Small Intestinal Bacterial Overgrowth Syndrome

Learning Luncheon
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Alimentary Pharmabiotic Center
University College Cork
Cork, Ireland

Objectives

• Small Intestinal Bacterial Overgrowth (SIBO): what is it?
• How to define/diagnose?
• Treatment
• Role in Irritable Bowel Syndrome (IBS)
The Context
Host-Microbe Interactions

Microbiota-Host Interactions in Gastrointestinal Disease

- Helicobacter
- Enteric infections
- Small intestinal bacterial overgrowth (SIBO)
- C. difficile, pseudomembranous colitis
- Necrotising enterocolitis
- IBD
  - Pouchitis
- Liver disease
  - NAFLD, Alcoholic liver disease, PSC, TPN-related liver disease
- Obesity
- IBS and constipation
Microbiota-Host Interactions: the Case of Dyspepsia and *Helicobacter pylori*
Why do some develop gastric cancer and others DU's?

- Individuals with gastritis predominantly localized to the antrum retain normal (or even high) acid secretion
- Individuals with extensive corpus gastritis develop hypochlorhydria and gastric atrophy, which are presumptive precursors of gastric cancer
Why do some develop cancer and others DU’s?

- Interleukin-(IL)1β
  - Initiates and amplifies the inflammatory response to *Helicobacter pylori*
  - Is a potent inhibitor of gastric acid secretion

- Pro-inflammatory genotypes of the IL-1 loci (IL-1B231T, IL-1RN*2/*2) increase
  - the likelihood of a chronic hypochlorhydric response
  - the risk of gastric cancer


Microbiota-Host Interactions in Gastrointestinal Disease

- *Helicobacter*
- Enteric infections
- Small intestinal bacterial overgrowth (SIBO)
- *C. difficile*, pseudomembranous colitis
- Necrotising enterocolitis
- IBD
  - Pouchitis
- Liver disease
  - NAFLD, Alcoholic liver disease, PSC, TPN-related liver disease
- Obesity
- IBS and constipation
Definitions
Focus on Malabsorption

• “a bacterial flora qualitatively resembling that found in the large intestine and faeces”

• “the occurrence of a bile salt tolerant flora consisting of both aerobic bacteria such as E. coli and S. faecalis and anaerobic bacteria such as Bacteroides and Bifidobacteria


SIBO: Definitions

• Culture
  → 10^5 Total
  → 10^3 Colonic

• Breath Tests
  – d-Xylose
  – Glucose
  – Lactulose

• Response to therapy

jejunal fluid
What is the basis for these definitions?


<table>
<thead>
<tr>
<th>Glucose Breath Hydrogen Test</th>
<th>Culture Positive</th>
<th>Culture Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>5/8</td>
<td>2/12</td>
<td></td>
</tr>
</tbody>
</table>

| Lactulose Breath Hydrogen Test | 13/19 | 9/16 |

Corazza et al, Gastroenterology 1990;98:302-9
Causes

- Drug therapy
- Immune deficiencies
- Pancreatic exocrine deficiency

Pathogenesis

- Defenses against SIBO
  - Gastric acid
  - Intestinal motility
  - Intact ileo-cecal valve
  - Immunoglobulins
  - Bacteriostatic properties of pancreatic and biliary secretions

- Causes
  - Achlorhydria
  - Motility disorders e.g. scleroderma
  - Anatomical defects e.g. fistula, resection, strictures
  - Immune deficiencies
  - Pancreatic exocrine deficiency
# Gastrointestinal Disorders

<table>
<thead>
<tr>
<th>Disease</th>
<th>Test Used</th>
<th>Outcome</th>
<th>Author</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crohn's Flare</td>
<td>GHBT</td>
<td>+</td>
<td>Klaus</td>
<td>25%</td>
</tr>
<tr>
<td>Tropical Enteropathy</td>
<td>Response to therapy</td>
<td>-</td>
<td>Trehan</td>
<td>No response</td>
</tr>
<tr>
<td>Coeliac Disease</td>
<td>Aspirate</td>
<td>+</td>
<td>Rubio-Tapia</td>
<td>9.3%</td>
</tr>
<tr>
<td>Coeliac Disease</td>
<td>LHBT</td>
<td>+</td>
<td>Chang</td>
<td>Resistant disease but no response to rifaximin</td>
</tr>
<tr>
<td>Post-Gastrectomy</td>
<td>GHBT</td>
<td>+</td>
<td>Paik</td>
<td>78 vs 7%</td>
</tr>
<tr>
<td>Erosive esophagitis</td>
<td>GHBT</td>
<td>+</td>
<td>Kim</td>
<td>67 vs 37%</td>
</tr>
<tr>
<td>Intestinal Failure</td>
<td>Culture</td>
<td>+</td>
<td>Gutierrez</td>
<td>PN use only risk factor</td>
</tr>
<tr>
<td>Pelvic radiotherapy</td>
<td>GHBT</td>
<td>+</td>
<td>Wedlake</td>
<td>26%</td>
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</table>

