Irritable Bowel Syndrome

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Definition

"A variable combination of chronic or recurrent gastrointestinal symptoms (attributed to the pharynx, esophagus, stomach, biliary tree, small or large intestine, or anorectum) not explained by structural or biochemical abnormalities."

Rome criteria, 1990

Rome II Criteria

At least 12 weeks in preceding 12 months of abdominal discomfort or pain and 2 of following:
- Pain relieved with defecation and/or
- Onset associated with change in frequency of stool and/or
- Onset associated with change in form (appearance) of stool

IBS - Rome Criteria Validation

Rome I + Absence of red flags = 63% Sensitivity
- Weight loss
- Nocturnal symptoms
- Blood in stools
- Recent antibiotics
- + FH colon cancer
- Abnormal PE

100% Specificity
98-100% PPV

U.S. Prevalence

IBS - Epidemiology

U.S. Prevalence

Age in Years

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>15-34</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-44</td>
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<tr>
<td>&gt;45</td>
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</table>
Prevalence of IBS in the World

IBS - Epidemiology

Doctor Visits by Gender

IBS - Psychosocial & Quality of Life

Prevalence of GI-related surgeries in IBS patients

IBS - Psychosocial

Concordance Among Twins

Amount of IBS visits by gender
Genetics In IBS

- Brain-Gut interactions:
  - Corticotropin-releasing hormone (CRH)
  - 5-hydroxytryptamine (5-HT)

- Enteric Nervous System
  - Enteric serotonin reuptake transporter

- Proposed candidate genes
  - 5-HT2A receptor gene (IBS)
  - B3-adrenoceptors (IBS)
  - Interleukin-10 (IBS)
  - Interleukin 1b (post-infectious IBS)

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**IBS - Early Life Influences**

**IBS - Psychosocial**

- Psychologic disturbance relates to patients who see physicians
- Psychosocial factors influence health care seeking

**IBS - Physiology**

- Stress affects GI function
- Pain sensitivity
- Clustered contractions
- CNS / ENS Autonomic reactivity

- Meas Pain / motility
- 3 cm pain motility
- Visceral hypersensitivity
- Post-Infectious IBS

- Motility
- Myoelectrical Marker
- Inflammation
- Visceral Hypersensitivity

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**IBS - Post-infection Gut Dysfunction**

- 94 Acute Gastroenteritis
- Psych testing Rectal biopsy +
- Psych -

- 22 IBS “Rome I”
- 72 No GI symptoms
- 18 Controls

Abnormal physiology + Rectal inflammation +

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**IBS - Post-infection Gut Dysfunction – Study Summary**


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**IBS - Psychosocial**

- Whitehead WE, et al., Gastroenterology 1988; 95;709

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**IBS - Physiologic Research**


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Pain Tolerance

IBS - Physiology

Lower Pain Tolerance in IBS Occurs Primarily in the Bowel - Whitehead, 1990

Cook IJ, et al., Gastroenterology 1987; 93:727

The Enteric Nervous System Functions as a Brain-in-the-Gut

IBS - Enteric Nervous System

Brain-in-the-Gut

Integrated Neural Circuits
- Program library
- Feedback control
- Reflexes
- Information processing

Myenteric plexus

IBS - Pathophysiology

Input Integration Effect

Cognition Affect

Sight Sound Small Somatosensory

Visceraesensory

Motority Secretion Blood Flow

Mayer EA, Gastroenterology 1990; 99:1688

IBS - fMRI During Rectal Distention

CNS Activation (fMRI) of Normals and IBS Subjects to Rectal Distension

Kane et al., Gastroenterology 2000; 119:842

IBS - Post Rectal Stimulation Activation (PET) in Normals and IBS

Anticipation of Distention 45 mm Hg of Distention

Mid Cingulate Cortex

Central nervous system
- Neurons

Digestive tract
- Neurons
- Enterochromaffin cells
- Mast cells

IBS - Serotonin Content (5-HT)

Central nervous system
- Neurons

Digestive tract
- Neurons
- Enterochromaffin cells
- Mast cells

Mayer EA, Gastroenterology 1990; 99:1688
Paul Lebovitz, MD
Irritable Bowel Syndrome
Washington Hospital Grand Rounds
August 20, 2003

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**IBS - Epidemiology**

Symptom Retention

- Initial survey: 17%
- 12-20 months later: 18%

Talley et al., Am J Epid 1992; 136:165

**IBS - Patient’s Agenda**

- My symptoms are worse
- Do I have cancer?
- I’m under more stress
- Why am I not getting better?
- Can’t function
- Why am I crazy?


**IBS - Treatment**

Placebo Response Rate

<table>
<thead>
<tr>
<th>Author</th>
<th>Drug</th>
<th>Placebo Response (%)</th>
<th>p&lt;.05</th>
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<tbody>
<tr>
<td>Piai ’81</td>
<td>Prifinium</td>
<td>33</td>
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<tr>
<td>Milo ’80</td>
<td>Domperidone</td>
<td>34</td>
<td>yes</td>
</tr>
<tr>
<td>Page ’81</td>
<td>Dicyclomine</td>
<td>54</td>
<td>yes</td>
</tr>
<tr>
<td>Heefner ’78</td>
<td>Desipramine</td>
<td>60</td>
<td>equivocal</td>
</tr>
<tr>
<td>Myren ’82</td>
<td>Trimiprimine</td>
<td>67</td>
<td>no</td>
</tr>
<tr>
<td>Longstreth ’81</td>
<td>Metamucil</td>
<td>71</td>
<td>no</td>
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<tr>
<td>Fielding ’81</td>
<td>Timolol</td>
<td>73</td>
<td>no</td>
</tr>
<tr>
<td>Fielding ’80</td>
<td>Trimebutine</td>
<td>88</td>
<td>no</td>
</tr>
</tbody>
</table>


