52 year old female with abdominal pain

- 5 year history of persistent right sided burning/sharp abdominal pain
- Not clearly related to eating or a bowel movement
- Occurs daily and interferes with her daily activities. She is on disability related to this pain
- She has seen her PCP, another GI, and a pain specialist. She is currently on vicodin daily
- Her bowel habits were normal until she started on vicodin
- “Dr. please help me – you are my last hope…”
**Functional Abdominal Pain Syndrome**

Must include *all* of the following* . . .

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

*Criteria fulfilled for the last 3 mos. with symptom onset at least 6 mos. before diagnosis

_Clouse, Gastroenterology 2006; 130:1492_

**CNS Contribution to GI Pain**

- Chronic abdominal pain (FAPS)
- Other functional pain disorders
  - IBS
  - Functional dyspepsia
  - Biliary type abdominal pain
CNS Contribution to GI Pain

- Chronic abdominal pain (FAPS)
- Other functional pain disorders
  - IBS
  - Functional dyspepsia
- Biliary type abdominal pain
  - Builds to steady level & lasts >30 minutes
  - Not related to BM
  - Not relieved by postural change or PPI
  - May radiate to back or scapula
  - May cause awakening from sleep

Clinical Spectrum: IBS and FAPS

<table>
<thead>
<tr>
<th></th>
<th>Mild/Mod IBS</th>
<th>Severe IBS</th>
<th>FAPS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population Frequency</td>
<td>5-10%</td>
<td>1-5%</td>
<td>&lt;1%</td>
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<tr>
<td>Abdominal Pain</td>
<td>+/-</td>
<td>++/+++</td>
<td>++/+++</td>
</tr>
<tr>
<td>Bowel Dysfunction</td>
<td>+/-</td>
<td>++/+++</td>
<td>0/+</td>
</tr>
<tr>
<td>Psychosocial Distress</td>
<td>++/+++</td>
<td>+++</td>
<td>0/+</td>
</tr>
<tr>
<td>Somatic Symptoms</td>
<td>0/+</td>
<td>+++</td>
<td>++/+++</td>
</tr>
<tr>
<td>Health Care Utilization</td>
<td>++/+++</td>
<td>++/+++</td>
<td></td>
</tr>
<tr>
<td>Treatment Method</td>
<td>Bowel&gt;CNS</td>
<td>CNS&gt;Bowel</td>
<td>CNS</td>
</tr>
</tbody>
</table>
FAPS - Multiple Contributions

Nociception
Recent stress
Culture & Early Life Events
Coping & Social support
Psychological status
Primary/Secondary gain

PAIN IS MAIN PREDICTOR OF HEALTH OUTCOME IN FGID

- Increased medical visits
- Increased health care utilization
- Increased illness severity
- More school and work absenteeism
- Poorer coping
- Poorer health related quality of life
SYMPTOM-RELATED BEHAVIORS OFTEN SEEN IN PATIENTS WITH FAPS

- Expressing pain through verbal and nonverbal methods
- Urgent reporting of intense symptoms
- Minimizing or denying a role for psychosocial contributors
- Requesting diagnostic studies or even exploratory surgery to validate the condition as “organic”
- Focusing attention on complete relief of symptoms rather than adaptation to a chronic disorder
- Seeking health care frequently
- Taking limited personal responsibility for self-management, while placing high expectations on physician to achieve symptom relief
- Making requests for narcotic analgesics

Clouse, Gastroenterology 2006; 130:1492
1. Accept the pain as real

- **Acknowledge the discomfort / distress**
- **Consider a pain diary to assess:**
  - Precipitating factors
  - Emotional responses
  - Cognitions
FAPS - Treatment

1. Accept the pain as real
2. Don’t just do something . . . Stand there!
   - Minimize diagnostic studies
   - Base decisions on the data . . . not patient requests

FAPS - Treatment

1. Accept the pain as real
2. Don’t just do something . . . Stand there!
3. Set reasonable goals:
   - Don’t expect a cure
   - Encourage improved function despite the pain
   - Know your limitations
FAPS - Treatment

1. Accept the pain as real
2. Don’t just do something . . . Stand there!
3. Set reasonable goals
4. Behavioral techniques:
   - *Increase patient control of symptoms*
   - *Reinforce healthy behaviors*
   - *Support the process, not the product*
   - *Don’t act on each symptom*
   - *Time management*

Treatment

Severity

Symptomatic medical treatment
Stress reduction
Exercise, yoga, etc.

