SIBO and good bacteria: The two sides of gut-microbiota

Disclosures

- Nothing to disclose

Objectives

- "Gut microbiota (GM)" a new organ within the body!
- Not all bacteria are our enemies, most of them are friendly
- SIBO is an example of bad bacteria or good becoming bad
- SIBO clinical features, diagnosis and treatment.
- The new story GM - a new organ.
- Clinical implications of dysbiosis of GM. Relevance to metabolic syndrome. Fatty liver. Insulin Resistance, obesity
- Therapeutic implications; prebiotic, probiotic, synbiotic.
- Future.

SIBO Small Intestinal Bacterial Over Growth Syndrome

Blind loop syndrome
Tropical sprue?
### Overview

- What is SIBO?
- Factors protecting against SIBO
- Associated Clinical Disorders
- Pathophysiology & Clinical Picture
- Testing for SIBO
- SIBO & Surgery
- The Gut Microflora in Healthy Individuals

### Small Intestinal Bacterial Overgrowth (SIBO)

**Definition**

The presence > 10⁵ (colony forming units) CFU/ml of small intestinal aspirate in the proximal small intestine.

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### Disorders Commonly Associated with SIBO

<table>
<thead>
<tr>
<th>Gut/gastrointestinal disorder</th>
<th>Pancreatic enzyme</th>
<th>Mobility disorder</th>
<th>Immune deficiency</th>
<th>GI structural defect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peptic ulcer disease</td>
<td>Chronic pancreatitis</td>
<td>Celiac sprue</td>
<td>Immunodeficiency</td>
<td>Pseudo-obstruction</td>
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<tr>
<td>Crohn’s disease</td>
<td>Cystic fibrosis</td>
<td>Cirrhosis</td>
<td>CD</td>
<td>Stricture</td>
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<td>Diverticulitis</td>
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<td>Fistula</td>
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<td>IBD (Crohn’s, ulcerative)</td>
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<td>IC valve resection</td>
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<td>J-tube resection</td>
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<td>GI malignancy</td>
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<td>Small bowel resection</td>
</tr>
</tbody>
</table>

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### Clinical Picture

- Abdominal pain, including cramping
- Constipation (methane)
- Diarrhea (hydrogen)
- Excessive flatus
- Massive absorption problems, i.e. fat soluble vitamins, vitamin B12, iron
- Systemic complaints such as fatigue, body pain, headaches

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<td>Vitamin B12, iron</td>
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<td>Systemic complaints</td>
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Overall 450 subjects were evaluated in this study. After SIBO eradication, bloating was improved or absent in 90%, diarrhea in 94%, and abdominal pain in 92% of the cases. 

Clinical Gastroenterology and Hepatology, 2010;8504-508.
Discovery of a new organ in the body, the gut microflora

Microbes ‘R’ Us

Irritable Bowel Syndrome (IBS) a disorder of Brain-Gut Axis dysfunction
- Symptom complex including abdominal pain, altered bowel function, bloating, mucosal inflammation, exaggerated stress response, increases in plasma pro-inflammatory cytokines
- IBS affects approximately 10-20% of the general population
- It is the most common disease diagnosed by gastroenterologists
- Large co-morbidity with anxiety & depression
- Current therapies are frequently ineffective
- Visceral Pain is a key symptoms of IBS
- Stress (including early life stress) plays a major role in the onset and exacerbation of symptoms in IBS
- Now viewed as a disorder of the Brain-Gut axis

Gastroenterologist: Gut disorder
Psychiatrist: Stress-related disorder
Neurobiologist/Neurologist: Chronic pain disorder

The human intestinal microbiota
- $10^{14}$ microorganisms; 10 times the number of cells in human body and 100-fold more genes than in human genome
- Acting at interfaces between food and epithelium
- A true organ, most often – protecting our health and well-being throughout all stages of our life

Expanding Number of Microbiome Publications

Welcome to the 21st Century
Are we ready?
A short primer of microbiology

- **Microbiome**: A collection of different microbes and their functions or genes found in an environmental habitat. Different parts of the body have different microbiomes, for example, the skin microbiome is different to the gut microbiome, but they are all part of the human microbiome.
- **Microbiota**: The types of organisms that are present in an environmental habitat, whether they are bacteria, viruses or eukaryotes.
- **Omic methods**:
- **Dysbiosis**: A disturbance or imbalance in a biological system, for example, changes in the types and numbers of bacteria in the gut which may lead to developing different diseases, such as IBD.
- **Metagenomics**: A method which allows us to create catalogues of what the bacteria can do based on the genes that they have.
- **Genome**: genetic material of an organism

**DYSBIOSIS**

- **Dysbiosis** is the abnormal microbial colonization of the intestine, where changes in Quantity and Quality of flora become Pathological & Harmful.
- When intestinal flora equilibrium is disturbed, the optimum expected health effects are lost → autoimmune conditions result (IBD, rheumatoid).
- A common cause of dysbiosis is antibiotic therapy (bacteriogenic).

**Cesarian birth**

- Swabbing a mother’s vagina and transferring it to her baby’s mouth, eyes and skin may stimulate microbiome development similarly to babies born naturally – and protect it from health issues later in life.
Cross-talk between bacterial pathogens and their host cells. Quorum sensing.

