Clinical Applications with DSL

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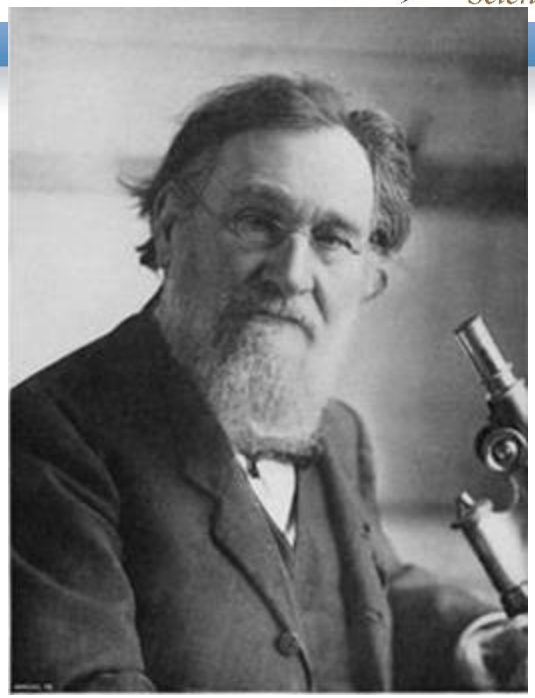
“Death Begins in The Colon”



- Ellie Metchnikoff, Russian biologist
- The rationale for the use of live microbes in the prevention and treatment of infections in 1907.
- He hypothesized that replacing or diminishing the number of bacteria in the gut, you could normalize bowel health and prolong life.

Potential Environmental Triggers

- Gluten
- Food Sensitivity
- Nutrient Deficiency
- Stress and Hormone Imbalance
- Dysbiosis
- Infections
- Toxins

What Patient Populations May Benefit from Stool Analysis?

- Inflammatory Bowel Issues
- Skin Conditions
- Fatigue of Unknown Origin
- Autoimmune Disorders
- Change in Bowel Habits

Conditions Associated with Dysbiosis and Intestinal Permeability

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Inflammatory Bowel Disease	Dermatitis Herpetiformis
Irritable Bowel Syndrome	Autism
Celiac Disease	Childhood Hyperactivity
Infectious Enterocolitis	Spondyloarthropathies
Cystic Fibrosis	Pancreatic Insufficiency
Chronic Fatigue Immune Deficiency Syndrome	Weight Gain
Acne	Neoplasia Treated with Cytotoxic Dr
Eczema	Hepatic Dysfunction
Psoriasis	Alcoholism
Urticaria	Environmental Illness

Unno N, Fink MP. Intestinal epithelial hyperpermeability. Mechanisms and relevance to disease. *Gastroenterol Clin North Am. 1998;27(2):289-307.*

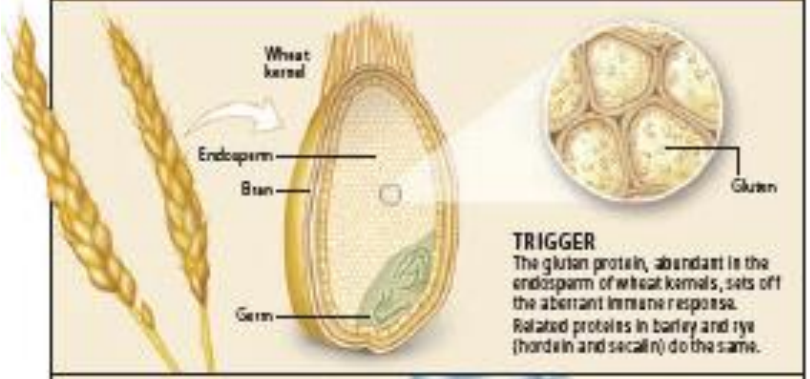
Intestinal barrier dysfunction

The gastrointestinal tract is 80% of our immune system. When inflammation is present, the tight junctions and intestinal mucosa can become damaged and inflamed causing gaps in the lining of the GI tract. Then toxic byproducts in the digestive tract can be absorbed into the bloodstream and carried on to the liver. The molecules of food and toxins are absorbed through the GI mucosa and then eventually they affect systems throughout the body causing inflammation in our joints, skin disorders, autoimmune conditions, and food sensitivities.

[OVERVIEW]

A TRIO OF CAUSES

Three factors underlie celiac disease: an environmental trigger, a genetic susceptibility and, according to the author's research, an unusually permeable gut (*below*). The author suspects that the same basic triad contributes to other autoimmune diseases, although each disorder will have its own triggers and genetic components.

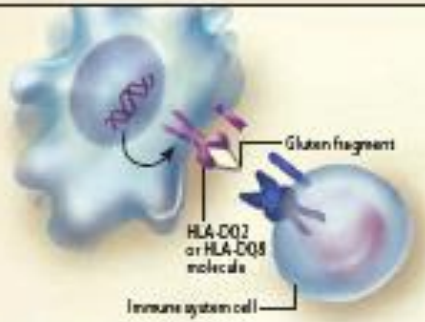


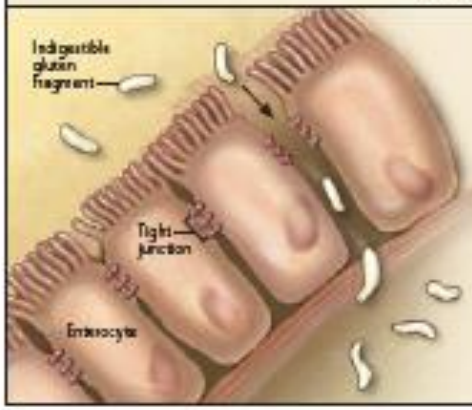
TRIGGER

The gluten protein, abundant in the endosperm of wheat kernels, sets off the aberrant immune response. Related proteins in barley and rye (hordein and secalin) do the same.

