CG OneGI SECOND ANNUAL GI & LIVER Summit

The Clinical Utility of Breath Tests & The Role of SIBO in IBS

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Heterogeneous Nature of IBS



SIBO Is Commonly Identified in IBS

Odds ratio meta-analysis plot [random effects]



SIBO in IBS patients and controls, all studies included

Study name		Stat	tistics for eac	h study		SIBO	/ Total		Odds ratio	and 95% CI	
	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value	IBS	Controls				
Posserud I et al*	4.013	0.503	32.026	1.311	0.190	10/162	1/62	12	1 -	+ - + -	- 1
Choung R et al	0.189	0.058	0.614	-2.771	0.006	3/148	52 / 527				
Pyleris E et al	5.640	3.098	10.267	5.660	0.000	42/112	20/208				
Giamarellos-Bourboulis E et al	1.345	0.860	2.102	1.299	0.194	33/252	65/645				
Shoshal U et al 2014*	15.581	0.883	275.075	1.875	0.061	34 / 80	0/10				
Pimental M et al	20.667	5.293	80.691	4.358	0.000	93/111	3/15				
Valters B et al	0.246	0.060	1.002	-1.958	0.050	4/42	6/20				
Bratten J et al	0.505	0.202	1.265	-1.458	0.145	166 / 224	34/40			+	
Scarpellini E et al	24.267	7.347	80.150	5.231	0.000	28/43	4/56				
Park JH et al*	2.484	0.274	22.536	0.809	0.419	7/38	1/12				
Collin B et al	18.041	6.547	49.712	5.593	0.000	68/75	14/40				_
Park JS et al*	1.214	0.558	2.642	0.489	0.625	34 / 76	16/40				
hao J et al*	7.778	0.968	62.498	1.929	0.054	35 / 89	1/13				_
upascu A et al*	10.889	3.517	33,710	4.141	0.000	20/65	4/102				-
Rana S et al 2008*	12.375	1.653	92.658	2,449	0.014	25/225	1/100				_
Parodi A et al*	4.303	1.236	14.979	2.293	0.022	21/130	3/70				
.ombardo L et al*	5.084	1.515	17.063	2.632	0.008	49/200	3/50				
Shoshal U et al 2010*	4,779	0.609	37.485	1,489	0.137	13/149	1/51				-
Rana S et al 2011*	9.994	1.275	78.341	2.191	0.028	11/175	1/150				_
Sachdeva S et al*	11,200	1.405	89.252	2.281	0.023	14/59	1/37				
Abbasi M et al*	4.317	2.144	8.691	4.096	0.000	40 / 107	13/107				
/loraru l et al*	6.504	2.920	14.490	4.582	0.000	105/331	7/105				
Galatola G et al	16.280	0.825	321.375	1.833	0.067	5/17	0/18				~
Schatz R et al	1 308	0.948	2.061	1.691	0.091	77/124	436 / 808			H	
Grover M et al*	2.289	0.892	5.873	1.723	0.085	52 / 158	6/34				
	3.696	2.261	6.042	5.215	0.000					•	
								0.01	0.1	1 10	100
									No SIBO	SIBO	

- Overall Prevalence Rates of SIBO in Rome IBS Using Breath Tests and/or Culture: 30-40%
- Predictors on SIBO in IBS patients: Female (OR 1.5) & IBS-D (OR 1.7)
- Overall quality of evidence low

Chen B et al. J Gastroenterol. 2018;53(7):807-818; Moayyedi P et al. JCAG. 2019;2:6-29; Shah A et al. Am J Gastroenterol. 2020;115:10-201; Takakura W and Pimentel M. Front Psychiatry. 2020;11:664.

Diagnostic Testing for SIBO/IMO



Breath Testing:

- · Simple, safe, widely available to diagnose SIBO
- Glucose (75g) or Lactulose (10g)
- Home or office-based procedure
- Significant heterogeneity in test performance, preparation, indications for testing, and interpretation of results)
- (+) H₂→indicative of SIBO but not directly associated with symptom production
- (+) CH₄→indicative of IMO associated with delayed transit and constipation (OR=3.51; higher the level the worse the constipation)
- (+) H₂S→associated with accelerated transit and diarrhea





Duodenal/Jejunal Quantitative Culturing:

- Gold standard but limited availability, invasive, expensive
- Debated but recommended threshold for (+) study >10³ CFU/ml
- Polymicrobial samples may indicate contamination
- · May miss distal small intestinal overgrowth

Capsule Technology is Coming

- Measure H₂ in vivo
- Collect samples of SI bacteria

Pimentel M et al. Am J Gastroenterol. 2020;115:165-178; Kalantar-Zadeh K et al. Nat Electronics. 2018;1:79-87; Kunkel D et al. DDS. 2011;56:56:1612-1618.

