The Gut Connection:
Solutions for SIBO, IBS, IBD and GERD

Dr. Kim Bretz ND
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?

NYC Subway Crawling with Germs

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.
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

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Factors in GI Disease

Starts Early…
...And Isn’t Stopping
Microbial Extinction

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

Sonnenburg ED, Smits SA, Timonov K, Kligler E, Wingreen NS, Sonnenburg JL.

Abstract
The gut is home to billions of microorganisms that mediate host metabolism. The reduced diversity of the gut microbiota presents the question of which taxa are essential for host health and disease. We studied the gut microbiota of mice consuming a Western diet (high in fat and simple carbohydrates) and found a significant loss of microbial diversity. In particular, Faecalibacterium prausnitzii, a key member of the Western microbiota, was significantly decreased in mice consuming a Western diet. However, over several generations, a low-MAC diet was reintroduced to restore the microbiota to its original state. Our data suggest that taxa driven to low abundance can be reintroduced successfully and transferred to the next generation, and at increased risk of becoming extinct within a growing Western microbiota and the microbiota is targeted therapeutically, microbiota richness could be increased through strategies that incorporate dietary MACs as well as taxa not currently present in the Western gut.
GI – The Basics

One microbe = one disease?
We identified fungal (Candida tropicalis) and bacterial (Serratia marcescens and Escherichia coli) species that are associated with CD dysbiosis.
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

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

Nylander L, Hermes M, Isolauri E, Salminen S, de Vos WM, Satokari R.

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

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

Jiang S1, Xie S1, Lv D1, Zhang Y1, Dong J1, Zeng L1, Chen Y2.

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 = -0.446, 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

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

G B Rogers, D J Keating, R L Young, M L Wong, J Licinio and S Wesselingh

Abstract

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, while 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

**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; TNF = tumor necrosis factor

"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."
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...”
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

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

PI-IBS is common after gastroenteritis from water contamination and often is diarrhea-predominant.
Acute gastroenteritis can trigger IBS symptoms that persist for at least 8 years.
We herein showed that sensitivity to colonic distension of IBS patients can be transferred to rats by the fecal microbiota.
IBS – Microbiota

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


**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 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/
In patients with self-reported non-celiac gluten sensitivity: Gluten-specific gastrointestinal effects were not reproduced.
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]
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
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
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 ($p = 0.0006$).

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.
The results of this study support the administration of 6g/day PHGG for IBS patients with bloating.
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.
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)
  o Inulin (including chicory root)
  o Fructo-oligosaccharides (FOS)

Generally helpful
  o Partially hydrolyzed guar gum
  o Arabinogalactans
  o Galacto-oligosaccharides
IBS - Probiotics

Stop saying you can recolonize the gut.

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

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Download PROBIOTIC GUIDE mobile app for free

[Icons for Google Play and App Store]
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
Several bacterial groups matching Faecalibacterium prausnitzii were more prevalent in stool samples with the probiotic versus placebo.
**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)
Visceral pain modulation represents another potential health benefit attributed to bifidobacteria and other GABA-producing species of the intestinal microbiome.
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.
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.
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?

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)
SIBO – Fad or Fact?

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%

FACT

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!
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

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

Furnari M¹, Parodi A, Gelmicini L, Giannini EG, Marasco S, Savarino E, Assanini L, Facio V, Bonfant 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 510 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.
Herbal therapies are at least as effective as rifaximin for resolution of SIBO by LBT.

**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=0.24). 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=0.17) 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=0.89). Adverse effects were reported among the rifaximin treated arm including 1 case of anaphylaxis, 2 cases of hives, 2 cases of diarhoea and 1 case of Clostridium difficile. Only one case of diarrhoea was reported in the herbal therapy arm, which did not reach statistical significance (P=0.22).

**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. Herbas 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
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.
SIBO – Motility

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

- Prokinetic options to help motility:
  - Medications: erythromycin, low dose naltrexone
  - Iberogast
  - 5-HTP**
  - Melatonin**
  - Ginger
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.
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.
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
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
- Cholesteryamine
- Bisphosphonates
- α and β adrenergic agonists
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.
IBS overlaps more frequently with FH than with GERD and HE, suggesting common pathways and treatment.
Don’t Make Your Patients Worse!

Warn your patients about rebound when stopping their PPIs.
Rebound Symptoms

Acid hypersecretion after PPI therapy is more pronounced, lasts longer, and could possibly be the cause of acid-related symptoms.
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
- Alginate
- Chewing non-mint gum
GERD – Treatment and Healing

- Melatonin (5-10g)
  - Gastroprotective
  - Inhibits NO production
  - Healing
  - Increases LES pressure
- Demulcients (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
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
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.
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.
H. Pylori

Increasing treatment failure:

14 day treatment (from 10 days)
Quadruple therapy (from triple)
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.
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.
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.
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
IBD: Physiology

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

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
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.
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 \( (21.1 ± 5.9 \text{ to } 7.8 ± 7.1, P = 0.011) \). 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 \( (P = 0.016 \text{ and } 0.027 \text{ compared to baseline}) \), 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.
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.
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.
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

<table>
<thead>
<tr>
<th>Probiotic</th>
<th>Formulation</th>
<th>Concentration</th>
<th>Quantity</th>
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<tbody>
<tr>
<td>Saccharomyces boulardii lyo</td>
<td>Capsule Sachet</td>
<td>5B/capsule 5B/sachet</td>
<td>1-2 capsules 1-2 sachets</td>
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<tr>
<td>Escherichia coli Nissle 1917</td>
<td>Capsule</td>
<td>2.5-25B/capsule</td>
<td>1-2 capsules</td>
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<tr>
<td>L. acidophilus SD5212</td>
<td>Sachet</td>
<td>450B/sachet</td>
<td>1-4 sachets</td>
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<tr>
<td>S. thermophilus SD5207</td>
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Clinical Guide to PROBIOTIC SUPPLEMENTS AVAILABLE IN CANADA: 2016 Edition
**IBD - PHGG**

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

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

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

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.
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.
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.
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

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