GENETIC PREDISPOSITION

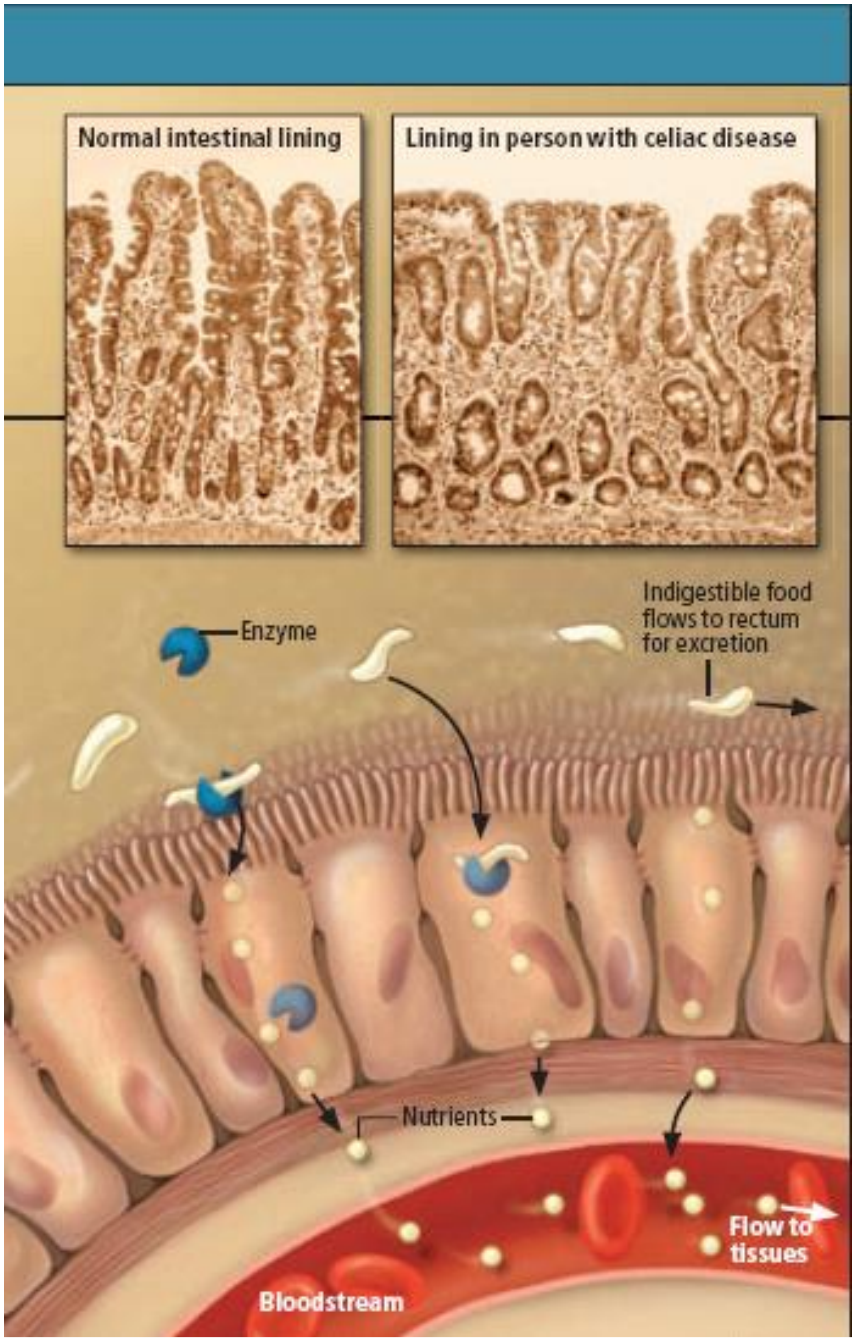
Almost all patients harbor a gene for either the HLA-DQ2 protein or the HLA-DQ8 protein, or both. These HLA molecules display gluten fragments to immune system cells, which then direct an attack on the intestinal lining. Other genes are likely to be involved as well, but these additional culprits may differ from person to person.





LEAKY SMALL INTESTINE

In most people, links known as tight junctions "glue" intestinal cells together. In those with celiac disease, the junctions come apart, allowing a large amount of indigestible gluten fragments to seep into the underlying tissue and incite immune system cells. Treatments that reduced leakiness could potentially ease not only celiac disease but also other autoimmune disorders involving unusually permeable intestines.



cholera. At that time, the cholera toxin was believed to be the sole cause of the devastating diarrhea characteristic of that infection. To test this hypothesis, my team deleted the gene encoding the cholera toxin from the bacterium *Vibrio cholerae*. Conventional wisdom suggested that bacteria disarmed in this way would make an ideal vaccine, because the remaining proteins on a living bacterial cell would elicit a strong immune response that would protect against diarrhea.

But when we administered our attenuated bacteria to volunteers, the vaccine provoked enough diarrhea to bar its use. I felt completely disheartened. Years of hard work were literally down the toilet, and we were faced with two unattractive options: giving up and moving on to another research project or persevering and trying to understand what went wrong. Some intuition that there was more to this story prompted us to choose the latter path, and this decision led us to discover a new toxin that caused diarrhea by a previously undescribed mechanism. It changed the permeability of the small intestine by disassembling those supposedly inert tight junctions, an effect that allowed fluid to seep from tissues into the gut. This "grout" was interesting after all.

