are not reality-based (e.g. they expect to be ‘cured’), treatment benefits are more limited. One of the first objectives of the physician is to help patients develop realistic expectations. To this end, it is very helpful to elicit the following information in the first meeting with new patients: what do the patients think they have, what are



**Figure 3 | The therapeutic ‘tree’ for FAPS with a therapeutic patient-physician relationship at its base.**

**Table 2 | Factors that can affect the patient-physician relationship in FAPS**

Patient-related	Positive expectations from treatment
	Readiness to enter into a therapeutic relationship
	Readiness to take responsibility for self-care
Physician-related	Ability to foster a therapeutic relationship
	Listen actively
	Empathise
	Identify and respond to concerns
	Validate
	Educate
	Reassure
	Present treatment options and set reasonable treatment goals
	Set reasonable limits
	Help patient take on responsibility for care
	Treatment options
	Continuity of care

their concerns and what do they expect from the physician or from treatment?

When these three points are sufficiently clarified and an understanding has been reached concerning the patients' expectations, the way is clear to a potentially successful treatment partnership.

*Patients' readiness to enter into a therapeutic relationship.* Many patients are used to a more acute model of care; a clinical sequence in which they present a symptom to the doctor, the doctor does tests, makes a diagnosis and then provides treatment that solves the problem. However, with chronic painful illnesses, the focus needs more to be on adaptation to constant symptoms with little chance of cure. Many patients may assume a more passive role with little personal responsibility for the care; often this leads the doctor to assume this responsibility. This is usually not effective for patient or doctor. For FAPS in particular, primary responsibility needs to be shared, with the patient actively participating in management decisions.

*The physician's ability to foster a therapeutic relationship.* Physicians play a key role in developing a therapeutic relationship with their patients to maintain a

therapeutic partnership. They need to know how to listen, show empathy and acknowledge that the patient's complaints are legitimate and that their distress is real. They need to know the full range of possible treatments, including the advantages and limitations of each. Based on this knowledge and the availability of various treatment modalities, they should be able to present therapeutic options, set treatment goals and help the patient take responsibility for care. Finally, they must expect to continue a long-term plan of care.

### Psychological therapy

There have been no specific studies designed to evaluate psychological therapy in FAPS. Thus, the following discussion is an extrapolation from studies on IBS and somatic functional syndromes like fibromyalgia.

Cognitive behavioural therapy, which identifies maladaptive thoughts, perceptions and behaviours, helps the patient develop new ways to increase control over symptoms. The beneficial effect of this modality has been shown in studies in FGIDs including FAPS.<sup>26</sup> Hypnotherapy has been extensively studied in IBS patients and shown to have beneficial effect in both short-term and long-term.<sup>27</sup> Other effective strategies are stress management techniques, which may be part of a multicomponent behavioural treatment programme and dynamic or interpersonal psychotherapy.<sup>28</sup> Some of these treatment modalities, particularly interpersonal psychotherapy may not be available in many medical centres.

One of the problems with psychological therapy in FAPS is that patients may minimise the role of the psychosocial aspects of their illness and deny any role for stress or psychopathology. Thus, they often resist any suggestion that psychological therapy can help and insist on medication. However, a positive patient-physician relationship can overcome this barrier.<sup>29</sup>

### Medical therapy

Medical therapy can be symptom-directed or directed more at the underlying causes, i.e. central pain mechanisms. Due to the persistent, debilitating abdominal pain, many patients demand and get pain medication, often opiates. This has become the refuge of overworked emergency room physicians faced with demanding patients with no clear cause for their pain.<sup>30</sup> Besides the obvious problems entailed in the over use of narcotic drugs, there is a less recognised potential complication, i.e. development of the narcotic bowel syndrome (NBS). This syndrome is characterised by chronic or frequently recurring abdominal pain that worsens with continued

or escalating dosages of narcotics.<sup>31</sup> As it is manifested with the same symptom as FAPS, the association between the pain and use of opiates is not understood and the response may be increased dosages of the opiate to relieve the pain, even if only temporarily. Recent research is beginning to elucidate the basis for the paradoxical visceral hyperalgesia caused by chronic narcotic use through a variety of mechanisms that are now being clarified.<sup>31, 32</sup> An animal model has recently been developed to facilitate further study into these mechanisms.<sup>33</sup> The treatment for this development is beyond the scope of this paper, but can be found in the above-cited papers.