# Motility Disorders

<table>
<thead>
<tr>
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<th>Test Used</th>
<th>Outcome</th>
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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic Fibrosis</td>
<td>GHBT</td>
<td>-</td>
<td>Lisowska</td>
<td>37 vs 13%</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>LHBT</td>
<td>-</td>
<td>Lisowska</td>
<td>Delayed OCTT</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>GHBT</td>
<td>-</td>
<td>Marie</td>
<td>43%</td>
</tr>
<tr>
<td>Scleroderma</td>
<td>LHBT</td>
<td>-</td>
<td>Parodi</td>
<td>56 vs 7% Delayed OCTT</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>GHBT</td>
<td>+</td>
<td>Lauritano</td>
<td>54 vs 5%</td>
</tr>
</tbody>
</table>
### Liver Disease

<table>
<thead>
<tr>
<th>Disease</th>
<th>Test</th>
<th>Outcome</th>
<th>Author</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>GHBT</td>
<td>+</td>
<td>Nancey</td>
<td>But not predictive of SBP</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>GHBT</td>
<td>+</td>
<td>Pande</td>
<td>49 vs 8% associated with severity</td>
</tr>
<tr>
<td>Cirrhosis EHPVO</td>
<td>GHBT</td>
<td>+</td>
<td>Lakshmi</td>
<td>24 vs 2%</td>
</tr>
<tr>
<td></td>
<td>GHBT</td>
<td>-</td>
<td></td>
<td>7 vs 2%</td>
</tr>
<tr>
<td>NAFLD</td>
<td>GHBT</td>
<td>+</td>
<td>Miele</td>
<td>Increased permeability</td>
</tr>
<tr>
<td>NASH</td>
<td>LHBT</td>
<td>+</td>
<td>Abu-Shanab</td>
<td>78 vs 31%</td>
</tr>
<tr>
<td>Minimal Encephalopathy</td>
<td>GHBT</td>
<td>+</td>
<td>Gupta</td>
<td>39% Delayed OCTT</td>
</tr>
</tbody>
</table>

### Metabolic Disorders

<table>
<thead>
<tr>
<th>Disease</th>
<th>Test</th>
<th>Outcome</th>
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<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>LHBT</td>
<td>+</td>
<td>Madrid</td>
<td>41% jejunal clusters</td>
</tr>
<tr>
<td>Obesity</td>
<td>GHBT</td>
<td>+</td>
<td>Sabate</td>
<td>17 vs 3% asstd with steatosis not NASH</td>
</tr>
<tr>
<td>Type I DM</td>
<td>+</td>
<td></td>
<td>Ojetti</td>
<td>44% with AN; 8% without</td>
</tr>
<tr>
<td>Type II DM</td>
<td>GHBT</td>
<td>+</td>
<td>Rana</td>
<td>15.5%</td>
</tr>
<tr>
<td>Bariatric Surgery</td>
<td>GHBT</td>
<td>+</td>
<td>Lakhani</td>
<td>Thiamine deficiency after Roux-en-Y</td>
</tr>
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</table>
## Miscellaneous Disorders

<table>
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<tr>
<th>Disease</th>
<th>Test</th>
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<th>Author Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Muscular Dystrophy</td>
<td>GHBT</td>
<td>+</td>
<td>Tarnopolsky 78 vs 7%</td>
</tr>
<tr>
<td>Parkinson's Disease</td>
<td>GHBT</td>
<td>+</td>
<td>Gabrielli 54 vs 8% linked to severity</td>
</tr>
<tr>
<td>Rosacea</td>
<td>GHBT</td>
<td>+</td>
<td>Parodi 46 vs 5% Improved with rifaximin</td>
</tr>
<tr>
<td></td>
<td>LHB</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urticaria</td>
<td>GHBT</td>
<td>-</td>
<td>Campanati</td>
</tr>
<tr>
<td>Restless Legs Syndrome</td>
<td>LHB</td>
<td>+</td>
<td>Weinstock 77% improved with treatment</td>
</tr>
<tr>
<td>Interstitial Cystitis</td>
<td>LHB</td>
<td>+</td>
<td>Weinstock 81%</td>
</tr>
<tr>
<td>Chronic Prostatitis</td>
<td>LHB</td>
<td>+</td>
<td>Weinstock 88%</td>
</tr>
</tbody>
</table>