Indeed, at nearly the same time, a series of seminal discoveries clarified that a sophisticated meshwork of proteins forms the tight junctions; however, little information was available on how these structures were controlled. Therefore, the discovery of our toxin, which we called the "*zonula occludens* toxin," or Zot (*zonula occludens* is Latin for "tight junction"), provided a valuable tool for clarifying the control process. It revealed that a single molecule, Zot, could loosen the complex structure of the tight junctions. We also realized that the control system that made this loosening possible was too complicated to have evolved simply to cause biological harm to the host. *V. cholerae* must cause diarrhea by exploiting a preexisting host pathway that regulates intestinal permeability.

Five years after the formulation of this hypothesis, we discovered zonulin, the protein that in humans and other higher animals increases intestinal permeability by the same mechanism as the bacterial Zot. How the body uses zonulin to its advantage remains to be established. Most likely, though, this molecule, which is secreted by intestinal epithelial tissue as well as by cells in other organs (tight junctions have important roles in tissues throughout the body), performs

[MYSTERY]

A Clue to Delayed Onset

People with celiac disease are born with a genetic susceptibility to it. So why do some individuals show no evidence of the disorder until late in life? In the past, I would have said that the disease process was probably occurring in early life, just too mildly to cause symptoms. But now it seems that a different answer, having to do with the bacteria that live in the digestive tract, may be more apt.

These microbes, collectively known as the microbiome, may differ from person to person and from one population to anot
progresses. Apparently they can also inf
at any given time. Hence, a person whos
gluten for many years might suddenly lo
a way that causes formerly quiet suscept
correct, celiac disease might one day be
helpful microbes, or "probiotics."

WHY REPLACING WHEAT IS HARD

Gluten is a major reason that wheat-based baked goods are light and airy. During baking, gluten strands trap water and carbon dioxide gas (from yeast and other leavening agents) and expand. To make gluten-free items, bakers generally combine several flours (as well as starches and additives), because no single variety mimics the properties of wheat flour. This demand adds significantly to the cost of the resulting product. It also explains why gluten-free foods have a hard time rivaling their gluten-containing counterparts for taste and texture. —*A. F.*

Discovery of zonulin prompted us to search the medical literature for human disorders characterized by increased intestinal permeability. It was then that we first learned, much to my surprise, that many autoimmune diseases—among them, CD, type 1 diabetes, multiple sclerosis, rheumatoid arthritis and inflammatory bowel diseases—all have as a common denominator aberrant intestinal permeability. In many of these diseases, the increased permeability is caused by abnormally high levels of zonulin. And in CD, it is now clear that gluten itself prompts exaggerated zonulin secretion (perhaps because of the patient's genetic makeup).

Therapies to Topple the Trinity

As I mentioned before, and as this theory would predict, removing gluten from the diet ends up healing the intestinal damage. Regrettably, a lifelong adherence to a strict gluten-free diet is not easy. Gluten is a common and, in many countries, unlabeled ingredient in the human diet. Further complicating adherence, gluten-free products are not widely available and are more

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Intestinal Barrier Dysfunction Develops at the Onset of Experimental Autoimmune Encephalomyelitis, and Can Be Induced by Adoptive Transfer of Auto-Reactive T Cells

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Abstract

Multiple
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Researchers at Lund University have published new research findings on the role of the intestinal barrier in the autoimmune disease multiple sclerosis (MS). Scientists at Lund University have previously shown that probiotics could provide a certain amount of protection against MS. Therefore, they questioned whether the intestinal barrier was affected, which led to their examination of inflammatory cells and processes in the intestine. As a result, they saw structural changes in the gastrointestinal mucosa of the small intestine and an increase in inflammatory T-cells. In addition, they saw a reduction in regulatory T-cells (immunosuppressive cells). These changes are often linked to inflammatory bowel diseases. Dr. Lavasani and his colleagues believe that future drugs to treat MS should not only focus on the central nervous system, but also on repairing and restoring the intestinal barrier. They hope for the development of a better treatment that looks at the intestinal barrier as a new therapeutic target.

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Funding: Th
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Competing Interests: The authors have read the journal's policy and declare that Dr. Shahram Lavasani (SL) is a part time employee and stakeholder of

Source: Intestinal Barrier Dysfunction Develops at the Onset of Experimental Autoimmune Encephalomyelitis, and Can Be Induced by Adoptive Transfer of Auto-Reactive T Cells. Mehrnaz Nouri, Anders Bredberg, Björn Weström, Shahram Lavasani. Published: September 03, 2014. DOI: 10.1371/journal.pone.0106335

Biochemical Individuality

- Patients with similar symptoms can have totally different test results
- Patients with similar test results can have totally different symptoms
- Protocol driven treatments can fail
- Test. Don’t Guess

Treatment Considerations Based on Test Results

- **GI – 4Rs**
  - **Remove** food sensitivities, alcohol, aspirin, NSAIDS from the diet. Use antimicrobials for dysbiosis, infections, and/or parasites.
  - **Replace** digestive enzymes and HCL if necessary.
  - **Reinoculate** the bowel with pre- and probiotics.
  - **Repair** the GI mucosa with healing nutrients and botanicals.

REMOVE

Remove food sensitivities, alcohol, aspirin, NSAIDS from the diet. Use antimicrobials for dysbiosis, infection, and/or parasites.