LHBT Measures Small Intestinal Transit Rather Than SIBO in IBS Patients



Yu, et al. Gut. 2011; 60:334; Simren M et al. Gut. 2013; 62:159; (Slide compliments of L. Chang, MD).

Positive Lactulose Hydrogen Breath Test Is Similar in Irritable Bowel Syndrome and Healthy Controls



Vanner SJ. Gut. 2008; 57:1315; (Slide compliments of L. Chang, MD).

Plusses and Minuses of Breath Testing for IBS

Competing Analytics: Which are Correct?

 Simple and safe test to diagnose SIBO 	Substrate	Test Dose	Sensitivity/ Specificity	Measured Gas ppm	Positive Study
 Useful in assessing conditions associated with bloating like IBS 		Modified	Sone:20-03%	Modified Rome &	Modified Rome: • Inc 12 ppm • Baseline > 20 ppm
 Significant heterogeneity in test performance, preparation, indications for testing, and interpretation of results 	Glucose	NAC: 75 gm	Spec:30-68%	NAC: H_2 or CH_4	NAC: • ≥ 20 ppm inc w/in 90 min H ₂ • ≥ 10 PPM CH ₄ at any time
 Historically 					Modified Rome:
 Glucose: more specific 					 Baseline > 20 ppm >20 ppm w/in 90
 Only samples proximal SB (high FN rate) due to distal SIBO 		Modified	Sens:17-68%	Modified Rome &	 min sustained increase > 10ppm above
 Lactulose: more sensitive 	Lactulose	Rome & NAC: 10 gm	Spec:44-86%	NAC: H_2 or CH_4	baseline
 Increased rate of orocecal transit (FPs) 		Ţ			NAC: • ≥ 20 ppm inc w/in 90 min H ₂ • ≥ 10 ppm CH ₄ at any time

Gasbarirni et al. APT. 2009;29(Suppl1):1-49; Rezaie A et al. AJG. 2017;112:775-78; Saad R et al. CGH. 2014;12:1964-1972.

Breath Testing in IBS: Lack of Consensus



ACG SIBO Guideline: "We **SUGGEST** the use of breath testing for the diagnosis of SIBO in patients with IBS" Conditional/Very Low Evidence ACG IBS 2021 Guideline: Not addressed

- AGA Guideline 2009: Insufficient evidence
- AGA Guideline Functional Diarrhea/IBS-D 2019: Not evaluated as not part of standard diarrhea evaluation
- AGA Practice SIBO Update 2020: Controversy concerning role of SIBO in pathogenesis of IBS
- AGA Guideline IBS 2021: Not Recommended

Pimentel M et al. *Am J Gastroenterol.* 2020;115:165-178; Lacy BE et al. *AJG.* 2021;116(1):17-44; Brandt LJ et al. *Am J Gastroenterol.* 2009;104 Suppl 1:S1-35; Carrasco-Labra-A et al. *Gastroenterology.* 2019;157:859-880; Quigley EMM et al. *Gastroenterology.* 2020;159(4):1526-1532; Chang L. *Gastroenterology.* 2021;161(4):1092–1098.

Pitfalls With Commercial Breath Testing

Table 2. Comparison of commercial entity diagnostic criteria for the positive diagnosis of intestinal overgrowth*

