The Gut Connection:

Solutions for SIBO, IBS, IBD and GERD

Dr. Kim Bretz ND

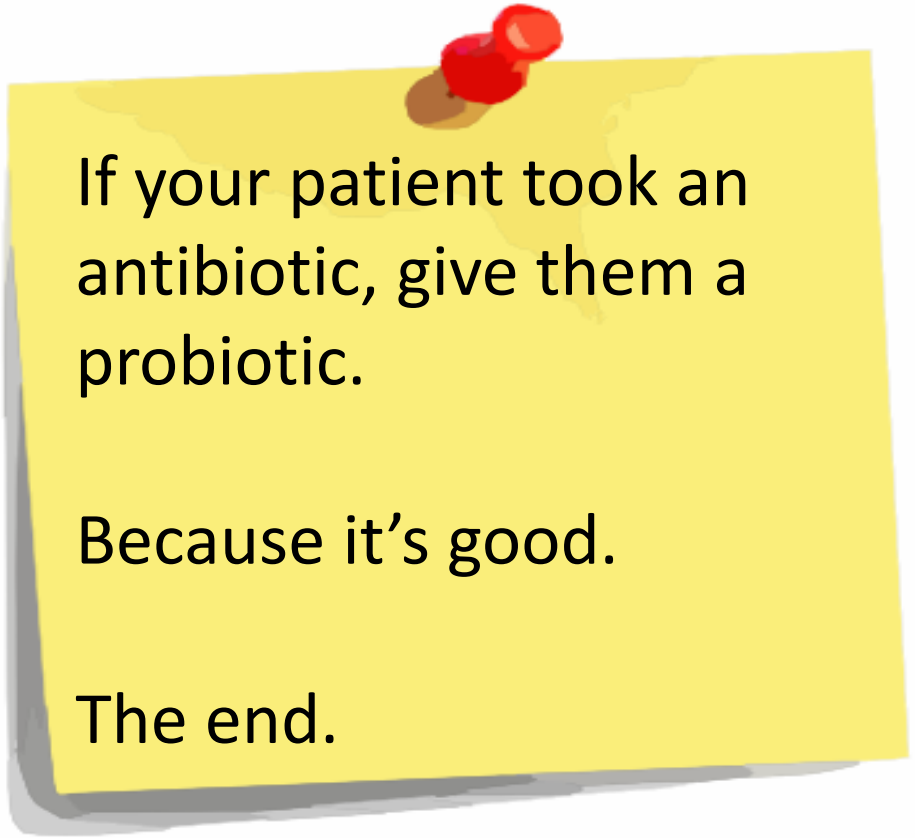
AARM

Association for the Advancement of Restorative Medicine

The Challenge of GI Health

Our understanding has changed…but not everyone knows it yet

Pub Med: 2017 (until Feb 8) – 481
2016 – 3174
2001 – 13
1997 – 5


If your patient took an antibiotic, give them a probiotic.
Because it’s good.
The end.

The Challenge of GI Health

The Volume

481 studies/39 = 12.33 studies per day

The Challenge of GI Health

But…aren't germs bad?

Study finds NYC subways are crawling with germs

Scientists discover a shocking number of different bacteria inside the NYC subway system. Source: CNN

The Challenges of GI Health

When you tell your patients about good bacteria they only half hear you.

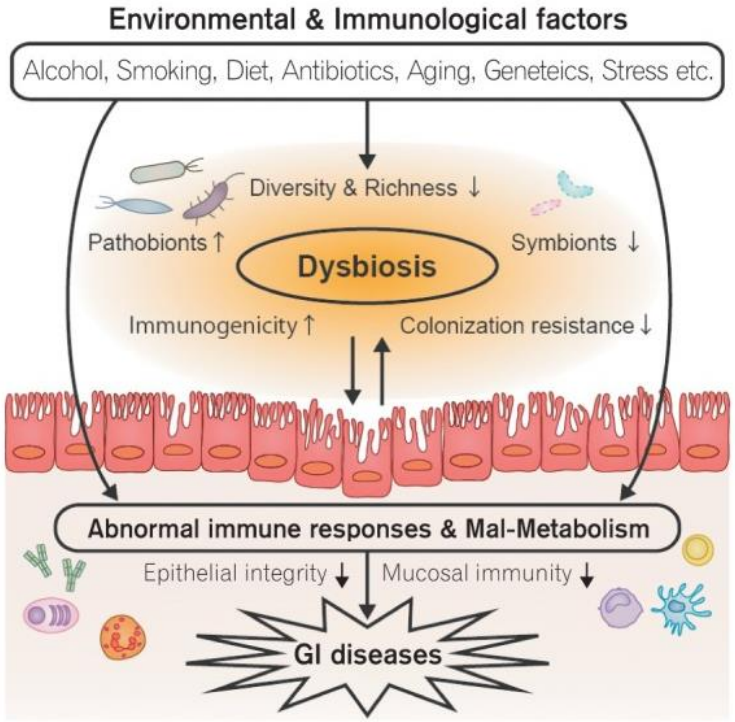
On a good day.


THNEEDS
And at that very moment, we heard a loud whack!
From outside in the fields came a sickening smack
of an axe on a tree. Then we heard the tree fall.
The very last Truffula Tree of them all!

The Lorax and The Microbiome

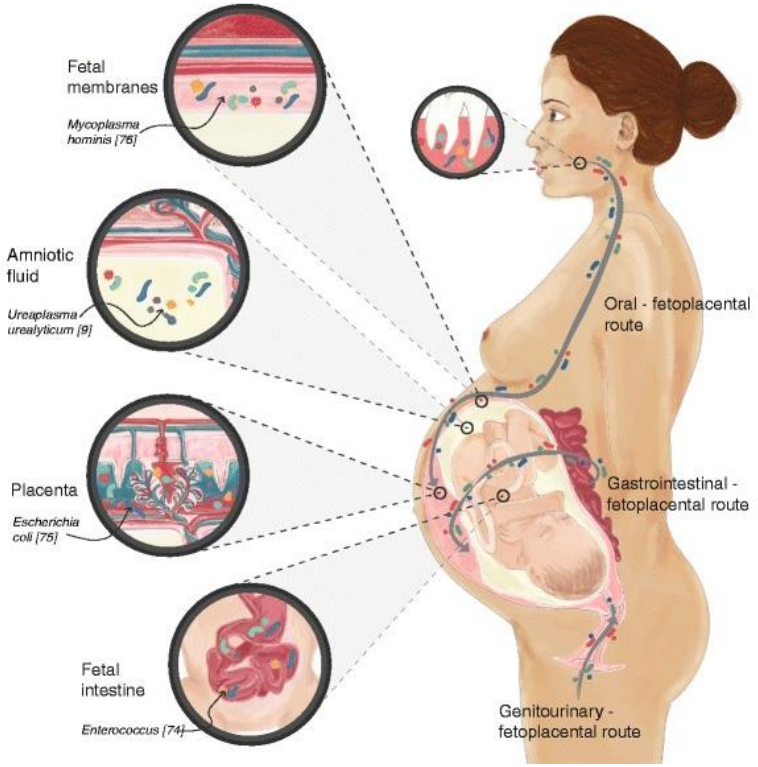
The Lorax	Us…as humans
Trees	Microbiome
Tree Canopy	Mucus Layer
Nutrients Lost/Soil Changes	Nutrients Lost/Intestinal Permeability
Scavengers/birds/animals	Pathobionts/pathogens/toxins
Local destruction	Gut health changes
Environmental destruction	Overall health is destroyed

Factors in GI Disease



Intest Res. 2016 Apr; 14(2): 127–138;

Starts Early…



BMC Med. 2016 Jun 17;14(1):91

…And Isn't Stopping

Microbial Extinction

Nature. 2016 Jan 14;529(7585):212-5. doi: 10.1038/nature16504.

Diet-induced extinctions in the gut microbiota compound over generations.

Sonnenburg ED[1], Smits SA[1], Tikhonov M[2,3], Higginbottom SK[1], Wingreen NS[4,5], Sonnenburg JL[1]

Author information

Abstract

The gut is home to trillions of microorganisms that
metabolism. The reduced diversity of
presents the question of wh
dietary fibre ha
carb
styles
ydrates (MACs) found in
Western diet (high in fat and simple
e microbiota of mice consuming a low-MAC
. However, over several generations, a low-MAC diet
reintroduction of dietary MACs. To restore the microbiota to its original
with dietary MAC consumption. Our data illustrate that taxa driven to low
iently transferred to the next generation, and are at increased risk of becoming extinct within
are linked to the Western microbiota and the microbiota is targeted therapeutically, microbiota
re
volve strategies that incorporate dietary MACs as well as taxa not currently present in the Western gut.

Save the... Faecalibacterium prausnitzii?

GI – The Basics

One microbe = one disease?

GI – The Basics

MBio. 2016 Sep 20;7(5). pii: e01250-16. doi: 10.1128/mBio.01250-16.

Bacteriome and Mycobiome Interactions Underscore Microbial Dysbiosis in Familial Crohn's Disease.

Hoarau G[1], Mukherjee PK[2], Gower-Rousseau C[3], Hager C[2], Chandra J[2], Retuerto MA[2], Neut C[1], Vermeire S[4], Clemente J[5], Colombel JF[6], Fujioka H[7], Poulain D[1], Sendid B[8], Ghannoum MA[9].

Author information

Abstract

Crohn's disease (CD) results from a complex interplay between host genetic factors and endogenous microbial communities. In the current study, we used Ion Torrent sequencing to characterize the gut bacterial microbiota (bacteriome) and fungal community

We identified fungal (Candida tropicalis) and bacterial (Serratia marcescens and Escherichia coli) species that are associated with CD dysbiosis.

of C. tropicalis was positively correlated with S. marcescens and E. coli, suggesting that these organisms interact in the gut. The mass and thickness of triple-species (C. tropicalis plus S. marcescens plus E. coli) biofilm were significantly greater than those of single- and double-species biofilms. C. tropicalis biofilms comprised blastospores, while double- and triple-species biofilms were enriched in hyphae. S. marcescens used fimbriae to coaggregate or attach with C. tropicalis/E. coli, while E. coli was closely apposed with C. tropicalis Specific interkingdom microbial interactions may be key determinants in CD.

IMPORTANCE: Here, we characterized the gut bacterial microbiota (bacteriome) and fungal community (mycobiome) in multiplex families with CD and healthy relatives and defined the microbial interactions leading to dysbiosis in CD. We identified fungal (Candida tropicalis) and bacterial (Serratia marcescens and Escherichia coli) species that are associated with CD dysbiosis. Additionally, we found that the level of anti-Saccharomyces cerevisiae antibodies (ASCA; a known CD biomarker) was associated with the abundance of C. tropicalis We also identified positive interkingdom correlations between C. tropicalis, E. coli, and S. marcescens in CD patients and validated these correlations using in vitro biofilms. These results provide insight into the roles of bacteria and fungi in CD and may lead to the development of novel treatment approaches and diagnostic assays.

GI – The Basics

Do YOU have Crohn's disease? The agonising bowel condition could be caused by a fungus in your intestines

- **Candida tropicalis alongside two other bacteria can cause the condition**
- **They together to produce a layer of microorganisms in the intestines**
- **This can cause inflammation which results in symptoms of Crohn's disease**

By STEPHEN MATTHEWS FOR MAILONLINE
PUBLISHED: 17:13 GMT, 21 September 2016 | **UPDATED:** 20:39 GMT, 21 September 2016

Fungus in the intestines could be responsible for the development of Crohn's disease, scientists have discovered.

Candida tropicalis works alongside two other bacteria to cause the debilitating bowel condition, experts found.

GI – The Basics

Type of bacteria

vs

Function

GI – The Basics

Allergy. 2015 Feb;70(2):241-4. doi: 10.1111/all.12549.

Severity of atopic disease inversely correlates with intestinal microbiota diversity and butyrate-producing bacteria.

Nylund L[1], Nermes M, Isolauri E, Salminen S, de Vos WM, Satokari R.

⊕ **Author information**

Abstract

The reports on atopic diseases and microbiota in early childhood remain contradictory, and both decreased and increased microbiota diversity have been associated with atopic eczema. In this study, the intestinal microbiota signatures associated with the severity of eczema in 6-month-old infants were characterized. Further, the changes in intestinal microbiota composition related to the improvement of this disease 3 months later were assessed. The severity of eczema correlated inversely with microbiota diversity ($r = -0.54$, $P = 0.002$) and with the abundance of butyrate-producing bacteria ($r = -0.52$, $P = 0.005$). During the 3-month follow-up, microbiota diversity increased ($P < 0.001$) and scoring atopic dermatitis values decreased ($P < 0.001$) in all infants. This decrease coincided with the increase in bacteria related to butyrate-producing Coprococcus eutactus ($r = -0.59$, $P = 0.02$). In conclusion, the high diversity of microbiota and high abundance of butyrate-producing bacteria were associated with milder eczema, thus suggesting they have a role in alleviating symptoms of atopic eczema.

GI – The Basics

Antonie Van Leeuwenhoek. 2016 Oct;109(10):1389-96. doi: 10.1007/s10482-016-0737-y. Epub 2016 Jul 18.

A reduction in the butyrate producing species Roseburia spp. and Faecalibacterium prausnitzii is associated with chronic kidney disease progression.

Jiang S[1], Xie S[1], Lv D[1], Zhang Y[1], Deng J[1], Zeng L[1], Chen Y[2].

⊕ **Author information**

Abstract

The human gut microbiota plays an important role in human health and might also be implicated in kidney disease. The interest in butyrate producing bacteria has recently increased and is a poorly understood faecal condition in chronic kidney disease (CKD). Therefore, we evaluated differences of the butyrate producing species Roseburia spp. and Faecalibacterium prausnitzii in the faeces of Chinese patients with CKD. A case-control study was carried out for 65 CKD patients and 20 healthy controls. Differences were quantitatively validated using quantitative real-time polymerase chain reaction (qPCR). Spearman rank correlation was used to analyse the correlation between gut microbiota and clinical variables. Roseburia spp. and F. prausnitzii were significantly different in CKD patients and controls ($p = 0.001$; $p = 0.025$, respectively) and reduced more markedly in end stage renal disease ($p = 0.000$; $p = 0.003$, respectively) and microinflammation ($p = 0.004$; $p = 0.001$, respectively). Roseburia spp. and F. prausnitzii were negatively associated with C-reactive protein in plasma ($r = -0.493$, $p = 0.00$; $r = -0.528$, $p = 0.000$; respectively) and Cystatin C ($r = -0.321$, $p = 0.006$; $r = -0.445$, $p = 0.000$; respectively). They were positively associated with eGFR ($r = 0.347$, $p = 0.002$; $r = 0.416$, $p = 0.000$; respectively). The negative correlation between Roseburia spp., F. prausnitzii and CRP and renal function suggested that the depletion of butyrate producing bacteria may contribute to CKD-associated inflammation and CKD progression. Roseburia spp. and F. prausnitzii may thus serve as 'microbiomarkers'.