	Patient:	Accession: 20160217-0002
	Collected: 02/15/2016	Received: 02/17/2016
	DOB:	Completed: 03/01/2016

Ordered by: Michael Jurgelewicz, DC

Pathogens

Bacterial Pathogens	Result	Expected
Campylobacter	Negative	Neg
C. difficile Toxin A	Positive	Neg
C. difficile Toxin B	Negative	Neg
E. coli O157	Negative	Neg
Enterotoxigenic *E. coli* LT	Negative	Neg
Enterotoxigenic *E. coli* ST	Negative	Neg
Shiga-like Toxin *E. coli* stx1	Negative	Neg
Shiga-like Toxin *E. coli* stx2	Negative	Neg
Salmonella	Negative	Neg
Shigella	Negative	Neg
Vibrio cholera	Negative	Neg
Yersinia enterocolitica	Negative	Neg
Parasitic Pathogens		
Cryptosporidium	Negative	Neg
Entamoeba histolytica	Positive	Neg
Giardia	Negative	Neg
Viral Pathogens		
Adenovirus 40	Negative	Neg
Adenovirus 41	Negative	Neg
Norovirus GI	Negative	Neg
Norovirus GII	Negative	Neg
Rotavirus A	Negative	Neg

Accession: 20160217-0002

Opportunistic Bacteria			
Potential Autoimmune Triggers	Result		Range
Citrobacter spp.	<dl		<1.0 E4
Klebsiella pneumoniae	<dl		<7.2 E3
Proteus spp.	<dl		<6.2 E3
Proteus mirabilus	<dl		<1.0 E3
Yersinia enterocolitica (from pg 1)	Negative		Neg
Additional Dysbiotic/Overgrowth Bacteria			
Morganella morganii	5.4 E3	High	<1.0 E3
Pseudomonas spp.	6.8 E3	High	<2.5 E3
Pseudomonas aeruginosa	<dl		<1.0 E3
Staphylococcus spp.	<dl		<1.0 E4
Streptococcus spp.	<dl		<1.0 E3
Parasites			
Blastocystis hominis	Negative		Neg
Dientamoeba fragilis	Negative		Neg
Endolimax nana	Negative		Neg
Entamoeba coli	Negative		Neg
Chilomastix mesnelli	Negative		Neg
Cyclospora cayetanenensis	Negative		Neg
Pentatrichomonas hominis	Negative		Neg
Fungi/Yeast			
Candida albicans	<dl		<5.0 E3
Candida spp.	Negative		Neg
Geotricum spp.	Negative		Neg
Microsporidia spp.	Negative		Neg
Trichosporon spp.	Negative		Neg

Gut Microbes and Systemic Pathology

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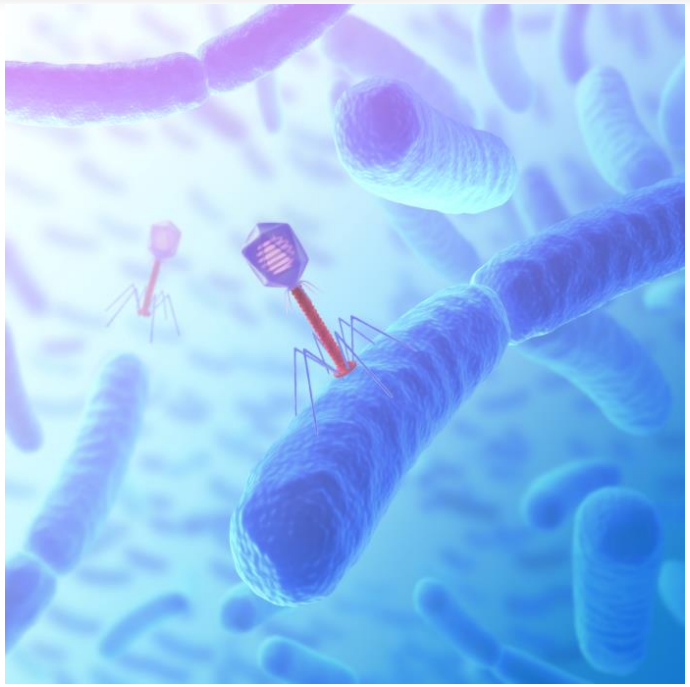
- Examples of epidemiologic associations between GI microbes and systemic autoimmune pathology:
  - *Klebsiella*: Ankylosing Spondylitis
  - *Citrobacter, Klebsiella,* Proteus Rheumatoid Arthritis
  - *Yersinia*: Grave's Disease & Hashimoto's Dz.
  - *S. Pyogenes*: Rheumatic Fever
  - *Camphylobacter jejuni*: Gullian Barre Syndrome
  - *E. coli*, Proteus: Autoimmunity in general

Modified from: Mayes MD. Epidemioloic studies of environmental agents and systemic autoimmune diseases. *Environ Health Perspect* 1999;107(suppl. 5):743-748

Remove

- Berberine – evidence against all microbes
- Wormwood & Black walnut – anti-parasitic
- Grapefruit & Bearberry – anti-bacterial, anti-fungal
- Caprylic acid – easily penetrates fatty cell membranes altering pathogen membrane fluidity
- Oil of Oregano- anti-fungal
- Allicin- anti-fungal
- Olive Leaf Extract- antimicrobial, antiviral
- Silver- antimicrobial, antiviral
- Monolaurin- antiviral
- Evidence supports sparing nature of the normal flora