	Commercial diagnostic cutoffs for intestinal overgrowth	Cutoffs in concordance with the ACG guidelines?	Length of test and other notes	Out-of-pocket cost ^b
Aerodiagnostics	H_{2^c} Change from baseline ≥20 CH ₄ : Rise ≥ 12 ppm H ₂ + CH ₄ : Level ≥ 15 ppm *may be suggestive* of SIBO	No	180min (CH₄ level ≥3 ppm with presence of constipation suggestive of SIBO)	\$209.74 (continental US) \$260.00 (outside continental US)
Commonwealth Diagnostics International, Inc.	$H_{2^{c}}$ Charge from baseline ≥ 20 ppm CH ₄ : ≥10 ppm at 90 min H ₂ + CH ₄ : Change from baseline ≥ 15 ppm	No	135min	\$175.00
Gemelli (trio-smart)	H_{2^c} Change from baseline ≥ 20 ppm CH _{4^c} Level ≥10 ppm at any time H_2S : ≥3 ppm at any time	Yes	120min Offers teleheaith service to guide use	\$289.00
Genova Diagnostics	H ₂ : Change from baseline ≥ 20 ppm CH ₄ : Level ≥10 ppm	Yes	120 or 180 min Lists H_2 + CH ₄ level, but this is not a diagnostic criterion	\$235.00 (listed on third-party site)
Metabolic Solutions, Inc.	H _≥ Change from baseline ≥ 20 ppm CH ₄ : Change from baseline ≥ 10 ppm	No	90 min glucose BT only	\$159.00
QuinTron	H₂: Change from baseline ≥ 20 ppm CH4: Level ≥ 12 ppm H₂ + CH₄ ≥ 15 ppm (12) "may suggest the presence" of SIBO	No	180min Glucose BTonly Portable analyzer available for purchase	\$215.00

BT, breath test; SIBO, small intestinal bacterial overgrowth.

*All information including pricing is derived from company websites unless otherwise referenced (diagnostic cutoffs derived from publicly available sample reports). *Charges vary based on whether billed as medical necessity and by insurance. Medicaid often not accepted.

Incorrect analytics:

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- 6 major commercial breath testing companies
- 2 with appropriate interpretation
- False positives → inappropriate treatment
- False negatives → unnecessary diagnostic testing
- Northwestern Review of Breath Testing:
 - 582 community breath tests performed
 - 16.3% FN (CH₄)
 - 3.2% FP (H₂ + CH₄)
 - THP: 20% of all breath tests reported incorrectly

Examples of Inaccurate Reporting:

]	Time	Sample No.	Hydrogen (PPM)	Methane (PPM)	Carbon dioxide (cf)		
	Baseline	1	0	24	1.09		
Ē	15 mins	2	0	23	1.09		
-se	30 mins	3	0	21	1.13		
1 E	45 mins	4	0	24	1.12		
1	60 mins	5	2	29	1.10		
Ë	75 mins	6	2	32	1.07		
0	90 mins	7	14	29	1.16		
E	105 mins	8	0	29	1.14		
1 8	120 mins	9	13	27	1.17		
ŭ	135 mins	10	23	39	1.14		
	Summary of 90-minute results						
	Greatest difference over baseline for each trace gas are presented below:						
	H ₂ production		0 ppm Normal <20 p				
	CH₄ productio	n	8 ppm	Norma	Normal <10 ppm		
	Combined		N/A ppm		Normal <15 ppm		
	He+ CHe production						
B	Based on the criteria used in this test, the presence of bacterial overgrowth is						
	not supported						

 $CH_4 > 10 PPM$ is a (+) study

b		Time	Sample No.	Hydrogen (PPM)	Methane (PPM)	Carbon dioxide (cf)		
		Baseline	1	0	0	1.00		
	Ē.	15 mins	2	18	0	0.95		
	est a	30 mins	3	14	0	0.89		
	1 E	45 mins	4	11	0	0.92		
	1	60 mins	5	4	0	0.88		
	Ê	75 mins	6	0	0	0.98		
	ŝ	90 mins	7	0	4	0.87		
	=	105 mins	8	0	4	0.93		
	8	120 mins	9	0	6	1.02		
	Ŭ	135 mins	10	0	0	0.88		
	Summary of 90-minute results							
	Greatest difference over baseline for each trace gas are presented below:							
		H ₂ production		18 ppm	Norma	Normal <20 ppm		
	CH ₄ production			4 ppm	Norma	Normal <10 ppm		
		Combined		22 ppm		Normal <15 ppm		
	H ₂ + CH ₄ production							
	Based on the criteria used in this test, the presence of bacterial overgrowth is							
	supported							

You cannot add H₂ and CH₄

Consensus Building: SIBO in IBS

Open

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

Ali Rezaie, MD, MSc, FRCP(C)¹, Michelle Buresi, MD³, Anthony Lembo, MD³, Henry Lin, MD⁴, Richard McCallum, MD⁵, Satish Rao, MD⁹, Max Schmulson, MD³, Miguel Valdovinos, MD⁵, Salam Zakko, MD⁹, Mark Pimentel, MD, FRCP(C)¹ and on behalf of The North American Consensus group on hydrogen and methanen-based breath testing

