Small Intestinal Bacterial Overgrowth

Clinical Considerations

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Technical Issues & Clinical Questions

Please type any technical issue or clinical question into either the “Chat” or “Questions” boxes, making sure to send them to “Organizer” at any time during the webinar.

We will be compiling your clinical questions and answering as many as we can the final 15 minutes of the webinar.

DISCLAIMER: Please note that any and all emails provided may be used for follow up correspondence and/or for further communication.
Need More Resources?
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Patient Population

- What is SIBO?
- Clinical impact
- Prevalence as it relates to IBS
Small Intestinal Bacterial Overgrowth Definitions

“Small Intestinal Bacterial Overgrowth is a heterogeneous syndrome characterized by an increased number and/or abnormal type of bacteria in the small bowel.”

Small Intestinal Bacterial Overgrowth Definitions

“Small intestinal bacterial overgrowth is a condition in which there is overgrowth of bacteria in small bowel in excess of 105 colony forming units per milliliter on culture of the upper gut aspirate.”

Commensal Bacteria Throughout the GI tract

- Lactobacilli
- Lactobacilli and Streptococci
- Clostridia
- Enterobacteria
- Enterococcus
- E. faecalis
- Bacteroides
- Bifidobacteria
- Fusobacteria
- Lactobacilli
- Peptococci
- Peptostreptococci
- Prevotellaceae
- Roseburia
- Ruminococci
- Verrucomicrobia

Microbial load per ml:
- Stomach: $10^2$ to $10^3$
- Duodenum: $<10^5$
- Jejunum: $10^3$ to $10^7$
- Ileum: $10^9$ to $10^{12}$
- Colon with caecum and appendix: $10^9$ to $10^{12}$
Clarifying the Terminology

- **SIBO**: Small Intestinal Bacterial Overgrowth
- **BOSI**: Bacterial Overgrowth of the Small Intestine
- **SBO**: Small Bowel Overgrowth
- **SBBO**: Small Bowel Bacterial Overgrowth
- **Dysbiosis**: An alteration of the gut microbiota

[http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3448089/]
Small Intestinal Bacterial Overgrowth

- **Predisposing factors:**
  - Loss of antibacterial mechanisms:
    - Achlorhydria/hypochlorhydria (PPI/H2 Blocker use)
    - Pancreatic exocrine deficiency
    - Immunodeficiency syndromes
  - Decreased motility in small intestine due to:
    - Diabetes
    - Hypothyroidism
    - Drugs
    - Other causes
  - Anatomical abnormalities
  - Surgical procedures and resulting bowel stasis
  - Food poisoning
Common Signs and Symptoms of SIBO

- Abdominal bloating
- Excessive gas or belching
- Abdominal cramps
- Diarrhea
- Constipation
- Steatorrhea
- Nutrient deficiencies
- Weight loss
- Food and supplement intolerances
Nutrient deficiencies

- **Iron**

- **Vitamin B12**
  - Bacteria in the small intestine absorb vitamin B-12, which is essential for the normal functioning of your nervous system and the production of blood cells and DNA. A severe B-12 deficiency can lead to weakness, fatigue, tingling and numbness in your hands and feet, and, in advanced cases, to mental confusion. Damage to your central nervous system resulting from a B-12 deficiency may be irreversible.

- **Calcium**
  - Over time, damage to your intestine from abnormal bacterial growth causes poor calcium absorption, and eventually may lead to bone diseases, such as osteoporosis.
  - Poor calcium absorption may also eventually result in kidney stones.