GI – The Basics

Butyrate:

- Anti-inflammatory
- Lower colonic pH – inhibit pathogens
- Anti-carcinogen properties
- Influence gut integrity/barrier function and immune defense of the small intestine
- Reduce oxidative stress

Strong views, loosely held

How I think about treatment

1. **Diet** – not always curative but always important to health
2. **Microbiota** – almost always contributes to the problem (probiotics, prebiotics, occasionally killing)
3. **Nutrient deficiencies** – will make healing and repair, as well as feeling good impossible if there are major deficiencies
4. **Healing and repair**
5. **Help –** enzymes, HCl stimulators, HCl, prokinetics

Gut Brain Connection

Mol Psychiatry. 2016 Jun; 21(6): 738–748.
Published online 2016 Apr 19. doi: 10.1038/mp.2016.50
PMCID: PMC4879184

From gut dysbiosis to altered brain function and mental illness: mechanisms and pathways

G B Rogers,[1,*] D J Keating,[2] R L Young,[3] M-L Wong,[4] J Licinio,[4] and S Wesselingh[1]

Author information ► Article notes ► Copyright and License information ►

Abstract

Go to:

The human body hosts an enormous abundance and diversity of microbes, which perform a range of essential and beneficial functions. Our appreciation of the importance of these microbial communities to many aspects of human physiology has grown dramatically in recent years. We know, for example, that animals raised in a germ-free environment exhibit substantially altered immune and metabolic function, whil the disruption of commensal microbiota in humans is associated with the development of a growing number of diseases. Evidence is now emerging that, through interactions with the gut–brain axis, the bidirectional communication system between the central nervous system and the gastrointestinal tract, the gut microbiome can also influence neural development, cognition and behaviour, with recent evidence that changes in behaviour alter gut microbiota composition, while modifications of the microbiome can induce depressive-

…And Sleep Matters Too

Medscape Gastroenterology > GI Common Concerns -- Computer Consult

COMMENTARY

Treating Gastrointestinal Disorders Through Improved Sleep

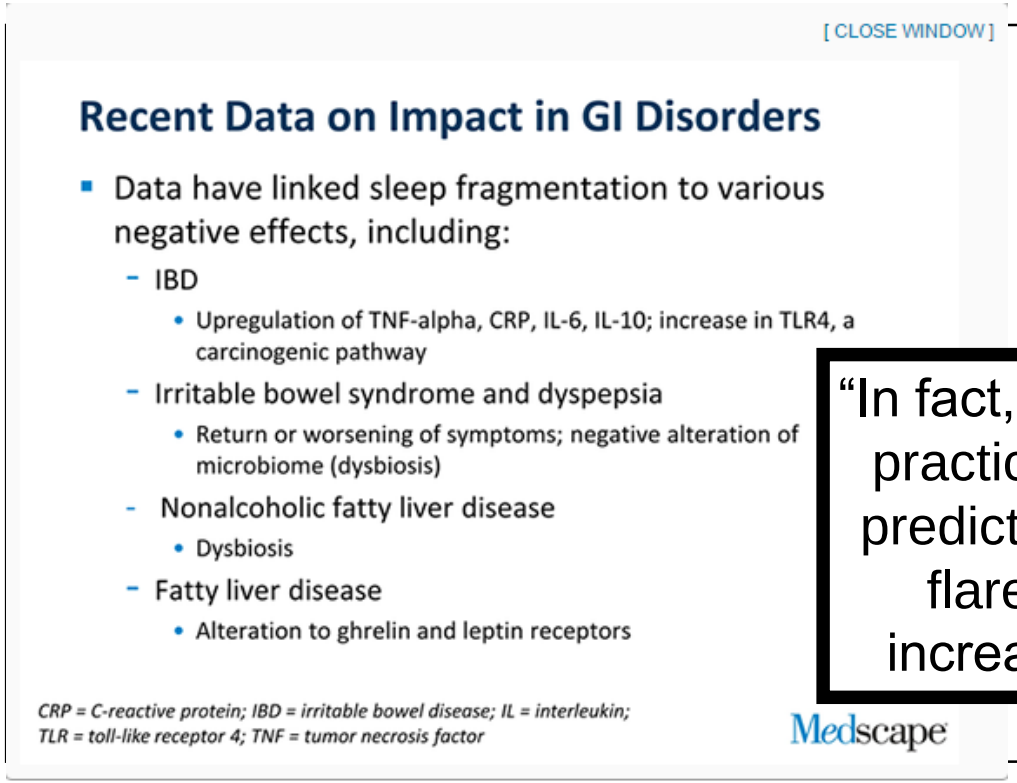
David A. Johnson, MD

Disclosures | December 19, 2016

IN THIS PROGRAM

- Sleep Fragmentation's Considerable Costs
- Identifying Sleep Disorders
- Impact in GI Disease
- Taking the Wider View

…And Sleep Matters Too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Recent Data on Impact in GI Disorders

- Data have linked sleep fragmentation to various negative effects, including:
  - IBD
    - Upregulation of TNF-alpha, CRP, IL-6, IL-10; increase in TLR4, a carcinogenic pathway
  - Irritable bowel syndrome and dyspepsia
    - Return or worsening of symptoms; negative alteration of microbiome (dysbiosis)
  - Nonalcoholic fatty liver disease
    - Dysbiosis
  - Fatty liver disease
    - Alteration to ghrelin and leptin receptors

CRP = C-reactive protein; IBD = irritable bowel disease; IL = interleukin; TLR = toll-like receptor 4; TNF = tumor necrosis factor

Medscape

"In fact, if you start asking the IBD patients in your practice about sleep fragmentation, it may be a predictor for who in remission is going to go to a flare in the next 6 months, with odds ratios increasing anywhere from two to three times."

IBS

Irritable bowel syndrome (**IBS**) is a group of symptoms—including abdominal pain and changes in the pattern of bowel movements without any evidence of underlying damage

"One could make the case it is now time to drop the arguably pejorative term functional..."

"...a purely symptom-based classification of the FGIDs will be extinct in the next two decades..."

Nature Reviews Gastroenterology & Hepatology 11, 649–650 (2014)

IBS – Diagnosis Rome IV

- Recurrent abdominal pain or discomfort at least 1 day a week in the last 3 months, associated with two or more of the following:
  - Symptoms improved by defecation
  - Onset associated with a change in frequency of stool
  - Onset associated with a change in form or appearance of stool

Alarm Features - IBS

- Unintended weight loss – more than 10% in 3 months
- Blood in stools – not caused by hemorrhoids
- Symptoms that waken pt during the night
- Fever associated with bowel symptoms
- Family history – CRC, IBD, celiac
- New onset – over 50 years old

IBS – Microbial Dysbiosis

Gastroenterology. 2006 Aug;131(2):445-50; quiz 660.

Incidence and epidemiology of irritable bowel syndrome after a large waterborne outbreak of bacterial dysentery.

Marshall JK[1], Thabane M, Garg AX, Clark WF, Salvadori M, Collins SM; Walkerton Health Study Investigators.

Author information

Abstract

BACKGROUND & AIMS: Postinfectious irritable bowel syndrome (PI-IBS) is a common clinical phenomenon. To better define its incidence and

PI-IBS is common after gastroenteritis from water contamination and often is diarrhea-predominant.

regression.

RESULTS: There were 2069 eligible study participants. Rome I criteria were met by 71 of 701 controls (10.1%) vs 249 of 904 subjects with self-reported gastroenteritis (27.5%) and 168 of 464 subjects with clinically suspected gastroenteritis (36.2%) (all comparisons, P < 001). Independent risk factors for PI-IBS included younger age, female sex, bloody stools, abdominal cramps, weight loss, and prolonged diarrhea. PI-IBS was more likely than sporadic IBS to show diarrhea-predominant features.

CONCLUSIONS: PI-IBS is common after gastroenteritis from water contamination and often is diarrhea-predominant. Characteristics of the acute illness identify patients at increased risk for PI-IBS.

IBS – Microbial Dysbiosis

Gut. 2010 May;59(5):605-11. doi: 10.1136/gut.2009.202234.

Eight year prognosis of postinfectious irritable bowel syndrome following waterborne bacterial dysentery.

Marshall JK[1], Thabane M, Garg AX, Clark WF, Moayyedi P, Collins SM; Walkerton Health Study Investigators.

⊕ Author information

Abstract

BACKGROUND: Although postinfectious irritable bowel syndrome (PI-IBS) is a well-recognised complication of acute gastroenteritis, its prognosis remains poorly defined. The natural history of PI-IBS was assessed among participants in the Walkerton Health Study (WHS), which has followed the long-term effects of a large outbreak of acute gastroenteritis related to municipal water contamination in May 2000.

METHODS: WHS participants were invited to return for annual assessment at a research clinic. Adult residents of Walkerton at the time of the outbreak who enrolled in 2002/2003 and returned for assessment in 2008 were eligible for a PI-IBS study cohort if they had no prior history of IBS or inflammatory bowel disease. A modified Bowel Disease Questionnaire was used to diagnose IBS by Rome I criteria and to identify IBS subtypes.

RESULTS: Of 4561 WHS participants, 2451 returned for their 8 year assessment and 1166 were eligible for the PI-IBS study cohort (688 females, mean age 46.2 years). The prevalence of IBS among 742 eligible subjects who suffered acute gastroenteritis during the outbreak declined from

Acute gastroenteritis can trigger IBS symptoms that persist for at least 8 years

enteric illness can predict the long-term risk of PI-IBS.

IBS - Microbiota

Neurogastroenterol Motil. 2013 Apr;25(4):e272-82. doi: 10.1111/nmo.12103. Epub 2013 Feb 25.

The hypersensitivity to colonic distension of IBS patients can be transferred to rats through their fecal microbiota.

We herein showed that sensitivity to colonic distension of IBS patients can be transferred to rats by the fecal microbiota.

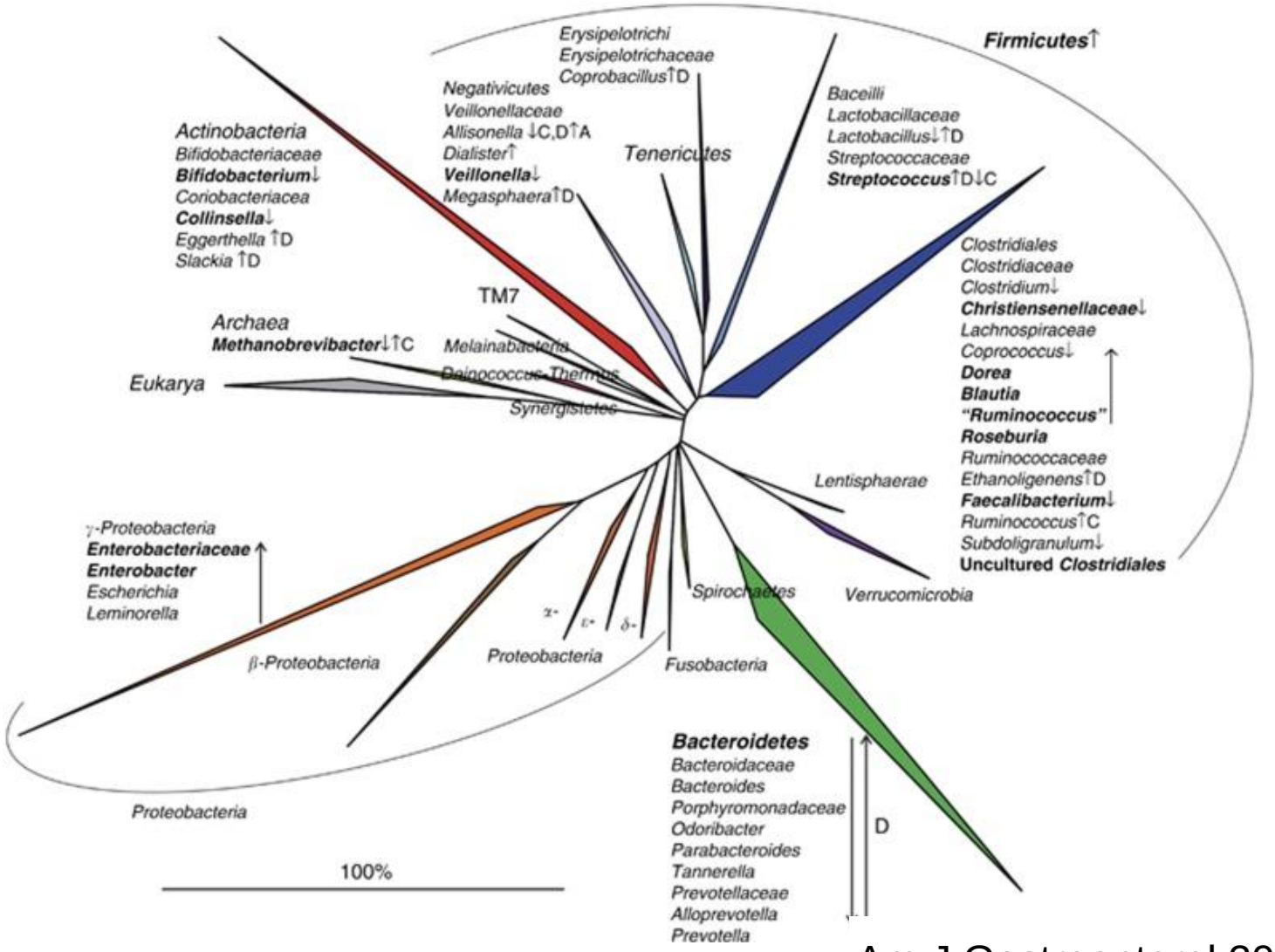
of our study was to determine whether the intestinal microbiota is involved in the visceral hypersensitivity in IBS.

METHODS: The painful response to colorectal distension and colonic mucosal parameters were assessed in gnotobiotic rats. Germfree (GF) rats were inoculated with the fecal microbiota from IBS patients characterized by hypersensitivity to colorectal distension (IBS HMA rats) or from non-hypersensitive healthy volunteers (Healthy HMA rats). Conventional rats were studied as normosensitivity control. Fecal microbial analyses were carried out in human and HMA rats fecal samples using cultural and molecular approaches.