European guideline on indications, performance, and clinical impact of hydrogen and methane breath tests in adult and pediatric patients: European Association for Gastroenterology, Endoscopy and Nutrition, European Society of Neurogastroenterology and Motility, and European Society for Paediatric Gastroenterology Hepatology and Nutrition consensus

Asian-Pacific consensus on small intestinal bacterial overgrowth in gastrointestinal disorders: An initiative of the Indian Neurogastroenterology and Motility Association

Uday C. Ghoshal ¹. Sanjeev Sachdeva² - Ujala Ghoshal² A Akh Misra¹ - Amarender Singh Puri² - Nitesh Pratap³ -Ayesha Shah³ - Nitesh Pratap³ - Kok Am Gover² - Victoria P Y Tan³ - Tahmed Ahmed¹ - Yeong Yeh Lee ^{11,12} -B S Ramakrishna³ - Ruppott Talukdar¹⁴ - S V Rana¹³ - Saroj K Sinha¹⁶ - Minhu Chen¹⁷ - Nayoung Kim¹⁶ -Gerald Holtman⁵



- 1. Mostly agree about criteria for SIBO
- 2. Mostly agree about dosing for substrates
- 3. Mostly agree that SIBO and IBS are interrelated

Nomenclature & Epidemiology of Intestinal Overgrowth Redefined

• Small Intestinal Bacterial Overgrowth (SIBO):

- Excessive concentrations of colonic bacteria identified in the small intestine causing symptoms
 - Escherichia coli, Klebsiella spp, Aeromonas spp→most common organisms
 - Streptococcal, Bacteroides, Lactobacillus spp→also commonly identified
 - Detected by elevated H₂ levels but these do not correlate with symptoms
 - Newest data suggests symptoms related to formation of hydrogen sulfide (H₂S)
- Intestinal Methanogenic Overgrowth (IMO):
 - Excess concentrations of archaea (single-cell organisms) in the small or large intestine
 - Methanobrevibacter smithii→primary methanogen
 - Delayed intestinal transit→constipation/IBS-C



Pimentel M et al. Am J Gastroenterol. 2020;115:165-178; Bouhnik Y et al. AJG 1999;94:1327.

Fermented Gas Microtyping



¹Leite, et al. *PlosOne.* 2019; ²Kunkel et al. *Dig Dis Sci.* 2011; ³Villanueva et al. DDW 2022.



Distinct Microtypes Drive IBS Subtypes

Villauneva—Millan M et al. AJG. 2022;117:2055-2066.

Can Positive Breath Test Predict Response to Therapy?



- Caveats
- Small retrospective analysis IBS-D N=93/2438
- Lack of comparison to responses in PBO cohort
- Does not assess retreatment
- 9 patients (+) LBT may have been misclassified and if (-) LBT w/(+) response now no difference between cohorts (P=0.324)

Rezaie A et al. AJG. 2019;11(4):1886-1893; Black CJ and Ford AC. AJG. 2020;115:955-956.

Evidence-Based Treatment:

ACG SIBO Guideline Recommendations:

 Table 5. Suggested antibiotics for treatment of small intestinal bacterial overgrowth

Antibiotic	Recommended dose	Efficacy
Nonabsorbable antibiotic		
Rifaximin	550 mg t.i.d.	61%-78%
Systemic antibiotic		
Amoxicillin-clavulanic acid	875 mg b.i.d.	50%
Ciprofloxacin	500 mg b.i.d.	43%-100%
Doxycycline	100 mg q.d. to b.i.d.	а
Metronidazole	250 mg t.i.d.	43%-87%
Neomycin	500 mg b.i.d.	33%-55%
Norfloxacin	400 mg q.d.	30%-100%
Tetracycline	250 mg q.i.d.	87.5%
Trimethoprim-sulfamethoxazole	160 mg/800 mg b.i.d.	95%

^aIn the study, no testing performed to reassess small intestinal bacterial overgrowth, although all participants had other objective measures of improvement.