- **Fat-soluble nutrients (Essential Fatty Acids and Fat-soluble Vitamins)**
  - Bacteria in your small intestine break down the bile salts needed to digest fats, thus patients with SIBO often have poor fat absorption. As a result, your body can't fully absorb the fat-soluble vitamins A, D, E and K.

http://www.mayoclinic.org/diseases-conditions/blind-loop-syndrome/basics/complications/con-20024503
Consequences of Long Term SIBO

Poor absorption of fats

• Incomplete absorption of fats leads to:
  – Diarrhea
  – Weight loss
  – Vitamin deficiency disorders

Damage to the intestinal lining

• Toxins that are released when bacteria break down stagnant food harm the mucous lining (mucosa) of the small intestine. As a result, most nutrients, including carbohydrates and proteins, are poorly absorbed, leading to serious malnourishment.
• A possible cause of leaky gut which may then lead to food sensitivities

http://www.mayoclinic.org/diseases-conditions/blind-loop-syndrome/basics/complications/con-20024503
Association with IBS
What is IBS?

• **Irritable Bowel Syndrome** is defined as a functional GI disorder that is characterized by abdominal discomfort and altered bowel habits, though often also includes symptoms of gas and bloating. It is specifically diagnosed by using the Rome criteria for functional bowel disorders.

• **Rome III Criteria for diagnosis of IBS:**
  
  – Recurrent abdominal pain or discomfort** at least 3 days/month in the last 3 months associated with *two or more* of the following:
    • Improvement with defecation
    • Onset associated with a change in frequency of stool
    • Onset associated with a change in form (appearance) of stool
  
  – The criteria must be fulfilled for at least the past 3 months with symptom onset at least 6 months prior to diagnosis

**“Discomfort” means an uncomfortable sensation not described as pain.

IBS Signs and Symptoms

- Abdominal pain or discomfort
- Diarrhea/ loose or watery stools
- Constipation/ hard or lumpy stools
- Feeling of incomplete bowel movement
- Passing mucous
- Abdominal bloating and distension
- Urgency
- Straining during a bowel movement

Classifications:

- IBS-D: Diarrhea predominant
- IBS-C: Constipation predominant
- IBS-M: Alternating or mixed constipation and diarrhea
- IBS-U: Unable to meet criteria

http://digestive.niddk.nih.gov/ddiseases/pubs/ibs/
Clinical Impact

**IBS symptoms are not well controlled in most patients**

- No single well established therapy is available
- Patients typically report extensive self-experimentation

**Evaluation and management of IBS is unstructured, prolonged, and frustrating**

- Patients typically report that years elapsed between first onset of symptoms and final diagnosis of IBS
- Leads to “doctor-shopping” for more testing
So....Is IBS Always a Functional Bowel Disorder?

Current research would point to → NO

We can find an underlying cause!
Bacterial Overgrowth of the Small Intestine and Irritable Bowel Syndrome

Though several studies reported an association between small intestinal bacterial overgrowth (SIBO) and IBS, the frequency of SIBO reported to vary between 4% and 78%. The current review suggests that the association between SIBO and IBS is definite.
GDX Index Test

- Bacterial Overgrowth of the Small Intestine Breath Test (BOSI)
Methodology for SIBO Breath Testing

Rana SV et al. Irritable bowel syndrome

Figure 1 Principle of breath testing.

Dietary Guidelines

Starting with dinner meal two nights before collection

• Foods to avoid:
  – Foods with high fiber content such as beans, legumes, whole grains, high starch/fiber vegetables and fruits, dried fruit, nuts and seeds and most dairy products

• Foods with no restrictions:
  – All meat and poultry, fish, shellfish, eggs, aged cheeses, juices, certain fruits and vegetables, condiments, sherbet, salad and cooking oils

• Foods to be eaten sparingly:
  – White bread and white crackers, highly refined cereals, white rice, tofu, rice or soy milk, certain fruits and vegetables, fruit jellies and sugar

• A more detailed list comes with kit
Bacterial Overgrowth of the Small Intestine Breath test

- **Advantages**
  - Non-invasive
  - Can be done at home or in physician’s office
  - Utilizes Lactulose, a synthetic disaccharide containing galactose and lactose, which is not absorbed by the intestinal lining and thus is only digested by intestinal bacteria
  - Hydrogen and methane identification
Interpretation of Results

Comparator Tests

- Intestinal aspirate and fluid culture
- Other types of breath tests
Small Intestine Aspirate and Fluid Culture

• Per Mayo clinic, this is the most **sensitive** test for bacterial overgrowth. To obtain the fluid sample, doctors pass a long, flexible tube (endoscope) down the throat and through the upper digestive tract to the small intestine. A sample of intestinal fluid is withdrawn and then tested in a laboratory for the growth of bacteria.

