Advances in Intestinal Hyperpermeability and Small Intestinal Bacterial Overgrowth

Corey Schuler, RN, MS, CNS, LN, DC, DBM DCBCN, FAAIM
Adjunct Assistant Professor, School of Health Sciences and Education, NYCC
Practitioner, Metabolic Treatment Center

October 15th, 2016
Disclosure

• Corey Schuler serves as Director of Clinical Affairs for Integrative Therapeutics
Outcomes

Participants will learn to work with patients

• for whom the elimination diet has failed
• who have increasingly difficult symptoms to manage
• who cannot tolerate conventional approaches.
Energy cost of digesting food

• ~10% of daily energy expenditure digesting and absorbing food.
• Protein requires ~20% of total calories to digest.
• Carbohydrates require ~5%.
• Fats require ~5%.


Thermic response to isoenergetic protein, carbohydrate or fat meals in lean and obese subjects.

Nair KS, Halliday D, Garrow JS.

Abstract
The thermic response of five lean and five obese subjects was measured by indirect calorimetry before, and for 157.5 min after a meal of protein, carbohydrate or fat, each of which provided 1.25 MJ. The change in plasma glucose, insulin and (in the case of the carbohydrate meal) the rate of exogenous glucose oxidation was also measured. There was no significant difference between the lean and obese groups in the magnitude of the thermic response to any of the three meals. In both weight groups the response was largest and most prolonged after the protein meal (P less than 0.01). The obese group showed a higher concentration of fasting plasma insulin (P less than 0.01) and a larger increase in plasma glucose (P less than 0.05) after the carbohydrate meal, but there was no significant difference in the oxidation of exogenous glucose when compared with the lean group. Previous studies on dietary-induced thermogenesis in lean and obese subjects have given conflicting results. In general reports of decreased thermogenesis in obese subjects are characterized by either (a) high pre-meal metabolic rates in the obese group, especially in diabetic subjects, or (b) a group classified as 'normal' who have been selected for their high thermogenic capacity.

PMID: 6347500 [PubMed - indexed for MEDLINE]
All Disease...

“All Disease begins in the gut”
~Hippocrates

Leaky Gut Syndrome

- **Disruption of Gut Lining**
  - Food intolerance, alcohol, stress, anti-inflammatory drugs, antibiotics, candida, fatty acid deficiencies can all disrupt the gut lining

- **Multiple Food Intolerances**
  - IgG antibodies produced to multiple foods as a result of gut inflammation

- **Leaky Gut**
  - Inflamed gut causes nutrients and waste to leak from the gut; worsens improper absorption and more IgG are produced

- **Improper Absorption**
  - Disrupted gut lining leads to improper absorption: food seen as an invader; IgG antibodies produced

- **Inflammation**
  - IgG antibodies form a complex with food antigens - the complexes are deposited in gut tissue, which leads to gut inflammation

Source: http://allergytreatmentsservices.com/digestion.html
Gas, bloating, pain, food intolerance, constipation and/or diarrhea

SIBO

Histamine

Methylation

IBS

Irritating

Debilitating
Gas, bloating, pain, food intolerance, constipation and/or diarrhea

- Breath
  - Glucose
  - Lactulose 2-3 hour test
  - Fructose

- Blood
  - Homocysteine
  - Methylmalonic acid
  - T-lymphocyte micronutrient assay
  - Genetic markers (i.e. MTHFR, MTRR)

- Urine
  - N-methylhistamine
  - Methylmalonic acid
  - Organic acids

What are the variants?
- C67T: There is a mutation from cytosine to adenine at position 677 within gene.
- A1298C: There is a mutation from adenine to cytosine at position 1298 within gene.

What are the possible genotypes?
- 677 - CC, CT, or TT
  - CC: homozygous normal
  - CT: one variant copy
  - TT: two variant copies

- 1298 - AA, AC, CC
  - AA: normal homozygous
  - AC or CC: one or two variant copies

These variants lead to amino acid differences in the protein that reduces its ability to function.
- Atopic Eczema
- Crohn's Disease
- Ulcerative Colitis
- Irritable Bowel Syndrome
- Leaky Gut Syndrome
- Detoxification
- Dysbiosis
- Chronic Inflammation
- Autoimmune Diseases
- Chronic Fatigue Syndrome (CFS)
- Fibromyalgia
- Myalgic Encephalomyelitis (ME)
- Systemic Exertion Intolerance Disease (SEID)
- Chronic Fatigue Immune Dysfunction Syndrome (CFIDS)

- Hypoallergenic requirements
- SIBO
- Pancreatic Insufficiency
- Multiple Food Protein Allergy/Intolerance
- Eosinophilic Esophagitis
- Pancreatitis
- Intestinal Failure

- Chronically Impaired GI Function
- Severely Impaired GI Function
- Malabsorption/Maldigestion

- Metabolic Syndrome
- Obesity

Intestinal Permeability
- Atopic Eczema
- Crohn's Disease
- Ulcerative Colitis
- Irritable Bowel Syndrome
- Leaky Gut Syndrome
- Detoxification
- Dysbiosis
- Chronic Inflammation
- Autoimmune Diseases
- Chronic Fatigue Syndrome (CFS)
- Fibromyalgia
- Myalgic Encephalomyelitis (ME)
- Systemic Exertion Intolerance Disease (SEID)
- Chronic Fatigue Immune Dysfunction Syndrome (CFIDS)

-Hypoallergenic Formula
-SIBO
-Pancreatic Insufficiency
-Multiple Food Protein Allergy/Intolerance
-Eosinophilic Esophagitis
-Pancreatitis
-Intestinal Failure

Is there a treatment common to these conditions?

-Chronically Impaired GI Function

-Severely Impaired GI Function
-Malabsorption/Maldigestion

-Metabolic Syndrome
-Obesity
How do you treat intestinal permeability?

- Supplements
- Biofeedback
- Diet
How do you treat intestinal permeability?

Many elimination diet proponents suggest the regimen can help find the cause of leaky gut syndrome or increased intestinal permeability. The idea is that some foods irritate the intestines and cause food proteins to leak through the intestinal wall where they shouldn’t be. Once there, the proteins come into contact with large numbers of immune cells that live just below the intestinal wall, says Dave Rakel, director of the University of Wisconsin Integrative Medicine Program at the School of Medicine and Public Health.

"The immune system along the gut is triggered to see friend or foe," says Dr. Rakel. If foe, an immune attack begins causing inflammation that can move throughout the body, he says.
Is the elimination diet the best?