Bacteriophages



- Inhibits *E. coli*
  (E.coli K-12, E.coli B, 16 ETEC strains, and 2 EHEC strains
- Prebiotic
- Effective in small doses
- Efficacious with hours
- Active in the small and large intestine
- Fermentation does not produce discomfort

H. pylori

H. pylori			
Helicobacter pylori	**2.5 E5**	**High**	<7.0 E3
Virulence Factor, cagA	**Positive**		Neg
Virulence Factor, vacA	**Negative**		Neg

Antibiotic Resistance Genes			
	Phenotype	Genotype	Expected
H. pylori			
Clarithromycin	**Negative**	**Negative**	Neg
Fluoroquinolones	**Positive**	**Positive**	Neg

Remove

- Mastic Gum
- Methylmethionesulfonium (Vitamin U)
- Deglycyrrhizinated Licorice (DGL)
- Zinc Carnosine
- Vitamin C

REPLACE

Replace digestive enzymes and HCL if necessary.

Digestion

Additional Tests			
	Result		Range
SIgA	**221**	Low	510-2040 ug/mL
Anti-gliadin	**0.7**		0.0-6.4 ug/mL
Elastase 1	**78**	Low	>200 ug/ml
Lactoferrin	**0.8**		0.0-7.2 ug/mL
Occult blood	Positive		neg

Elastase 1

- Excreted by the pancreas exclusively and has a direct correlation with pancreatic function.
- Not affected by pancreatic enzyme replacement therapy

Digestion

- Elastase, unlike chymotrypsin, has been found via quantitative studies to remain unaffected during intestinal transit and to be stable in stool samples for up to a week at room temperature.
- Elastase can not be detected in bovine or porcine pancreatic enzyme preparations. Unlike chymotrypsin, it is not affected by oral pancreatic enzyme replacement therapy.

Digestion

Elastase is also *Not Affected* by:

- Previous Gastrointestinal Surgery
- Gastric Dysmotility
- Mucosal Disease of the Small Intestine.

Digestion

Additional Tests			
	Result		Range
Secretory IgA	**1491**		510 - 2010 ug/g
Anti-gliadin IgA	**209**	**High**	0 - 100 U/L
Elastase-1	**139**	**Low**	>200 ug/g
Calprotectin	**5**		<50 ug/g
b-Glucuronidase	**1892**	**High**	<1123 U/mL
Steatocrit	**33**	**Very High**	<15 %
Fecal Occult Blood	**Negative**		Negative

Fecal Fat

- a marker of fat breakdown and absorption
- under normal conditions, the bulk of dietary fat is digested and absorbed in the small intestine, leaving only small amounts for delivery to the colon and fecal stream. Fecal fat measurements determine the amount of fat in stool, and may therefore identify fat maldigestion, malabsorption, or steatorrhea.
- Treatment
  - Treat underlying issue
  - Support digestion
    - HCL, pepsin, digestive enzymes, bile salts

Fecal Fat

- Causes
  - Malabsorption
    - Diarrhea
    - Dysbiosis
    - Parasites
    - Colitis
    - Gluten intolerance
    - Food allergy
    - Pancreatic or bile salt insufficiency
    - Chronic NSAID Use
  - High dietary fat intake
  - Medications designed to bind and eliminate fats
  - SIBO

REINOCULATE

Reinoculate the bowel with pre- and probiotics.

Commensal Bacteria

Normal Bacterial Flora			
Bifidobacter	**6.8 E9**	**Low**	>8.9 E9
Enterococcus	**4.1 E4**		1.2 E4 - 3.1 E6
E. coli	**3.5 E7**		1.0 E4 - 7.6 E7
Lactobacillus	**7.3 E5**	**Low**	1.0 E6 - 5.8 E9

Low Commensal Bacteria

- Causes
  - Antibiotics, diarrhea, Imbalanced diet
- ↑ risk of opportunistic and/or pathogenic organisms
- Re-inoculate with pre- and probiotics

RESEARCH ARTICLE

Same Exposure but Two Radically Different Responses to Antibiotics: Resilience of the Salivary Microbiome versus Long-Term Microbial Shifts in Feces

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Department of Preventive Dentistry, Academic Centre for Dentistry Amsterdam, University of Amsterdam and VU University Amsterdam, Amsterdam, The Netherlands[a]; Swammerdam Institute for Life Sciences, University of Amsterdam, Amsterdam, The Netherlands[b]; Research Group Microbiology and Systems Biology, TNO Earth, Life and Social Sciences, Zeist, The Netherlands[c]; Department of Laboratory Medicine, Karolinska Institute, Karolinska University Hospital, Stockholm, Sweden[d]; Helperby Therapeutics Limited, London, United Kingdom[e]; Genetics and Genomic Medicine Programme, UCL Institute of Child Health, London, United Kingdom[f]; Department of Microbial Diseases, UCL Eastman Dental Institute, London, United Kingdom[g]

ABSTRACT Due to the spread of resistance, antibiotic exposure receives increasing attention. Ecological consequences for the different niches of individual microbiomes are, however, largely ignored. Here, we report the effects of widely used antibiotics (clindamycin, ciprofloxacin, amoxicillin, and minocycline) with different modes of action on the ecology of both the gut and the oral microbiomes in 66 healthy adults from the United Kingdom and Sweden in a two-center randomized placebo-controlled clinical trial. Feces and saliva were collected at baseline, immediately after exposure, and 1, 2, 4, and 12 months after administration of antibiotics or placebo. Sequences of 16S rRNA gene amplicons from all samples and metagenomic shotgun sequences from selected baseline and post-antibiotic-treatment sample pairs were analyzed. Additionally, metagenomic predictions based