• But what about **specificity**? This test can have high rates of **false negatives**
Small Intestine Aspirate and Fluid Culture

Disadvantages:

• Invasive procedure as the small intestine must be intubated so that aspirates can be collected

• Culture-based techniques do not allow for growth of all organisms, thus may underestimate the bacterial population

• Potential for contamination of instrumentation and inaccurate sampling due to technical problems

• Endoscopy can only reach the upper portion of the small intestine and colonoscopy can only reach the lower, thus the substantial middle section of the small intestine is not accessible by this method

Substrates for SIBO Breath Test
Glucose – Lactose – Sucrose - Xylose

Lactulose

- Cannot be digested or absorbed by humans, thus passes through entire length of small intestine
- **Advantage**: can diagnose **distal overgrowth** which is thought to be more common
- **Disadvantage**: not as sensitive as glucose

Glucose

- Glucose is absorbed within first few feet of small intestine, thus can only diagnose proximal overgrowth
- **Advantage**: accurate diagnosis of proximal overgrowth
- **Disadvantage**: cannot diagnose distal overgrowth
Gas Collection for SIBO Breath Test

- Important to measure both hydrogen (H2) & methane (CH4) gases
- Treatment may differ based on gas findings
Testing of H2 alone overlooks the importance of CH4 as a fermentation product. 30%-50% of human population are producers of CH4. Synthesis of CH4 mostly consumes large amounts of H2, this may waiver diagnostic accuracy of breath testing when alone H2 is considered.
Outcomes

- Test Interpretation
- Importance of clinical correlation
- Therapeutic interventions
- Follow-up testing
Test Interpretation: Negative Result

Total Hydrogen and Methane Breath Gases

Hydrogen & Methane (ppm)

<table>
<thead>
<tr>
<th>Minutes</th>
<th>Baseline</th>
<th>20</th>
<th>40</th>
<th>60</th>
<th>90</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogen (H₂)</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Methane (CH₄)</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>1</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td>4</td>
</tr>
</tbody>
</table>

Increase over Baseline

<table>
<thead>
<tr>
<th>Change in H₂ &amp; CH₄ ppm</th>
<th>Normal</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;= 11</td>
<td>12 - 32</td>
<td>&gt;= 33</td>
<td></td>
</tr>
</tbody>
</table>

Baseline Evaluation

<table>
<thead>
<tr>
<th>Baseline Level</th>
<th>ppm</th>
<th>Normal</th>
<th>Elevated</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;= 20</td>
<td>&gt;= 21</td>
<td></td>
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</tr>
</tbody>
</table>

This test was developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.

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Test Interpretation: Two Peak - Mild

Total Hydrogen and Methane Breath Gases

Hydrogen & Methane (ppm)

<table>
<thead>
<tr>
<th>Minutes</th>
<th>Base-line</th>
<th>20</th>
<th>40</th>
<th>60</th>
<th>90</th>
<th>120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogen (H₂)</td>
<td>3</td>
<td>14</td>
<td>20</td>
<td>15</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Methane (CH₄)</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>16</td>
<td>22</td>
<td>17</td>
<td>11</td>
<td>28</td>
</tr>
</tbody>
</table>

Increase over Baseline

<table>
<thead>
<tr>
<th>Change in H₂ &amp; CH₄ ppm</th>
<th>Normal</th>
<th>Mild</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤ 11</td>
<td>12 - 32</td>
<td>≥ 33</td>
</tr>
</tbody>
</table>

Baseline Evaluation

<table>
<thead>
<tr>
<th>Baseline Level</th>
<th>Normal</th>
<th>Elevated</th>
</tr>
</thead>
<tbody>
<tr>
<td>ppm</td>
<td>≤ 20</td>
<td>&gt; 21</td>
</tr>
</tbody>
</table>