THIS IS THE BEST!
Progress report

Elemental diets

The term ‘elemental diet’ is applied to a food which contains an elemental protein source, in the form of amino acids, with other easily digestible nutrients, minerals, and vitamins added; fat is present in very small quantities. Such a diet may also be described as ‘chemically defined’, the elemental components being pure chemical entities.
Composition of an Elemental Diet

- **Free form amino acids**
  - 14-18% of calories
  - 42-76% of calories
  - 6-43% of calories

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein:</td>
<td>16</td>
<td>14</td>
<td>15</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>Carbohydrate:</td>
<td>51</td>
<td>44</td>
<td>42</td>
<td>76</td>
<td>68</td>
</tr>
<tr>
<td>Fat:</td>
<td>33</td>
<td>42</td>
<td>43</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

**What about micronutrient levels?**
Micronutrients

- Micronutrient levels must be sufficient for sole source nutrition for up to 3 weeks at a time.

- However, micronutrient levels must not exceed safe levels, even for impaired individuals.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vit B6</td>
<td>mg</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>mcg</td>
</tr>
<tr>
<td>Vit B12</td>
<td>mcg</td>
</tr>
<tr>
<td>Biotin</td>
<td></td>
</tr>
<tr>
<td>Pantothenic</td>
<td>mg</td>
</tr>
<tr>
<td>Phosphorus</td>
<td></td>
</tr>
<tr>
<td>Iodine</td>
<td></td>
</tr>
<tr>
<td>Magnesium</td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td></td>
</tr>
<tr>
<td>Selenium</td>
<td></td>
</tr>
<tr>
<td>Copper</td>
<td></td>
</tr>
<tr>
<td>Manganese</td>
<td></td>
</tr>
<tr>
<td>Vitamin A</td>
<td>IU</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>mg</td>
</tr>
<tr>
<td>Calcium</td>
<td></td>
</tr>
<tr>
<td>Iron</td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>IU</td>
</tr>
<tr>
<td>Vit E</td>
<td>IU</td>
</tr>
<tr>
<td>Vitamin K</td>
<td></td>
</tr>
<tr>
<td>Thiamin</td>
<td>mg</td>
</tr>
<tr>
<td>Riboflavin</td>
<td>mg</td>
</tr>
<tr>
<td>Niacin</td>
<td>mg</td>
</tr>
</tbody>
</table>
Why are Elemental Diets Used?

Elemental Diet Products

Semi-Elemental Diets

Meal Replacements

Targeted Protein Products
Elemental vs Semi-elemental

- Semi-elemental diet is a subset of elemental diet
- Semi-elemental diets traditionally taste better
- Semi-elemental diets are used for less severe cases
- Semi-elemental diets can be introduced more quickly
- Semi-elemental diets use hydrolyzed protein rather than amino acids
Elemental vs Meal Replacement

- Both can be used as sole nutrition
- Meal Replacements are more designed for weight loss or weight gain
- Elemental diets have not been studied in metabolic syndrome
- Meal Replacements contain whole proteins which are not suitable for compromised systems
Elemental vs Targeted Protein

- TPPs contain **whole proteins**
- TPPs are NOT designed for sole nutrition
- TPPs are not hypoallergenic
- TPPs are not indicated for severely impaired GI function
- Some practitioners inappropriately use TPPs as a replacement for elemental diet
- Both used for dysbiosis and inflammatory bowel
Elemental diet as first option

- Atopic Eczema
- Crohn's Disease
- Ulcerative Colitis
- Irritable Bowel Syndrome
- Leaky Gut Syndrome
- Detoxification
- Dysbiosis
- Chronic Inflammation
- Autoimmune Diseases
- Chronic Fatigue Syndrome (CFS)
- Fibromyalgia
- Myalgic Encephalomyelitis (ME)
- Systemic Exertion Intolerance Disease (SEID)

Elemental Diet Products

- 100% Free Form Amino Acid Formula
- Hypoallergenic Formula
- SIBO
- Pancreatic Insufficiency
- Multiple Food Protein Allergy/Intolerance
- Eosinophilic Esophagitis
- Pancreatitis
- Intestinal Failure
- Early Post Operative Feeding

Semi-Elemental Diets

- Chronically Impaired GI Function
- Gut Rest

Meal Replacements

- Readily Absorbed Nutrients
- Severly Impaired GI Function
- Malabsorption/Maldigestion

Targeted Protein Products

- Metabolic Syndrome
- Obesity

- Sole source Nutrition
• There are no federal standards or definitions that govern the use of the term “hypoallergenic.”
• Intact proteins are common sources of allergic responses.
• Hypoallergenicity must be maintained throughout the entire supply chain.
• Even ingredients “derived from” potentially allergenic sources should be eliminated so that hypoallergenicity can be maintained.
Hypoallergenic

• Common source of carbohydrates in elemental diet is maltodextrin.
  – Maltodextrin often comes from corn.
  – Corn is a common allergen.
• Many elemental diets claim lactose-free but do not indicate dairy-free.
• Allergen-free vitamins must be used. No allergens in carriers.
  – Vitamin A (corn), Vitamin E (soy), Vitamin C (corn), amino acids.
• Should additionally be free of peanuts, tree nuts, fish, shellfish, eggs, wheat, gluten, and soy.
• Ideally, would be free of artificial coloring, flavoring, or preservatives, or ingredients of animal origin.
Hypoallergenic

- Hypoallergenic refers to the strict avoidance of common allergens including measurable amounts in the finished product, original sources of vitamins, minerals, and macronutrients as well as carriers and manufacturing aids.


On chart review, subjects who successfully normalized their breath test had a 66.4 +/- 36.1% improvement in bowel symptoms, compared to 11.9 +/- 22.0% in those who failed to normalize (P < 0.001).
An elemental diet for 2 weeks resulted in a clinical improvement in patients with active rheumatoid arthritis, and was as effective as a course of oral prednisolone 15 mg daily in improving subjective clinical parameters.
This improvement was not present following food reintroduction.

There was a high default rate, only 38% of those patients originally enrolled completed the study.
Assessment at four and 12 weeks showed that the patients treated with the elemental diet had improved as much as and by some criteria more than the steroid treated group. Elemental diet is a safe and effective treatment for acute Crohn's disease.
Effectiveness of an 'half elemental diet' as maintenance therapy for Crohn's disease: A randomized-controlled trial.