KEY RESULTS: The microbial dysbiosis of the IBS gut microbiota (more sulfate-reducing bacteria and Enterobacteriaceae and less bifidobacteria) could be maintained in gnotobiotic rats. The number of abdominal contractions in response to colorectal distensions was significantly higher in IBS HMA rats than in healthy HMA rats. No difference was observed between healthy HMA and conventional rats. Colorectal compliance, epithelial paracellular permeability, and density of colonic mucosal mast cells were similar in the three groups of rats.

CONCLUSIONS & INFERENCES: We herein showed that sensitivity to colonic distension of IBS patients can be transferred to rats by the fecal microbiota. Mucosal alterations associated with microbiota transfer are not involved in this hypersensitivity. The altered IBS microbiota may have important role in the hypersensitivity characterizing IBS patients through specific bacterial metabolites.

IBS – Microbiota



Am J Gastroenterol 2015 Feb; 110(2):278-287

IBS - Diet

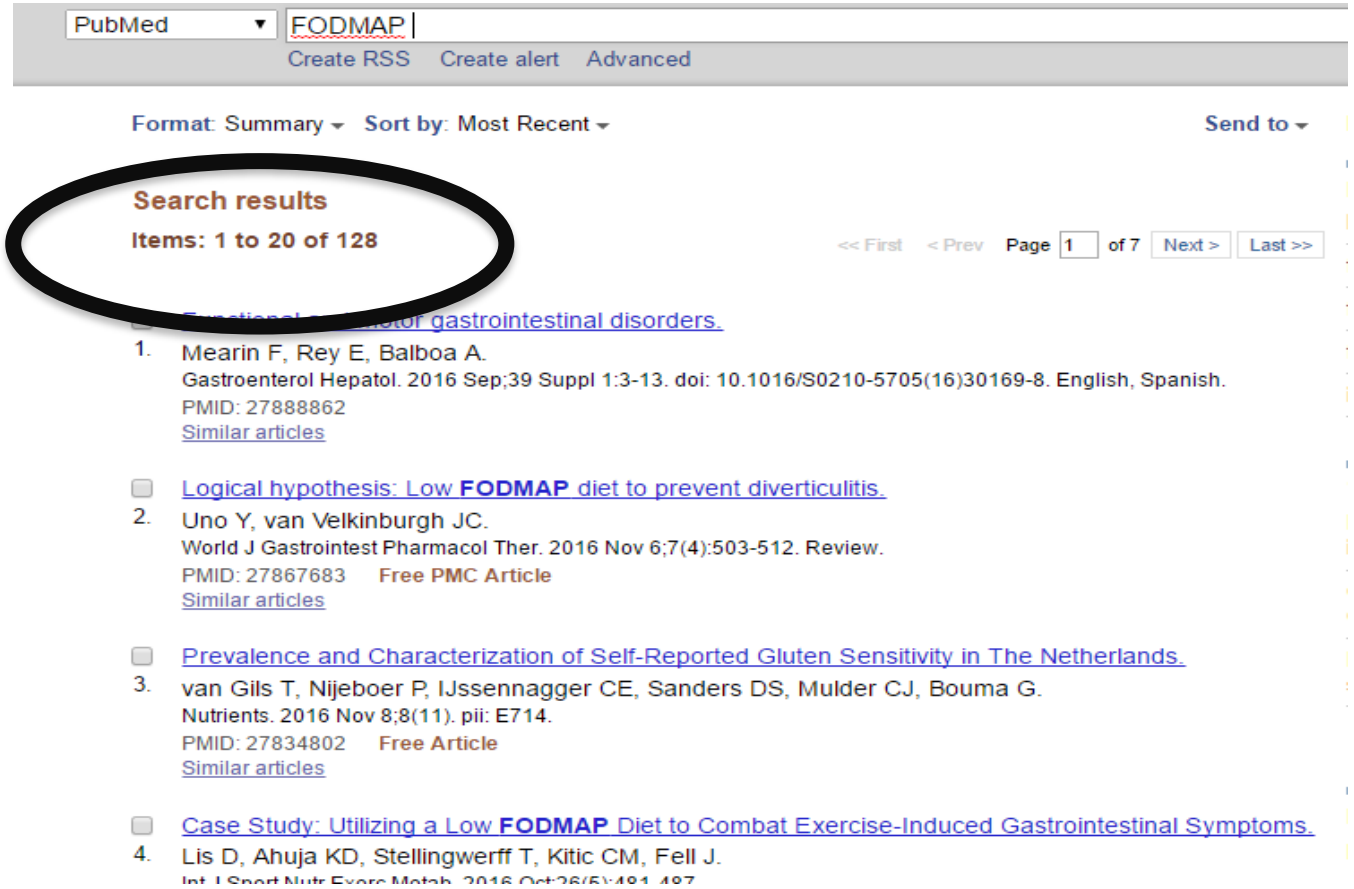
Most recently, and belatedly, the important role of the ubiquitous interloper into the gastrointestinal environment, food, has begun to be recognized and serious research efforts devoted to understanding its role in IBS and to the development of dietary approaches to the management of IBS.

Eamonn M.M. Quigley

IBS – Diet?

- Allergies
- Intolerances
- Elimination Diets
- Hypoallergenic Diets
- Rotation Diets
- Lactose, gluten, non-celiac wheat sensitivity…

Low-FODMAP Diet



IBS – FODMAP Diet

TABLE 1

Patterns of malabsorption of FODMAPs

Oligosaccharides
Fructans: no suitable small-intestinal hydrolases—negligible absorption
Galacto-oligosaccharides: no human alpha-galactosidase—minimal absorption

Disaccharides (lactose)
No absorption if lactase is deficient

Fructose
Absorptive capacity limited when in excess of glucose—low in 30% (considered to have fructose malabsorption)

Polyols
Slow passive diffusion and absorption only (< 20%)

FODMAPs = fermentable oligosaccharides, disaccharides, monosaccharides, and polyols

IBS – Low FODMAP Diet

PROS

- 70-86% success in patients – and fast

CONS

- Microbiota change - bad (and good?)
- Constipation
- Nutrient lack?

IBS – Low-FODMAP Diet

Gut. 2016 Mar 14. pii: gutjnl-2015-311339. doi: 10.1136/gutjnl-2015-311339. [Epub ahead of print]

FODMAPs alter symptoms and the metabolome of patients with IBS: a randomised controlled trial.

McIntosh K[1], Reed DE[2], Schneider T[2], Dang F[2], Keshteli AH[3], De Palma G[4], Madsen K[3], Bercik P[4], Vanner S[2].

IBS symptoms are linked to FODMAP content and associated with alterations in the metabolome. In subsets of patients, FODMAPs modulate histamine levels and the microbiota, both of which could alter symptoms.

RESULTS: Thirty-seven patients (19 low FODMAP; 18 high FODMAP) completed the 3-week diet. The IBS-SSS was reduced in the low FODMAP diet group ($p<0.001$) but not the high FODMAP group. LBTs showed a minor decrease in H_2 production in the low FODMAP compared with the high FODMAP group. Metabolic profiling of urine showed groups of patients with IBS differed significantly after the diet ($p<0.01$), with three metabolites (histamine, p-hydroxybenzoic acid, azelaic acid) being primarily respons between the two groups. Histamine, a measure of immune activation, was reduced eightfold in the low FODM FODMAP diet increased Actinobacteria richness and diversity, and high FODMAP diet decreased the relative involved in gas consumption.

CONCLUSIONS: IBS symptoms are linked to FODMAP content and associated with alterations in the metabolome. In subsets of patients, FODMAPs modulate histamine levels and the microbiota, both of which could alter symptoms.

Histamine was reduced eightfold

IBS – Low-FODMAP Diet

Do not let your patients find their own information online – make your own handouts based on Monash information or get them to buy them app themselves

IBS – Low-FODMAP Diet

http://www.med.monash.edu/cecs/gastro/fodmap/

IBS – Gluten Effect?

Gastroenterology. 2013 Aug;145(2):320-8.e1-3. doi: 10.1053/j.gastro.2013.04.051. Epub 2013 May 4.

No effects of gluten in patients with self-reported non-celiac gluten sensitivity after dietary reduction of fermentable, poorly absorbed, short-chain carbohydrates.

Biesiekierski JR[1], Peters SL, Newnham ED, Rosella O, Muir JG, Gibson PR.

In patients with self-reported non-celiac gluten sensitivity: Gluten-specific gastrointestinal effects were not reproduced.

reduced FODMAPs, and were then placed on high-gluten (16 g gluten/d), low-gluten (2 g gluten/d and 14 g whey protein/d), or control (16 g whey protein/d) diets for 1 week, followed by a washout period of at least 2 weeks. We assessed serum and fecal markers of intestinal inflammation/injury and immune activation, and indices of fatigue. Twenty-two participants then crossed over to groups given gluten (16 g/d), whey (16 g/d), or control (no additional protein) diets for 3 days. Symptoms were evaluated by visual analogue scales.

RESULTS: In all participants, gastrointestinal symptoms consistently and significantly improved during reduced FODMAP intake, but significantly worsened to a similar degree when their diets included gluten or whey protein. Gluten-specific effects were observed in only 8% of participants. There were no diet-specific changes in any biomarker. During the 3-day rechallenge, participants' symptoms increased by similar levels among groups. Gluten-specific gastrointestinal effects were not reproduced. An order effect was observed.

CONCLUSIONS: In a placebo-controlled, cross-over rechallenge study, we found no evidence of specific or dose-dependent effects of gluten in patients with NCGS placed diets low in FODMAPs.

IBS – Spelt Sourdough

PLoS One. 2014 Oct 30;9(10):e111225. doi: 10.1371/journal.pone.0111225. eCollection 2014.

Effect of breadmaking process on in vitro gut microbiota parameters in irritable bowel syndrome.

Costabile A[1], Santarelli S[1], Claus SP[1], Sanderson J[2], Hudspith BN[2], Brostoff J[2], Ward JL[3], Lovegrove A[3], Shewry PR[4], Jones HE[5], Whitley AM[6], Gibson GR[1].

In conclusion, breads fermented by the traditional long fermentation and sourdough are less likely to lead to IBS symptoms compared to bread made using the Chorleywood Breadmaking Process. [short processing time, lower quality wheat]

donors showed a significant increase in bifidobacteria (P<0.005) after 8 h of fermentation of a bread produced using a sourdough process (type C) compared to breads produced with commercial yeasted dough (type B) and no time fermentation (Chorleywood Breadmaking process) (type A). A significant decrease of δ-Proteobacteria and most Gemmatimonadetes species was observed after 24 h fermentation of type C bread in both IBS and healthy donors. In general, IBS donors showed higher rates of gas production compared to healthy donors. Rates of gas production for type A and conventional long fermentation (type B) breads were almost identical in IBS and healthy donors. Sourdough bread produced significantly lower cumulative gas after 15 h fermentation as compared to type A and B breads in IBS donors but not in the healthy controls. In conclusion, breads fermented by the traditional long fermentation and sourdough are less likely to lead to IBS symptoms compared to bread made using the Chorleywood Breadmaking Process.

IBS – Low-FODMAP Diet

Even though your patients might feel better eliminating the foods in this diet, it is not the solution. Re-introduce foods, asap.

IBS – Low-FODMAP Diet

Re-introduction:

- Starting by week 6 – I often start earlier
- Remember, the food isn't the problem

IBS - Prebiotics

Non-digestible food ingredients that beneficially affect the host by selectively stimulating the growth and/or the activity of a bacterium or a limited number of bacteria in the colon that can improve host health

IBS - Prebiotics

Warning: These bars may cause your IBS patients to explode

IBS - Prebiotics

Are your patients avoiding all prebiotics?

IBS - PHGG

Beneficial Function

- Supports bifidogenic and lactogenic growth
- Increases the concentration of short chain fatty acids (SCFAs) in the distal intestine due to its fermentability
- Effective in the treatment of acute diarrhea in children and adult patients of intensive care units
- Alleviate irritable bowel syndrome (IBS) symptoms

Food Funct., 2016, 7, 1833

IBS - PHGG

Anaerobe. 2016 Aug 30;42:60-66. doi: 10.1016/j.anaerobe.2016.08.006. [Epub ahead of print]

In vitro analysis of partially hydrolyzed guar gum fermentation on identified gut microbiota.

Carlson J[1], Gould T[2], Slavin J[3].

PHGG stimulates growth of Parabacteroides, a genus of bacteria that have been inversely associated with IBS and ulcerative colitis

METHOD: Fecal donations were collected from six healthy individuals consuming a non-specific Western diet, free of antibiotic treatments in the past year, not affected by any GI diseases and not consuming any probiotic or prebiotic supplements. Fecal samples were exposed to 0.5 g of PHGG and measured for bacterial changes at 0, 12 and 24 h based on 16S rRNA sequencing.

RESULTS: Parabacteroides increased from 3.48% of sequence reads to 10.62% of sequence reads after 24 h ($p = 0.0181$) and Bacteroidetes increased from 45.89% of sequence reads to 50.29% of sequence reads ($p = 0.0008$).

CONCLUSIONS: PHGG stimulates growth of Parabacteroides, a genus of bacteria that have been inversely associated with IBS and ulcerative colitis. PHGG provides stimulation of beneficial Bacteroidetes (Bacteroides and Parabacteroides), which may be correlated with many positive health markers and outcomes. PHGG is a prebiotic dietary fiber that is readily fermentable.

IBS - PHGG

Nutr Metab (Lond). 2016 Feb 6;13:10. doi: 10.1186/s12986-016-0070-5. eCollection 2016.

Randomized clinical study: Partially hydrolyzed guar gum (PHGG) versus placebo in the treatment of patients with irritable bowel syndrome.

The results of this study support the administration of 6g/day PHGG for IBS patients with bloating

fiber. To assess the effects of PHGG on clinical symptoms of IBS patients in a prospective randomized double blind placebo-controlled study.

METHODS: Suitable IBS patients were recruited into an 18-week-long study (2 weeks of run-in, 12 weeks of treatment and 4 weeks of follow-up). They were blindly randomized to receive 6 gr of PHGG or placebo. Treatment efficacy was evaluated by the Francis Severity IBS score, the IBS quality-of-life scores and scored parameters of weekly journal of symptoms. Deltas of changes between the final and baseline scores were compared between two groups.

RESULTS: Of 121 patients who underwent randomization, 108 patients (49 in the PHGG group and 59 in the placebo group) had all the data needed for intention-to-treat analysis. A 12-week administration of PHGG led to a significant improvement of journal bloating score in the PHGG group versus placebo (-4.1±13.4 versus -1.2±11.9, P=0.03), as well as in bloating+gasses score (-4.3±10.4 versus -1.12±10.5, P = 0.035). The effect lasted for at least 4 weeks after the last PHGG administration. PHGG had no effect on other journal reported IBS symptoms or on Severity and Quality of life scores. There were no significant side effects associated with PHGG ingestion. The rate of dropouts was significantly higher among patients in the placebo group compared with the PHGG group (49.15% versus 22.45%, respectively, P = 0.01).