Another serious obstacle to successful medical treatment in patients with severe IBS or FAPS patients is their tendency to report serious adverse effects and discontinue treatment close to its inception. Thiwan *et al.*<sup>34</sup> studied 57 women who received the tricyclic antidepressant desipramine as part of a clinical trial to see whether the symptoms they reported were side effects of the medication or reflected a general behavioural tendency to report symptoms. They found that the majority of symptoms often attributed to side effects of desipramine were actually present prior to treatment, suggesting that most symptoms considered as side effects were not related to drug *per se*. They recommended that clinicians consider the possibility that 'side effects' may relate more to psychological distress than to drug effects.

The cornerstone of current medical therapy is treatment with antidepressant medications.<sup>2</sup> The rationale is that these drugs can modulate pain perception by modulating central regulatory mechanisms and to some degree visceral hypersensitivity. They have been used with success in the treatment of chronic neuropathic pain.<sup>35</sup> A recent systematic review and meta-analysis of antidepressants [tricyclic antidepressants (TCA), selective serotonin reuptake inhibitors (SSRI), serotonin and norepinephrine reuptake inhibitors (SNRI)] and psychological therapy (cognitive-behavioural therapy) showed that these treatment modalities were all effective with a number needed to treat (NNT) of four for both antidepressants and psychological therapy.<sup>36</sup>

New insights into the mechanism of action of antidepressants in chronic pain are emerging<sup>37</sup> based on the concept of neuroplasticity. There is evidence that nerve cells may die as a result of abuse and war (PTSD), depression and chronic pain disorders.<sup>38, 39</sup> Brain-derived neurotrophic factor BDNF, a member of the 'neurotrophin' family of growth factors, supports the survival of existing neurons and encourages the growth and

differentiation of new neurons and synapses. Antidepressants can increase the concentration of BDNF and there is evidence that they can therefore lead to regeneration of neurons in the affected regions reversing the effect of chronic pain on BDNF levels and activity.<sup>38, 40</sup>

Although all families of antidepressants can be effective in FAPS, there is logic to initiating therapy with a TCA drug as this group is particularly effective for chronic pain. Another alternative is an SNRI drug such as duloxetine, which has been used successfully for chronic neuropathic pain. Tables 3 and 4 provide information on the major TCA drugs (Table 3) and SSRI and SNRI drugs (Table 4), including receptor activity and dosage schedules. It should be noted that the TCA doses usually used for FGIDs are considerably lower than those prescribed by psychiatrists for clinical depression.

Among the major issues with antidepressant therapy for FGIDs are side effects and the perception by many patients that as they are being given a 'psychiatric' drug, the physician thinks that their problems are all in their head. For this reason, it is important to 'frame' the rea-

**Table 3 | Receptor activity and dosages for TCA antidepressants**

Drug	Receptor activity				Dosage	
	NE	5-HT	H <sub>1</sub>	ACh	Initial	Range
Amitriptyline	+2	+2	+4	+4	10-50	25-150
Imipramine	+2	+2	+4	+2	10-50	25-150
Desipramine	+4	+2	+1	+1	10-50	25-150
Nortriptyline	+3	+2	+2	+2	10-50	25-150

NE, norepinephrine; 5-HT, 5-hydroxytryptamine; H<sub>1</sub>, histamine-H<sub>1</sub> receptor; ACh, acetylcholine.

**Table 4 | Receptor activity and dosages for SSRI and SNRI antidepressants**

Drug	Receptor activity			Dosage	
	NE	5-HT	ACh	Initial	Range
Fluoxetine	-	+4	-	10-20	20-80
Fluvoxamine	-	+4	-	25-50	50-300
Paroxetine	-	+4	+1	10-20	20-60
Sertraline	-	+4	-	25-50	50-200
Venlafaxine	+4	+3	-	25-50	25-150
Duloxetine	+4	+4	-	20-40	20-80

NE, norepinephrine; 5-HT, 5-hydroxytryptamine; H<sub>1</sub>, histamine-H<sub>1</sub> receptor; ACh, acetylcholine.



sons for prescribing these drugs in a way that will convince the patient to try them and, at the same time, reduce the incidence of side effects. Table 5 presents ways that the physician can accomplish this in the framework of the patient–physician partnership.