IMPORTANCE Many health care professionals use antibiotic prophylaxis strategies to prevent infection after surgery. This practice is under debate since it enhances the spread of antibiotic resistance. Another important reason to avoid nonessential use of antibiotics, the impact on our microbiome, has hardly received attention. In this study, we assessed the impact of antibiotics on the human microbial ecology at two niches. We followed the oral and gut microbiomes in 66 individuals from before, immediately after, and up to 12 months after exposure to different antibiotic classes. The salivary microbiome recovered quickly and was surprisingly robust toward antibiotic-induced disturbance. The fecal microbiome was severely affected by most antibiotics: for months, health-associated butyrate-producing species became strongly underrepresented. Additionally, there was an enrichment of genes associated with antibiotic resistance. Clearly, even a single antibiotic treatment in healthy individuals contributes to the risk of resistance development and leads to long-lasting detrimental shifts in the gut microbiome.

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11/10/2015

Probiotics

- Single and multispecies probiotics
- *Saccharomyces boulaurdii*

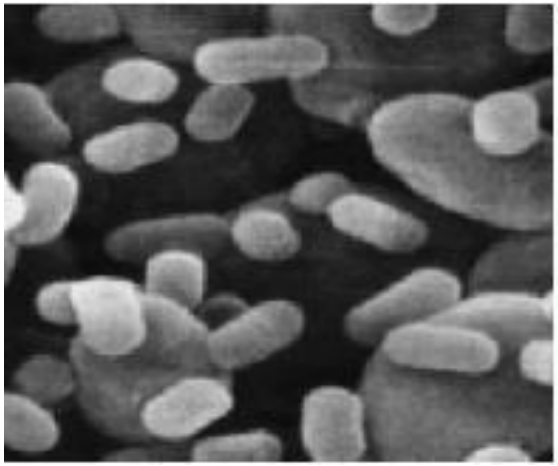
Saccharomyces boulardii

- A nonpathogenic, probiotic yeast.
- Protects the intestinal epithelial cells and supports intestinal barrier function.
- Increases sIgA secretion
- Directly inhibits colonization of harmful bacteria.

Saccharomyces boulardii

- Protects gastrointestinal tract during antibiotic therapy
- Restores normal intestinal function in children and adults with diarrhea
- Prevents traveler's diarrhea
- *C. difficile*
- Inflammatory Bowel Disease

Saccharomyces boulardii



Binding of enterohaemorrhagic E.coli

S. boulardii through its mannose-dominant outer membrane has the ability to bind E. coli and Salmonella, bacteria responsible for diarrhea, especially traveller's diarrhea. The large cell surface of the yeast allows the binding of many bacterial cells limiting their capacity to bind to the intestinal epithelium. In this way the bacteria are likely to be eliminated in the stools.

In a placebo-controlled study (Surawicz *et al*.,1989) on patients under antibiotic treatment the following results were obtained:

Although *S. boulardii* does not suppress all antibiotic-associated diarrhea, the fact that it reduces the risk by half is significant (Marteau,2000).

