



Advancing GI Patient Care 2021

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Beyond Gut Instincts

Latest Advances in Diagnosis & Management of IBS, and Gut Microbiome Developments

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Chair, Institutional Review Boards for Human Subject
Protection, Baylor Scott & White Research Institute

Faculty Disclosures

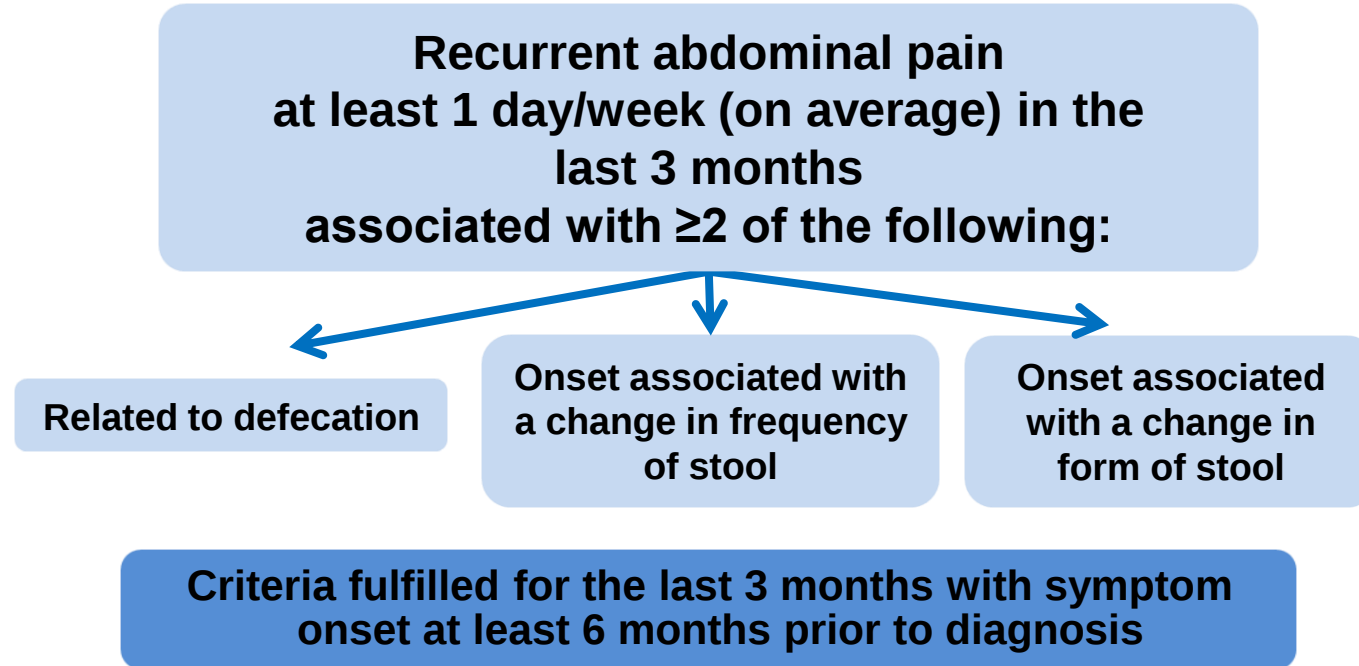
Lawrence R. Schiller, MD

- Dr. Schiller has received honoraria for Speakers' Bureaus and Advisory Boards for:
 - Red Hill Pharmaceuticals
 - Phathom Pharmaceuticals
 - Salix Pharmaceuticals

Irritable Bowel Syndrome – What Is It?

- Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by a group of symptoms accompanied together that include abdominal pain and changes in the consistency of bowel movements. These symptoms occur over a long time, often years.