CONCLUSIONS: The results of this study support the administration of 6 g/day PHGG for IBS patients with bloating.

IBS - PHGG

World J Gastroenterol. 2013 Jan 14;19(2):235-40. doi: 10.3748/wjg.v19.i2.235.

Partially hydrolyzed guar gum in pediatric functional abdominal pain.

Romano C[1], Comito D, Famiani A, Calamarà S, Loddo I.

Author information

Abstract

AIM: To assess the effects of partially hydrolyzed guar gum (PHGG) diet supplement in pediatric chronic abdominal pain (CAP) and irritable bowel syndrome (IBS).

METHODS: A randomized, double-blind pilot study was performed in sixty children (8-16 years) with functional bowel disorders, such as CAP or IBS, diagnosed according to Rome III criteria. All patients underwent ultrasound, blood and stool examinations to rule out any organic disease. Patients were allocated to receive PHGG at dosage of 5 g/d (n = 30) or placebo (fruit-juice n = 30) for 4 wk. The evaluation of the efficacy of fiber

Although the cause of pediatric functional gastrointestinal disorders is not known, the results show that the complementary therapy with PHGG may have beneficial effects on symptoms control

tendency toward normalization of bowel movements, but there was no difference in the prevalence of improvement in two bowel habit subsets. PHGG was therefore better tolerated without any adverse effects.

CONCLUSION: Although the cause of pediatric functional gastrointestinal disorders is not known, the results show that complementary therapy with PHGG may have beneficial effects on symptom control.

IBS - PHGG

Dig Dis Sci. 2014 Sep;59(9):2207-14. doi: 10.1007/s10620-014-3135-1. Epub 2014 Apr 8.

Partially hydrolyzed guar gum accelerates colonic transit time and improves symptoms in adults with chronic constipation.

Four-week PHGG use accelerates colon transit time in patients with chronic constipation, especially in those with slow transit, and improves many of their symptoms including frequency of bowel movements.

usage diaries. They also recorded their symptom-related satisfaction weekly and treatment adverse events.

RESULTS: Forty-nine patients received treatment; 39 (80 %) completed the study. Treatment significantly reduced colon transit time, from 57.28 ± 39.25 to 45.63 ± 37.27 h ($p = 0.026$), a reduction more prominent in slow transit patients (from 85.50 ± 27.75 to 63.65 ± 38.11 h, $p = 0.016$). Overall, the weekly number of complete spontaneous and spontaneous bowel movements increased significantly ($p < 0.001$); the latter correlated significantly with the acceleration of CTT in the overall population and in slow transit patients ($B = 0.382$; $p = 0.016$ and $B = 0.483$; $p = 0.023$, respectively). In addition, the number of bowel movements with straining decreased ($p < 0.001$) and stool form improved ($p < 0.001$), while days with laxative intake and days with abdominal pain decreased ($p = 0.001$ and $p = 0.027$, respectively).

CONCLUSION: Four-week PHGG use accelerates colon transit time in patients with chronic constipation, especially in those with slow transit, and improves many of their symptoms including frequency of bowel movements.

Prebiotics

Use caution (bloating likely)

- Inulin (including chicory root)
- Fructo-oligosaccharides (FOS)

Generally helpful

- Partially hydrolyzed guar gum
- Arabinogalactans
- Galacto-oligosaccharides

IBS - Probiotics

Stop saying you can recolonize the gut.

Seriously.

IBS - Probiotics

Genome Med. 2016 May 10;8(1):52. doi: 10.1186/s13073-016-0300-5.

Alterations in fecal microbiota composition by probiotic supplementation in healthy adults: a systematic review of randomized controlled trials.

Kristensen NB[1], Bryrup T[2], Allin KH[2], Nielsen T[2], Hansen TH[2], Pedersen O[2].

⊕ Author information

Abstract

BACKGROUND: The effects of probiotic supplementation on fecal microbiota composition in healthy adults have not been well established. We aimed to provide a systematic review of the potential evidence for an effect of probiotic supplementation on the composition of human fecal microbiota as assessed by high-throughput molecular approaches in randomized controlled trials (RCTs) of healthy adults.

This systematic review of the pertinent literature demonstrates a lack of evidence for an impact of probiotics on fecal microbiota composition in healthy adults.

found that probiotic supplementation significantly modified the overall structure of the fecal bacterial community in terms of β-diversity when compared to placebo.

CONCLUSIONS: This systematic review of the pertinent literature demonstrates a lack of evidence for an impact of probiotics on fecal microbiota composition in healthy adults. Future studies would benefit from pre-specifying the primary outcome and transparently reporting the results including effect sizes, confidence intervals, and P values as well as providing a clear distinction of between-group and within-group comparisons.

IBS - Probiotics

J Clin Gastroenterol. 2011 Nov;45 Suppl:S115-9. doi: 10.1097/MCG.0b013e318227414a.

Impact of probiotics on colonizing microbiota of the gut.

Sanders ME[1].

Further research will provide insight into the degree of permanence of probiotic-induced changes, although research to date suggests that continued probiotic consumption is needed for sustained impact

bacteria is a matter of debate, increased levels of Bifidobacterium and Lactobacillus in the gut correlate with numerous health endpoints. Microbiota changes due to probiotic intake include increased numbers of related phylotypes, decreasing pathogens and their toxins, altering bacterial community structure to enhance evenness, stabilizing bacterial communities when perturbed (eg, with antibiotics), or promoting a more rapid recovery from a perturbation. Further research will provide insight into the degree of permanence of probiotic-induced changes, although research to date suggests that continued probiotic consumption is needed for sustained impact.

IBS - Probiotics

Effects of Probiotics on the Microbiota:

- Production of inhibitory compounds (i.e. antimicrobial peptides)
- Producing substrates that might promote the growth of colonizing microbes
- Promoting immune responses against specific microbes

J Clin Gastroenterol Volume 45, Supp. 3,

IBS - Probiotics

Effects of Probiotics on the Microbiota:

- Inhibiting attachment through stimulated mucin production
- Decreased colonic pH
- Reinforcing gut barrier effects - repair of hyperpermeable epithelial barriers
- Increase production of SCFAs including butyrate
- Downregulation of gut inflammation

J Clin Gastroenterol Volume 45, Supp. 3,

Probiotics

Clinical Guide to Probiotic Supplements

Available in Canada: 2016 Edition

Indications, Dosage Forms and Clinical Evidence to Date

Author: Dragana Skokovic-Sunjic BScPhm RPh NCMP

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Medical Editor: Ivana Sunjic MSc

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IBS - Probiotics

- ***L. plantarum 299v*** – 10B/capsule (1-2 daily): level 1

- ***L. acidophilus CUL60*** – 10-25B/capsule (1-2 daily): level 2
  L. acidophilus CUL21
  B. bifidum CUL20
  B. lactis CUL34

- ***Saccharomyces cerevisiae I-3856*** – 40B/capsule (1 daily): level 1

IBS - Probiotics

J Am Coll Nutr. 2015;34(6):459-69. doi: 10.1080/07315724.2014.983249. Epub 2015 Apr 24.

Lactobacillus gasseri KS-13, Bifidobacterium bifidum G9-1, and Bifidobacterium longum MM-2 Ingestion Induces a Less Inflammatory Cytokine Profile and a Potentially Beneficial Shift in Gut Microbiota in Older Adults: A Randomized, Double-Blind, Placebo-Controlled, Crossover Study.

Spaiser SJ[1], Culpepper T[1], Nieves C Jr[1], Ukhanova M[2], Mai V[2], Percival SS[1], Christman MC[3,4], Langkamp-Henken B[1].

Several bacterial groups matching Faeacalibactierium prausnitzii were more prevalent in stool samples with the probiotic versus placebo.

but did not change with the probiotic (44% ± 3% to 42% ± 3%) and log-transformed concentrations of interleukin-10 increased with the probiotic (1.7 ± 0.2 to 3.4 ± 0.2, $p < 0.0001$) but not the placebo (1.7 ± 0.2 to 2.1 ± 0.2). With the probiotic versus the placebo a higher percentage of participants had an increase in fecal bifidobacteria (48% versus 30%, $p < 0.05$) and lactic acid bacteria (55% versus 43%, $p < 0.05$) and a decrease in Escherichia coli (52% versus 27%, $p < 0.05$). Several bacterial groups matching Faeacalibactierium prausnitzii were more prevalent in stool samples with the probiotic versus placebo.

CONCLUSIONS: The probiotic maintained CD4+ lymphocytes and produced a less inflammatory cytokine profile possibly due to the changes in the microbial communities, which more closely resembled those reported in healthy younger populations.

IBS - Enzymes

Digestive enzymes are classified based on their target substrates:

- Proteases and peptidases split proteins into small peptides and amino acids.
- Lipases split fat into three fatty acids and a glycerol molecule
- Amylases split CHO such as starch and sugars into simple sugars such as glucose

IBS - Enzymes

If your patient responds to a low-FODMAP diet, they don't likely need amylases, lipases or proteases

IBS - Enzymes

- **Alpha-galactosidase** – beans, veg, whole grains (esp. cruciferous)
- **Lactase** – milk lactose
- **Hemi-cellulase & cellulase** – plant cell wall/fiber
- **Pectinase** – breaks down pectin (polysaccharide) found in cell walls (fruits/veg)
- **Xylanase** – structural components of cell walls (fruits, veg, nuts, grains)

IBS – Gut/Brain Connection

Neurogastroenterol Motil. 2016 Jul 25. doi: 10.1111/nmo.12904. [Epub ahead of print]

GABA-producing Bifidobacterium dentium modulates visceral sensitivity in the intestine.

Visceral pain modulation represents another potential health benefit attributed to bifidobacteria and other GABA-producing species of the intestinal microbiome.

central pain perception from peripheral afferent neurons. Although gut bacteria are reported to produce GABA, it is not known whether the microbial-derived neurotransmitter modulates abdominal pain.

METHODS: To investigate the potential analgesic effects of microbial GABA, we performed daily oral administration of a specific Bifidobacterium strain (B. dentiumATCC 27678) in a rat fecal retention model of visceral hypersensitivity, and subsequently evaluated pain responses.

KEY RESULTS: We demonstrate that commensal Bifidobacterium dentium produces GABA via enzymatic decarboxylation of glutamate by GadB. Daily oral administration of this specific Bifidobacterium (but not a gadB deficient) strain modulated sensory neuron activity in a rat fecal retention model of visceral hypersensitivity.

CONCLUSIONS & INFERENCES: The functional significance of microbial-derived GABA was demonstrated by gadB-dependent desensitization of colonic afferents in a murine model of visceral hypersensitivity. Visceral pain modulation represents another potential health benefit attributed to bifidobacteria and other GABA-producing species of the intestinal microbiome. Targeting GABAergic signals along this microbiome-gut-brain axis represents a new approach for the treatment of abdominal pain.

IBS – Gut/Brain Connection

Genes Nutr. 2015 Nov;10(6):47. doi: 10.1007/s12263-015-0497-8. Epub 2015 Oct 15.

GABA selectively increases mucin-1 expression in isolated pig jejunum.

Braun HS[1], Sponder G[1], Pieper R[2], Aschenbach JR[1], Deiner C[3].

GABA selectively increases the expression of MUC1, a cell surface mucin that prevents the adhesion of microorganisms, because of its size and negative charge, and therefore propose that the well-described positive effects of glutamine on enterocytes and intestinal integrity are partly attributable to effects of its metabolite GABA.

treatment groups showed a significantly higher MUC1 expression than the control group. We conclude that GABA selectively increases the expression of MUC1, a cell surface mucin that prevents the adhesion of microorganisms, because of its size and negative charge, and therefore propose that the well-described positive effects of glutamine on enterocytes and intestinal integrity are partly attributable to effects of its metabolite GABA.

IBS – Gut/Brain Connection

Life Sci. 2016 Dec 2. pii: S0024-3205(16)30684-1. doi: 10.1016/j.lfs.2016.11.031. [Epub ahead of print]

Melatonin's role as a co-adjuvant treatment in colonic diseases: A review.

Melatonin has been studied as a co-adjuvant treatment in several gastrointestinal diseases including irritable bowel syndrome (IBS), constipation-predominant IBS (IBS-C), diarrhea-predominant IBS (IBS-D), Crohn's disease, ulcerative colitis, and necrotizing enterocolitis.

through its direct and indirect actions. In addition, the dysregulation of the circadian system is observed to be related with alterations in colonic motility and cell disruptions due to the modifications of clock genes expression. In the gastrointestinal tract, the activities of melatonin are mediated by melatonin receptors (MT2), serotonin (5-HT), and cholecystokinin B (CCK2) receptors and via receptor-independent processes. The levels of melatonin in the gastrointestinal tract exceed by 10-100 times the blood concentrations. Also, there is an estimated 400 times more melatonin in the gut than in the pineal gland. Gut melatonin secretion is suggested to be influenced by the food intake. Low dose melatonin treatment accelerates intestinal transit time whereas high doses may decrease gut motility. Melatonin has been studied as a co-adjuvant treatment in several gastrointestinal diseases including irritable bowel syndrome (IBS), constipation-predominant IBS (IBS-C), diarrhea-predominant IBS (IBS-D), Crohn's disease, ulcerative colitis, and necrotizing enterocolitis. The purpose of this review is to provide information regarding the potential benefits of melatonin as a co-adjuvant treatment in gastrointestinal diseases, especially IBS, Crohn's disease, ulcerative colitis, and necrotizing enterocolitis.

IBS – Gut/Brain Connection

Melatonin Function:

- Regulation of GI motility – excitatory AND inhibitory effect on gut smooth muscle
- Anti-inflammatory effect
- Moderation of visceral sensation – analgesic effect
- Sleep promotion, mood regulation, anti-stress effects

IBS – Gut/Brain Connection

Melatonin – Regulation of GI Function

- High dose – decrease transit time
- Low dose – increase transit time

SIBO

Condition in which there is overgrowth of bacteria in small bowel in excess of 10^5 colony forming units per milliliter on culture of the upper gut aspirate

SIBO – Fad or Fact?

Am J Gastroenterol. 2003 Feb;98(2):412-9.

Normalization of lactulose breath testing correlates with symptom improvement in irritable bowel syndrome. a double-blind, randomized, placebo-controlled study.