Clinicians prescribing these drugs should keep in mind that the therapeutic benefit may take 4 to 6 weeks to achieve, while side effects, if they occur, usually do so at the beginning of treatment. Treatment can be started at a low dose. It is helpful to follow-up in the first week and maintain ongoing care. A common error is prescribing a suboptimal dose or failing to increase the dose when the patient has an incomplete response.<sup>41</sup>

Recently, Grover *et al.* published a preliminary report on the use of quetiapine, an atypical antipsychotic drug, for severe refractory FGIDs.<sup>42</sup> The rationale for using this drug was that it might benefit patients by providing an independent analgesic effect, augmenting the effect of antidepressants, and mitigating associated anxiety and sleep disturbances. In addition, quetiapine has a relatively safe

side effect profile, especially at lower dosages. Their retrospective study of 21 patients with refractory symptoms who were treated with quetiapine showed that at low doses, it improved the condition of more than 50% of refractory patients who stayed on the medication. Thus, this medication provided symptom relief in patients who had previously failed on all other treatment attempts.

### Augmentation therapy

Another treatment strategy that has been adapted from psychiatric treatment of depression to the treatment of severe FGIDs is augmentation therapy,<sup>43</sup> which is based on the idea of potentiating the effect of one agent or modality by adding another agent or modality with a different mechanism of action to maximise efficacy and minimise side effects. Augmentation therapy may involve combinations of two types of antidepressants, an antidepressant with an anxiolytic drug (e.g. buspirone), an antidepressant with an atypical antipsychotic (e.g. quetiapine), an antidepressant with psychological therapy, or a central modality with a peripheral one (antidepressant or psychological therapy with a GI-directed agent, e.g. an anticholinergic drug). Table 6 describes these options further.

**Table 5 | Working with patients to improve chances of successful treatment with antidepressants**

Physician should	Barriers/actions
Address patient resistance/concerns	'Didn't work'
	'Caused side effects'
	'Don't want a mind-altering drug'
	'Don't have a psychiatric problem'
Reframe patient's understanding	Central analgesic
	Not just for psychiatric conditions
	Used in many medical conditions such as migraine, post-herpetic neuralgia, diabetic neuropathy
	Works in doses lower than used by psychiatrists
	May take time to show effect
Be familiar with	Minor side effects are transient
	First choice does not always work
	Dosage Initial, optimal, length treatment period
Learn to combine	Adverse effects
	Indications to stop therapy or switch preparation
	Different central and peripheral agents and non-pharmacological therapeutic modalities

**Table 6 | Options for combining treatment modalities in augmentation therapy**

Combination	Examples
Central drug with central drug	SSRI with TCA
	SNRI with SSRI
Central drug with peripheral drug	SSRI with anticholinergic drug
	TCA with pregabalin or gabapentin
Non-pharmacological treatment with central drug	Hypnosis with TCA
	CBT with SSRI
Non-pharmacological treatment with peripheral drug	Hypnosis with anticholinergic
	CBT with pregabalin or gabapentin
Central drug with non-pharmacological treatment and peripheral drug	Hypnosis with SSRI and anticholinergic agent
	CBT with SNRI and pregabalin
CBT, cognitive-behavioural therapy.	

## CONCLUSIONS

Functional abdominal pain syndrome is a difficult-to-treat, debilitating chronic abdominal pain disorder. It is related to alterations in endogenous pain modulation systems, including dysfunction of descending pain modulation and cortical pain modulation circuits. The diagnosis is symptom-based with further diagnostic evaluation depending on the absence or presence of alarm features. The approach to successful treatment is rooted in the biopsychosocial philosophy with a therapeutic patient-

physician partnership at its base. Therapeutic modalities include nonpharmacological therapy and pharmacological therapy. These treatments can be combined in various ways to produce an augmentation effect. Although few studies have been designed to assess FAPS or its treatment specifically, the treatment strategies outlined in this paper appear to be effective.

## ACKNOWLEDGEMENT

*Declaration of personal and funding interests:* None.

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