Rome IV Criteria for IBS



Rome Criteria Identify a Set of Patients

- Who are unlikely to have structural diseases (such as IBD or cancer) at time of diagnosis
- Who are unlikely to develop structural disease for up to 10 years after diagnosis
- Who do not need extensive evaluation for structural disease
- Can be tried empirically on medications aimed at symptom control

Current Orthodoxy About IBS

- Identify patient's symptoms
- If criteria for IBS met → make “positive” diagnosis
 - Unlikely to have IBD, cancer
 - Minimal initial evaluation
 - For IBS-D: CBC, celiac serologies, serum CRP, fecal calprotectin or lactoferrin
- Begin treatment for IBS

Problems With Current Orthodoxy

- Little evidence that patients who meet Rome criteria are different from those with similar symptoms who do not
- Once a “diagnosis” is made, physicians stop thinking about cause of symptoms in the patient
- Treatable conditions are overlooked

IBS: Is It Still a Relevant Diagnosis?

- IBS highlights pain as major issue
 - May not be much difference in patients with or without pain
- Spectrum of chronic constipation
 - IBS-C $\leftrightarrow$ chronic constipation (depending on amount of pain)
- Spectrum of chronic diarrhea
 - IBS-D $\leftrightarrow$ chronic diarrhea (depending on amount of pain)

IBS: Is It Still a Relevant Diagnosis?

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**WHAT IF WE FORGET ABOUT IBS AS A FINAL DIAGNOSIS
AND CONSIDER DIFFERENTIAL DIAGNOSES FOR
CONSTIPATION AND DIARRHEA?**

Differential Diagnosis of IBS-C

- Chronic idiopathic constipation (~75%)
 - Normal transit
 - Slow transit
 - Methanogenic bacteria¹
 - Define by breath testing: increased methane (fasting & after CHO)
 - Treat with antibiotics (not FDA-approved: neomycin, rifaximin)
- Outlet obstruction constipation (~25%)
 - Do a rectal examination!

¹Bin Waqar SH, Rehan A. Methane and constipation-predominant irritable bowel syndrome: Entwining pillars of emerging neurogastroenterology. *Cureus*. 2019 May 28;11(5):e4764.

Differential Diagnosis of IBS-D

- Food intolerances
- Bile acid diarrhea
- Small intestinal bacterial overgrowth (SIBO) or dysbiosis
- Everything else
 - Celiac disease
 - Microscopic colitis
 - Mast cell disorders/eosinophilic gastroenteritis

Specific Diagnoses in IBS-D

Diagnosis	Estimated frequency in IBS-D	Diagnostic strategy	Empiric trials
Food intolerances	20–67%	Diet and symptom diary; exclusion diet	Low FODMAPs diet
Bile acid diarrhea	10–40%	SeHCAT test, C4, fecal BA	Bile acid sequestrant
SIBO	23–45%	Breath tests, quant. culture	Antibiotics

Specific Diagnoses in IBS-D

Diagnosis	Estimated frequency in IBS-D	Diagnostic strategy	Empiric trials
Microscopic colitis	5–10%	Colon biopsies	Rx only with Dx
Celiac disease	0.4–4%	IgA anti-tTG, duodenal biopsies	Rx only with Dx

Advice About Diagnosis of IBS

- Don't consider IBS to be a final diagnosis
- Think about common disorders presenting as IBS
- Consider outlet problems in all constipated patients
 - Do a rectal examination in all; anorectal manometry, defecography selectively
- Selective testing or empiric trials for common disorders causing IBS-D
 - Food intolerances; may need dietician help
 - Bile acid diarrhea; trial of bile acid sequestrant
 - SIBO/dysbiosis; breath test, antibiotic trial

What's New About the Gut Microbiome?

It's Even More Complicated Than We Thought

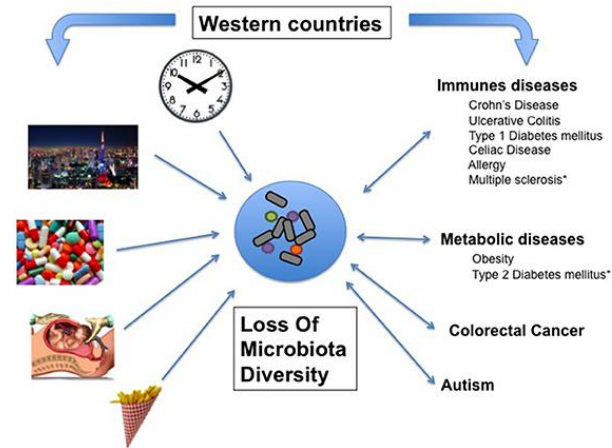
- It's more than bacteria
 - Viruses
 - Protozoa, fungi
- It metabolizes chemicals in the lumen
 - Nutrients
 - Antigens
 - Drugs
 - Bile acids