Pimentel M[1], Chow EJ, Lin HC

111 IBS subjects (55 neomycin, 56 placebo) entered the study, with **84% having an abnormal LBT**, compared with 20% in healthy controls ($p < 0.01$)

of treatment, subjects returned for repeat LBT. A symptom questionnaire was administered on both days.

RESULTS: After exclusion criteria were met, 111 IBS subjects (55 neomycin, 56 placebo) entered the study, with 84% having an abnormal LBT, compared with 20% in healthy controls ($p < 0.01$). In an intention-to-treat analysis of all 111 subjects, neomycin resulted in a 35.0% improvement in a composite score, compared with 11.4% for placebo ($p < 0.05$). Additionally, patients reported a percent bowel normalization of 35.3% after neomycin, compared with 13.9% for placebo ($p < 0.001$). There was a graded response to treatment, such that the best outcome was observed if neomycin was successful in normalizing the LBT (75% improvement) (one-way ANOVA, $p < 0.0001$). LBT gas production was associated with IBS subgroup, such that methane excretion was 100% associated with constipation-predominant IBS. Methane excretors had a mean constipation severity of 4.1, compared with 2.3 in all other subjects ($p < 0.001$).

CONCLUSIONS: An abnormal LBT is common in subjects with IBS. Normalization of LBT with neomycin leads to a significant reduction in IBS symptoms. The type of gas seen on LBT is also associated with IBS subgroup.

SIBO – Fad or Fact?

Park et al[86]	Prospective (Case-control)	34/76 (44.7)	16/40 (40)	19/76 (25)	10/40 (25)	LHBT
Scarpellini et al[88]	Prospective (Case-control)	28/43 (65)	4/56 (7)	4/43 (9.3)	0	LHBT
Carrara et al[14]	Prospective	55/127 (43)	NCG	ND	ND	LHBT
Mann and Limoges-Gonzales[87]	Prospective	89/258 (34.5)	NCG	ND	ND	LHBT
Nucera et al[89]	Prospective	64/98 (65)	NCG	ND	ND	LHBT
Majewski et al[94]	Prospective (Case-control)	93/204 (46)	NCG	27/204 (13.2)	ND	GHBT
Cuoco and Salvangnini[75]	Retrospective	44/96 (45.8)	NCG	ND	ND	GHBT
Lupascu et al[95]	Prospective (Case-control)	20/65 (31)	4/102 (4)	ND	ND	GHBT
Ghoshal et al[16]	Prospective (Case-control)	11/129 (8.5)	1/51(2)	ND	ND	GHBT
Posserud et al[12]	Prospective	6/162 (4)	1/26 (4)	ND	ND	Hydrogen breath test and culture

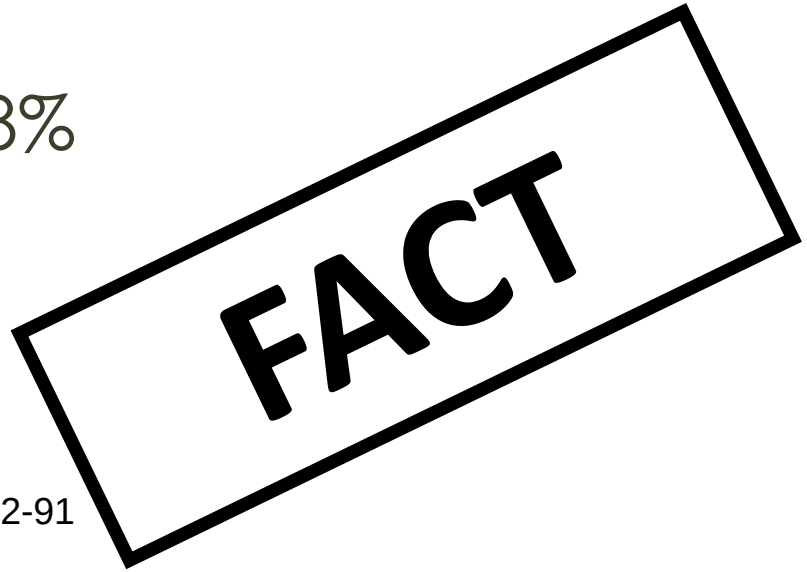
Irritable bowel syndrome and small intestinal bacterial overgrowth: Meaningful association or unnecessary hype?

World J Gastroenterol 2014 Mar 14;20(10):2482-91

SIBO – Fad or Fact?

2014 review of studies on SIBO among patients with IBS

- Patients with IBS: 4% to 78%
- Controls: 1% and 40%



World J Gastroenterol 2014 Mar 14;20(10):2482-91

SIBO – Fact…But…

Stop saying 84% of people with IBS have SIBO. Please.

SIBO Testing

Lactulose Breath Testing

- Diagnose overgrowth in the distal end of the SI
- LBT – can over-estimate frequency in studies

Glucose Breath Testing

- Successfully and accurately diagnoses proximal overgrowth (less common form)
- Cannot diagnose distal overgrowth – may under-estimate frequency of SIBO

SIBO Testing

There is no universally accepted standard for interpretation of SIBO testing, at present

SIBO – Associated Diseases

- IBS
- Acne rosacea
- Systemic sclerosis
- Fibromyalgia
- Unresponsive celiac disease
- NAFLD
- Parkinson's disease

SIBO - Treatment

- Reduce the bacteria
- Dietary components
- Gut healing

DEAL WITH THE CAUSE!

SIBO - Eradication

Aliment Pharmacol Ther. 2007 Apr 1;25(7):781-6.

High dosage rifaximin for the treatment of small intestinal bacterial overgrowth.

Scarpellini E[1], Gabrielli M, Lauritano CE, Lupascu A, Merra G, Cammarota G, Cazzato IA, Gasbarrini G, Gasbarrini A.

Author information

Abstract

BACKGROUND: Rifaximin is a broad spectrum non-absorbable antibiotic used for treatment of small intestinal bacterial overgrowth. Doses of 1200 mg/day showed a decontamination rate of 60% with low side-effects incidence.

AIMS: To assess efficacy, safety and tolerability of rifaximin 1600 mg with respect to 1200 mg/day for small intestinal bacterial overgrowth treatment.

Rifaximin 1600 mg/day showed a significantly higher efficacy for small intestinal bacterial overgrowth treatment with respect to 1200 mg with similar compliance and side-effect profile.

differences in patient compliance and incidence of side effects were found between groups.

CONCLUSIONS: Rifaximin 1600 mg/day showed a significantly higher efficacy for small intestinal bacterial overgrowth treatment with respect to 1200 mg with similar compliance and side-effect profile.

SIBO - Eradication

Aliment Pharmacol Ther. 2010 Oct;32(8):1000-6. doi: 10.1111/j.1365-2036.2010.04436.x. Epub 2010 Aug 18.

Clinical trial: the combination of rifaximin with partially hydrolysed guar gum is more effective than rifaximin alone in eradicating small intestinal bacterial overgrowth.

Furnari M[1], Parodi A, Gemignani L, Giannini EG, Marenco S, Savarino E, Assandri L, Fazio V, Bonfanti D, Inferrera S, Savarino V.

The combination of rifaximin with partially hydrolysed guar gum seems to be more useful in eradicating SIBO compared with rifaximin alone.

METHODS: A 50 g-glucose breath test was given to 500 consecutive patients. Patients with a positive glucose breath test and predisposing conditions to SIBO entered into the study, and were randomized to receive rifaximin 1200 mg/day or rifaximin 1200 mg/day plus partially hydrolysed guar gum 5 g/day for 10 days. Patients completed a symptom questionnaire and glucose breath test both in basal condition and 1 month after withdrawal of therapy.

RESULTS: Seventy-seven patients had SIBO. Eradication rate of SIBO was 62.1% in the rifaximin group (both on per-protocol and intention-to-treat analyses), and 87.1% (per-protocol, P=0.017) and 85.0% (intention-to-treat, P=0.036) in the rifaximin-plus-partially hydrolysed guar gum group. Clinical improvement was observed in 86.9% and 91.1% of eradicated cases in rifaximin and rifaximin-plus-partially hydrolysed guar gum groups respectively (P=0.677).

CONCLUSION: The combination of rifaximin with partially hydrolysed guar gum seems to be more useful in eradicating SIBO compared with rifaximin alone.

SIBO - Eradication

Glob Adv Health Med. 2014 May;3(3):16-24. doi: 10.7453/gahmj.2014.019.

Herbal therapy is equivalent to rifaximin for the treatment of small intestinal bacterial overgrowth.

Chedid V[1], Dhalla S[2], Clarke JO[3], Roland BC[4], Dunbar KB[5], Koh J[6], Justino E[7], Tomakin E[8], Mullin GE[9].

⊕ **Author information**

Herbal therapies are at least as effective as rifaximin for resolution of SIBO by LBT.

rifaximin 1200 mg daily vs herbal therapy for 4 weeks with repeat LBT post-treatment.

RESULTS: Three hundred ninety-six patients underwent LBT for suspected SIBO, of which 251 (63.4%) were positive 165 underwent treatment and 104 had a follow-up LBT. Of the 37 patients who received herbal therapy, 17 (46%) had a negative follow-up LBT compared to 23/67 (34%) of rifaximin users (P=.24). The odds ratio of having a negative LBT after taking herbal therapy as compared to rifaximin was 1.85 (CI=0.77-4.41, P=.17) once adjusted for age, gender, SIBO risk factors and IBS status. Fourteen of the 44 (31.8%) rifaximin non-responders were offered herbal rescue therapy, with 8 of the 14 (57.1%) having a negative LBT after completing the rescue herbal therapy, while 10 non-responders were offered triple antibiotics with 6 responding (60%, P=.89). Adverse effects were reported among the rifaximin treated arm including 1 case of anaphylaxis, 2 cases of hives, 2 cases of diarrhea and 1 case of Clostridium difficile. Only one case of diarrhea was reported in the herbal therapy arm, which did not reach statistical significance (P=.22).

CONCLUSION: SIBO is widely prevalent in a tertiary referral gastroenterology practice. Herbal therapies are at least as effective as rifaximin for resolution of SIBO by LBT. Herbals also appear to be as effective as triple antibiotic therapy for SIBO rescue therapy for rifaximin non-responders. Further, prospective studies are needed to validate these findings and explore additional alternative therapies in patients with refractory SIBO.

SIBO – Eradication SE

- **Rifaximin**
  - Anaphylaxis (1)
  - Hives (2)
  - Diarrhea (2)
  - C. diff infection (1)
- **Herbal Therapy**
  - Diarrhea (1)

SIBO – Herbal Eradication

- **Hydrogen SIBO**
  - Berberine herbs (2000-5000mg/d)**
  - Oregano (50 mg tid)

- **Methane SIBO**
  - Allicin extract (450 mg tid)

SIBO - Diets

- Nothing has been proven as a gold standard
- Not to be done in isolation
- Usually done after microbe eradication (many symptoms should be gone BEFORE starting)

SIBO – Diet Options

1. Specific Carbohydrate Diet
2. GAPS diet
3. Low FODMAP diet
4. SIBO Specific Food Guide (Dr Allison Siebecker)**
5. Cedars-Sinai Diet (Dr Pimentel)

SIBO - Diets

Belief:

Bacteria ONLY consume carbohydrates

SIBO - Diets

BMC Microbiol. 2013 Jan 11;13:6. doi: 10.1186/1471-2180-13-6.

Ammonia production by human faecal bacteria, and the enumeration, isolation and characterization of bacteria capable of growth on peptides and amino acids.

Protein fermentation by human faecal bacteria in the absence of sugars not only leads to the formation of hazardous metabolic products, but also to the possible proliferation of harmful bacteria.

from peptides, followed by casein and amino acids, which were similar. The amino acids metabolized most extensively were Asp, Ser, Lys and Glu. Monensin inhibited the rate of ammonia production from amino acids by 60% (P = 0.001), indicating the involvement of Gram-positive bacteria. Enrichment cultures were carried out to investigate if, by analogy with the rumen, there was a significant population of asaccharolytic, obligately amino acid-fermenting bacteria ('hyper-ammonia-producing' bacteria; HAP) in the colon. Numbers of bacteria capable of growth on peptides or amino acids alone averaged 3.5% of the total viable count, somewhat higher than the rumen. None of these were HAP, however. The species enriched included Clostridium spp., one of which was C. perfringens, Enterococcus, Shigella and Escherichia coli.

CONCLUSIONS: Protein fermentation by human faecal bacteria in the absence of sugars not only leads to the formation of hazardous metabolic products, but also to the possible proliferation of harmful bacteria. The kinetics of protein metabolism were similar to the rumen, but HAP bacteria were not found.

SIBO – Motility

Am J Physiol Gastrointest Liver Physiol. 2016 Feb 15;310(4):G228-33. doi: 10.1152/ajpgi.00212.2015. Epub 2015 Dec 10.

Redefining the functional roles of the gastrointestinal migrating motor complex and motilin in small bacterial overgrowth and hunger signaling.

During the **fasting state** the upper gastrointestinal tract exhibits a specific periodic migrating contraction pattern that is known as the migrating motor complex (MMC)

hinted in the beginning of the 20th century by both Cannon (Cannon W, Washburn A. Am J Physiol 29: 441-454, 1912) and Carlson (Carlson A. The Control of Hunger in Health and Disease. Chicago, IL: Univ. of Chicago Press, 1916). The discovery of motilin in 1973 shed more light on the control mechanisms of the MMC. Motilin plasma levels fluctuate together with the phases of the MMC and induce phase III contractions with a gastric onset. Recent research suggests that these motilin-induced phase III contractions signal hunger in healthy subjects and that this system is disturbed in morbidly obese patients. This minireview describes the functions of the MMC in the gut and its regulatory role in controlling hunger sensations.

SIBO - Motility

- Prokinetic options to help motility:
  - Medications: erythromycin, low dose naltrexone
  - Iberogast
  - 5-HTP**
  - Melatonin**
  - Ginger

SIBO – Motility

World J Gastroenterol. 2014 Mar 14;20(10):2492-8. doi: 10.3748/wjg.v20.i10.2492.

Melatonin for the treatment of irritable bowel syndrome.

Siah KT[1], Wong RK[1], Ho KY[1].

Author information

Melatonin plays an important part in gastrointestinal physiology which includes regulation of gastrointestinal motility, local anti-inflammatory reaction as well as moderation of visceral sensation

at bedtime as the standard dose of trial. However, all studies had consistently showed improvement in abdominal pain, some showed improvement in quality of life of IBS patients. Melatonin is a relatively safe drug that possesses potential in treating IBS. Future studies should focus on melatonin effect on gut mobility as well as its central nervous system effect to elucidate its role in IBS patients.