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Test Interpretation: Two Peak - Severe

Total Hydrogen and Methane Breath Gases

This test was developed and its performance characteristics determined by Genova Diagnostics, Inc. It has not been cleared or approved by the U.S. Food and Drug Administration.
Test Interpretation: Severe
Test Interpretation: Methane Predominant

Total Hydrogen and Methane Breath Gases

<table>
<thead>
<tr>
<th>Collection Times</th>
<th>Baseline</th>
<th>20 min</th>
<th>40 min</th>
<th>60 min</th>
<th>90 min</th>
<th>120 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrogen (H₂)</td>
<td>3</td>
<td>18</td>
<td>12</td>
<td>10</td>
<td>20</td>
<td>12</td>
</tr>
<tr>
<td>Methane (CH₄)</td>
<td>37</td>
<td>71</td>
<td>71</td>
<td>81</td>
<td>81</td>
<td>47</td>
</tr>
<tr>
<td>Total</td>
<td>40</td>
<td>89</td>
<td>83</td>
<td>81</td>
<td>101</td>
<td>59</td>
</tr>
</tbody>
</table>

Increase over Baseline

- Change in H₂ & CH₄: 61 ppm
- Normal: <= 11 ppm, Mild: 12 - 32 ppm, Severe: >= 33 ppm

Baseline Evaluation

- Baseline Level: 40 ppm
- Normal: <= 20 ppm, Elevated: >= 21 ppm

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Case Example

72 yo Male

• Presenting Symptoms:
  – Constipation- hard stools, once every other day
  – Bloating
  – Symptoms were better initially after probiotics and fiber, then worse again

• Previous testing:
  – Initial GI Effects stool test showed dysbiosis and low beneficial bacteria
  – Follow up GI Effects showed elevated fecal fats and protein products
  – Screening colonoscopy at age 65 negative

• Additional Evaluation:
  – BOSI test ordered
Methane-Predominant SIBO

- Elevated baseline typical with SIBO
- Botanical antimicrobial regimen started
- Discontinued probiotics and supplemental fiber
- Low-carb diet
### GI Effects Test

**Euryarchaeota Phylum**

| Methanobrevibacter smithii | 4.4E7 | <=8.6E7 |

<table>
<thead>
<tr>
<th><strong>Methanobrevibacter smithii</strong></th>
<th>IBS</th>
<th>Inflammation</th>
<th>Immune Modulation</th>
<th>Metabolic Disorders</th>
<th>Autism</th>
<th>Diversity Association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euryarchaeota phylum</td>
<td>L/H</td>
<td>L/H</td>
<td>L/H</td>
<td>HD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Abundance associated with higher bacterial gene richness in the gut
- Lower counts of *Methanobrevibacter* species reported in human obesity; higher amounts reported in anorexia; in contrast, one study confirmed a positive association with increased BMI and body fat in methanogen-colonized populations
- Higher levels linked to IBS-C; reduced levels linked with IBS-D
- Methanogens found higher in people with colon cancer, colonic polyposis, ulcerative colitis, and diverticular disease (sigmoidoscopy enema samples)
- Some studies have reported lower counts in IBD, conversely, other have reported increased abundance

**Breath-testing study, an accepted indirect measure of gut methanogens; although *M. smithii* is currently considered the dominant methanogenic archaeon in the gut, other methanogenic bacteria may also be contributors to breath methane.**
SIBO Therapeutic Interventions

• Rifaximin
• Rifaximin in combination with other antibiotics (neomycin)
  – Methane-predominant SIBO
• Herbal antibiotics
• Dietary interventions
  – Low FODMAPs
  – Low Carbohydrate diet
  – Elemental diets
• Treat underlying cause
  – Maldigestion (hypochlorhydria/pancreatic insufficiency)
  – Motility issues
  – Poor diet (high starch/refined carbohydrates)
3 Month Follow-up

- Results slightly improved
- Patient still experiencing constipation and bloating
- Rifaxamin with neomycin
Follow-up