It's Even More Complicated Than We Thought

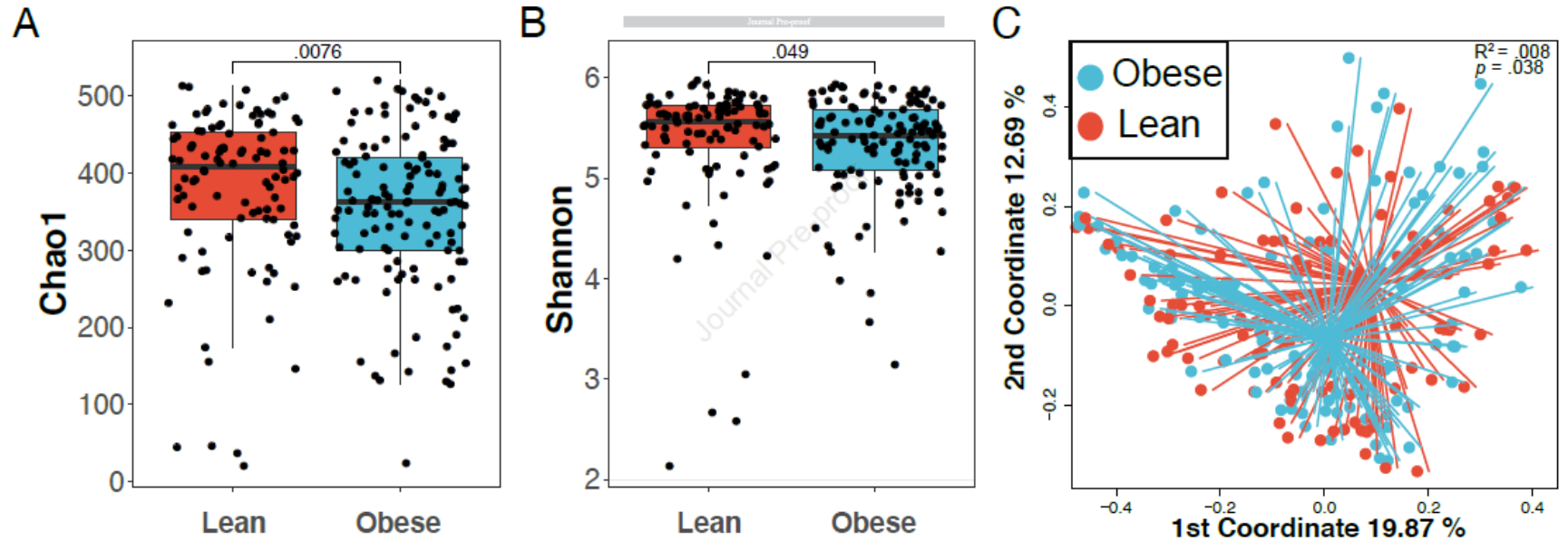
- It communicates chemically with our human cells
 - Peptides (“enterotoxins”) → enterocytes
 - Modulates human immune cell function → T cells
 - Alters human hormone actions → PTH
- Our hormones affect bacterial metabolism
 - Norepinephrine → increased *E. coli* virulence
- Our immune system modifies components of gut microbiome

We Have Limited Ability to Measure It

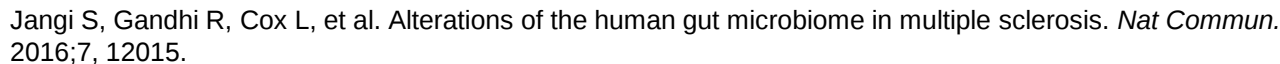
- PCR techniques allow assessment of the types of organisms present and relative prevalence
- Decreased microbial diversity (“dysbiosis”) seen in several conditions
 - Inflammatory bowel diseases
 - Obesity
 - Diabetes
 - Inflammatory diseases
 - Colon cancer



