Irritable Bowel Syndrome: Diagnosis, Evaluation, and Treatment

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Irritable Bowel Syndrome

Most common GI Condition

Commonly seen in Primary Care - IBS pts tend to visit physicians frequently

Accounts for 25% to 50% of all GI referrals

Saito, YA. Am J Gastroenterol. 2002
American College of Gastroenterology Task Force of Irritable Bowel Syndrome. Am J Gastroenterol 2009
Chial H, Camilleri M. J Gender Specif Med 2002
IBS: Epidemiology

- 10-15% of US population
- 2:1 female predominance in North America
IBS Subtypes

- IBS is classified by the predominant bowel habit:

  **Diarrhea-predominant** ($\geq 25\%$ loose, $<5\%$ hard stools)

  **Constipation-predominant** ($\geq 25\%$ hard, $<25\%$ loose)

  **Mixed** ($\geq 25\%$ hard, $\geq 25\%$ loose)

  **Untyped** - insufficient abnormality of stool consistency to meet the other subtypes
Risk Factors:

Family history of first-degree relatives with IBS

History of sexual abuse

Diagnosis of anxiety or depression
Anxiety/Depression:

- Not all patients with IBS have a mood or anxiety disorder:
  - The *lifetime prevalence* of a mood or anxiety disorder is *approximately 50%* in IBS pts.

Case #1

- Your patient comes in for an IBS f/u appt. Which of the following signs or symptoms WOULD make you reevaluate the diagnosis of IBS?
Case #1

a. Associated GERD
b. Mucousy discharge with stools
c. Nocturnal diarrhea that prevents sleep
d. Nausea
e. Change in stools from predominantly diarrhea to predominantly constipation
f. Feeling of incomplete evacuation after BM
Clinical Manifestations
ABDOMINAL PAIN

A **Prerequisite** clinical feature of IBS

- Often Cramp-like
- Exacerbated by eating or emotional stress
- Improvement with defecation
- Women may report **worsening symptoms during premenstrual period**
Alteration of Bowel Movements

- Loose or hard stools are a common feature of IBS.

- **Most** patients will **change subtypes** in as little as 1 year (Constipation, Diarrhea, Mixed)
Other Clinical Manifestations

- Urgency even to the point of fecal incontinence
- Straining with BMs
- Abdominal Bloating

ACG Guidelines, Am J Gastroenterol 2009
Other Clinical Manifestations

- Evacuation followed by: feeling of incomplete evacuation OR significant relief

- About 50% of all patients with IBS will complain of mucus discharge with stools

- 25-50% also have Upper GI symptoms

ACG Guidelines, Am J Gastroenterol 2009
Non-GI sx:

- Impaired sexual function
- Dysmenorrhea
- Increased urinary frequency or urgency
- Fibromyalgia symptoms
To meet diagnostic criteria for IBS:

Abdominal discomfort must be present at least **12 weeks** (don’t need to be consecutive) out of the last **12 months**
“Red Flag” Alarm Features:

- Bloody stools
- Fever
- Unintentional Weight loss
- Nocturnal Diarrhea that prevents sleep
- Anemia
- First degree relative with IBD or early colon cancer
- >50 y.o at onset

“Alarm Sxs” should make an examiner consider other diagnoses
Differential Diagnosis:
Differential Diagnosis

- Malignancy

Others: Parasitic infections, Endometriosis, Thyroid/Parathyroid D/Os, Laxative abuse

Diarrhea Predominant:

- Inflammatory Bowel Disease
- Lactose Intolerance
- Celiac Disease
Case #2

- A 40 y.o. female presents with symptoms consistent with IBS-C. She denies any red flag alarm symptoms. Based on current AGA recommendations and current EBM, which of the following tests would you order before you can accurately make the diagnosis of Constipation-Predominant Irritable Bowel Syndrome.
Case #2

a. CBC
b. CMP
c. Colonoscopy
d. Anti-endomesial antibody
e. Hydrogen Breath Testing
f. CRP
Diagnostic Testing
AGA Guidelines recommend a stool **Hemoccult and CBC** for all patients to rule out the “red flag” alarm feature of Anemia or rectal bleeding.
Diagnostic Tests:

- No evidence to support other routine diagnostic testing in patients without alarm features and in those without diarrhea.

No evidence for routine:

- CMP
- Thyroid tests
- Stool examination
- Abdominal imaging

ACG Position Statement 2009
AGA Recommendations
Different Groups for Evaluation:

- **Constipation-Predominant**: No further evaluation if no red flags. Abdominal Xray if clinical concern for obstruction.