## Autism and the Microbiota

- **Increased** *Bacteroidetes*, reduced *Firmicutes*; increased *Desulfovibrio* and *B. vulgatus*
  
  Finegold et al. Anaerobe 2010;16:444-53

- **Decreased** *Bacteroidetes*; increased F/B ratio and *Betaproteobacteria*. Correlated with decreased expression levels of disaccharidases and hexose transporters
  

- Reduced *Akkermansia mucinophilia* and *Bifidobacteria* spp
  

- **Desulfovibrio** associated with regressive autism
  

- **Sutterella** and autism with GI symptoms
  
  Williams et al. MBio 2012;10:3

- **No differences** between autism (+ or - GI symptoms) and neurotypical siblings
  
Positive Duodenal Aspirates

- Retrospective review of 675 duodenal aspirates
  - 8% positive overall
    - Predictors
      - Older age
      - Steatorrhoea
      - Narcotic use
      - IBD
      - Small bowel diverticula
      - Pancreatitis
  - 2% of IBS positive for SIBO


- Prospective review of 320 duodenal aspirates
  - 19.4% positive overall (68% had IBS)
    - Predictors
      - IBS
      - Type II DM
      - PPI use
      - Not having gastritis
  - 38% of IBS positive for SIBO
    - 60% D-IBS
    - 27% non D-IBS

SIBO Consequences: Direct

- $B_{12}$ malabsorption - mucosal changes
- Bile acid deconjugation
- Mucosal injury
  - Loss of b.b. enzymes
  - Altered permeability
  - PLE
- Intraluminal protein digestion
- Enterotoxins

SIBO Consequences: Indirect

- Nutritional effects
- Translocation; systemic sepsis
- Other systemic effects
  - Liver
  - Reactive arthropathy
  - Other "auto-immune" disorders
- Immune-mediated enteropathy
**SIBO Consequences: Pathology**

- Decreased villous to crypt ratio more frequent in SIBO than controls (24% vs 7%)
- Duodenal biopsies from patients with SIBO slightly less likely to be judged within reference range than controls (52% versus 64%)

Lappinga et al. Arch Pathol Lab Med 2010;134:264-70

**SIBO Consequences: Symptoms**

- None
- Those of malnutrition or specific deficiencies
- Steatorrhea
- Diarrhea, especially in the elderly
- Bloating
- Flatulence
- Abdominal discomfort
- Weight loss
SIBO Consequences: Symptoms

- None
- Those of malnutrition or specific deficiencies
- Steatorrhea
- Diarrhea
- Bloating
- Flatulence
- Abdominal discomfort
- Weight loss

Clinical Syndromes

- Malabsorption syndrome ("Classic" SIBO)
- Altered permeability
  - Enhanced absorption of Vitamin K, impact on warfarin dose
    Giuliano et al. Thromb Res 2010;126:12-7
- Flora-immune engagement
  - Normal flora
  - Abnormal flora
    - Mucosal
    - Systemic
- Metabolic activity
  - Obesity
  - NAFLD
- "Functional" symptoms: IBS
Diagnostic Approaches

- Quantify
- Measure
- Products of Fermentation

Assess Consequences

- Pathogen displacement
- Nutrient competition
- Receptor competition
- Production of anti-microbial factors e.g., lactobacilli, lactic acids

- Breath Tests
  - Substrates
    - Lactose
    - Fructose
    - Glucose
    - Lactulose
    - $^{14}$C-Xylose

- Expired products
  - $^{14}$CO$_2$
  - H$_2$

- Intraluminal bacterial metabolism of substrate
- Colonic fermentation of unabsorbed carbohydrates
- Vitamin K synthesis
- Bile salts
- Short-chain fatty acids
- Short-chain fatty acids
- Increase or decrease in intestinal absorption
- Ferment non-digestible dietary residue and endogenous epithelial-derived residue
- Salute of energy
- Control IEC differentiation and proliferation
- Modulate dietary carcinogens
- Synthesize vitamins e.g., both, thiamine
- Barrier fortification
- Reduction of H$_2$
- Apical tightening of tight junctions
- Immune system development
- Control IEC differentiation and proliferation
- Modulate dietary carcinogens
- Synthesize vitamins e.g., both, thiamine