Abstract

BACKGROUND: Although thiopurines have a proven role in maintenance therapy for Crohn's disease, an alternative therapy is needed for patients intolerant or resistant to thiopurines.

AIM: To evaluate the effectiveness of home enteral nutrition as a maintenance therapy regimen in which half of the daily calorie requirement is provided.

CONCLUSION: This randomized-controlled trial shows the effectiveness of an half elemental diet, which is a promising maintenance therapy for Crohn's disease patients.

The relapse rate in the half elemental diet group was significantly lower [34.6% vs. 64.0%; multivariate hazard ratio 0.40 (95% CI: 0.16-0.98)] than that in the free diet group after a mean follow-up of 11.9 months.
Quality of life of patients and medical cost of "half elemental diet" as maintenance therapy for Crohn’s disease: secondary outcomes of a randomised controlled trial.


Abstract

BACKGROUND/AIM: Quality of life (QOL) of the patients and medical costs are important in current medical treatments, especially those for chronic diseases. We have reported the effectiveness of 'half elemental diet (ED)' as maintenance therapy for patients with Crohn's disease (CD). The aim of this study was to evaluate the QOL of CD patients and medical costs of half-ED.

METHODS: Fifty-one CD patients in remission were randomly assigned to a half-ED group (n=26) or a free diet group (n=25). The primary outcome measure was the occurrence of relapse during a 2-year period. This time, we investigated the QOL of the patients and medical costs of half-ED, as

This study has confirmed this half-ED therapy is beneficial for patients with Crohn's disease.

CONCLUSION: This study has confirmed this half-ED therapy is beneficial for patients with Crohn’s disease.

PMID: 18945653 [PubMed - indexed for MEDLINE]
## Why use an elemental diet?

- Severe Gut Problems
- Autoimmune Conditions
- Complex, Chronic Cases
- Systemic Conditions of GI origin
- Food Intolerances
- Pre/Post Surgical
Gut Rest

Repairing leaky gut (intestinal hyperpermeability) requires gut rest.

Zonulin and its regulation of intestinal barrier function: the biological door to inflammation, autoimmunity, and cancer.


Zonulin and its regulation of intestinal barrier function: the biological door to inflammation, autoimmunity, and cancer.
Fasano A1.

Author information

Abstract
The primary functions of the gastrointestinal tract have traditionally been perceived to be limited to the digestion and absorption of nutrients and to electrolytes and water homeostasis. A more attentive analysis of the anatomic and functional arrangement of the gastrointestinal tract, however, suggests that another extremely important function of this organ is its ability to regulate the trafficking of macromolecules between the environment and the host through a barrier mechanism. Together with the gut-associated lymphoid tissue and the neuroendocrine network, the intestinal epithelial barrier, with its intercellular tight junctions, controls the equilibrium between tolerance and immunity to non-self antigens. Zonulin is the only physiological modulator of intercellular tight junctions described so far that is involved in trafficking of macromolecules and, therefore, in tolerance/immune response balance. When the finely tuned zonulin pathway is deregulated in genetically susceptible individuals, both intestinal and extraintestinal autoimmunity, inflammatory, and neoplastic disorders can occur. This new paradigm subverts traditional theories underlying the development of these diseases and suggests that these processes can be arrested if the interplay between genes and environmental triggers is prevented by reestablishing the zonulin-dependent intestinal barrier function. This review is timely given the increased interest in the role of a "leaky gut" in the pathogenesis of several pathological conditions targeting both the intestine and extraintestinal organs.

“Zonulin is the only physiological modulator of intercellular tight junctions described so far that is involved in trafficking of macromolecules and, therefore, in tolerance/immune response balance.”

“When the finely tuned zonulin pathway is deregulated in genetically susceptible individuals, both intestinal and extraintestinal autoimmune, inflammatory, and neoplastic disorders can occur.”
• TPN or fasting causes mucosal atrophy


Enteral nutrient deprivation in patients leads to a loss of intestinal epithelial barrier function.
Ralls MW\textsuperscript{1}, Demehri FR\textsuperscript{1}, Feng Y\textsuperscript{1}, Woods Ignatowski KM\textsuperscript{1}, Teitelbaum DH\textsuperscript{2}.

Abstract

OBJECTIVE: To investigate the effects of total parenteral nutrition (TPN) or fasting on epithelial barrier function (EBF). Studies have shown that TPN or fasting causes mucosal atrophy, but the results in decreased EBF. This work was designed to determine whether TPN or fasting can cause a loss of EBF.

DESIGN: Small bowel specifically and in humans undergoing total parenteral nutrition (TPN) or fasting were assessed by immunohistochemical and epidermal growth factor receptor (EGFR) expression. Tight junctions and adherens junctions were also evaluated.

RESULTS: Because of TPN administration, the development of mucosal atrophy and a loss of epithelial barrier function (EBF) was observed. The loss of EBF was most evident in TPN-fed segments (P < .05). Immunohistochemical staining showed marked declines in intensity of ZO-1, occludin, E-cadherin, and claudin-4 in unfed intestinal segments, as well as a loss of structural formation of tight junctions. Analysis of cytokine and TLR expression showed significant increases in tumor necrosis factor (TNF)-\alpha and TLR4 in unfed segments of bowel compared with fed segments from the same individual.

CONCLUSION: EBF declined in unfed segments of human small bowel. This work represents the first direct examination of EBF from small bowel derived from nutrient-deprived humans and may explain the increased incidence of infectious complications seen in patients not receiving enteral feeds.
Even regular food causes stress to the gut mucosal integrity, but more so in compromised subjects.

*The effect of route of nutrient administration on the nutritional state, catabolic hormone secretion, and gut mucosal integrity after burn injury.*


**Abstract**

So that the efficacy of route of nutrient administration in thermal injury could be determined, a comparison was made between immediate enteral vs parenteral feedings in burned guinea pigs. Thirty-five guinea pigs underwent both catheter gastrostomy and jugular vein catheterization. On postoperative day 8, burned animals [30% total body surface area (TBSA)] were divided into an intragastrically (ig) fed group (N = 14) and a parenterally (iv) fed group (N = 14). Animals in each group received 175 kcal/kg/day with a solution of identical nutrient value beginning 2 hr after burn. The body weight change until postburn day (PBD) 8 and the average nitrogen balance were significantly better in the ig group than in the iv group. Values were also higher for the iv group than for the ig group in the early postburn period for urinary vanillyl mandelic acid (VMA) (p less than 0.05), plasma cortisol (p less than 0.05), and plasma glucagon (p less than 0.05). Also, the iv group showed reduced mucosal weight and thickness compared to the ig group on PBD 1 (p less than 0.02). There were significant negative correlations between VMA excretion and body weight change, and between plasma cortisol and jejunal mucosal structure (thickness and weight). These findings suggest that immediate postburn enteral nutrition can provide better nutritional support than parenteral nutrition through the maintenance of gut mucosal integrity and the prevention of increased secretion of catabolic hormones.