SIBO - Treatment

J Physiol Pharmacol. 2011 Dec;62(6):591-9.

Stress and the gut: pathophysiology, clinical consequences, diagnostic approach and treatment options.

Konturek PC[1], Brzozowski T, Konturek SJ.

⊕ Author information

Abstract

Stress, which is defined as an acute threat to homeostasis, shows both short- and long-term effects on the functions of the gastrointestinal tract.

Additionally, **melatonin** an important mediator of brain gut axis, has been shown to exhibit important protective effects against stress-induced lesions in the gastrointestinal tract

multifactorial approach and includes pharmacotherapy targeted against the predominant symptom, behavioural and psychological treatment, dietary alterations, education, reassurance and effective patient-physician relationship. When evaluating for the stress-induced condition in the upper GI tract, the diagnostic testing includes mainly blood tests and gastroscopy to rule out GERD and peptic ulcer disease. The therapy for these conditions is mainly based on the inhibition of gastric acid by proton pump inhibitors and eradication of Helicobacter pylori-infection. Additionally, melatonin an important mediator of brain gut axis has been shown to exhibit important protective effects against stress-induced lesions in the gastrointestinal tract. Finally, probiotics may profoundly affect the brain-gut interactions ("microbiome-gut-brain axis") and attenuate the development of stress-induced disorders in both the upper and lower gastrointestinal tract. Further studies on the brain-gut axis are needed to open new therapeutic avenues in the future.

GERD

Backwards movement of stomach acid secretions or bile/gastric acid secretions into the esophagus, causing symptoms (with or without esophagitis)

GERD - Symptoms

- A burning sensation in the chest, can spread to the throat
- Sour taste in the mouth
- Chest pain
- Dry cough
- Regurgitation of food or sour liquid (acid reflux)
- Sensation of a lump in your throat

GERD - Symptoms

Less common:

- Hoarseness and sore throat
- Difficulties swallowing
- Asthma
- Sinusitis
- Nausea and vomiting

GERD - Facts

A diagnosis of refractory GERD is made if no other causes are identified and a patient's symptoms persist in spite of proton pump inhibitor dose escalation to twice daily; typically, this represents 19% to 32% of GERD patients

Can J Gastroenterol. 2010 Jul; 24(7): 431-434

Is It Really GERD?

Functional heartburn: the same heartburn symptoms that are caused by GERD without any evidence of abnormal esophageal acid exposure, physiologic acid reflux exposure that highly correlates with symptoms and recognized esophageal motility disorders.

GERD – Causes

- Peristaltic motility disorders
- Valve incompetency
- Delayed gastric emptying
- Hiatal hernia
- Poor dietary habits
- Obesity, pregnancy
- Medications

GERD – Medications

- Anti-cholinergic drugs
- Birth control pills
- Ca channel blockers
- Diazepam, TCA
- Cholestryamine
- Bisphosponates
- a and β adrenergic agonists

GERD-IBS Overlap

Scand J Gastroenterol. 2015 Feb;50(2):162-9. doi: 10.3109/00365521.2014.983157. Epub 2014 Dec 19.

Overlap of symptoms of gastroesophageal reflux disease, dyspepsia and irritable bowel syndrome in the general population.

Rasmussen S[1], Jensen TH, Henriksen SL, Haastrup PF, Larsen PV, Søndergaard J, Jarbøl DE.

Author information

Of individuals meeting the criteria of one or more of the conditions GERD, FD and IBS, about one-third are suffering from at least **two** of them.

RESULTS: The overall response rate was 52.2%. The prevalence of GERD, FD and IBS was 11.2%, 7.7% and 10.5%, respectively, and overlap between two or three of these conditions was seen among 6.5% of the respondents. Among individuals meeting the criteria of one or more of the conditions GERD, FD and IBS, 30.7% had overlap between two or all three conditions.

CONCLUSION: GERD, FD and IBS are common conditions in the general population and the overlap between these conditions is also quite common. When diagnosing patients with GERD, FD and IBS, physicians should keep in mind that these patients could be suffering from more than one of these conditions.

Functional Heartburn & IBS

Am J Gastroenterol. 2016 Dec;111(12):1711-1717. doi: 10.1038/ajg.2016.432. Epub 2016 Sep 20.

Functional Heartburn Overlaps With Irritable Bowel Syndrome More Often than GERD.

de Bortoli N[1], Frazzoni L[2], Savarino EV[3], Frazzoni M[4], Martinucci I[1], Jania A[5], Tolone S[6], Scagliarini M[7], Bellini M[1], Marabotto E[8], Furnari M[8], Bodini G[8],

IBS overlaps more frequently with FH than with GERD and HE, suggesting common pathways and treatment

METHODS: Patients underwent a structured interview based on questionnaires for GERD, IBS, anxiety, and depression. Off-therapy upper-gastrointestinal (GI) endoscopy and 24 h MII-pH monitoring were performed in all cases. In patients with IBS, fecal calprotectin was measured and colonoscopy was scheduled for values >100 mg/kg to exclude organic disease. Multivariate logistic regression analysis was performed to identify independent risk factors for FH.

RESULTS: Of the 697 consecutive heartburn patients who entered the study, 454 (65%) had reflux-related heartburn (GERD+HE), whereas 243 (35%) had FH. IBS was found in 147/454 (33%) GERD/HE but in 187/243 (77%) FH patients (P<0.001). At multivariate analysis, IBS and anxiety were independent risk factors for FH in comparison with reflux-related heartburn (GERD+HE).

CONCLUSIONS: IBS overlaps more frequently with FH than with GERD and HE, suggesting common pathways and treatment. HE showed intermediate characteristic between GERD and FH.

Don’t Make Your Patients Worse!

Warn your patients about rebound when stopping their PPIs

Rebound Symptoms

Dig Dis. 2011;29(5):482-6. doi: 10.1159/000331514. Epub 2011 Nov 16.

Acid inhibition and the acid rebound effect.

Lerotić I[1], Baršić N, Stojsavljević S, Duvnjak M

Acid hypersecretion after PPI therapy is more pronounced, lasts longer, and could possibly be the cause of acid-related symptoms.

acid hypersecretion after the cessation of therapy with H(2) antagonists and proton-pump inhibitors (PPIs). While most of those studies had small patient numbers, the findings generally demonstrate that RAH after H(2) antagonist therapy is of low magnitude, short duration, and has questionable clinical significance. On the contrary, acid hypersecretion after PPI therapy is more pronounced, lasts longer, and could possibly be the cause of acid-related symptoms. Potential for causing symptoms has recently been confirmed in two randomized placebo-controlled studies, and while we witness the increasing use of PPIs, RAH could become a proven cause of failure to withdraw therapy in a proportion of patients with reflux or dyspeptic symptoms.

GERD – Food Allergies

Pediatr Allergy Immunol. 2013 Sep;24(6):582-8. doi: 10.1111/pai.12103. Epub 2013 Aug 2.

Development of food allergies in patients with gastroesophageal reflux disease treated with gastric acid suppressive medications.

Trikha A[1], Baillargeon JG, Kuo YF, Tan A, Pierson K, Sharma G, Wilkinson G, Bonds RS.

⊕ **Author information**

Abstract

BACKGROUND: The prevalence of food allergy has steadily increased, especially in children. Reflux disease, a very common problem in children, is often treated with gastric acid suppressive (GAS) medications which may alter the processing of food allergens, thereby

Treatment with GAS medications is associated with the occurrence of food allergy, an effect not apparently related to a diagnosis of GERD alone.

RESULTS: In comparison to the referent (children without GERD who received no GAS medications), children with GERD who were treated with GAS were more likely to be diagnosed with a food allergy (Hazard ratio (HR): 3.67, 95% CI 2.15-6.27), as were children with GERD diagnosis but who were not treated with GAS medications (HR: 2.15, 95% CI: 1.21-3.81). A direct comparison of the two GERD cohorts showed that children with GERD who were treated with GAS had a greater risk of food allergy than those with GERD who were untreated (HR, 1.68, 95%CI, 1.15-2.46).

CONCLUSION: Treatment with GAS medications is associated with the occurrence of food allergy, an effect not apparently related to a diagnosis of GERD alone.

GERD - Diet

Commonly considered foods:

- Fatty or fried foods
- Tomato sauce, citrus, spicy
- Alcohol
- Chocolate
- Mint
- Garlic, onions – especially raw
- Coffee, tea

GERD - Diet

Poor habits

- Over-eating
- Eating late at night
- Eating too quickly, not chewing enough
- Lying down after eating
- Smoking

GERD - Diet

Biggest successes

- Gluten-free
- Alcohol decrease, especially if excessive
- Mint – watch toothpastes, gums, candies
- Low FODMAP diet – especially for refractory cases/functional heartburn or those with IBS-type symptoms**

GERD – Treatment and Healing

Acute Care:

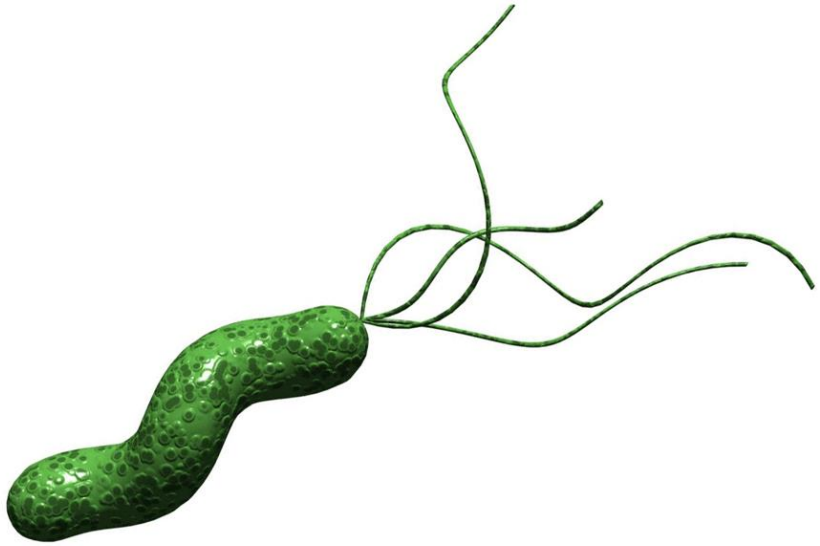
- 2 Tbsp aloe vera juice in water or chamomile tea
- Slippery elm gruel or tea
- DGL tablets –1-2 tabs, as needed (max qid)
- 1 Tbsp ACV in large glass of water
- Alginates
- Chewing non-mint gum

GERD – Treatment and Healing

- Melatonin (5-10g)
  - Gastroprotective
  - Inhibits NO production
  - Healing
  - Increases LES pressure
- Demulcents (capsules or slippery elm gruel)
- Aloe vera juice (1-3 oz before meals) or in smoothie
- HCl stimulator (instead of HCl) – gentian, ACV, dandelion, chamomile, bitters combo

H. Pylori

The poster child for missing bacteria



sing

and asthma

ic ulcer with

H. Pylori

- Role in regulating stomach acid
- Role in decreasing risk of allergies and asthma
- In its absence – lowered risk of peptic ulcer with increased GERD

H. Pylori

Am J Epidemiol. 2013 Dec 15;178(12):1721-30. doi: 10.1093/aje/kwt234. Epub 2013 Oct 11.

Decreased risk of celiac disease in patients with Helicobacter pylori colonization.

Lebwohl B, Blaser MJ, Ludvigsson JF, Green PH, Rundle A, Sonnenberg A, Genta RM.

We conclude that H. pylori presence and CD are inversely associated, a relationship that persists after adjustment for socioeconomic factors. Future studies should address whether H. pylori modulates immune responses to ingested gluten.

0.0001). After adjustment for the above covariates, this inverse relationship remained strong (adjusted odds ratio (OR) = 0.48, 95% confidence interval (CI): 0.40, 0.58). The relationships were similar in men (unadjusted OR = 0.51, 95% CI: 0.38, 0.69) and women (unadjusted OR = 0.46, 95% CI: 0.36, 0.58) and in all age groups. We conclude that H. pylori presence and CD are inversely associated, a relationship that persists after adjustment for socioeconomic factors. Future studies should address whether H. pylori modulates immune responses to ingested gluten.

H. Pylori

Cell Rep. 2016 Feb 16;14(6):1395-407. doi: 10.1016/j.celrep.2016.01.017. Epub 2016 Feb 4.

Gastric Helicobacter pylori Infection Affects Local and Distant Microbial Populations and Host Responses.

Helicobacter pylori is a late-in-life human pathogen with potential early-life benefits. These studies indicate that H. pylori influences the microbiota and host immune responses not only locally in the stomach, but distantly as well, affecting important target organs

gastric and pulmonary tissues revealed increased expression of multiple immune response genes, conserved across mice and over time in the stomach and more transiently in the lungs. Moreover, H. pylori infection led to significantly different population structures in both the gastric and intestinal microbiota. These studies indicate that H. pylori influences the microbiota and host immune responses not only locally in the stomach, but distantly as well, affecting important target organs.

H. Pylori

Gastroenterology 2016;151:51–69

CONSENSUS STATEMENT

The Toronto Consensus for the Treatment of *Helicobacter pylori* Infection in Adults

Carlo A. Fallone,[1] Naoki Chiba,[2,3] Sander Veldhuyzen van Zanten,[4] Lori Fischbach,[5] Javier P. Gisbert,[6] Richard H. Hunt,[3,7] Nicola L. Jones,[8] Craig Render,[9] Grigorios I. Leontiadis,[3,7] Paul Moayyedi,[3,7] and John K. Marshall[3,7]

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This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e25. Learning Objective: Upon completion of this examination, successful learners will be able to establish a treatment plan for patients with *H pylori* infection.

BACKGROUND & AIMS: *Helicobacter pylori* infection is increasingly difficult to treat. The purpose of these consensus statements is to provide a review of the literature and specific, updated recommendations for eradication therapy in adults. **METHODS:** A systematic literature search identified studies

Although the prevalence of *H pylori* is decreasing in some parts of the world, the infection remains present in 28% to 84% of subjects depending on the population tested.[1] Even studies in Western nations, which tend to have the lowest general prevalence,[1–4] report high proportions of

Increasing treatment failure:

14 day treatment (from 10 days)

Quadruple therapy (from triple)

GERD - Probiotics

Eur J Clin Invest. 2011 Apr;41(4):417-22. doi: 10.1111/j.1365-2362.2010.02425.x. Epub 2010 Nov 26.

Lactobacillus reuteri accelerates gastric emptying and improves regurgitation in infants.

Indrio F[1], Riezzo G, Raimondi F, Bisceglia M, Filannino A, Cavallo L, Francavilla R.