- Anaerobic genera
  - Bifidobacterium
  - Clostridium
  - Eubacterium
  - Butyricoccus

- Aerobic genera
  - Enterobacteriaceae
  - Bacteroides
  - Akkermansia
Interpretation

• No gold standard
• No community values
• Aspirate and culture
  – Proximal only
  – Will not detect un-culturables
  – Invasive
  – Diagnostic thresholds based on jejunal not duodenal aspirates
Diagnosis

• Breath tests
  – Non-invasive
  – Significant issues with false positives and negatives
    • Sensitivity 70-90%
    • Specificity 40-100%
    - Glucose more accurate but proximal only
    - 15-27% do not produce hydrogen with lactulose

• Jejunal biopsy
  Chandra et al. Ind J Gastroenterol 2010;29:226-30

• Molecular
  – In development

The New Context
The Molecular Era
Where we should really be looking - Colonic Biofilm

CD  |  Self-Limited Colitis  |  IBS

- *Bacteroides fragilis*
- *Eubacterium rectale*
Considerable variability in fecal flora
Minimal variability in Biopsy flora

Therapy of SIBO

- Correct cause
- Nutritional replacement
- Prokinetics
- Antibiotics
  - Short course
  - Repeated
  - Continuous, rotating
- Prebiotics
- Probiotics

Few Trials
Antibiotics and a Probiotic in SIBO

Norfloxacin does not suppress anaerobes

Attar et al, 1999

Effects of Therapy on $H_2$ Breath Test

$\text{Amoxicillin-clavulanic acid}$
$\text{Norfloxacin}$
$\text{S. boulardii}$
$\text{Placebo}$

Time (min)
**Rifaximin**

- Normalization of Glucose Breath Hydrogen Tests with rifaximin

- Superior to chlortetracycline

- Effective in Crohn’s with SIBO

- Inferior to metronidazole in those with a blind loop

<table>
<thead>
<tr>
<th>Daily Dose (mg)</th>
<th>Normalization (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>600</td>
<td>17</td>
</tr>
<tr>
<td>800</td>
<td>27</td>
</tr>
<tr>
<td>1200</td>
<td>60</td>
</tr>
</tbody>
</table>

**Rifaximin in SIBO**

- Compared Rifaximin 1200 mg/dy vs Rifaximin 1200 mg + Guar gum/dy for 10 days
  - Eradication rates:
    - Rifaximin 62%
    - Rifaximin + Guar gum 85%
    - Clinical response in 87-91%
      - Furnari et al. Aliment Pharmacol Ther 2010;32:1000-6

- Rifaximin 1200 mg vs Metronidazole 750 mg
  - Eradication rates
    - Rifaximin 63%
    - Metronidazole 44%
    - Less AE’s with rifaximin
SIBO in IBS

• SIBO at baseline
  – 20% controls
  – 84% IBS
  – 100% Fibromyalgia
    • Pimentel, et al. 2004
  – Associated with lower MMC frequency
    • Pimentel, et al. 2002
  – Pattern of gas excretion predicts symptoms

• Response to eradication
Bacterial Overgrowth in IBS

- 84% SIBO at baseline
- Eradication resolved
  - Diarrhoea
  - Pain
  - NOT bloating

Pimentel et al, Am J Gastro 2000

SIBO in IBS

- Other studies negative:
  - Walters and Vanner. Am J Gastro 2005
    - lactulose and xylose breath tests
    - Glucose breath hydrogen test
  - Ruff, et al. ACG 2006
    - Jejunal culture
  - Bratten, Spanier and Jones. Am J Gastro 2008
    - Methane associated with constipation in IBS
SIBO in IBS

Other studies:
- Posserud et al, Gut 2007
  - 162 IBS subjects
  - All had jejunal cultures
  - SIBO (> 10^5) in 4% of IBS and controls
  - Mild increase in bacterial counts 43%
  - Enteric dysmotility more common in IBS with SIBO

Systematic Review

- 12 studies, 1921 subjects
- Pooled prevalence of a positive lactulose or glucose hydrogen breath test was 54% (95% CI, 32%-76%) and 31% (95% CI, 14%-50%)
- Prevalence of a positive jejunal aspirate and culture was 4% (95% CI, 2%-9%)
- OR for any positive test for SIBO in IBS vs controls was 3.45 (95% CI, 0.9-12.7) or 4.7 (95% CI, 1.7-12.95), depending on the criteria used to define a positive test
SIBO in IBS: Why do study results vary?