PMID: 3102769 [PubMed - indexed for MEDLINE]
Gut Rest

- Support upstream organs by addressing intestinal health


The role of the intestine in the pathophysiology and management of severe acute pancreatitis.
Flint RS¹, Windsor JA.

Author information

Abstract

BACKGROUND: The outcome of severe acute pancreatitis has scarcely improved in 10 years. Further impact will require new paradigms in pathophysiology and treatment. There is accumulating evidence to support the concept that the intestine has a key role in the pathophysiology of severe acute pancreatitis which goes beyond the notion of secondary pancreatic infection. Intestinal ischaemia and reperfusion and barrier failure are implicated in the development of multiple organ failure.

DISCUSSION: Conventional management of severe acute pancreatitis has tended to ignore the intestine. More recent attempts to rectify this problem have included 1) resuscitation aimed at restoring intestinal blood flow through the use of appropriate fluids and splanchnic-sparing vasoconstrictors or inotropes; 2) enteral nutrition to help maintain the integrity of the intestinal barrier; 3) selective gut decontamination and prophylactic antibiotics to reduce bacterial translocation and secondary infection. Novel therapies are being developed to limit intestinal injury, and these include antioxidants and anti-cytokine agents. This paper focuses on the role of the intestine in the pathogenesis of severe acute pancreatitis and reviews the implications for management.

An elemental diet

• Researchers and clinicians have been evaluating and using elemental diets for moderate-to-severe gastrointestinal impairment.
• Published studies have shown efficacy in small intestinal bacterial overgrowth (SIBO), irritable bowel (IB), Crohn's disease and other conditions.
• While clinicians used commercially available preparations, several problems with those products remained.
  – All contained artificial preservatives.
  – None were strictly hypoallergenic.
  – Most problematic was taste and thus compliance.
Medical foods

- A medical food, as defined in section 5(b)(3) of the Orphan Drug Act (21 U.S.C. 360ee(b)(3)), is “a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.”
Medical foods

• The FDA has made some specific guidance on what IS and what IS NOT a medical food.
• Dietary supplement companies have come under fire for not following the guidance.
• Product must adhere to the guidance and qualifies as a medical food.
• [http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm054048.htm](http://www.fda.gov/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ucm054048.htm)
Example of a protocol

- 14 days on elemental diet
- Re-test (if you tested) and possibly continue for 7-14 more days
- Continue with a “half-elemental diet” with a focus on intermittent fasting. Intermittent fasting extends gut rest. In this context keep all meals within an 8 hour period each day excluding the elemental meal. For example, if you use the elemental meal for breakfast and eat lunch at noon, be sure to finish dinner by 8 pm. Tighter windows may be more effective but also more difficult.
- During this step, you will also begin actively healing using intestinal permeability factors and balancing microbiota as part of gastrointestinal restoration.
  - NOTE: Most clinicians recommend waiting 3 months following a negative SIBO test before introducing probiotic supplements
Patient encounter

• 30 year old male with relatively unexplained acute anxiety.
• Panic attack resulted in emergency room visit.
• CT reveals no pancreatitis.
• No abnormalities in blood chemistry from ER.
• Reports fear/ anxiousness ever since (2 weeks).
• Lifestyle includes meditation most days and reports feeling calm and centered prior to ER visit.
• Getting married in the next few months, and have C7 neck issues, potentially myelopathy, causing numbness in middle finger, weak triceps with atrophy.
• Reports a day of binge drinking the day prior to panic attack.
• Panic relieved by bowel movements.
• Self-initiated a gluten-free, dairy-free diet but continued to have loose stools and stomach/intestinal soreness with pressure on abdomen.
• Anxiety gets worse 4pm-7pm each day and then mostly resolves.
Patient encounter

- Recommended elemental diet for 5 days as well as oral lavender @160 mg daily. Patient had initiated lavender a few days prior to initial visit.
- “Just as an update, I stuck to elemental diet for 3 days, bowels normalized within like 2-3 days, still getting some anxiety symptoms but not building on themselves like they had been.”
  - AR, Phoenix, AZ
Patient encounter

• Prescribed intestinal defense products
• 10g glutamine product with water dispersible turmeric 3x/day, soothing gastric products and digestive enzymes with meals.

• “I feel mostly normal although a little sluggish, and I get butterflies in my stomach feeling in waves leading up to a bowel movement usually like 2-3pm, 6-7pm, and then when I lay down at night....but I'm not carrying around anti-anxiety meds like I was OCD about when this was at its worst.”
Hey! I have a question!

Does anyone else become bloated if they don't eat after being hungry for a while? My bloating is almost completely gone, except that I usually get bloated if I don't eat "on time". Does this happen to anyone else?

I get really nauseated if my stomach is empty for very long.

I get bloated and nauseous if I don't eat for too long... love the irony... sick if I eat... sick if I don't eat!!! ughh lol

“I feel like I can’t win. Does everyone feel this defeated?”
What we know so far

- Elemental diet is a suitable intervention for complex, chronic diseases as well as pre/post operative.
- Gut rest is key to healing intestinal hyperpermeability.
- An Elemental diet can be hypoallergenic.
- An Elemental diet is perhaps one of the most powerful tools for conditions of GI origin including autoimmune conditions, severe gut dysfunction, and food intolerances.
A SIBO Protocol

SIBO Treatment Protocol
Variation of the Cedars-Sinai Protocol (Pimentel 2006)
Siebecker & Sandberg-Lewis (2014)

SIBO Suspected

Non-Diagnostic Tests
1. PE: TCV, Acid Peristalsis Reflex
2. Blood Test: CBC, RSR, Thyroid, CV, KD
3. Stool Test (fat malabsorption)
4. Strep/Gastro-TotTest or Heidelberg
5. Celiac, Intestinal permeability,
   Food allergy/sensitivity
6. Endo Colonoscopy