**IBS - Diagnosis**

Rediagnosis Follow-up

- Owens ’95: 1, Follow-up Months: 24-360
- Harvey ’87: 0, 60-64
- Svendsen ’85: 4.5, 60
- Sullivan ’83: 4, 29
- Holmes ’82: 5, >72
- Hawkins ’71: 3.7, 24-240


**IBS - Diagnostic Approach**

- Establish symptom-based diagnosis
- Identify dominant symptom
  - Pain
  - Diarrhea
  - Constipation
- Consider other clinical factors
- Perform diagnostic tests
- Initiate treatment
- Reassess in 3-6 weeks

Drossman DA, et al., Gastroenterology 1997; 112:2187

- Establish symptom-based diagnosis
- Identify dominant symptom
- Perform diagnostic tests
- Consider other clinical factors
- Initiate treatment
- Reassess in 3-6 weeks
**IBS - Diagnosis**

**Physical**
- Abnormal exam
- Fever
- Positive occult stool

**Red Flags**
- Weight loss
- Onset in older patients
- Nighttime awakening
- Family history of cancer / IBD

**Initial Labs**
- Hgb
- WBC
- ESR
- Abnormal chemistry

**IBS - Diagnostic Approach**

1. Establish symptom-based diagnosis
2. Identify dominant symptom
3. Consider other clinical factors
4. Perform diagnostic tests
5. Initiate treatment
6. Reassess in 3 - 6 weeks

**IBS - Treatment Approach**

1. Education / Reassurance
2. Dietary Modifications
3. Monitoring and modification
4. Pharmacotherapy of gut symptoms
5. Psychological treatments
6. Referral for pain management
7. Set realistic goals
8. Antidepressants
9. Referral for medical / pain management
10. Focus on health, not illness

**Dietary Modifications**
- Eliminate offending items:
  - Lactose
  - Sorbitol gum
  - Caffeine
  - Large meals
  - Fatty foods
  - Food sensitivity
  - Alcohol
  - Gas producing foods
- Increase fiber (constipation)

**Symptom Diary**

<table>
<thead>
<tr>
<th>Date/ Time</th>
<th>Symptom Severity (1 - 10)</th>
<th>Associated Factors</th>
<th>Emotional Response</th>
<th>Thoughts/ Cognitions</th>
</tr>
</thead>
<tbody>
<tr>
<td>pain, diarrhea</td>
<td>diet, activity, stress</td>
<td>angry, sad, anxious</td>
<td>out of control, hopeless</td>
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</tbody>
</table>

**IBS - Psychological Treatment Studies**

**Controlled Trials**
- Cognitive-Behavioral therapy
- Psychotherapy - interpersonal therapy
- Hypnosis
- Relaxation training

8/9 studies continued to show benefit
10/13 studies favored psychological treatment

**Drossman et al., Gut 1999; 45:II30**

**IBS - Treatment Approach**

- **Pharmacotherapy of gut symptoms**
  - Pain
  - Diarrhea
  - Constipation


**IBS - Treatment**

**Pharmaceutical Agents**

<table>
<thead>
<tr>
<th>Pain</th>
<th>Diarrhea</th>
<th>Constipation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antispasmodics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Anticholinergics</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Peppermint oil</td>
<td></td>
<td></td>
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<tr>
<td>Opioid-like Agents</td>
<td></td>
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</tr>
<tr>
<td>- Dextromethorphan</td>
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<td></td>
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<tr>
<td>- Trimebutine</td>
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<td></td>
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<tr>
<td>- Loperamide</td>
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<tr>
<td>- Cholestyramine</td>
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<tr>
<td>- Alosetron</td>
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<td></td>
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<tr>
<td>- Fiber</td>
<td></td>
<td></td>
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<tr>
<td>- Osmotic laxatives</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Tegaserod</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Misoprostil</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- PEG solution</td>
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</tr>
</tbody>
</table>


**IBS - Effect of 5-HT3 Antagonist**

**Relief of Abdominal Pain and Discomfort**


**Antibiotics**
- SIBO testing
- Rifaximin
- FDA approval? Denied 2011
TCAs for IBS

- First high quality randomized trial comparing TCA (desipramine) and placebo
- Mixed message:
  - ITT - no significant difference
  - Per-protocol analysis - 73% vs. 49% (p=0.006)
  - 28% dropouts

SNRI

- Efficacy of Cymbalta in the treatment of IBS (all subtypes) in patients with GAD.

Kaplan, Lebovitz, 2011 in progress
IBS Treatment

New Therapeutic Options

- 5-HT3 antagonist
- NK antagonist
- CCK antagonists
- Anti-depressants
  - TCAs
  - SSRIs / SNRIs
- x opioid agonist
  - Opioid antagonists
- prokinetic agent
  - Metoclopramide

IBS - Treatment Approach

Referral for symptom management
- Psychologist
- Psychiatrist
- Pain center

Conference Evaluations

Online evaluations at:
www.pacnp.org/conference