- Patient selection
  - Acquisition bias

- Test artifact
  - Diagnostic cut-off
  - Accelerated small bowel transit in IBS

- Other confounders
  - Obesity
  - PPI use

Role of Substrate

<table>
<thead>
<tr>
<th>Substrate</th>
<th>IBS</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactulose</td>
<td>34</td>
<td>30</td>
</tr>
<tr>
<td>Glucose</td>
<td>6</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Rana et al. Digestion 2012;85:243-7
<table>
<thead>
<tr>
<th>Diagnostic method</th>
<th>N. of IBS patients</th>
<th>N. of controls</th>
<th>Percentage of SIBO in IBS subjects</th>
<th>Percentage of SIBO in controls</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>LHBT</td>
<td>76</td>
<td>40</td>
<td>44.7%</td>
<td>40.0%</td>
<td>Park et al.</td>
</tr>
<tr>
<td>LHBT</td>
<td>43</td>
<td>56</td>
<td>65%</td>
<td>7%</td>
<td>Scarpellini et al.</td>
</tr>
<tr>
<td>LHBT</td>
<td>127</td>
<td>—</td>
<td>43%</td>
<td>—</td>
<td>Carrara et al.</td>
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<tr>
<td>LHBT</td>
<td>258</td>
<td>—</td>
<td>34.5%</td>
<td>—</td>
<td>Mann and Limoges-Gonzales</td>
</tr>
<tr>
<td>LHBT</td>
<td>98</td>
<td>—</td>
<td>65%</td>
<td>—</td>
<td>Nucera et al.</td>
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<tr>
<td>GHBT</td>
<td>59</td>
<td>37</td>
<td>23.7%</td>
<td>2.7%</td>
<td>Sachdeva et al.</td>
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<tr>
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<td>98</td>
<td>—</td>
<td>36%</td>
<td>—</td>
<td>Reddymasu et al.</td>
</tr>
<tr>
<td>GHBT</td>
<td>200</td>
<td>50</td>
<td>24.5%</td>
<td>6%</td>
<td>Lombardo et al.</td>
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<td>GHBT</td>
<td>1921</td>
<td>—</td>
<td>31%</td>
<td>—</td>
<td>Ford et al.</td>
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<td>GHBT</td>
<td>130</td>
<td>70</td>
<td>16.1%</td>
<td>4.2%</td>
<td>Parodi et al.</td>
</tr>
<tr>
<td>GHBT</td>
<td>225</td>
<td>100</td>
<td>11.1%</td>
<td>1%</td>
<td>Rana et al.</td>
</tr>
<tr>
<td>GHBT</td>
<td>204</td>
<td>—</td>
<td>46%</td>
<td>—</td>
<td>Majewski et al.</td>
</tr>
<tr>
<td>GHBT</td>
<td>96</td>
<td>—</td>
<td>45.8%</td>
<td>—</td>
<td>Cuoco and Salvangini</td>
</tr>
<tr>
<td>GHBT</td>
<td>65</td>
<td>102</td>
<td>31%</td>
<td>4%</td>
<td>Lupascu et al.</td>
</tr>
<tr>
<td>GHBT</td>
<td>129</td>
<td>51</td>
<td>8.5%</td>
<td>2%</td>
<td>Ghoshal et al.</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>158</td>
<td>34</td>
<td>32.9%</td>
<td>17.9%</td>
<td>Grover et al.</td>
</tr>
<tr>
<td>Breath test and aspirate culture</td>
<td>162</td>
<td>26</td>
<td>4%</td>
<td>4%</td>
<td>Posserud et al.</td>
</tr>
</tbody>
</table>

Spiegel et al. Am J Gastroenterol 2008;103:2972-6
SIBO and PPI

- 450 consecutive patients on PPI for a median of 36 months; 200 with IBS and no PPI for at least 3 years; 50 controls, no PPI for >10 years
  - Positive GHBT: PPI 50%, IBS 25%, Controls 6%

- Retrospective review of 1191 patients who underwent a GHBT between 2004-2010
  - 566 were on a PPI
  - Predictors of positive GHBT
    - Older age
    - Diarrhea or use of anti-diarrheals
    - Not PPI’s

Positive LHBT in IBS: SIBO or altered transit?