SIBO Lactulose Breath Test
Or: Glucose Breath Test

Hx
Gx: Eros Gx, Mst, Dx

Treat SIBO
2 options

Diet
SCD, SIBO food guide

Elemental Diet
x 2-3 wks

Herbal Antibiotics
1. Berberine containing herbs
2. Aillicin (methane)
3. Oregano
4. Nemen
1-3 caps 2-3 x day x 4 weeks
Optional: Probiotic, Antifungal

Feel Better: 90%

Partial Improvement: Not Better
Re-Assess

Antibiotics
1. Rifaximin: Diarrhea/Alternating
500mg bid x 14 days
2. Rifaximin + Neomycin: Constipation
150mg tid = 500mg bid x 14 days
or Ruf = Metronidazole 500mg bid x 14 days
Optional: Probiotic, Antifungal

Prevention
1. Diet (SCD, SIBO food guide, etc)
2. Prokinetic x 3 mo
   Erythromycin 250mg qhs x 3 mo
   Prucalopride 0.5-2 mg qhs x 3 mo
   LDN 2.5-4.5 gq x 2 mo
3. Probiotic: 4 HC1
4. BB healing supplements (optional)

Relapse

SIBO Re-Test

SIBO (-)
Consider other Dx
Re-Treat

SIBO (+)
The GUT, a lot more than digestion

- Digestion and Elimination of waste products
- 80% Immune System
- Production of neurotransmitter, Serotonin
- One Cell Paradox.
The One Cell Paradox
Microbiota involved in multiple physiological functions of the GI Tract

• Reduction in pathogen colonization
• Degradation of non-digestible dietary substances
• Production of SCFA, folic acid and vitamins
• Stimulation of normal epithelial turnover
• Shaping of mucosal immunity
Gut Barrier
Claudins regulate the intestinal barrier in response to immune mediators.

Kinugasa T¹, Sakai N², Tsuchiya K², Nishida M², Carole NM², Sato T², Nakamura M², Takatori Y², Takeshita K², Moriguchi Y², Imanishi K², Sakamoto N³, Kato E³, Kanemoto K³, Li X¹, Sakurada T¹, Takahashi Y¹, Tsuchiya K², Sakai N²

Abstract

BACKGROUND: Claudins are a large family of integral membrane proteins in the tight junction that are involved in the regulation of claudin-mediated paracellular permeability in epithelial cells. The aim of this study was to investigate the role of claudin-mediated paracellular permeability in intestinal epithelial cells.

METHODS: Expression of claudins and activation of extracellular signal-regulated kinases (ERK) mitogen-activated protein kinases (MEK) was determined by immunoblotting. IL-17 expression was assessed by immunoblotting. The regulation of claudin-1 and claudin-2 gene transcription was characterized through transfection of claudin promoter constructs. The claudin-mediated paracellular flux was measured by the transmembrane flux of horseradish peroxidase.

RESULTS: IL-17 induced the development of a paracellular barrier of T84 cell monolayers. Inhibition of ERK activation with the MEK inhibitor PD98059 blocked IL-17 as well as basal development of tight junctions in T84 cells. IL-17 induced formation of tight junctions correlated with up-regulation of claudin-1 and claudin-2 gene transcription. Inhibition of MEK reduced the activated and basal expression of claudin-2 messenger RNA and protein expression. Functional MEK was required for the expression and membrane association of claudin-2 but not claudin-1 in T84 cells.

CONCLUSIONS: MEK activity is required for claudin-mediated formation of tight junctions. IL-17 is able to regulate the intestinal barrier through the ERK MAPK pathway.

PMID: 10833473 [PubMed]
Claudin-2 as a mediator of leaky gut barrier during intestinal inflammation.
Luetig J1, Rosenthal R1, Barmeyer C1, Schulzke JD1.

Abstract
The epithelial tight junction determines the tightness of the paracellular pathway, including antigens, in an uncontrolled paracellular pathway for small cations and water and for the paracellular transport of macromolecules in intestinal diseases (celiac disease), and enhances the flux mechanism. In parallel to the absorptive flux, absorptive passage of macromolecules is enhanced.

Claudin-related intestinal diseases.
Barmeyer C1, Schulzke JD1, Fromm M2.

Abstract
With up to 200 m(2) the human intestine is the organ with the largest absorptive surface of the body. It is lined by a single layer of epithelial cells. The intestinal epithelium provides both, selective absorption of nutrients, ions, a protective barrier function and the first line of defense against environmental antigens. The paracellular part of the intestinal barrier is provided by tight junction (TJ) proteins, especially the large family of claudins. Changes in abundance or molecular structure result in three typical effects, (i) decreased absorptive passage, (ii) increased secretory passage of small solutes and water, and (iii) increased absorptive passage of macromolecules which may induce inflammatory processes. Several intestinal diseases result from such changes that can result in intestinal inflammation and symptoms like weight loss, abdominal pain or diarrhea. This recurrent knowledge on barrier dysfunction and claudin dysregulation in several intestinal diseases gastroenterologists are treating. These diseases include inflammatory bowel disease, microscopic colitis, celiac disease, irritable bowel syndrome, gallstones and infectious diseases like Campylobacter jejuni and Clostridium perfringens infection.

Copyright © 2015 Elsevier Ltd. All rights reserved.

KEYWORDS: Claudin; Inflammatory bowel disease; Intestinal disease; Intestine; Tight junction

PMID: 25999319 [PubMed - in process]
Glutamine

• Reduces inflammation but cannot overcome protein deprivation

---

Glutamine decreases lipopolysaccharide-induced intestinal inflammation and neutrophil transendothelial migration in neonatal rats.

Li N, Liboni K, Fang MZ, Samuelson D, Lewis P, Patel R, Neu J.

Abstract
Using a gastrostomy-fed (GF) rat infant "pup-in-a-cup" model, the effects of glutamine (Gln) and glutamate (Glu) supplementation on growth and small intestine morphometry in gastrostomy-fed rat pups were examined to test the hypothesis that Gln decreases the protein-critical effects of Gln and Glu on gut health and intestinal cytokine-induced neutrophil chemoattractant (CINC) peptide (P < 0.05). Gln blunted intestinal CINC peptide expression and provided 100 and 25% protein was elevated approximately 13-fold. Intestinal CINC peptide by 73 and 80%, respectively. GF, LPS-treated Glu decreased plasma CINC peptide by 73 and 80%, respectively. An approximate 13-fold increase was observed in the LPS-induced inflammatory response in infant rat intestine under GF conditions.

Effects of protein deprivation on growth and small intestine morphometry in gastrostomy-fed rat pups.

