Intestinal Microbial Overgrowth

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Conflict of interest

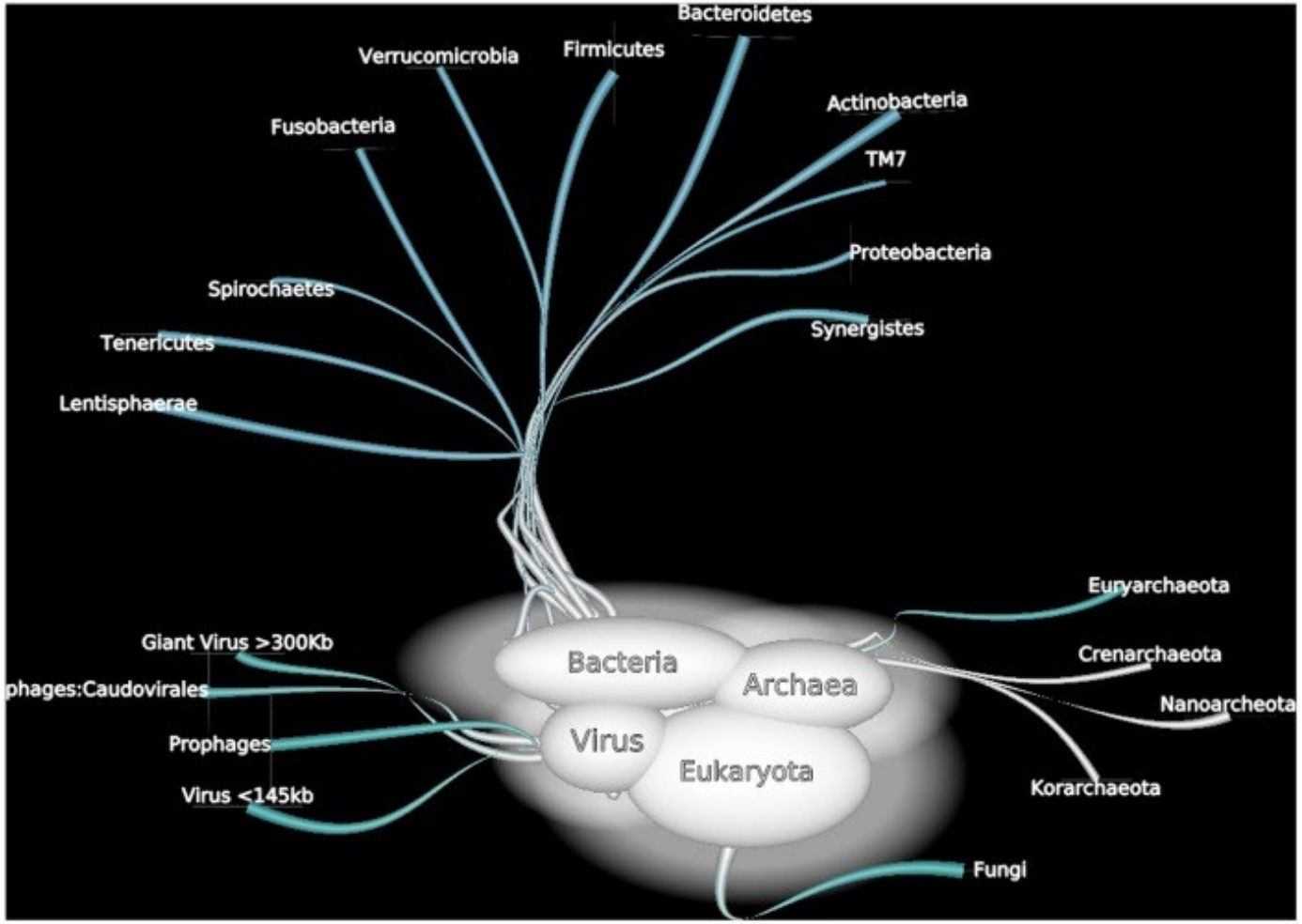
- Bausch Health, Gemelli Biotech, BetterBiome
- This application is put forward personally by Drs.Rezaie and Pimentel and is not sponsored by industry