At 2 months
• Regular twice daily bowel movements easy to pass
• No bloating

At 4 months
• Symptoms remain resolved
• Remains on low carb diet
Conclusion:
Rifaximin improves IBS symptoms for up to 10 weeks after the discontinuation of therapy.
CONCLUSIONS: Rifaximin plus neomycin is superior to neomycin alone in improving multiple C-IBS symptoms. This effect is predicted by a reduction in breath methane.
Herbal Therapy Is Equivalent to Rifaximin for the Treatment of Small Intestinal Bacterial Overgrowth

Victor Chedid, MD, United States; Sameer Dhalla, MD, United States; John O. Clarke, MD, United States; Bani Chander Roland, MD, United States; Kerry B. Dunbar, MD, United States; Joyce Koh, MD, United States; Edmundo Justino, MD, United States; Eric Tomakin, RN, United States; Gerard E. Mullin, MD, United States

What is new here?

The high prevalence rate for SIBO of 64% in a tertiary care referral gastroenterology practice.

The response rate for normalizing breath hydrogen testing in patients with SIBO was 46% for herbal therapies vs 34% for Rifaximin.

Herbal therapy may be an effective treatment for patients with SIBO.

Patients with SIBO refractory to rifaximin can be given the choice of herbal therapy as rescue therapy.
“While there has only been one published report of herbal antibiotics in the treatment of SIBO, our experience is that they have similar effectiveness to antibiotics. We have used the following botanicals: Allium sativum, Hydrastis canadensis, and other berberine-containing herbs, Origanum vulgare, cinnamon, and Azadirachta indica. We have used these as both single agents and in various combinations at dosages that are at the upper end of label suggestions × 30 days. Specific single dosages we have used include allicin extract of garlic: 450 mg b.i.d.–t.i.d., goldenseal/berberine: 5g q.d. in split dosage, emulsified oregano: 100 mg b.i.d., and neem: 300 mg t.i.d. Our breath testing has validated the need for the longer treatment period of 30 days for herbal antibiotics compared with 14 days for antibiotics. We have also observed with this method prolonged die-off reactions, which can last for the duration of treatment course. Studies on herbal antibiotics for SIBO are needed, particularly to identify botanicals effective in reducing methane.”

http://www.townsendletter.com/FebMarch2013/ibs0213.html
Herbal Antimicrobial Therapeutics Overview

• There is no standardized treatment at this time with regards to herbs being used or time frame of use

• It seems that most clinicians agree that herbal therapy usually requires longer treatment periods when compared to prescription antibiotics such as Rifaximin

• Further studies are needed to provide added clarification on the specifics of products and dosing
Other Considerations for Similar Symptoms

- GI Effects can identify:
  - Pancreatic insufficiency
  - Inflammation
  - Dysbiosis
  - Yeast overgrowth
  - Parasitic infection
- Food Antibody panel
- Celiac and Gluten Sensitivity panel
GI Effects Comprehensive Profile

Important:
GI Effects profile can NOT identify Small Intestinal Bacterial Overgrowth

There are markers on this profile that can be suggestive of SIBO in the right patient population:

• Elevations in Products of Protein Breakdown
• Elevations in Fecal Fats (due to interrupted enterohepatic recirculation)
• Unexpected or extreme elevations in Beneficial SCFAs and n-butyrate
Follow-up Support

- Nutritional testing (NutrEval/ION)
  - B vitamin status
  - Fatty Acid profile
  - Fat-soluble vitamin status
- Intestinal Permeability Panel
- Food Antibody Panel
Today’s Presenters

Christine Stubbe, ND
Stephen Goldman, DC

Questions?

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- **Test Menu** – Detailed test profile information
- **MY GDX** – Order materials and get results

Christine Stubbe, ND
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UK Client Services: 020.8336.7750

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- How Genova’s profiles might support patients in your clinical practice, or
- To review a profile that has already been completed on one of your patients

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• January 2016:
  – Nutritional Status and Hormone Balance
    • Dr. Marion Owen

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