- **> 50 years old**: Colonoscopy (can also bx for microscopic colitis)

- **Diarrhea-Predominant, Mixed, Other**: Consider more testing: IBD, Celiac, Lactose Intolerance
Case #3

A 40 y.o. female presents with 6 months of diarrhea and bloating. + family history of IBD (unknown if UC or Crohns) in her MGF. No associated wt loss or f/s/c. Guiac is negative and CBC nml. Fecal calprotectin and CRP are normal. Based on current evidence, you can be relatively convinced that you have ruled out which diagnosis?
Case #3

A. Lactose intolerance
B. Celiac Disease
C. Active Crohn’s disease
D. Abdominal malignancy
E. Parasitic Infection
F. Irritable Bowel Disease
Ruling Out Inflammatory Bowel?

- CRP (better than ESR)
- Fecal Calprotectin (at least as good as CRP)


Sipponen T, et al. Inflamm Bowel Dis. 2008
Inflammatory Markers: CRP

- CRP is increased in:
  - Virtually All pts with active Crohn’s dz
  - About 50% with active Ulcerative Colitis
  - Should not be significantly elevated with functional bowel symptoms

Using highly sensitive CRP (ELISA) to differentiate IBS from new cases of IBD:

A cut-off value of 2.3 mg/l has:

- 100% sensitivity
- 67% specificity

Mean CRP Values

- 0.38 mg/l constipation-predominant IBS
- 1.43 mg/l diarrhea-predominant IBS
- 1.45 mg/l quiescent IBD
- 8.89 mg/l new active ulcerative colitis
- 13.12 mg/l new active Crohn's disease

Inflammatory Markers: Fecal Calprotectin

- A cut off of 30 μg/g had 100% sensitivity in discriminating active Crohn’s Disease from IBS in a small pt study

In other studies, the detection of Crohns and UC with Fecal Calprotectin:

Sensitivity of 87-95%

Specificity 92-93%

Studies comparing CRP and Fecal Calprotectin found it slightly more sensitive

Sipponen T, et al. Inflamm Bowel Dis. 2008
Take Home: IBD Screening

- Both CRP and Fecal Calprotectin are excellent tests for ruling out Crohn’s Dz.

- CRP and Fecal Calprotectin are not as good at detecting Ulcerative Colitis, but are still very sensitive for active disease.

- Fecal Calprotectin shows slightly better sensitivity for IBD than CRP (may depend on type of CRP used).
Lactose Intolerance

- Occurs more frequently in IBS than controls (35% vs 26%)
- Avoidance Diet Vs Hydrogen Breath Testing
In a meta-analysis of 14 IBS studies:

Celiac disease was **four times as likely** than in controls without IBS.

Celiac Screen

Screening with:

IgA anti-endomysial antibodies

Serum test with highest overall sensitivity and specificity
Take Home: Diarrhea Predominant IBS

Rule out the following:

- **Celiac Dz:** IgA antiendomysial antibodies
- **Lactose Intolerance:** Elimination Diet Vs Hydrogen Breath Test
- **Inflammatory bowel:** CRP and/or fecal calprotectin
I’ve Screened for my Differential Diagnoses and Have no Red Flags:

What do I do next?
Diagnosing IBS:

Can’t order confirmatory blood work/labs:
No diagnostic markers exist to confirm

Diagnosis is ultimately based on clinical presentation

American Gastroenterological Association recommends that the diagnosis should be based on Rome criteria
Case #4

A 45 y.o. female presents to you with alternating diarrhea and constipation for the last 4 months. Your examination is normal. Based on the Rome Criteria for IBS diagnosis, what question would you ask to help elicit the MOST useful information regarding IBS?
Case #4

a. Have you been having any associated abdominal discomfort?

b. Have you had straining or urgency with stool passage?

c. Have your symptoms been associated with the passage of mucous with stools

d. Have you had any associated abdominal bloating?

e. Do you have a history of anxiety or depression?
According to Rome Criteria,

- IBS **must** be associated with abdominal pain

- Painless diarrhea or constipation does not fulfill diagnostic criteria for IBS.
Rome Criteria

>12 weeks (need not be consecutive) in last year of ABDOMINAL PAIN or DISCOMFORT

AND

At least 2 of 3 features:

1. Relieved with defecation
2. Associated with change in stool frequency
3. Associated with change in stool form (appearance)
Before Reviewing Treatment...Must Understand the Proposed Pathophysiology
Pathophysiology of IBS

The pathophysiologic cause may differ between individuals with similar symptoms.