LHBT in IBS


Simmén M et al. Gut doi:10.1136
SIBO and IBS

• Unlikely that SIBO is the predominant cause of IBS; lactulose hydrogen breath test may not have measured SIBO
• No evidence of SIBO being absent before and present after IBS emerges
• No dose-response between microbiota and IBS symptoms
• SIBO-IBS relationship inconsistent
• Many IBS therapies do not address SIBO at all, yet have a more favorable NNT than antibiotics
• IBS does not behave like a traditional infectious disease
• Other factors may confound the relationship
• Whereas the brain-gut hypothesis is evolutionary sensible, the bacterial hypothesis is harder to defend from an evolutionary perspective

Spiegel BM. CGH 2011;9:461-9

SIBO and IBS

• Bacteria may contribute to some IBS symptoms, but cannot be the only explanation; a causal link between SIBO and IBS is not secure

Spiegel BM. CGH 2011;9:461-9
But IBS responds to Antibiotic Therapy: “Target” Trials

• 1,260 patients with non-constipation irritable bowel syndrome (IBS) recruited in the US and Canada

• Rifaximin **550 mg, 3 times daily**, for 2 weeks

• Primary endpoint:
  - The proportion of subjects who achieved adequate relief of IBS symptoms for at least 2 weeks during the first 4 weeks (weeks 3-6) of the 10-week follow-up phase

• Also assessed relief of IBS bloating and symptom responses at 12 weeks (10 weeks after end of therapy)


## Hitting the Target!

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>Target 1 Rif vs Placebo</th>
<th>Target 2 Rif vs Placebo</th>
<th>Combined Rif vs Placebo</th>
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</thead>
<tbody>
<tr>
<td>Adequate relief of IBS symptoms</td>
<td>41% vs 31%</td>
<td>41% vs 32%</td>
<td>41% vs 32%</td>
</tr>
<tr>
<td>Adequate relief of IBS bloating</td>
<td>40% vs 29%</td>
<td>41% vs 32%</td>
<td>40% vs 30%</td>
</tr>
</tbody>
</table>

All p<0.03  
What is the Explanation for the Rifaximin Effect in IBS?

• “Classical” SIBO may not be common
  – ? Lesser degrees; ? Distal small bowel only
• Effect on colonic flora would decrease fermentation
  – Rifaximin effect on symptoms
    • Not dependent on abnormal baseline breath test
    • Parallel reduction in breath hydrogen excretion
    Sharara et al. Am J Gastroenterol 2010
• Anti-inflammatory effect

When to consider SIBO?

• 72 yo retired
  – Hx of IBS, Diverticular Disease, A Fib
  – Wife terminally ill with myeloma
  – Significant traumas in recent past
  – Depression with suicidal ideation
• Dyspepsia, urgency and diarrhoea
• Gastroscopy and duodenal bx - normal
• Colonoscopy and colonic biopsies:
  – Diverticula +++
  – Minor inflammatory changes in bx from sigmoid
• CT abdomen and thorax: stable ascending aortic aneurysm
Two years later...........

- Loose bowel movements, bloating, urgency
- Loperamide 2 mg b.i.d.
- 2 episodes incontinence
- A lot of distress: 4 bereavements
- Meds:
  - Anti-spasmodics
  - Peppermint oil
  - B12 injections
  - Seeing psychologist
Lactulose Breath Test

<table>
<thead>
<tr>
<th>Time (mins)</th>
<th>0</th>
<th>20</th>
<th>40</th>
<th>60</th>
<th>80</th>
<th>100</th>
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</thead>
<tbody>
<tr>
<td>Hydrogen</td>
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<tr>
<td>Methane</td>
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<td></td>
</tr>
</tbody>
</table>

ppm

Hydrogen
Methane
Progress

• Alternating cipro and metronidazole
• No diarrhoea or bloating
• Gained 3 kg
• Still concerned re incontinence

Summary

• SIBO is a somewhat arbitrarily defined condition; needs revision based on modern microbiological methods
• Symptoms of SIBO, of whatever cause, are non-specific
• Causes can be predicted on the basis of a knowledge of the factors that normally prevent colonisation
• There is no gold standard in diagnosis; aspirate and breath tests have their limitations
• Treatment remains, for the most part, empiric though rifaximin looks promising
• There is much to do!
  – (Remember Helicobacter pylori)
Thank you!

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