Li N, Lassman BJ, Liu Z, Liboni K, Neu J.

Abstract
OBJECTIVES: Critically ill neonates often have their enteral intake severely limited shortly after birth; to preserve intestinal structure and function in the neonate undergoing limited enteral feeding, they need to be fed a protein rich diet to prevent intestinal structure in the developing small intestine of infant rats fed a low protein diet.

METHODS: Using a gastrostomy-fed "pup-in-a-cup" rat model, the effects of Gln and Glu supplementation in groups of 6- to 7-day-old pups were fed rat milk substitute (RMS) via gastrostomy tube. One group of the protein normally received from their mothers. Two of the groups fed 25% protein replaced by Gln or Glu. RESULTS: Pups receiving the 100% protein RMS were larger than pups receiving the 25% protein RMS diet (P < 0.001). Average villus height (P < 0.01) and area (P < 0.01) were greater in pups receiving the 100% protein RMS diet. There was no significant difference among the groups in mucosal maltase or alkaline phosphatase activity. Ocludin-1 or claudin-1 activity was significantly higher in the group fed 100% protein RMS diet, while claudin-1 or claudin-1 in rats fed 25% protein.

CONCLUSIONS: These results suggest that neither Gln nor Glu supplementation can support small intestine for the outcomes that were evaluated.
Glutamine reduce intestinal hyperpermeability

L-Glutamate supplementation improves small intestinal architecture and enhances the expressions of jejunal mucosa amino acid receptors.

Lin M^1, Zhang B^1, Yu C^1, Li J^1, Zhang

Abstract

L-Glutamate is a major oxidative fuel, and the key metabolite. This study investigated the effects of L-Glutamate on jejunal mucosal barrier function in weanling piglets.

Lin M^1, Zhang B^1, Yu C^1, Li J^1, Zhang

Abstract

Glutamine enhances tight junction protein expression and modulates corticotropin-releasing factor signaling in the jejunum of weanling piglets.

Wang H^1, Zhang C^1, Wu G^2, Sun Y^1, Wang B^1, He B^1, Dai Z^1, Wu Z^3

Abstract

L-Glutamate Enhances Barrier and Antioxidative Functions in Intestinal Porcine Epithelial Cells.

Jiao N^1, Wu Z^2, Ji Y^1, Wang B^1, Dai Z^1, Wu G^3

Abstract

L-Glutamine Enhances Tight Junction Integrity by Activating CaMK Kinase 2-AMP-Activated Protein Kinase Signaling in Intestinal Porcine Epithelial Cells.

Wang B^1, Wu Z^2, Ji Y^1, Sun K^1, Dai Z^1, Wu G^3

Abstract

1-Glutamine Enhances Tight Junction Integrity by Activating CaMK Kinase 2-AMP-Activated Protein Kinase Signaling in Intestinal Porcine Epithelial Cells.

Wang B^1, Wu Z^2, Ji Y^1, Sun K^1, Dai Z^1, Wu G^3

Abstract

BACKGROUND: The tight junctions (TJs) are essential for maintenance of the intestinal mucosal barrier integrity. Results of our recent work show that dietary l-glutamine (Gln) supplementation enhances the protein abundance of TJ proteins in the small intestine of piglets. However, the underlying mechanisms remain largely unknown.

PMID: 25368996 [PubMed - indexed for MEDLINE]
Other amino acids

• L-Cysteine, Aspartate, and potentially other amino acids are involved in intestinal health.

Abstract
Zehe Song and Guo Tong are co-first authors.

L-Cysteine protects intestinal injury by modulating TNF-α and NF-κB and Nrf2 pathways in weaned pigs after LPS challenge.

Eur J Nutr. 2016 Feb 23. [Epub ahead of print]

Aspartate attenuates intestinal injury and inhibits TLR4 and NODs/NF-κB and p38 signaling in weaned pigs after LPS challenge.

Wang H¹, Liu Y², Shi H¹, Wang X¹, Zhu H¹, Pi D¹, Leng W¹, Li G¹.

Author information

Additional information

Innate Immun. 2016 Feb 25; pii: 1753425715606821

L-Cysteine protects intestinal injury and inhibits TLR4 and NODs/NF-κB and p38 signaling in weaned pigs after LPS challenge. Song ZH¹, Tong G², Xiao K¹, Jiao LF².

Abstract

PURPOSE: This study was conducted to investigate whether aspartate (Asp) could alleviate Escherichia coli lipopolysaccharide (LPS)-induced intestinal injury by modulating intestine inflammatory response.

METHODS: Twenty-four weaned piglets were divided into four treatments: (1) non-challenged control; (2) LPS-challenged control; (3) LPS + 0.5 % Asp; and (4) LPS + 1.0 % Asp. After feeding with control, 0.5 or 1.0 % Asp-supplemented diets for 21 days, pigs were injected intraperitoneally with saline or LPS. At 4 h postinjection, blood and intestine samples were obtained.

RESULTS: Asp supplementation to LPS-challenged pigs improved intestinal morphology, indicated by higher jejunal and ileal villus height/crypt depth ratio and lower ileal crypt depth linearly or quadratically. Asp also improved intestinal barrier function, indicated by increased jejunal and ileal diamine oxidase activities as well as enhanced protein expression of jejunal claudin-1 linearly or quadratically. In addition, Asp decreased plasma, jejunal and ileal tumor necrosis factor-α concentration and ileal caspase-3 protein expression linearly and quadratically. Moreover, Asp down-regulated the mRNA expression of toll-like receptor 4 (TLR4) and nucleotide-binding oligomerization domain protein (NOD) signaling-related genes, nuclear factor-κB (NF-κB) p65 and p38, decreased phosphorylation of jejunal p38, and increased phosphorylation of ileal extracellular signal-related kinase 1/2 linearly or quadratically. Finally, Asp increased mRNA expressions of TLR4 and NOD signaling negative regulators including radioprotective 105, suppressor of cytokine signaling 1, toll-interacting protein, Erbb2 interacting protein and centaurin β1 linearly or quadratically.