American Gastroenterology Association
Pathophysiology of IBS

- Altered Gastric Reactivity
- Visceral Hypersensitivity
- Inflammation
- Alteration in GI flora
- Post-infectious
- Small Bowel Overgrowth
Altered Gastrointestinal Reactivity

Altered GI reactivity in IBS (motility or secretion) results in symptoms of diarrhea or constipation

Altered reactivity may be a response to:
- Certain foods
- Stress
Visceral Hypersensitivity

- Enhanced perception of normal motility and visceral pain (i.e. like fibromyalgia of GI tract)
- Only found in a subset of IBS patients
- **Seratonin** may play a role

Mayer EA, Gebhart GF. Gastroenterology 1994
Mertz H, Naliboff B, Munakata J. Gastroenterology 1995
Inflammation:

- **Conventional wisdom:** no inflammation occurs in patients with IBS

- **Recent evidence** shows that some patients with IBS *(particularly diarrhea-predominant)* have increased microscopic inflammation of the GI tract

*Barbara, G, Stanghellini, V, et al. Gastroenterology 2004*


*Liebregts T, et al. Gastroenterology 2007*

*Tornblom et. Al. Gastroenterology 2002*
Inflammation in IBS

Mean CRP:

- 0.383 mg/l in constipation-predominant IBS
- 1.435 mg/l in diarrhea-predominant IBS
- 1.455 mg/l in quiescent IBD

Alteration in Fecal Microflora

- Fecal flora in IBS patients differs from those in healthy controls

- Treatment of patients with probiotics have yielded promising results

Kassinen A. Gastroenterology 2007
Yamazaki S, et al. Microflora 1982
Post-Infectious IBS

- IBS may develop after infectious enteritis and may occur in as high as 25% of patients after severe acute enteritis.


- Related to the severity of GE
Proposed Mechanisms for Post-Infectious IBS

- Disruption of mucosal nerves, which could lead to irritability
- Development of postinfectious bile acid malabsorption
- Alteration in colonic flora (tx with Abx?)
Small Intestinal Bacterial Overgrowth?

- Highly controversial

- Original study showed 78% of IBS pts had SIBO (based on lactose hydrogen breath test)

- Future studies showed less than 20% using same criteria

- Studies do not show improvement of symptoms with normalization of hydrogen breath test

Treatment
Treatment: Patient Education

- Education regarding the proposed mechanisms of IBS

- Patients should be informed of the chronic and benign nature of IBS and that they should have a normal life span
What Do Patients Think?

Can IBS develop into cancer?
22% yes  38% no

Will IBS shorten my life span?
23% yes  51% no

Caused by a lack of digestive enzymes?
52% yes  17% no

Problem Needing Surgery?
34% yes  27% no

Halper, A et al.  Am J Gastroenterology 2007
Case #5

- You have a patient with **Constipation-predominant IBS** who is *not responding to fiber*. Based on **current medical evidence**, which of the following choices would you prescribe as the **MOST EFFECTIVE and appropriate** treatment?
Case #5

a. Amitryptiline (Elavil)
b. Sertraline (Zoloft)
c. Loperamide
d. Avoiding flatogenic foods
e. Exercise
f. Increase fluid intake
Non-Medication Tx:

Safe But UNPROVEN Remedies:

- Avoiding flatogenic foods
- Increasing fluid intake
- Avoidance of caffeine and simple sugars
- Exercising
- Losing excess weight
Common INITIAL Treatments:

- Loperamide – diarrhea
- Fiber – constipation (and diarrhea)
- Polyethylene Glycol (MiraLax) – constipation
- Antispasmodics – (spasmotic pain)
- Probiotics – any symptoms of IBS

*Note: Combining treatments is often helpful

*ACG Guidelines, Am J Gastroenterol 2009*
Anti-Diarrheal Agents

- Loperamide is the most commonly used antidiarrheal agent for IBS
- More effective than placebo for treating diarrhea
- Does not improve global IBS symptoms or abdominal pain.

*American College of Gastroenterology EBM-Based Position Statement, Am J Gastroenterol 2009*
Increasing fiber intake might also help reduce symptoms of both constipation and diarrhea, although a systematic review of fiber for IBS showed no significant benefit.

Brandt LJ, et al. (Systematic review) Am J Gastroenterol 2002
Polyethylene Glycol

- Laxative

- Shown to be more effective and have less side effects than FDA approved medication for IBS-C

*Di Palma, Jack A et al. The American Journal of Gastroenterology, 2007*
Symptoms of Spasmotic Pain

- Antispasmodic drugs appear to *provide short-term relief*
- Long-term efficacy has not been proven.
- Response should be evaluated in 3–6 weeks

*American College of Gastroenterology EBM-Based Position Statement, Am J Gastroenterol 2009*
*Lynn RB, Friedman LS. N Engl J Med 1993*
Treatment: Antispasmodics

- Anticholinergic: Dicyclomine
- Antimuscarinic: Hyoscyamine
- Smooth muscle relaxant: Peppermint
Treatment: Peppermint

- A 2005 review article of 16 clinical trials showed mean response rate:
  - 58% for peppermint
  - 29% for placebo


- Other meta-analyses show a significant benefit, but a lower response rate
Treatment: Probiotics

- *Lactobacillus* and *Bifidobacteria*, are widely used in yogurts and other products
Treatment: Probiotics