ACG IMO Guideline Recommendations:



Retrospective Analysis: IBS-C Patients

We suggest the use of antibiotics in SYMPTOMATIC patients with SIBO to eradicate overgrowth and resolve symptoms:

We suggest....NOTHING. Not enough evidence to support

Pimentel M et al. Am J Gastroenterol. 2020;115:165-178; Low K et al. J Clin Gastroenterol. 2010;44:547-550.

Best of the Rest?

SIBO:

- Diet Modification: Starve the bacteria reducing fermentable substrates (FODMAPS) but no studies
- Probiotics: Fight bacteria with bacteria or cause SIBO?
 - MA: OR dec H₂ production 1.61
 - Small poor-quality studies
- Fecal Transplant: Patients receiving these may experience increased GI symptoms esp if donor has (+) breath test

IMO:

- Diet Modification: Pilot study at Northwestern using low-FODMAP diet
- Herbal preparation: Atrantil® assessing symptomatic efficacy (bloating/constipation) and resolution of CH₄ (+) breath test

Herbal Intervention for IMO

Botanical (Neutraceutical)	Active compounds	Effects	
Quebracho (common name used to describe a type of hardwood from Central and South America)	Tannins	Free radical scavengers that bind hydrogen and fiber, disrupt bacterial lipid layers	
Horse chestnut or conker tree extract (Aesculus hippocastanum)	Saponins (escins)	Free radical scavengers that bind hydrogen, reduction of methane emissions, promote intestinal motility	
Peppermint (Mentha balsamea Wild) extract	Menthol	Smooth muscle relaxant, modulator of visceral pain, bactericidal effects	



Herbal Intervention for IMO

- Open label N=39 with GBT/LBT (+) IMO \geq 10 PPM •
- Atrantil 2 capsules TID x 4 wks
- Symptoms Response (GI PROMIS); CH4 reduction; Correlation between the two
- Adverse Events: Diarrhea (1); Bloating (2); Belching/Stomach Burning (1) •



- Abdominal Pain/Gas Bloating significantly improved
- Median Δ CH₄ from baseline 5 PPM
- Constipation symptoms improved trend toward significance
- 56% endorsed AR
- Liu JJ....Brenner DM. ACG. 2022:S579.

- 86% of all CH₄ breath tests still (+) after treatment
- No significant correlation between symptoms and CH₄

Potential Treatment for Hydrogen Sulfide

GASTROENTEROLOGY 1998;114:923-929

Bismuth Subsalicylate Markedly Decreases Hydrogen Sulfide Release in the Human Colon

FABRIZIS L. SUAREZ, JULIE K. FURNE, JOHN SPRINGFIELD, and MICHAEL D. LEVITT Research Department, Minneapolis Veterans Affairs Medical Center, Minneapolis, Minnesota

Background & Aims: Hydrogen sulfide is one of the main malodorous compounds in human flatus. This toxic gas also has been implicated in the pathogenesis of ulcerative colitis. Therefore, a treatment that reduces colonic H₂S levels could be clinically useful in the treatment of flatus odor and of ulcerative colitis. In this study the ability of bismuth subsalicylate, a compound that binds H₂S, to reduce H₂S release in the colon, was tested. Methods: Homogenates made from human and rat feces were incubated with and without bismuth subsalicylate, and gas production was measured. Fecal samples from 10 healthy subjects were analyzed before and after ingestion of bismuth subsalicylate (524 mg four times a day) for 3-7 days. Results: Fecal homogenates showed a dose-dependent relationship between the concentration of bismuth subsalicylate and H₂S release. Treatment of subjects with bismuth subsalicylate produced a >95% reduction in fecal H₂S release. Conclusions: The ability of bismuth subsalicylate to dramatically reduce H₂S could provide a clinically useful means of controlling fecal and/or flatus odor and of decreasing the putative injurious effects of H₂S on the colonic mucosa.

containing compounds to the colon could also limit H_2S production. However, a variety of endogenous compounds (e.g., mucin and taurocholic acid) as well as dietary substances (e.g., amino acids and sulfate) serve as sources of sulfur for the colonic bacteria,⁷ and it seems unlikely that delivery of sulfur to the colon can be drastically reduced.

A simple approach to reducing H_2S release in the colon would be the administration of a compound that binds H_2S . In the test tube, bismuth reacts with sulfide to form very insoluble bismuth sulfide. In the present report, we carried out a series of experiments in rats and humans to determine whether bismuth subsalicylate (BSS) decreases the fecal release of H_2S .