CONCLUSIONS: These results indicate that Asp supplementation is associated with inhibition of TLR4 and NODs/NF-κB and p38 signaling pathways and concomitant improvement of intestinal integrity under an inflammatory condition.
Etiology of Systemic Conditions

- SIBO Dysbiosis
- Increased Gut Permeability
- Sympathetic Response
- PAMPS endotoxins
- Translocation of microbes
  - Gut Dysfunction
  - Autoimmune
  - Food Intolerances
  - Mitochondrial Dysfunction
A myriad of effects

- Tight junction proteins are dysregulated
  - impaired paracellular transport
    - e.g. causing magnesium loss in the kidney
  - increased paracellular transport of solutes and water
    - e.g. causing leak-flux diarrhea in the intestine
  - increased permeability to large molecules
    - e.g. unwanted intestinal pathogen uptake fueling inflammatory processes.

Optimize the HPA Axis

- Increased corticotropin releasing factor (CRF) leads to increased intestinal hyperpermeability.
Peripheral corticotropic releasing factor (CRF) affects colonic motility
Optimize the HPA Axis

- Stress constricts the small bowel and may cause deep visceral pain.
The receptor for corticotropic releasing hormone (CRH or CRF) can be antagonized to help those with IBS.
Food residues

- Pesticides affect intestinal permeability


**Increased gut permeability and bacterial translocation after chronic chlorpyrifos exposure in rats.**

Joly Condette C¹, Khorsl-Cauet H¹, Morlière P², Zablijak L³, Reygner J¹, Bach V¹, Gay-Quéhéillard J¹.

**Author information**

**Abstract**

The epithelium's barrier function is crucial for maintaining homeostasis and preventing the passage of food antigens and luminal bacteria. This function is essentially subserved by tight junctions (TJs), multiprotein complexes located in the most apical part of the lateral membrane. Some gastrointestinal disease states are associated with elevated intestinal permeability to macromolecules. In a study on rats, we determined the influence of chronic, daily ingestion of chlorpyrifos (CPF, a pesticide that crosses the placental barrier) during pre- and postnatal periods on intestinal permeability and TJ characteristics in the pups. Fluorescein isothiocyanate (FITC)-dextran was used as a marker of paracellular transport and mucosal barrier dysfunction. Pups were gavaged with FITC-dextran solution and blood samples were collected every 30 min for 400 min and analyzed spectrofluorimetrically. At sacrifice, different intestinal segments were resected and prepared for analysis of the transcripts (qPCR) and localization (using immunofluorescence) of ZO-1, occludin and claudins (scaffolding proteins that have a role in the constitution of TJs). In rats that had been exposed to CPF in utero and after birth, we observed a progressive increase in FITC-dextran passage across the epithelial barrier from 210 to 325 min at day 21 after birth (weaning) but not at day 60 (adulthood). At both ages, there were significant changes in intestinal TJ gene expression, with downregulation of ZO-1 and occludin and upregulation of claudins 1 and 4. In some intestinal segments, there were changes in the cellular localization of ZO-1 and claudin 4 immunostaining. Lastly, bacterial translocation to the spleen was also observed. The presence of CPF residues in food may disturb epithelial homeostasis in rats. Changes in TJ protein expression and localization may be involved in gut barrier dysfunction in this model. Uncontrolled passage of macromolecules and bacteria across the intestinal epithelium may be a risk factor for digestive inflammatory diseases.
Alcohol

• “alcohol is able to increase the intestinal epithelial barrier permeability in a dose- and time-dependent manner. Alcohol induces a change in the expression of the tight junction-associated proteins, ZO-1 and claudin-1, which are two major sites of alcohol action, thus increasing intestinal epithelial barrier permeability.”


Effects of alcohol on intestinal epithelial barrier permeability and expression of tight junction-associated proteins.

Abstract
The present study aimed to investigate the effects of alcohol on intestinal epithelial barrier permeability and expression of the tight junction-associated proteins, zonula occludens-1 (ZO-1) and claudin-1. An alcohol-treated Caco-2 intestinal epithelial cell monolayer in vitro model was used to investigate whether alcohol is able to induce intestinal barrier dysfunction and decrease expression of ZO-1 and claudin-1. MTT assay results revealed unaltered cell viability at alcohol concentrations of <5%. Caco-2 cells in the 5% alcohol-treated groups exhibited a significant time-dependent decrease in transepithelial electrical resistance (TEER) and an increase in fluorescent yellow flux rate compared with the control cells. ZO-1 expression exhibited a progressive decline following 20 min of incubation, reached its minimum levels at 60 min and then showed an increasing trend
Melatonin

• Melatonin to the rescue; dose per clinical need


**Long-term oral melatonin administration reduces ethanol-induced increases in duodenal mucosal permeability and motility in rats.**

Sommansson A¹, Yamskova O, Schlöth HB, Nylander O, Sjöblom M.

+ Author information

**Abstract**

**AIM:** Increased intestinal epithelial permeability is associated with intestinal inflammation and dysfunction. The aim of the present study was to investigate the role of long-term oral melatonin administration on ethanol-induced increases in duodenal mucosal permeability and hypermotility.

**METHODS:** Male Sprague-Dawley rats were administered melatonin in their tap water (0.1 mg mL(-1) or 0.5 mg mL(-1)) for 2 or 4 weeks. After the treatment period, the rats were anaesthetized with Inactin®, and a 30-mm duodenal segment was perfused in situ. The effects on duodenal mucosal paracellular permeability, bicarbonate secretion, fluid flux and motor activity were studied. The expression levels of the tight junction components, zona occludens (ZO)-1, ZO-2, and ZO-3, claudin-2, claudin-3, claudin-4, occludin, and myosin light chain kinase and of the melatonin receptors MT1 and MT2 were assessed using qRT-PCR.
NAC provides protective effect.

Am J Physiol Gastrointest Liver Physiol. 2016 Jan 28;ajpgi.00314.2015. doi: 10.1152/ajpgi.00314.2015. [Epub ahead of print]

Rapid Disruption of Intestinal Epithelial Tight Junction and Barrier Dysfunction by Ionizing Radiation in Mouse Colon in vivo: Protection by N-Acetyl L-Cysteine.

Shukla PK1, Gangwar R2, Manda B1, Meena AS3, Yadav N3, Szabo E3, Balogh A3, Lee SC3, Tigyi GJ4, Rao RK5.