⊕ **Author information**

Abstract

In infants with functional GER, L. reuteri DSM 17938 reduce gastric distension and accelerate gastric emptying. In addition, this probiotic strain seems to diminish the frequency of regurgitation.

infants was similar to the control group as regards anthropometric and physiological data. The median fasting antral area was significantly reduced, (P = 0·01) the delta in gastric emptying rate was significantly increased (P = 0·01) and the median episodes per day of regurgitation was reduced (, P < 0·001) in the probiotic group compared to the placebo group. In the whole group, the frequency of regurgitation and the basal antral area showed a positive correlation (r = 0·53, P = 0·004).

CONCLUSIONS: In infants with functional GER, L. reuteri DSM 17938 reduce gastric distension and accelerate gastric emptying. In addition, this probiotic strain seems to diminish the frequency of regurgitation.

GERD - Probiotics

World J Gastroenterol. 2012 Nov 21;18(43):6250-4. doi: 10.3748/wjg.v18.i43.6250.

Helicobacter pylori eradication: sequential therapy and Lactobacillus reuteri supplementation.

Efrati C[1], Nicolini G, Cannaviello C, O'Sod NR, Valabrega S

The sequential treatment regimen achieved a significantly higher eradication rate of H. pylori compared with standard 7-d regimen. L. reuteri supplementation could reduce the frequency and the intensity of antibiotic-associated side-effects.

Successful eradication therapy was defined as a negative urea breath test at least 4 wk following treatment.

RESULTS: Ninety adult dyspeptic patients were enrolled, and 83 (30 male, 53 female; mean age 57 ± 13 years) completed the study. Nineteen patients were administered a 7-d triple treatment: 11 with L. reuteri supplementation during and 8 after therapy. Sixty-four patients were administered a sequential regimen: 32 with L. reuteri supplementation during and 32 after therapy. The eradication rate was significantly higher in the sequential group compared with the 7-d triple regimen (88% vs 63%, P = 0.01). No difference was found between two types of PPI. No difference in eradication rates was observed between patients submitted to L. reuteri supplementation during or after antibiotic treatment. Compliance with therapy was excellent in all patients. No difference in adverse effects was observed between the different antibiotic treatments and between patients submitted to L. reuteri supplementation during and after antibiotic treatment. There was a low incidence of adverse effects in all groups of patients with sequential therapy, probably due to the presence of the L. reuteri supplementation.

CONCLUSION: The sequential treatment regimen achieved a significantly higher eradication rate of H. pylori compared with standard 7-d regimen. L. reuteri supplementation could reduce the frequency and the intensity of antibiotic-associated side-effects.

GERD - Probiotics

J Clin Gastroenterol. 2014 May-Jun;48(5):407-13. doi: 10.1097/MCG.0000000000000007.

Lactobacillus reuteri strain combination in Helicobacter pylori infection: a randomized, double-blind, placebo-controlled study.

L. reuteri combination alone is able to exert an inhibitory effect on H. pylori growth, and when administered with eradication therapy, it determines a significant reduction in antibiotic-associated side effects.

positive naive patients received either L. reuteri combination (2×10 Colony Forming Units) or placebo during a 3-phase study (pre-eradication, eradication, and follow-up). All underwent C urea breath test (C-UBT), blood assessments of gastrin-17 (G17), endoscopy, and the Gastrointestinal Symptom Rating Scale. Eradication was confirmed by C-UBT 8 weeks after the completion of therapy.

RESULTS: Fifty patients were allocated in each group. During pre-eradication period, C-UBT δ decreased by 13% in L. reuteri combination as compared with a 4% increase in placebo (-13.2±34% vs. 4.3±27%; P<0.03). During eradication, GSRS increased significantly in placebo as compared with L. reuteri combination (6.8±2.9 vs. 4±3.1; P<0.01). Significantly less patients in L. reuteri combination as compared with placebo-reported side effects (40.9% vs. 62.8%; P<0.04). An abnormal G17 value was found in patients receiving placebo as compared with L. reuteri combination (28% vs. 12%; P<0.02). Eradication rate was 75% in L. reuteri combination and 65.9% in placebo (P=NS). L. reuteri combination increased eradication rate by 9.1% (odds ratio: 1.5).

CONCLUSIONS: L. reuteri combination alone is able to exert an inhibitory effect on H. pylori growth, and when administered with eradication therapy, it determines a significant reduction in antibiotic-associated side effects. Moreover, L. reuteri combination was able to decrease serum G17 levels and to (not significantly) increase the H. pylori-eradication rate.

GERD/H. pylori – Probiotics

- **L. reuteri DSM 17938 (Adjunctive with some eradication)**
  - 100M/tab – daily
- **L. rhamnosus GG (Adjunctive)**
  - 10B/cap – daily
- **Saccharomyces boulardii lyo (Adjunctive)**
  - 5B/capsule – 1-2 daily

Inflammatory Bowel Disease

- Group of inflammatory autoimmune disorders affecting the gut – anywhere from mouth to rectum

- Most common types: Crohn's Disease and Ulcerative Colitis

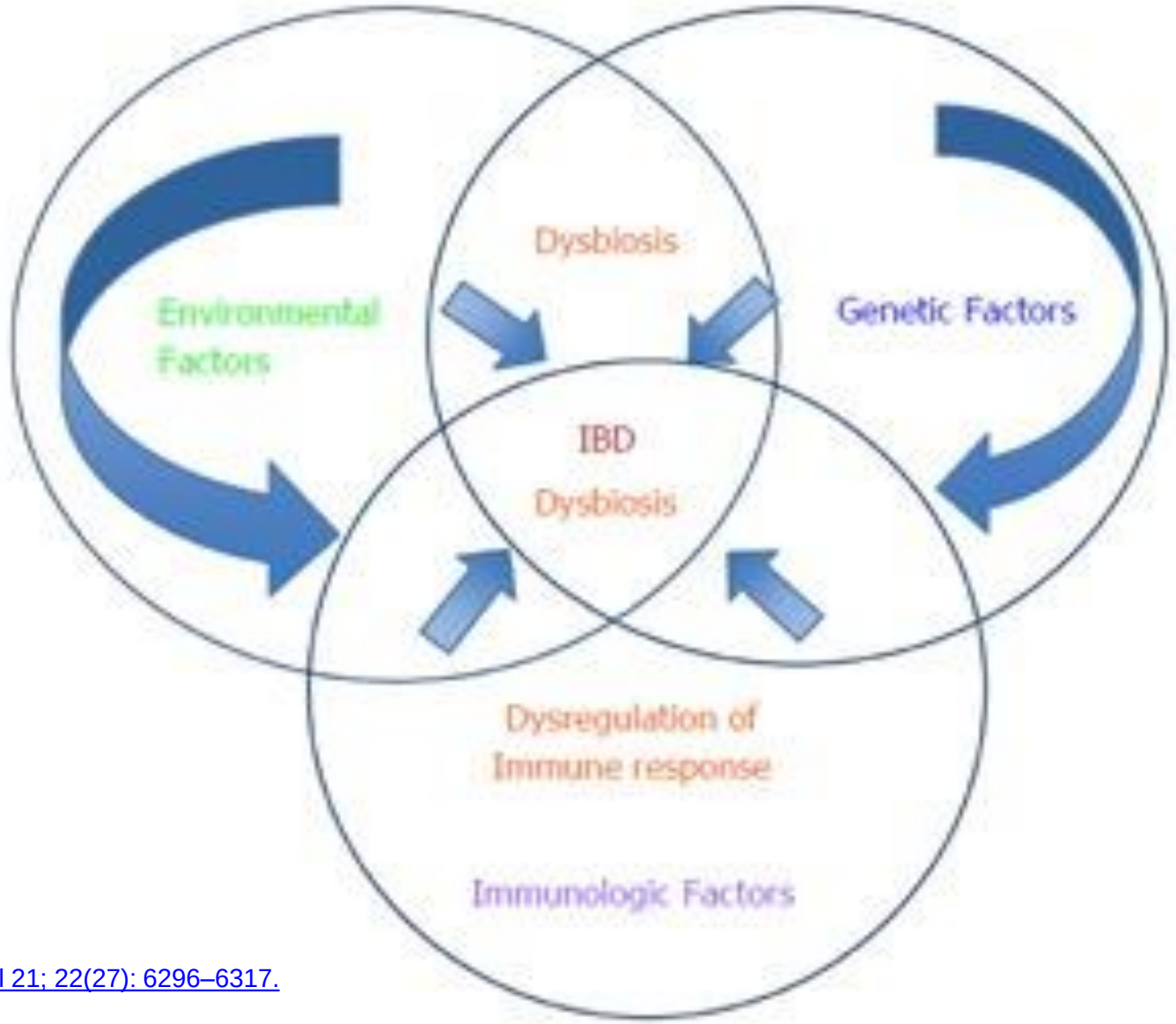
Inflammatory Bowel Disease

Symptoms related to inflammation of the GI tract:

- Diarrhea
- Rectal bleeding
- Urgent need to move bowels
- Abdominal cramps and pain
- Sensation of incomplete evacuation
- Constipation (can lead to bowel obstruction)

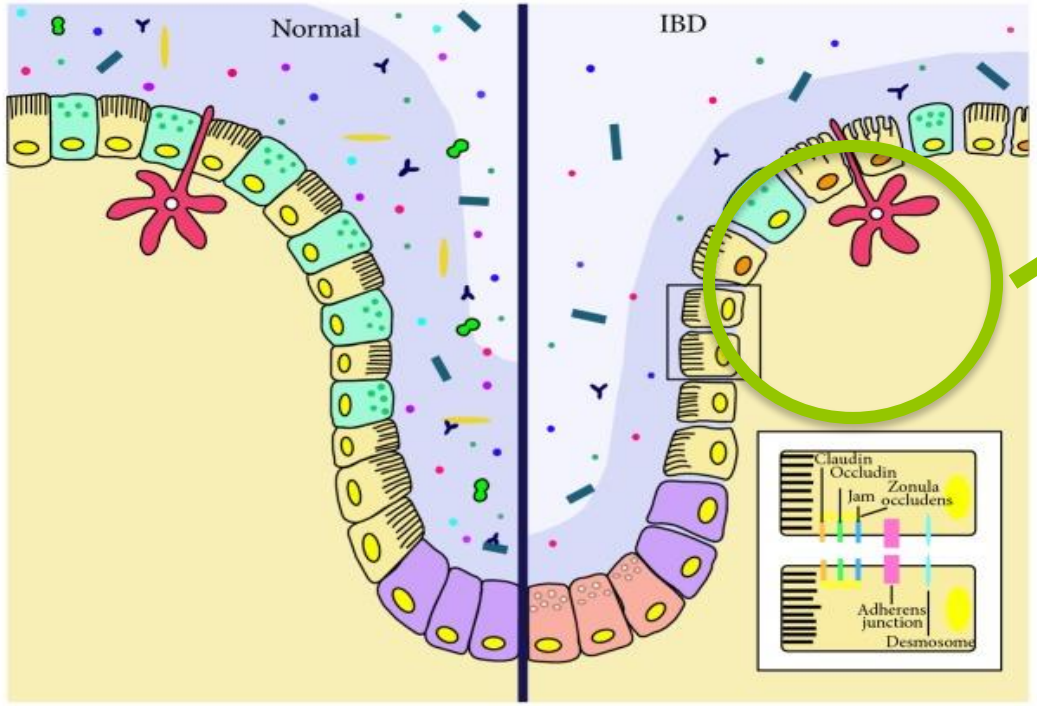
General symptoms that may also be associated with IBD:

- Fever
- Loss of appetite
- Weight Loss
- Fatigue
- Night sweats
- Loss of normal menstrual cycle



World J Gastroenterol. 2016 Jul 21; 22(27): 6296–6317.

IBD: Physiology



- Increased paracellular permeability
- Tight junction abN
- TNF-*a*
  - altered permeability
  - apoptosis of enterocytes
  - increased rate of shedding, and hindering the redistribution of TJs that should seal the gaps left

PMC full text: Mediators Inflamm. 2015; 2015: 628157.

IBD: History Of Antibiotic Use

UK study following a total of 1 072 426 subjects from 1994-2009

- IBD rates: **anti-anaerobic antibiotic** unexposed and exposed subjects were 0.83 and 1.52/10000 person-years, respectively
- 84% relative risk increase
- Dose-response effect existed with more than 2 courses of antibiotics

Pediatrics 2012 Oct;130(4):e794-803.

IBD – Decreased Butyrate-Producing Bacteria Species

Digestion. 2016;93(1):59-65. doi: 10.1159/000441768. Epub 2016 Jan 14.

Reduced Abundance of Butyrate-Producing Bacteria Species in the Fecal Microbial Community in Crohn's Disease.

The dysbiosis of CD patients is characterized by reduced abundance of multiple butyrate-producing bacteria species.

SUMMARY: Fecal samples from 10 inactive CD patients and 10 healthy individuals were subjected to 16S rRNA sequencing. The V3-V4 hypervariable regions of 16S rRNA were sequenced by the Illumina MiSeq™II system. The average of 62,201 reads per CD sample was significantly lower than the average of 73,716 reads per control sample. The genera Bacteroides, Eubacterium, Faecalibacterium and Ruminococcus significantly decreased in CD patients as compared to healthy controls. In contrast, the genera Actinomyces and Bifidobacterium significantly increased in CD patients. At the species level, butyrate-producing bacterial species, such as Blautia faecis, Roseburia inulinivorans, Ruminococcus torques, Clostridium lavalense, Bacteroides uniformis and Faecalibacterium prausnitzii were significantly reduced in CD patients as compared to healthy individuals ($p < 0.05$). These results of 16S rRNA sequencing were confirmed in additional CD patients ($n = 68$) and in healthy controls ($n = 46$) using quantitative PCR. The abundance of Roseburia inulinivorans and Ruminococcus torques was significantly lower in C-reactive protein (CRP)-positive CD patients as compared to CRP-negative CD patients ($p < 0.05$).

KEY MESSAGE: The dysbiosis of CD patients is characterized by reduced abundance of multiple butyrate-producing bacteria species.

IBD - Diet

A low-FODMAP diet does not seem to improve IBD

IBD - Diet

World J Gastroenterol. 2016 Apr 21;22(15):4009-19. doi: 10.3748/wjg.v22.i15.4009.

Follow-up of patients with functional bowel symptoms treated with a low FODMAP diet.

Maagaard L[1], Ankersen DV[1], Végh Z[1], Burisch J[1], Jensen L[1], Pedersen N[1], Munkholm P[1].