Materials and Methods

In Vitro Studies

The ability of BSS to bind the three major sulfur gases present in human flatus⁸ was studied by incubating 1 mL of a 1:10 dilution of BSS (4.84 µmol of bismuth) in the form of Pepto-Bismol (Procter & Gamble, Cincinnati, OH) in buffer (0.1 mol/L sodium phosphate, pH 7.0) with 20 mL of N-

- Fecal samples 10 healthy subjects
- Analyzed before/after bismuth consumption
- 524 mg QID 3-7 days
- >95% reduction in production H₂S

NEEDS VALIDATION IN IBS-D RCTs

Treatment: "SIBO" Search

What happens when our patients google "SIBO" or "SIBO diet"



Services and Products

Testing, medical treatment/ counseling, Osteopathic manipulation, naturopathic interventions, nutritional interventions, psychological interventions (hypnotherapy), acupuncture, massage, podcasts, yoga, YouTube videos, vitamins, minerals, herbals, probiotics, prebiotics, nutraceuticals, food products (i.e., bone broth, LOW FODMAP food products), books





SIBO Test Video

Order

Each SIBO kit costs \$180.00. We only ship within the United States. If you are outside of the U.S. Please contact the SIBO lab to discuss your optic

TWO MONTH PROGRAM: 2395.00

This program is ideal if you want support shifting onto a customized SIBO protocol, ongoing symptoms addressed, ongoing support and reassessment of progress with bi-monthly adaptation of your plan to address SIBO

You can start with this program, or if you move from the Two Week to the Two Month Program, you simply pay the difference in price.

- · Starts with Two Week Intensive Program and continues for eight more weeks
- In addition to the Two Week Program, that is detailed above:
- · 45 minute calls held every two weeks for eight weeks

SIX MONTH PROGRAM:

5395.00

This program is ideal for those who want to address SIBO to the fullest extent, working through rotating customized protocols that knock down the microbes, use diet to heal the gut, immune support and flora rebalancing.

You can start with this program, or if you move from the Two Week Program to the Six Month Program, you simply pay the difference in price.

- Starts with Two Week Intensive Program and continues for twenty-two more weeks.
- In addition to the Two Week Program, which is detailed above:
- 45 minute calls held every two weeks for twenty-two weeks
- Includes ongoing research on your case
- Continue journaling: tracking eating, lifestyle habits and symptoms





The SIBO Diet Plan: Four Weeks To

Relieve Symptoms And Manage SIBO

Amazon.com



\$29.97 Free Shipping Amazon.com

The SIBO Solution: Your Comprehensive Guide To Eliminating

Where Are We in 2023?

Known:

- SIBO develops with loss of anatomic or functional protective factors
- SIBO and IMO are pathogenically distinct
- $H_2 \rightarrow$ not correlated with any symptoms but is indicative of SIBO
- CH₄→associated with delayed intestinal transit and constipation (IBS-C)
- H₂S→associated with accelerated transit and diarrhea
- (IBS-D)
- Bloating most common symptom c/o patients
- Unknown:
 - Best diagnostic strategy, substrate, and positive thresholds
 - Best treatments if antibiotics fail
- Overblown:
 - Benefits and of natural, behavioral, and dietary "cures" which require more robust studies

ACG Clinical Guideline: Small Intestinal Bacterial Overgrowth

Mark Pimentel, MD, FRCP (C), FAO3¹, Richard J. Saad, MD, FAO3², Mille D. Long, MD, MPH, FAO3 (GRADE Methodologist)^a and Satish S. C. Rao, MD, PhD, FRCP, FAO3⁴

Small intestinal bacterial overgrowth is defined as the presence of excessive numbers of bacteria in the small bowel, causing gastrointestinal symptoms. This guideline statement evaluates oriteria for diagnosis, defines the optimal methods for diagnosis testing, and summarizes treatment options for small intestinal bacterial overgrowth. This guideline provides an evidence-based evaluation of the literature through the Gand ing of Recommend ations Ass essment, Development, and Evaluation (GRADE) process. In instances where the available evidence was not appropriate for a formal GRADE recommendation, key concepts were developed using expert consensus.