Objectives

- Definition, diagnosis, and treatment of intestinal microbial overgrowth
  - Small intestinal bacterial overgrowth (SIBO)
    - Hydrogen subtype
    - Hydrogen sulfide subtype
  - Small intestinal fungal overgrowth (SIFO)
  - Intestinal methanogen overgrowth (IMO)
- The need for ICD-10-CM codes

Gut microbiome

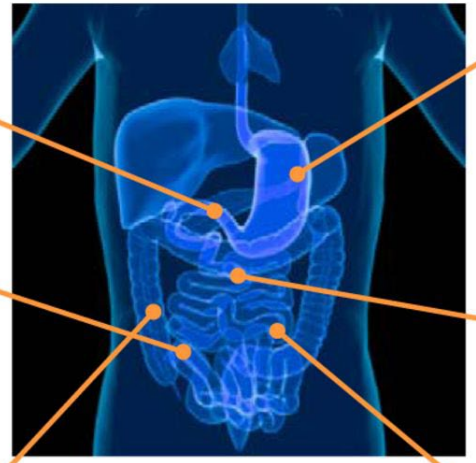
- Gut microbiota consist of living microorganisms (bacteria, fungi and archaea) and viruses
- Impairment of the delicate balance of our gut microbiome is linked to various diseases and symptoms



Lagier et al. Front Cell Infect Microbiol. 2012
Rezaie A et al. Am J Gastro. 2019

Microbial distribution of GI tract is quite variable

- Unlike colon (10^{12} CFU/ml), our small bowel is relatively sterile (<10^3 CFU/ml)
- SIBO and SIFO are dislocation of colonic bacteria/fungi to the small bowel: A type of dysbiosis and not an infection
- SIBO: Concentration of bacteria in the small bowel ≥1,000 CFU/ml using endoscopic aspiration
- SIFO: Concentration of fungi in the small bowel ≥1,000 CFU/ml using aspiration
- IMO: Overgrowth of methanogenic archaea to increase exhaled breath methane to 10ppm (exclusive biomarker)



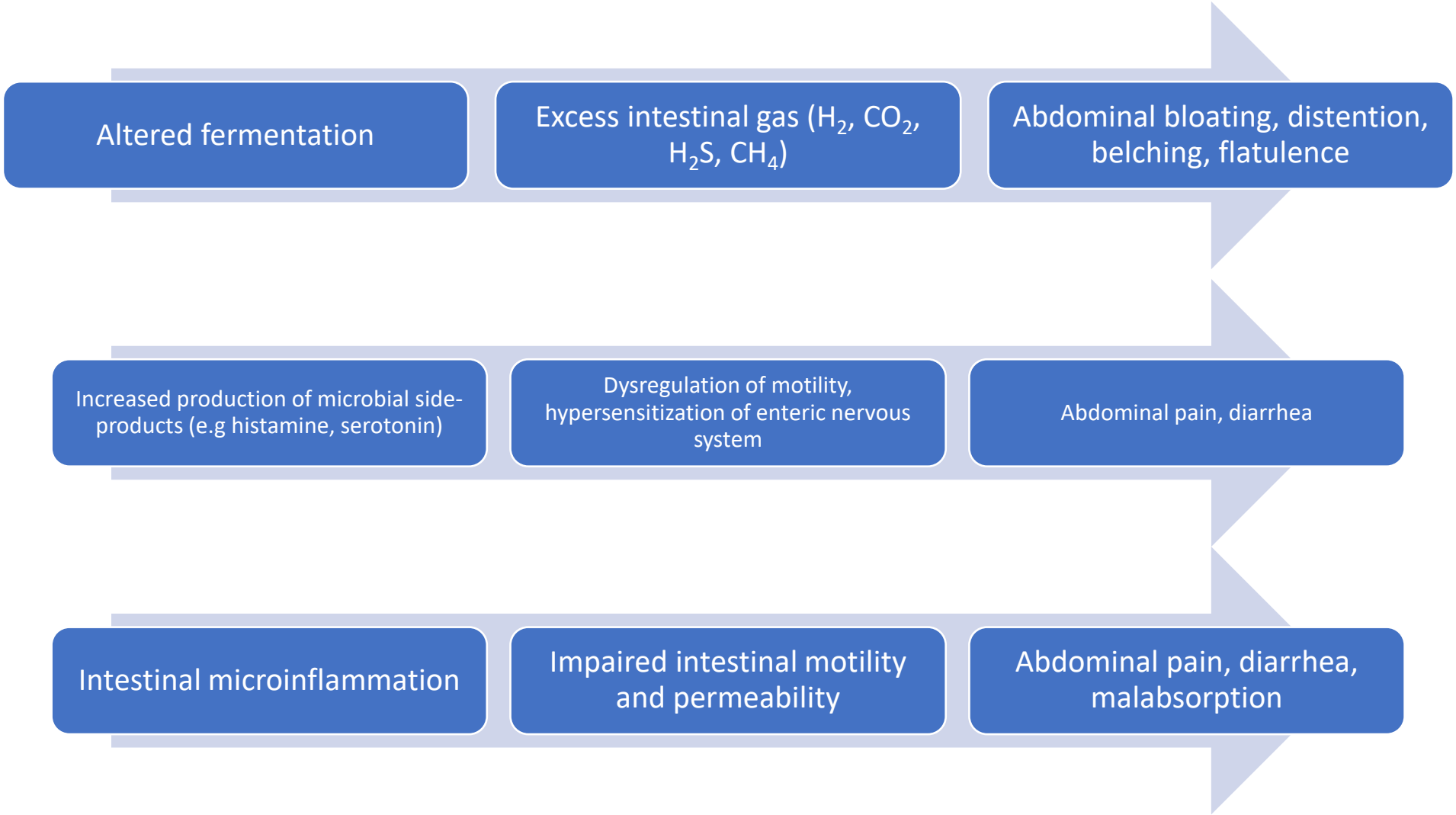
Rezaie A et al. North American consensus. AJG 2017
Greiner AK et al. Am J of Physiology 2014