	Placebo group	*S. boulardii* group
% of patients with diarrhea	21.8 %	**9.5** %

Saccharomyces boulardii

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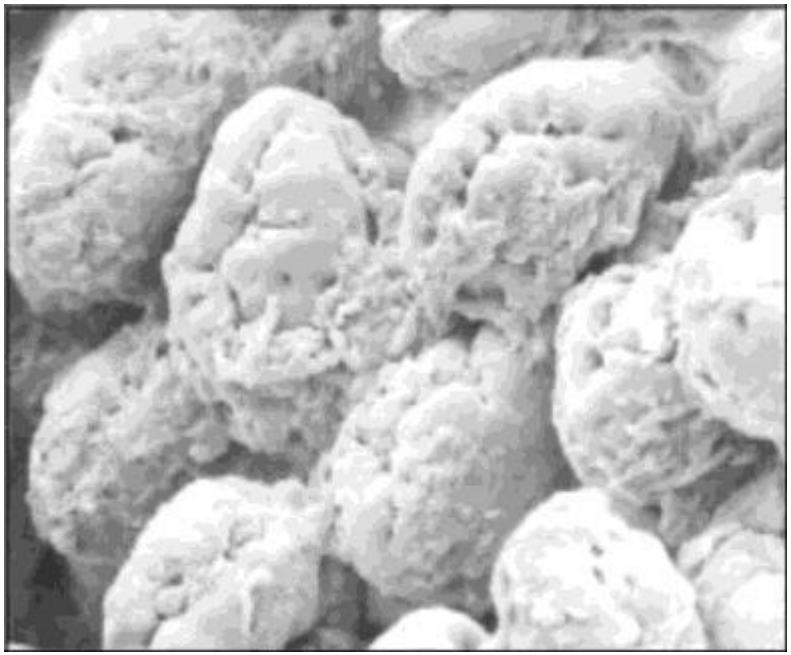
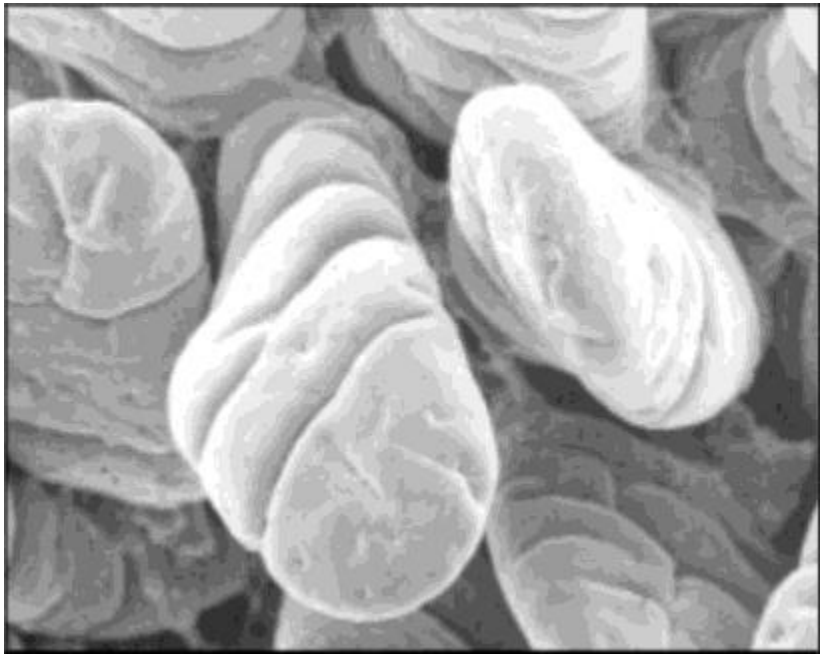
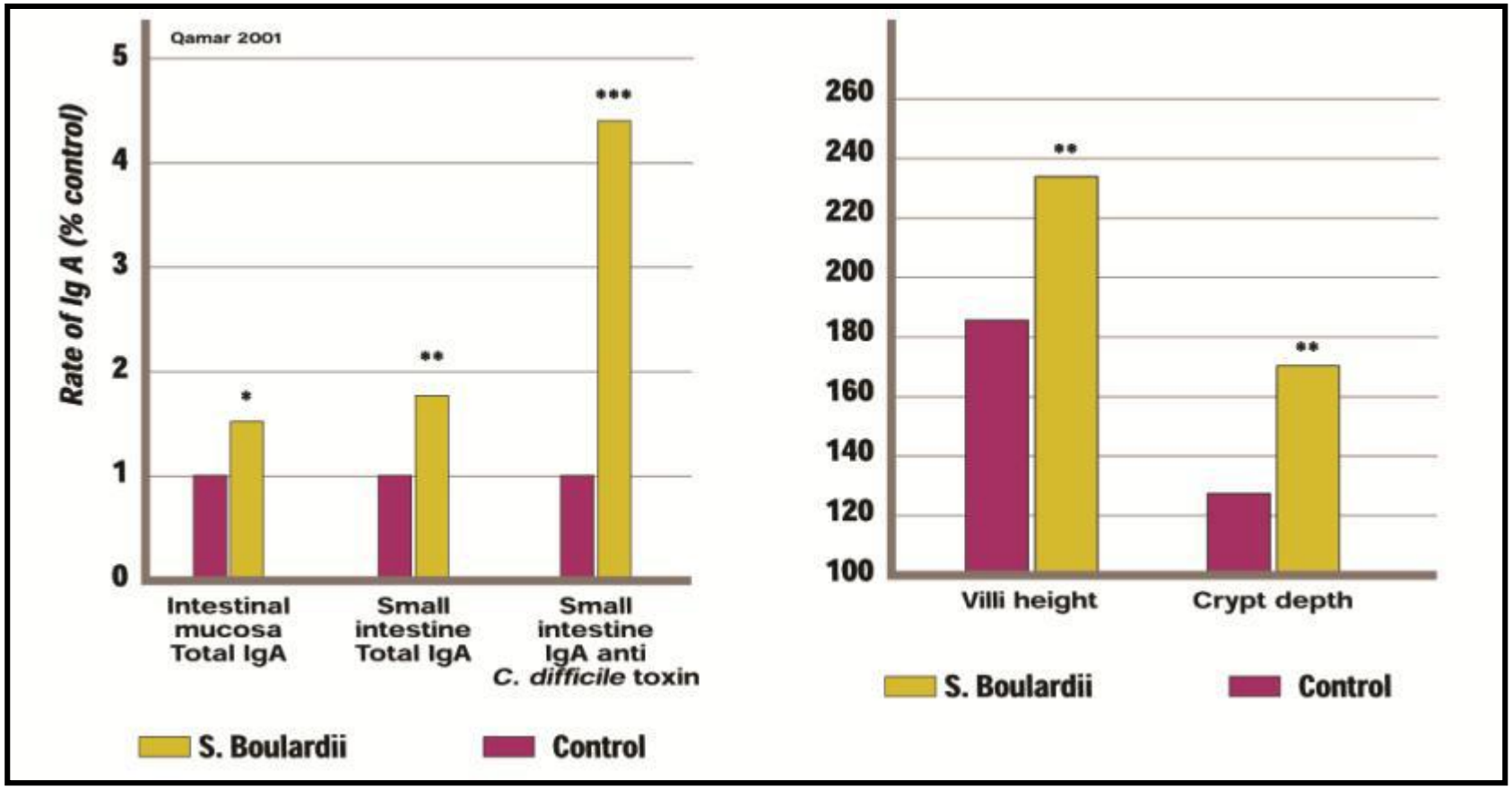


Jejunum of mice infected by Clostridium difficile



Jejunum of mice protected by S.boulardii after infection with Clostridium difficile

Saccharomyces boulardii



Efficacy and safety of the probiotic *Saccharomyces boulardii* for the prevention and therapy of gastrointestinal disorders

Ther Adv Gastroenterol
(2012) 5(2) 111–125
DOI: 10.1177/1756283X11428502

Theodoros Kelesidis and Charalabos Pothoulakis

Abstract: Several clinical trials and experimental stud
Saccharomyces boulardii as a biotherapeutic agent for
several gastrointestinal diseases. *S. boulardii* mediates
effects of the normal healthy gut flora. The multiple m
and its properties may explain its efficacy and benefici
gastrointestinal diseases that have been confirmed by
taken in patients with risk factors for adverse events.
for efficacy and safety of *S. boulardii* as a probiotic for
gastrointestinal disorders in humans.