- Two-way biochemical interactions leading to responses in both the pathogen and host cell.
- The epithelium is armed with active means of keeping intestinal bacteria in check.
- The intestinal epithelium must also be able to readily discriminate between resident flora and enteric pathogens.

Bacterial colony an organ?.

- "With considerable metabolic activity GM is a virtual organ within the host.
- Profound influence on normal structural and functional development of the GIT mucosal immune system.
- A powerful influence on health and disease.
- Bacterial flora has a combined metabolic activity equal to that of a well formed organ within the host, but not so far well recognized, it is a "forgotten organ" within the human body."

Manipulation of the Gut Microbiota as a Novel Treatment Strategy for Gastrointestinal Disorders.


What kinds of microbes are found in the gut?

Isabel Moreno-Indias, L 2014

The main bacterial phyla in the gut are 6:

- **Firmicutes** (Gram-positive) (mycoplasma, bacillus, clostridium)
- **Bacteroidetes** (Gram-negative) (Bacteroides, Prevotella),
- **Actinobacteria** (Gram-positive) (Bifidobacterium).
- **Proteobacteria**
- **Verrucomicrobia**
- **Fusobacteria**
  - > 1000 species
  - 10-100 trillion organisms

Collective weight of about 1kg in human intestine.

The aging gut

Stability and diversity declines

- Physiological changes
- Living situation community dwelling, hospitalization, nursing care
- Diet and nutritional status
- Medications

Decline in commensal anaerobes. Bacteroides.

Rise in proteolytic and pathogenic bacteria. Fusobacteria, Propionibacteria, Clostridia, and E. coli.

Phylogenetic view: gut bacteria in the "family" tree of life

Classification memo:
- Domain: Bacteria
- Phylum:
  - Firmicutes
  - Bacteroidetes
  - Actinobacteria

Single gene: 16S rDNA sequence:
- 3 major phyla among the >50 within currently known bacterial diversity.
Bacteria in the Intestines May Help Tip the Bathroom Scale, Studies Show

In the bypass mice, the microbial populations quickly changed, and the mice lost weight. In the sham group, the microbiota did not change much — even in those on the weight-loss diet.

Next, the researchers transferred intestinal contents from each of the groups into other mice, which lacked their own intestinal bacteria. The animals that received material from the bypass mice rapidly lost weight; stool from mice that had the sham operations had no effect.

Gut Microbiota: The Neglected Endocrine Organ

Antibiotics and childhood obesity

5. Antibiotics, obesity and the link to microbes - what are we doing to our children?

In a 2014 New York Times article, “The Fat Drug” Pagan Kennedy “that inappropriate antibiotic use, already associated with the antibiotic resistance crisis, had been tentatively linked to yet another “epidemic”: the dramatically increasing (and incompletely explained) obesity rates across the US.”

Martin Blaser in his best-selling book, Missing Microbes, audiences have been asked to consider whether the same antibiotics used to stimulate the growth of livestock have also stimulated our own waistlines by altering our intestinal flora.
Probable beneficial effects of GM.

Type 1 DM

Insulin Resistance

Microbiota associated with type 2 diabetes and its related complications
Yong Zhang, Heping Zhang, Food Science and Human Wellness 2013, 2;167-172

- Clinical studies
- Obese people with insulin resistance characterized by an altered composition of gut microbiota,
- An elevated Firmicutes/Bacteroidetes ratio compared with healthy people
- Microbiota in obesity modulates intestinal permeability and increases metabolic endotoxin secretion that lead to chronic low-level inflammation, the pathogenesis of insulin resistance and onset of T2DM.
Intestinal Bacteria Role in NAFL / NASH

Gut flora promote
- absorption of dietary lipids
- hepatic fatty acid synthesis

Gut-derived bacterial products
- escape steatotic livers
- stimulate cytokine production by peripheral fat

The vast majority of our immune system is located in the gut

Metabolic Syndrome

Hepatic Fatty Acids

TNF
- pro-inflammatory
- pro-apoptotic
- recruits WBC’s
- stimulates insulin resistance

Adiponectin
- anti-inflammatory
- inhibits FA uptake
- stimulates FA oxidation & lipid export
- enhances insulin sensitivity

Prebiotics, probiotics, synbiotics

Prebiotics are indigestible carbohydrates that act as food for probiotics. They are found in whole grains, bananas, onions, garlic, honey, and artichoke.

Probiotics are organisms found in yogurts. In addition, probiotics and prebiotics can be added to some foods and available as dietary supplements.

A synbiotic is created when probiotics and prebiotics are combined; they form because they contain live bacteria and the fuel they need to thrive.

Therapeutic possibility?

- Low calorie diet, and exercise remain the mainstay of treatment of obesity.
- Therapeutic manipulation of the gut microbiota represents a novel approach for treating obesity.
- Use of antibiotics, prebiotics, and probiotics may result in nonspecific modulation of the gut microbiota in the future treatment of obesity.
- Restoration of "healthy microbiota" a promising therapeutic strategy for controlling metabolic syndrome.