Patient – Physician Relationship
FAPS - Treatment

1. Accept the pain as real
2. Don’t just do something...Stand there!
3. Set reasonable goals
4. Behavioral techniques
5. Pharmacotherapy:
   - ASA / NSAIDs not helpful
   - Avoid narcotics
   - Antidepressants (TCA, SSRI, SNRI)
   - Anticonvulsants (gabapentin/pregabalin)?

FGID – Pain Treatment

Potential Targets & Associated Treatments

- CNS
  - SSRIs / SNRIs
  - Antipsychotics?
  - Anticonvulsants
  - Tricyclics
  - Probiotics
  - Diet
  - NA antibiotics
  - Anti-spasmodics
  - Opioid agonists
  - Prosecretories
  - 5-HT agents

- Altered motility / secretion
- Altered sensation
Treatment

Severity

Psychiatric referral

Augmentation

4-6 wks

2 drugs

Increase dose

Low dose

TCA or SNRI

CBT

Hypnosis

IP psychotherapy

Stress management

Symptomatic medical treatment

Stress reduction

Exercise, yoga, etc.

Patient - Physician Relationship

* Monitor side effects

CBT vs. EDU and DES vs. PLA for Moderate to Severe FBD

CBT/EDU Responder Analysis*

P<0.0001

P=0.0002

n=110

n=51

n=100

n=46

DES/PLA Responder Analysis*

P=0.128

P=0.021

P=0.006

n=107

n=57

n=89

n=80

n=55

* Responder defined as % $\geq$ 3.5 on Satisfaction scale at end of treatment

Drossman, et. al., Gastroenterology 2003; 125:19-31
### Antidepressant Receptor Site Effects

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<tr>
<th></th>
<th>NE</th>
<th>5HT</th>
<th>Histamine</th>
<th>Ach</th>
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<tbody>
<tr>
<td><strong>TCAs (10-150 mg)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline (3°)</td>
<td>+++</td>
<td>+++</td>
<td>++++</td>
<td>+++</td>
</tr>
<tr>
<td>Doxepin (3°)</td>
<td>++</td>
<td>+++</td>
<td>++++</td>
<td>++</td>
</tr>
<tr>
<td>Desipramine (2°)</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Nortriptyline (2°)</td>
<td>+++</td>
<td>+</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td><strong>SSRIs (1-2 pills)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>nil</td>
<td>++++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>nil</td>
<td>++++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>nil</td>
<td>++++</td>
<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>nil</td>
<td>++++</td>
<td>nil</td>
<td>+</td>
</tr>
<tr>
<td>Sertraline</td>
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<td>++++</td>
<td>nil</td>
<td>nil</td>
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<tr>
<td><strong>SNRI’s (variable)</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Venlafaxine</td>
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<td>nil</td>
<td>nil</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>+++</td>
<td>+++</td>
<td>nil</td>
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</table>