Author information

Abstract

AIM: To investigate patient-reported outcomes from, and adherence to, a low FODMAP diet among patients suffering from irritable bowel syndrome and inflammatory bowel disease.

METHODS: Consecutive patients with irritable bowel syndrome (IBS) or inflammatory bowel disease (IBD) and co-existing IBS fulfilling the ROME III criteria, who previously attended an outpatient clinic for low FODMAP diet (LFD) dietary management and assessment by a gastroenterologist, were invited to participate in a retrospective questionnaire analysis. The questionnaires were sent and returned by regular mail and gathered information on recall of dietary treatment, efficacy, symptoms, adherence, satisfaction, change in disease course and stool type, and quality of life. Before study enrolment all patients had to sign an informed written consent.

These data suggest that a diet low in FODMAPs is an efficacious treatment solution in the **management of functional bowel symptoms for IBS and IBD patients**

duration of dietary course ($P < 0.001$). Satisfaction with dietary management was seen in 83 (70%) IBS patients and 24 (55%) IBD patients. Eighty-four percent of patients lived on a modified LFD, where some foods rich in FODMAPs were reintroduced, and 16% followed the LFD by the book without deviations. Wheat, dairy products, and onions were the foods most often not reintroduced by patients.

CONCLUSION: These data suggest that a diet low in FODMAPs is an efficacious treatment solution in the management of functional bowel symptoms for IBS and IBD patients.

IBD - Diet

J Pediatr Gastroenterol Nutr. 2014 Oct;59(4):516-21. doi: 10.1097/MPG.0000000000000449.

Clinical and mucosal improvement with specific carbohydrate diet in pediatric Crohn disease.

Cohen SA[1], Gold BD, Oliva S, Lewis J, Stallworth A, Koch B, Eshee L, Mason D.

Clinical and mucosal improvement with specific carbohydrate diet in pediatric Crohn disease; N = 9

METHODS: Eligible patients with active CD (Pediatric Crohn's Disease Activity Index [PCDAI] ≥ 15) underwent a patency capsule and, if passed intact, capsule endoscopy (CE) was performed. Patients taking SCD were monitored for 52 weeks while maintaining all prescribed medications. Demographic, dietary, and clinical information, PCDAI, Harvey-Bradshaw Index (HBI), and Lewis score (LS) were collected at 0, 12, and 52 weeks. CEs were evaluated by an experienced reader blinded to patient clinical information and timing.

RESULTS: Sixteen patients were screened; 10 enrolled; and 9 completed the initial 12-week trial-receiving 85% of estimated caloric needs before, and 101% on the SCD. HB significantly decreased from 3.3 ± 2.0 to 0.6 ± 1.3 (P = 0.007) as did PCDAI (21.1 ± 5.9 to 7.8 ± 7.1, P = 0.011). LS declined significantly from 2153 ± 732 to 960 ± 433 (P = 0.012). Seven patients continued the SCD up to 52 weeks; HB (0.1 ± 0.4) and PCDAI (5.4 ± 5.5) remained improved (P = 0.016 and 0.027 compared to baseline), with mean LS at 1046 ± 372 and 2 patients showed sustained mucosal healing.

CONCLUSIONS: Clinical and mucosal improvements were seen in children with CD, who used SCD for 12 and 52 weeks. In addition, CE can monitor mucosal improvement in treatment trials for pediatric CD. Further studies are critically needed to understand the mechanisms underlying SCD's effectiveness in children with CD.

IBD - Diet

Nutrition. 2016 Apr;32(4):418-25. doi: 10.1016/j.nut.2015.08.025. Epub 2015 Nov 30.

Specific carbohydrate diet for pediatric inflammatory bowel disease in clinical practice within an academic IBD center.

This retrospective review provides evidence that the SCD can be integrated into a tertiary care center and may improve clinical and laboratory parameters for pediatric patients with nonstructuring, nonpenetrating CD as well as UC.

METHODS: In this retrospective study, we reviewed the medical records of patients with IBD on SCD.

RESULTS: We analyzed 26 children on the SCD: 20 with CD and 6 with UC. Duration of the dietary therapy ranged from 3 to 48 mo. In patients with active CD (Pediatric Crohn's Disease activity index [PCDAI] >10), PCDAI dropped from 32.8 ± 13.2 at baseline to 20.8 ± 16.6 by 4 ± 2 wk, and to 8.8 ± 8.5 by 6 mo. The mean Pediatric Ulcerative Colitis Activity Index for patients with active UC decreased from a baseline of 28.3 ± 10.3 to 20.0 ± 17.3 at 4 ± 2 wk, to 18.3 ± 31.7 at 6 mo.

CONCLUSION: This retrospective review provides evidence that the SCD can be integrated into a tertiary care center and may improve clinical and laboratory parameters for pediatric patients with nonstructuring, nonpenetrating CD as well as UC. Further prospective studies are needed to fully assess the safety and efficacy of the SCD in pediatric patients with IBD.

IBD-AID Nutritional Regime

Nutr J. 2014 Jan 16;13:5. doi: 10.1186/1475-2891-13-5.

An anti-inflammatory diet as treatment for inflammatory bowel disease: a case series report.

Olendzki BC[1], Silverstein TD, Persuitte GM, Ma Y, Baldwin KR, Cave D.

Author information

Abstract

BACKGROUND: The Anti-Inflammatory Diet (IBD-AID) is a nutritional regimen for inflammatory bowel disease (IBD) that restricts the intake of certain carbohydrates, includes the ingestion of pre- and probiotic foods, and modifies dietary fatty acids to demonstrate the potential of an adjunct dietary therapy for the treatment of IBD.

METHODS: Forty patients with IBD were consecutively offered the IBD-AID to help treat their disease, and were retrospectively reviewed. Medical

After following the IBD-AID, all (100%) patients were able to **discontinue at least one of their prior IBD medications**, and all patients had symptom reduction including bowel frequency.

CONCLUSION: This case series indicates potential for the IBD-AID as an adjunct dietary therapy for the treatment of IBD. A randomized clinical trial is warranted.

IBD-AID Nutritional Regime

There are 4 basic parts to the diet that need to be included on a daily basis + texture changes to food:

1. Prebiotic food
2. Probiotic food
3. Good balanced diet
4. Avoidance of certain foods (modified specific CHO diet)

- No processed foods, trans, refined sugar, grains (except oats), lactose

http://www.umassmed.edu/nutrition/ibd/ibdaid/

IBD – Strain Specific Probiotics

Saccharomyces boulardii lyo	Capsule Sachet	5B/capsule 5B/sachet	1-2 capsules 1-2 sachets
Escherichia coli Nissle 1917	Capsule	2.5-25B/capsule	1-2 capsules
L. acidophilus SD5212 *L. casei SD5218* *L. bulgaricus SD5210* *L. plantarum SD5209* *B longum SD5219* *B. infantis SD5220* *B. breve SD5206* *S. thermophilus*	Sachet	450B/sachet	1-4 sachets

Clinical Guide to PROBIOTIC SUPPLEMENTS AVAILABLE IN CANADA: 2016 Edition

IBD - PHGG

Food Funct. 2016 Jul 13;7(7):3176-83. doi: 10.1039/c6fo00177g.

Partially hydrolyzed guar gum enhances colonic epithelial wound healing via activation of RhoA and ERK1/2.

PHGG promotes colonic epithelial cell wound. These findings indicate that PHGG could be utilized as a therapeutic agent for patients with intestinal mucosal damage such as those with IBD.

MATERIALS AND METHODS: Young adult mouse colonic (YAMC) epithelial cells were scraped with a 10 µl micro-pipette tip to denude a round of the monolayer and were incubated with PHGG. The area of cell migration was measured using Image J software. Meanwhile, Rho activation assays were utilized to monitor Rho activation levels. To assess in vivo effects, C57B6 mice were treated with DSS for 7 days and then provided food supplemented with PHGG for 8 days.

RESULTS: YAMC cells treated with PHGG exhibited significantly enhanced wound healing compared to the control cells; however, this enhancement was inhibited by both Y-27632 (RhoA inhibitor) and U0126 (ERK1/2 inhibitor). Likewise, there was a PHGG-dependent increase in F-actin accumulation and Rho kinase activity that was blocked by U0126. Meanwhile, PHGG-dependent ERK1/2 activity was not inhibited by Y-27632. In the DSS-induced mouse colitis model, animals that received food supplemented with PHGG exhibited significant recovery of the colonic mucosa.

CONCLUSIONS: In this study, we demonstrate that PHGG promotes colonic epithelial cell wound healing via activation of RhoA, which occurs downstream of ERK1/2 activation. These findings indicate that PHGG could be utilized as a therapeutic agent for patients with intestinal mucosal damage such as those with IBD.

IBD - PHGG

J Nutr. 2016 Sep 7. pii: jn232538. [Epub ahead of print]

Dietary Fermentable Fiber Reduces Intestinal Barrier Defects and Inflammation in Colitic Mice.

Hung TV[1], Suzuki T[2].

⊕ **Author information**

Abstract

BACKGROUND: Dietary fiber (DF) and its fermentation metabolites play an important role in establishing and maintaining intestinal health.

OBJECTIVE: This study investigated the effects of fermentable DF, guar gum (GG), and partially hydrolyzed GG (PHGG) on the epithelial tight junction (TJ) barrier and inflammation in a murine model of dextran sodium sulfate (DSS)-induced colitis.

METHODS: In Expt. 1, male, 7-wk-old BALB/c mice weighing ~21 g were fed diets with 0%, 5%, and 10% GG for 12 d and administered distilled water with 2% DSS for 7 d beginning 5 d after the start of feeding. In Expt. 2, mice were provided diets with or without 10% PHGG and GG for 13 d and administered distilled water with 2% DSS for 8 d from 5 d after the start of feeding. In Expt. 3, mice were provided diets with or without 10%

These findings suggest that microbial metabolites of PHGG **reduce intestinal barrier defects and inflammation** in colitic mice.

inflammation in colitic mice.

IBD - Melatonin

BMC Gastroenterol. 2002 Apr 24;2:9.

Melatonin reduces TNF-a induced expression of MAdCAM-1 via inhibition of NF-kappaB.

Shown to block the induction of drug-induced colitis in mice if **premedicated with melatonin**

dependent induction and progress of inflammatory bowel disease (IBD). Melatonin, a relatively safe, potent antioxidant, has shown efficacy in several chronic injury models may limit MAdCAM-1 expression and therefore have a therapeutic use in IBD.

METHODS: We examined how different doses of melatonin reduced endothelial MAdCAM-1 induced by TNF-a in an in vitro model of lymphatic endothelium. Endothelial monolayers were pretreated with melatonin prior to, and during an exposure, to TNF-a (1 ng/ml, 24 h), and MAdCAM-1 expression measured by immunoblotting.

RESULTS: MAdCAM-1 was induced by TNF-a. Melatonin at concentrations over 100 microm (10(-4) M) significantly attenuated MAdCAM-1 expression and was maximal at 1 mM.

CONCLUSIONS: Our data indicate that melatonin may exert therapeutic activity in IBD through its ability to inhibit NF-kappaB dependent induction of MAdCAM-1.

IBD - Melatonin

Curr Pharm Des. 2011 Dec;17(38):4372-8.

Melatonin, a promising supplement in inflammatory bowel disease: a comprehensive review of evidences.

The majority of these studies indicate that melatonin has a **positive impact on IBD** with no or negligible side effects. Such results have been mostly explained through free radical scavenging and diminishing inflammation.

melatonin has a positive impact on IBD with no or negligible side effects. Such results have been mostly explained through free radical scavenging and diminishing inflammation. It is yet crucial to determine the efficacy of melatonin in combination with other established drugs in more clinical trials, not only for further confirmation of its efficacy, but also to investigate its possible side effects in longer durations of therapy.

IBD – Nutrient Deficiencies

World J Gastroenterol. 2016 Jan 21;22(3):895-905. doi: 10.3748/wjg.v22.i3.895.

Diet and nutritional factors in inflammatory bowel diseases.

Due to chronic inflammation as well as side effects of chronically used medications, patients with IBD are also at increased risk of nutritional factor deficiencies, **including iron, calcium, vitamin D, vitamin B12, folic acid, zinc, magnesium and vitamin A**

consumption of alcohol and sulfur products may have a negative effect on the disease course. Attempts are also made at employing diets composed in detail in order to supplement IBD therapy. A diet with a modified carbohydrate composition, a semi-vegetarian diet and a diet low in fermentable oligosaccharides, disaccharides, monosaccharides and polyols are under investigation. Due to chronic inflammation as well as side effects of chronically used medications, patients with IBD are also at increased risk of nutritional factor deficiencies, including iron, calcium, vitamin D, vitamin B12, folic acid, zinc, magnesium and vitamin A. It should also be remembered that there is no single common diet suitable for all IBD patients; each of them is unique and dietary recommendations must be individually developed for each patient, depending on the course of the disease, past surgical procedures and type of pharmacotherapy.

IBD – Nutrient Deficiencies

- Decreased food intake
- Increased intestinal loss
- Malabsorption
- Hypermetabolic state
- Drug interactions
- Long-term total parenteral nutrition

IBD – Nutrient Deficiencies

- **Anemia**
  - Iron, folate, vitamin B12
- **Bone disease**
  - Calcium, D
- **Hypercoagulability**
  - Folate, B12
- **Wound healing**
  - Zinc, A & D
- **Colorectal cancer risk**
  - Folate, D

IBD – Nutrient Deficiencies

Rev Med Chir Soc Med Nat Iasi. 2016 Jan-Mar;120(1):34-9.

ANEMIA IN INFLAMMATORY BOWEL DISEASE MORE THAN AN EXTRAINTESTINAL COMPLICATION.

Nemeş RM, Pop CS, Calagiu D, Dobrin D, Chetroiu D, Jantea P, Postolache P.

Abstract

The most common hematologic complication of inflammatory bowel disease (IBD)--ulcerative colitis and Crohn's Disease is anemia. Anemia in patients with IBD may be a result of iron, vitamin B12 or folate deficiency; anemia of chronic disease and hemolytic anemia are other causes in these patients. Factors contributing to the development of anemia include chronic gastrointestinal blood loss, vitamin B12 malabsorption

Factors contributing to the development of anemia include chronic gastrointestinal blood loss, vitamin B12 malabsorption secondary to terminal ileitis, folate deficiency as a result of **sulfasalazine therapy**

IBD – Nutrient Deficiencies

Iron Measurements:

- In patients without clinical symptoms and normal C-reactive protein (CRP), a ferritin of under 30 = Fe deficiency anemia
- If CRP is elevated, use iron & transferrin levels
- Monitor within 4 weeks - serum ferritin and transferrin levels - earlier in symptomatic patients