We Have Limited Ability to Measure It



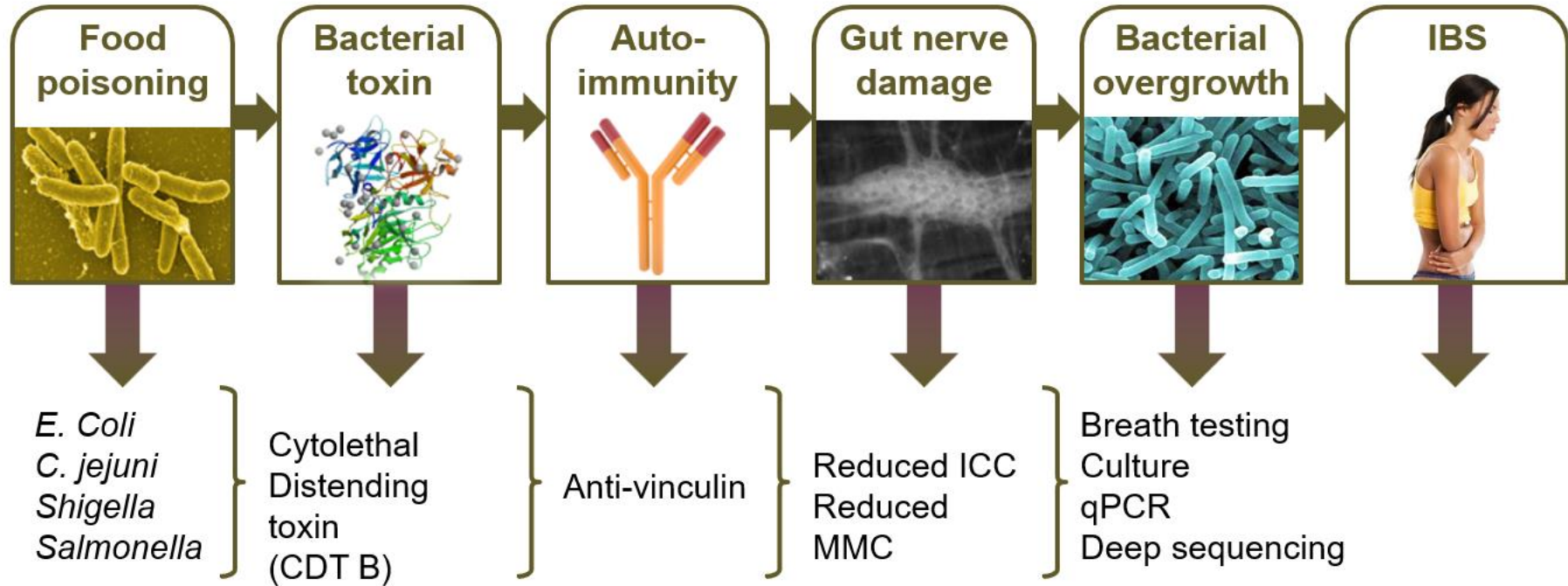
- Information overload
- Can see that there are differences, but it's not clear what it means
- Potential interactions and effects not defined



Microbiome Studies 2021

- Current technology still limited in analyzing complex community of organisms
- Implications of changes in microbiome uncertain; mechanism by which changes → disease states unknown
 - Changes in metabolome?
 - Impacts on human physiology?
 - Impacts on epithelium, immune system?

Pathogenesis of Postinfectious IBS-D?



ICC, interstitial cells of Cajal; MMC, migrating motor complex; qPCR, quantitative polymerase chain reaction. Pimentel M et al. *PLoS ONE*. 2015;10(5):e0126438.

Summary

- Current orthodoxy about IBS may need to change
- IBS-C
 - Consider outlet problems → digital rectal examination
 - Consider methanogenic flora → breath test
- IBS-D
 - Consider big three factors: food intolerances, bile acid diarrhea, SIBO/dysbiosis
 - Empiric trials of diet, bile acid sequestrants, antibiotics may be helpful in absence of decisive laboratory tests