### Antidepressant Treatment

<table>
<thead>
<tr>
<th></th>
<th>TCA (pain)</th>
<th>SSRI (pain)</th>
<th>SNRI (pain)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Potential benefits</strong></td>
<td>depression</td>
<td>depression, panic, anxiety, OCD</td>
<td>depression</td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td>Sedation, Hypotension, Constipation, Dry mouth/eyes, Arrhythmias, Weight gain, Sex dysfunction</td>
<td>Insomnia, Agitation, Diarrhea, Night sweats, Headache, Weight loss, Sex dysfunction</td>
<td>Nausea, Agitation, Dizziness, Sleep disturbance, Fatigue, Liver dysfunction</td>
</tr>
<tr>
<td><strong>Risk of overdose</strong></td>
<td>moderate</td>
<td>minimal</td>
<td>minimal</td>
</tr>
<tr>
<td><strong>Dose Adjustment</strong></td>
<td>yes</td>
<td>not usual</td>
<td>varies</td>
</tr>
<tr>
<td><strong>Cost / month</strong></td>
<td>$5-50</td>
<td>$20-250</td>
<td>$80-250</td>
</tr>
</tbody>
</table>
GENERAL APPROACH TO PRESCRIBING ANTIDEPRESSANTS

• **Assess symptoms**
  - IBS symptoms: pain, diarrhea, etc
  - Non-GI symptoms: poor sleep
  - Co-morbid conditions: anxiety, depression, fibromyalgia

• **Leverage side effect profile**

• **Consider cost**

• **Consider previous medication experiences and preferences**
  - Intolerance to medications or short duration of treatment adherence – benefits may not occur for 4-6 weeks
  - May want to start at low doses and gradually increase to lowest, most effective dose

GENERAL GUIDELINES

• **If patient has IBS and predominant symptom is pain**
  - Low dose TCA (choice dependent on sleep, bowel habit)
  - Consider SSRI or SNRI (Duloxetine)

• **If patient has predominant psychological symptoms thought to amplify pain**
  - SSRI (avoid Paroxetine if IBS-C)
  - SNRI
  - Mirtazepine but can cause weight gain
  - Behavioral/psychological treatment
  - Can consider combination therapy
  - ? Antipsychotics (e.g. Seroquel- helps sleep and anxiety?)
IBS - Behavioral Treatments

• Cognitive - behavioral
  Uses diaries and exercises to reframe maladaptive thoughts and increase control over symptoms

• Psychotherapy - Interpersonal
  Identify and address difficulties in relationships and emotional conflicts via bowel symptoms

• Hypnosis
  Suggestion used to produce overall relaxation and reduce gut sensations

• Relaxation training
  Uses imagery and relaxation techniques to reduce autonomic arousal and stimulate muscular relaxation

When to Refer for Behavioral Treatment

• Consider referral for:
  • Any level of symptoms
    • Daily severe symptoms is a negative predictor of outcome
  • Patient recognizes a relation to stress
  • Maladaptive coping/catastrophizing
  • Motivated to try behavioral therapy
Limitations of Psychological Treatment

• Requires a motivated, engaged patients
• Therapist must be experienced with GI problems
• Variable reimbursement from third party payers
• Typically requires ongoing medical care – not usually a replacement for the gastroenterologist

Treatment

Severity

Combined AD + psych

Psychiatric referral

Augmentation 2 drugs

Increase dose

/4-6 wks

Low dose

TCA or SNRI or SSRI

CBT

Hypnosis

IP psychotherapy

Stress management

Symptomatic medical treatment

Stress reduction

Exercise, yoga, etc.

Patient - Physician Relationship

* Monitor side effects
COMBINING ANTIDEPRESSANTS & BEHAVIORAL TREATMENTS

• Brain Imaging
  Antidepressants may have central and peripheral effects, acting on limbic/paralimbic regions which modulate pain
  Psychological treatments may have “top down” effects on prefrontal cognitive areas improving “executive” function as well as limbic regions

• Clinical trials show combined treatments > monotherapy for headache, depression and other psych disorders

CONCLUSIONS

• FAPS is characterized by chronic abdominal pain not associated with physiologic events
• Limited scientific evidence concerning pathophysiology and treatment
• Treatment management based on therapeutic patient-provider relationship and centrally targeted therapies
• Rationale for use of TCAs and SSRIs/SNRIs to treat FAPS
  – Central effects: affects cortico-limbic processing of emotional stimuli and may enhance descending pain inhibition
• Discourage use of narcotics to avoid addiction and Narcotic Bowel Syndrome (NBS)