- **Bifidobacterium**: probiotic with most evidence for efficacy

**Improves:**
- Abdominal pain/discomfort
- Bloating
- Straining
- Feelings of incomplete evacuation

**Doesn’t help with:**
- Stool frequency

Yamazaki S, et al. Microflora 1982
AGA Recs: Probiotics

- *Lactobacilli* DOES NOT appear to be effective for the treatment of IBS

- *Bifidobacteria* and some combinations of probiotics do appear to be effective

- Most of the studies were short-term; long-term data are lacking
Antibiotics for IBS

- Based on idea of SI bacterial overgrowth

- Recent study compared non-absorbable antibiotic Vs placebo for IBS-D or IBS-mixed

- Endpoint: global relief and reduced bloating

- Results: Antibiotic response rate 41%
  Placebo group: 32%

_Pimental, M et. al. NEJM 2011_
Antidepressants

- **First line** for pts with co-existing anxiety or depression
Treatment: Antidepressants

- Antidepressants are effective

- A 2009 meta-analysis concluded that antidepressants effective for relief of pain and global symptoms of IBS.

- Efficacy similar for selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs)

What type of Antidepressants

- TCA or SSRI based on type of IBS?

- **TCA** – tend to constipate (anticholinergic)

- **SSRIs** – tend to cause diarrhea
Antiflatuance Meds

- Data regarding simethicone are conflicting.
Anticonvulsants

- Examples: Gabapentin, Pregabalin
- Few data support their use for IBS
Behavioral Therapies

Combining medication AND behavioral therapies improves likelihood of successful IBS treatment

American College of Gastroenterology EBM-Based Position Statement, Am J Gastroenterol 2009
Cognitive Behavioral Therapy

The methods include:

- Problem-solving strategies for stress
- Muscle relaxation exercises
- Cognitive restructuring

A meta-analysis of 17 studies on CBT for IBS showed a greater than 50% reduction in GI symptoms.

*Lackner JM, et al. Gastroenterology 2007*
Meds to Avoid

Benzodiazepines are of limited usefulness.

Risk of drug interactions, habituation, addiction, and rebound withdrawal.

Furthermore, benzodiazepines may lower pain thresholds by stimulating gamma aminobutyric acid (GABA), which can lead to a decrease in brain serotonin.
CAM Treatment: Acupuncture

- Can be considered for patients who desire complementary and alternative treatments for their IBS.

- Multiple, mostly poor-quality studies have used acupuncture to treat IBS with mixed results

FDA Approved Meds:

- Alosetron
- Tagaserod
- Lubiprostone
- Linaclotide
5-HT3 Receptor Agonists/Antagonists

- **Zelnorm (Tegaserod)** – 5HT3 antagonist used for **IBS-C**, but was removed from the market in March 2007 due to cardiovascular side effects.

- **Alosetron (Lotronex)** – 5HT3 agonist used for **IBS-D**, FDA removed from the market due to ischemic colitis and severe constipation; allowed back under strict regulation.
Chloride Channel Activators

- Enhance chloride-rich intestinal fluid secretions without changing sodium and potassium concentrations in the serum.

- **Lubiprostone** FDA approved for **IBS with constipation** in women aged 18 years and older.

- Efficacy is still questionable and it is expensive

- Best reserved for patients with IBS and severe constipation in whom other approaches have been unsuccessful
Guanylate Cyclase Agonists

- Class of newest FDA approved IBS treatment (08/12)
- Increased levels of chloride and bicarbonate in the intestinal lumen and speeds up gastrointestinal transit.
- Linzess (linaclotide) treats IBS with constipation (IBS-C) in adults; came to market in August 2012
- Only effective in small percentage of IBS-C patients
Not FDA Approved

- Antidepressants
- Antispasmodics
- Probiotics
- Antibiotics
- Antidiarrheals
- Laxatives
Take Home: Treatment

Counseling patient is the first step in treatment

1st line Agents:
Loperamide
Fiber
Polyethylene Glycol
Antispasmodics
Probiotics
Antidepressants (if mood d/o)

Combining treatments is often more effective (particularly Behavioral and Medication tx)

FDA approved meds are all reserved for more severe IBS non-responsive to 1st line tx
FIVE KEY POINTS

• Abdominal discomfort is a prerequisite for the diagnosis of IBS. Diarrhea and constipation without abdominal discomfort does not meet criteria for IBS.

• No specific serologic markers exist for IBS; Diagnosed clinically based on Rome Criteria

• IBS should not cause rectal bleeding (without hemorrhoids), fever, weight loss, anemia, or nocturnal diarrhea that prevents sleep.

• Counseling patients about IBS is the first step in treatment

• Most successful treatment will be comprehensive and involve multiple strategies.
Questions from the Audience?