Am J Gatrometerol 2020 115:16-178. https://doi.org/10.14309/ag.0000000000001; published online January 8, 2020

INTRODUCTION

Small intestinal bacterial overgrowth (SIBO) has been recognized as a medical phenomenon for many decades. Although its definition has been debated, the principle concept is that the normal small bowel has lower levels of microbial colonization compared with the colon and this normal balance is significantly altered in SIBO. SIBO is defined as the presence of excessive numbers of bacteria in the small bowel causing gastrointestinal (GI) symptoms. These bacteria are usually coliforms, which are typically found in the colon and include predominantly Gram-negative aerobic and anaerobic species that ferment carbohydrates producing gas (1). Since the late 1990s, there has been a resurgence in SIBO research which has been further enhanced by the increasing knowledge of the gut microbiome and its roles in human health and disease (2). These include a series of articles linking SIBO to diseases such as irritable bowel syndrome (IBS) (3.4), inflammatory howel disease (IBD) (5), systemic sclerosis (6), motility disorders (7,8), cirrhosis (9), fatty liver (10), postgastrectomy syndrome (11), and a variety of other conditions. Although these findings are important, a recent consensus document identified a number of strengths and weaknesses in the published work in this area (12). As such an effort has been underway to re-evaluate the criteria for the diagnosis of SIBO and define the optimal methods for diagnostic testing to identify this condition. Furthermore, treatment for SIBO has been largely empirical, has not undergone the scrutiny of sponsored clinical trials, and requires appraisal. In this guideline, we provide an evidence-based evaluation of the literature and assess the current unmet needs in SIBO research.

The guideline is structured in sections, each with recommendations, key concepts, and summaries of the evidence. Each recommendation statement has a n associated assessment of the quality of evidence and strength of recommendation based on the

Grading of Recommendations Assessment, Development, and Evaluation (GRADE) process. The GRADE system was used to evaluate the quality of supporting evidence (13). A "strong" recommendation is made when the benefits clearly out weigh the nexatives and/or the result of no action. "Conditional" is used when some uncertainty remains about the balance of bere fit sand potential harms. The quality of the evidence is graded from high to low. "High" quality evidence indicates that further research is unlikely to change the authors' confidence in the estimate of effect, and that we are very confident that the true effect lies close to that of the estimate of the effect. "Moderate" quality evidence is associated with moderate confidence in the effect estimate, although further research would be likely to have an impact on the confidence of the estimate, whereas "low" quality evidence indicates that further study would likely have an important impact on the confidence in the estimate of the effect and would likely change the estimate. "Very low" quality evidence indicates very little confidence in the effect estimate, and that the true effect is likely to be substantially different than the estimate of effect.

Key concepts are statements that are not amenable to the GRADE process either because of the statement or because of the swillable evidence. In some instances, key concepts are based on estrapolation of evidence and/or expert opinion. Tables I and 2 summarise the recommendations andkey concepts, are proceeding, in this guideline.

DEFINITION OF SIB O

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Medically Associated Sciences and Technology (MAST) Program, Coden-Simil Medical Dentes, Lon Angeles, California, ULA, Wellium, Medicina, University of Wellium, Ann Anton, Michigan, ULA, "Obision of Garcherotrology and Hopping Linking Medical Pathol Ecology, Linking California, ULA, Wellium, Linki, Augusta, Caerga, ULA, Comego and nones Merk Pimertel, MD, PROPE), RAGE, E-mail presentemborh.org. Received February 13, 2019 accessed Newmber 12, 2019

Summary: Clinical Utility of Breath Tests & Role of SIBO in IBS

- Our understanding of pathogenesis of excreted gases detected via breath testing is evolving
- Consensus a subpopulation of individuals meeting criteria for IBS also meet current criteria for SIBO
 - Is that IBS or SIBO?
- Multiple controversies and caveats to using breath testing to define SIBO/IMO in IBS or otherwise
- Guidelines on breath tests don't help as most do not weigh in on the controversy
 - Likely lack of consensus due to inefficiencies in data
- Treatments limited even if study (+): Not for IBS but for SIBO/IMO associated with IBS
 - SIBO: Antibiotics, Antibiotics, Antibiotics (?) Pepto
 - IMO: Rifaximin +/- Neomycin or Metronidazole or Atrantil
 - Overall: Diet (starve the bug) or Probiotics (survival of fittest) remains unvalidated
- My line in sand 2023: Honestly still trying to figure it out but overall, I argue no need to initially perform breath testing in individuals with IBS.
 - When they ask for it (glucose)
 - Rule out PBO effect