Symptoms of microbial overgrowth

- Post-prandial abdominal distention
- Post-prandial bloating
- Early satiety
- Nausea
- Abdominal discomfort/pain
- Diarrhea/urgency (more common with H_2 or H_2S-predominant overgrowth)
- Constipation (More common in intestinal methanogen overgrowth)
- Malabsorption

Rezaie A, Pimentel M, Rao SS. Curr Gastroenterol Report. 2016
Rao SS et al. CTG 2018

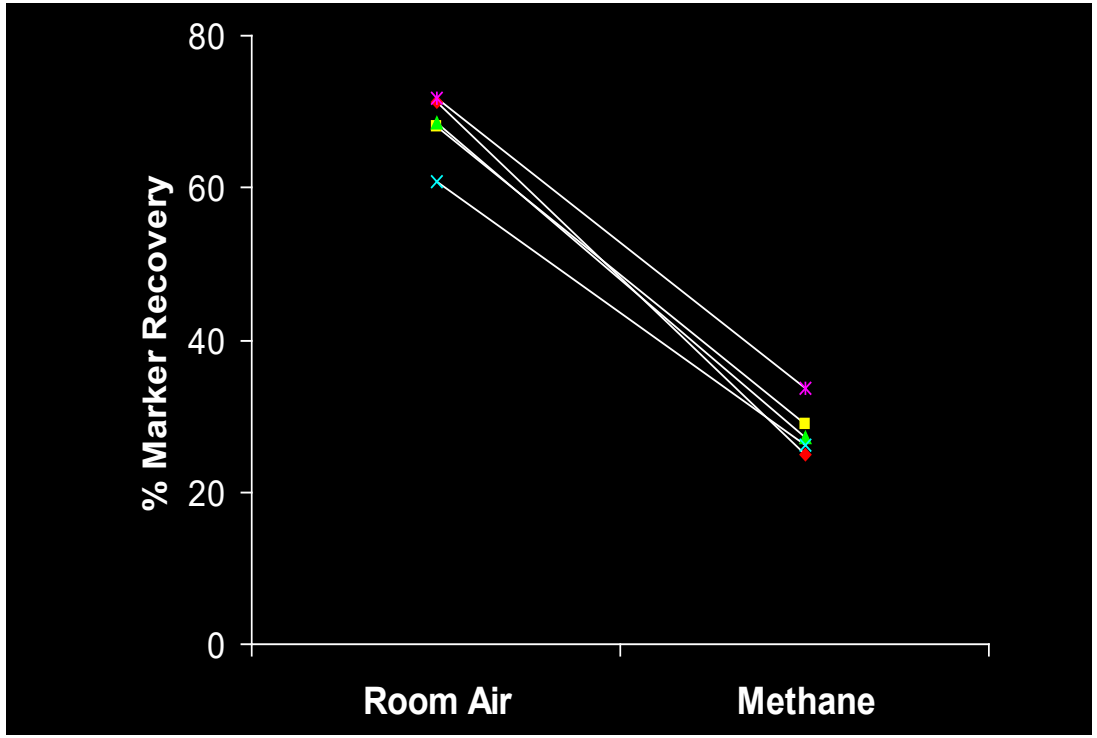
Selected pathogenesis pathways



Rezaie A, Pimentel M, Rao SS. Curr Gastroenterol Report. 2016
Raskov H et al. *Gut Microbes.*2016
De palma et al. Sci Trans Med. 2022

Methane decreases intestinal transit

- Infusion of methane gas into canine small bowel slows the transit by 69%
- Methanogen overgrowth can occur in small bowel or the colon; hence, the name "*Intestinal* methanogen overgrowth"



Pimentel, et al. Am J Physiol, 2006

Diagnosis of intestinal microbial overgrowth

	Breath testing	Small bowel aspiration and culture	Deep sequencing of intestinal content*
Intestinal methanogen overgrowth (IMO)	Yes	No	Yes
Small intestinal fungal overgrowth (SIFO)	No	Yes	Yes
Small intestinal bacterial overgrowth (H_2 subtype)	Yes	Yes	Yes
Small intestinal bacterial overgrowth (H_2S subtype)	Yes	No	Yes

* Currently limited to research studies

Rezaie A et al. AJG 2017
Rao SS et al. CTG. 2018
Leite G et al. Plos One. 2020

Diagnosis

Hydrogen and Methane-Based Breath Testing in Gastrointestinal Disorders: The North American Consensus

Ali Rezaie, MD, MSc, FRCP(C)[1], Michelle Buresi, MD[2], Anthony Lembo, MD[3], Henry Lin, MD[4], Richard McCallum, MD[5], Satish Rao, MD[6], Max Schmulson, MD[7], Miguel Valdovinos, MD[8], Salam Zakko, MD[9], Mark Pimentel, MD, FRCP(C)[1] and on behalf of The North American Consensus group on hydrogen and methane-based breath testing