Abstract
The goals of this study were to evaluate the effects of ionizing radiation on apical junctions in colonic epithelium and mucosal barrier function in mice in vivo. Adult mice were subjected to total body irradiation (TBI; 4 Gy) with or without N-acetyl L-cysteine (NAC) feeding for 5 days prior to irradiation. At 2-24 h post-irradiation, the integrity of colonic epithelial tight junctions (TJ), adherens junctions (AJ) and the actin cytoskeleton was assessed by immunofluorescence microscopy and immunoblot analysis of detergent-insoluble fractions for TJ and AJ proteins. The barrier function was evaluated by measuring vascular-to-luminal flux of FITC-inulin in vivo and luminal-to-mucosal flux in vitro. Oxidative stress was evaluated by measuring protein thiol oxidation. Confocal microscopy showed that radiation caused redistribution of occludin, ZO-1, claudin-3, E-cadherin and β-catenin, as well as the actin cytoskeleton as early as 2 h post-irradiation, and this effect was sustained for at least 24 h. Feeding NAC prior to irradiation blocked radiation-
Endotoxins and their origins

• Any toxin secreted by a microorganism and released into the surrounding environment only when it dies.

• Technically only gram-negative bacteria release lipopolysaccharides, but clinically relevant to use a broader definition including anything released by gut bacteria.

• Metabolites produced by gut bacteria can enter the bloodstream by translocation through impaired gut barrier function.

• Up to one-third of the small molecules in human blood can be derived from gut bacteria
Endotoxins

• Pathogen-associated molecular patterns (PAMPs)
  – Highly conserved motifs in pathogens
  – Lipopolysaccharide (LPS) is the most well studied, considered prototypic activator of innate immunity, and often referred to as “endotoxin”.
  – Other PAMPs includes mannans in the yeast cell wall, formylated peptides and various bacterial cell-wall components such as lipopeptides, peptidoglycans and teichoic acids
• Toll like receptors (TLRs), are immune sensors of PAMPs
  – TLRs initiate an adaptive immune response and a signaling cascade leading to activation of pro-inflammatory genes, such as tumor necrosis factor (TNF)-α and interleukins-6, -8, and -12
LPS: Prototypic Endotoxin

- LPS represents ~80% of the cell wall mass of Gram negative bacteria
- **Toxic compounds localized on the surface of bacterial cells as a part of the outer membrane.**
- Constituted by an antigen-O specific chain, hetero-oligosaccharide, and by a lipid A region representing the toxic part of the LPS
- Taken up by the Lipopolysaccharide Binding Protein (LBP)

![LPS Diagram](image)
Autoimmune Disease

• Clinical Research has shown a relationship between autoimmune diseases and increased gut permeability
• Medical treatment for autoimmune disease centers around target markers and symptomology.

Examples:

**Rheumatoid Arthritis:** RA Factor, anti-CCP (cyclic citrullinated peptide), ESR, CRP
Current Pharmacological Interventions

- **NSAIDS**
- **Steroids**
- **Acetaminophen**

**DMARDs** (dz modifying antirheumatic agents)
Eg: methotrexate, Plaquenil

**Biologic Response Modifiers**
(Remicade, monoclonal antibody)
Endotoxins up-regulate inflammation

![Diagram showing the effects of endotoxins on various biological processes]

- Interleukin-1 and interleukin-2
- Histamine
- Tumor necrosis factor
- Activation of coagulation system
- Prostaglandin, thromboxane, leukotriene, and prostacyclin release
- Myocardial depressant factor
- Anaphylatoxins C5a and C3a
- Platelet-activating factor
- Oxygen-derived free radicals
- Bradykinin
- Beta-endorphins
GI Permeability
A Potential Cause of Autoimmune Disease

Increased Gut Permeability

Antigen

Enzymes

T Cell

B Cell
What if it isn’t SIBO?

**SIBO Treatment Protocol**

*Variation of the Cedars-Sinai Protocol (Pimentel 2006)*

Siebecker & Sandberg-Lewis (2014)

**SIBO Suspected**

- **Non-Diagnostic Tests**
  1. PE: TCV, Acid Resistant Reflex
  2. Blood Tests: CBC, ESR, Thyroid, CV, KD
  3. Stool Test (fatty malabsorption)
  4. Stool/Gastro-Test or Heidelberg
  5. Celiac, Intestinal permeability, Food allergy/sensitivity
  6. Endo Colonoscopy

- **SIBO Lactulose Breath Test**
  Or: Glucose Breath Test

- **Hx**
  - GI: Erosa, GT, Motility

- **Treat SIBO**
  - 4 options

**Diet**
- SCD
- Elemental Diet
  - x 2-3 wks

**Herbal Antibiotics**
- 1. Berberine containing herbs
- 2. Allicin (methion)
- 3. Oregano
- 4. Neem
- 1-3 caps 2-3 x day x 4 weeks
- Optional: Probiotic, Anti-fungal

- **Feel Better: 90%**

**Prevention**
- 1. Diet (SCD, SIBO foodguide, etc)
- 2. Prokinetic x 3 mo^-
  - Esomeprazole 20mg qhs x 3 mo^-
  - Pantoprazole 0.5-2 mg qhs x 3 mo^-
  - LDN 2.5-4.5 mg x 2 mo^-
- 3. Probiotic: 4 HCl
- 4. BB healing supplements (optional)

**Antibiotics**
- 1. Rifaximin: Diarrhea/Alternating
  - 550mg tid x 14 days
- 2. Rifaximin + Neomycin: Constipation
  - 550mg tid = 500mg bid x 14 days
  or Flu = Metronidazole 250mg tid x 14 days
- Optional: Probiotic, Anti-fungal

- **Partial Improvement/Not Better**
  - Re-Assess

- **SIBO Breath Re-Test**

- **SIBO (-)**
  - Consider other Dx
  - Re-Treat

- **SIBO (+)**
  - Consider other Dx
  - Re-Treat

**Relapse**
a) 2 weeks elemental-only according to caloric needs
b) 2-4 weeks of half-elemental diet/ half-well tolerated foods/ GI support supplements
c) 2-4 months of half-elemental diet/ reintroduction of foods, one at a time/ probiotics/ GI support
d) Elemental diet-only as needed for 1-3 days during exacerbations
e) Elemental diet-only as needed for 1-3 days for “gut rest” immediately prior to implementing other supplementation and/or dietary protocols
Food re-introduction

• Start with KNOWN tolerated foods for 2-4 weeks
  – Keep inflammation low
  – Provides gut rest
  – Prevents major shifts in microbiota

• Reintroduce foods one at a time for 2-4 months
  – Just like elimination diet
  – Expands diet choices
  – Reduces dependence on supplementation
WHEREVER THE ART OF MEDICINE IS LOVED, THERE IS ALSO A LOVE OF HUMANITY.

Hippocrates
Greek Scientist
Questions, Comments, or Concerns?

- info@metabolic-treatment-center.com