Provides a standardized protocol on indications, preparation, performance and interpretation of breath testing for diagnosis of microbial overgrowth including SIBO and IMO

Rezaie A et al. Am J Gastro. Apr 2017

Three pillars of management

- Addressing the modifiable underlying cause(s) of overgrowth
  - Decreasing inflammation if underlying Celiac or Crohn's disease
  - Better control of diabetes
- Induction of remission
  - Antimicrobials
    - IMO: Neomycin plus rifaximin
    - SIBO (H2 subtype): Rifaximin, metronidazole, ciprofloxacin, trimethoprim-sulfamethoxazole
    - SIBO (H2S subtype): Bismuth subsalicylate, rifaximin
    - SIFO: Fluconazole
  - Elemental diet
- Maintenance of remission
  - Low fermentation diet
  - Promotility medications

Rezaie A et al. Curr Gastr Report. 2016
Pimentel M et al. Dig Dis Sci. 2004
Rao SS et al. Clin Trans Gastr. 2018
Pimentel M et al. Am J Gast. 2020
Suarez F. Gastroenterology. 1998
Rezaie A. Am J Gast. 2020

Management

ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth

Mark Pimentel, MD, FRCP(C), FACG[1], Richard J. Saad, MD, FACG[2], Millie D. Long, MD, MPH, FACG (GRADE Methodologist)[3] and Satish S. C. Rao, MD, PhD, FRCP, FACG[4]

Provides clinical guidelines on diagnosis and treatment of microbial overgrowth including SIBO and IMO

Pimentel M et al. Am J Gastro. 2020

Conclusions

- Microbial overgrowth consists of multiple distinct diseases (i.e. SIBO, SIFO and IMO) with substantial chronic symptoms. There have been significant advancements in our understanding of theses diseases and specific diagnostic tests and therapeutic algorithms are used to manage patients.
- Currently, there are no specific ICD-10-CM codes for microbial overgrowth or any of the subtypes.
- ICD-10-CM codes will enable us to:
  - Use a common language to record, report and monitor microbial overgrowth
  - Determine the incidence and prevalence rates
  - Encourage research