Keywords: efficacy, gastrointestinal disorders, probiot

Introduction

There is increasing evidence that the gastrointestinal microflora is a major regulator of the immune system, not only in the gut, but also in other organs [Gareau *et al.* 2010]. The nonpathogenic yeast *Saccharomyces boulardii* has been prescribed in the past 30 years for prophylaxis and treatment of diarrheal diseases caused by bacteria. Importantly, *S. boulardii* has demonstrated clinical and experimental effectiveness in gastrointestinal diseases with a predominant inflammatory component, indicating that this probiotic might interfere with cellular signaling pathways common in many inflammatory conditions. The goal of this study is to review the clinical evidence for efficacy and safety of *S. boulardii* in the prevention and treatment of gastrointestinal disorders with diverse etiology.

Saccharomyces boulardii as a probiotic

An increasing number of potential health benefits are being attributed to probiotic treatments [Gareau *et al.* 2010; Szajewska *et al.* 2006]. However, only a limited number have been confirmed in well-designed and conducted randomized controlled trials (RCTs) and even less in the pediatric population. *S. boulardii* is a live yeast used extensively as a probiotic and often

a scarcity of data [Floch *et al.* 2008]. In a small pilot study of 31 patients with Crohn's disease in remission all patients continued their maintenance medications and were randomized to either *S. boulardii* for 3 months or placebo [Garcia *et al.* 2008]. Those treated with *S. boulardii* were found to have a significant reduction in colonic permeability compared with those given placebo, thus reducing the risk of bacterial translocation in these patients [Garcia *et al.* 2008]. Two RCTs tested *S. boulardii* for patients with Crohn's disease [Guslandi *et al.* 2000; Plein and Hotz, 1993]. In a small randomized study of 20 patients with Crohn's disease all patients continued their maintenance medications and were randomized to either *S. boulardii* for 7 weeks or placebo. Patients treated with *S. boulardii* were significantly improved compared with the placebo group [Plein and Hotz, 1993]. Finally, in a study of 32 patients with Crohn's disease who were in remission, significantly fewer patients treated with *S. boulardii* (6%) relapsed than the control group (38%) [Guslandi *et al.* 2000]. Further studies to establish the efficacy of *S. boulardii* in treatment of Crohn's disease are needed.

REPAIR

Repair the GI mucosa with healing nutrients and botanicals.

GI repair nutrients

Zinc Carnosine- *Intestinal lining*

- Mucosal- protective and anti-ulcerative
- Protects the intestinal lining against damage due to strong anti-inflammatory medications often associated with intestinal mucosal damage.

L-Glutamine- *Intestine repair*

- Supports tissue repair, particularly high turnover tissue such as the epithelial cells of the intestinal lining.
- Shown to have specific GI mucosal protective action:
    - immunomodulatory
    - anticatabolic/anabolic
- Antioxidant activity as it is a precursor for glutathione synthesis
- Essential in maintaining proper intestinal permeability

Mucin-*Intestinal lining support*

- A glycoprotein, used to coat the intestinal lining and to neutralize intestinal antigens and sIgA.

GI Repair Nutrients

N-Acetyl Glucosamine- *GI tissue support*

- Promotes the production of health supportive structures for the cells of the intestinal lining
- Supports increased production of glycosaminoglycans (GAGs) for proper mucosal health and reduced intestinal permeability.

DGL, Slippery Elm, Marshmallow, Chamomile, Okra, and Cat's Claw *GI soothing*

- Provides comprehensive enhancement of intestinal function by coating and soothing the intestinal lining.

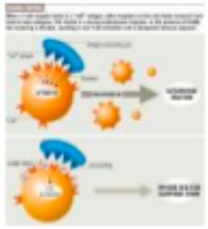
Omega-3 fatty acids and Polyphenols - curcumin, boswellia, ginger, quercetin, rutin, rosemary, resveratrol, EGCg - *Reduction of inflammation*

- Can reduce the chronic inflammation of the intestinal lining
- Quercetin can provide direct anti-inflammatory action by stabilizing intestinal mast cells

Sugar supplement may treat immune disease

07 June 2007 by Aria Pearson
Magazine issue 2607. Subscribe and get 4 free issues.

A sugar supplement may sweeten the overactive immune cells responsible for autoimmune diseases such as multiple sclerosis (MS) and type 1 diabetes and stop them attacking the body's tissues.



Crowd control

Enlarge image

Autoimmune diseases are triggered when receptors on the outside of immune cells called T-helper 1 (Th1) cells start binding "self" antigens rather than pieces of foreign invaders. Anything that decreases the amount of binding should suppress the autoimmune response.

Previous studies suggested that glucosamine, a dietary supplement commonly taken by people with osteoarthritis, has some immunosuppressive effects. This led Michael Demetriou and colleagues at the University of California, Irvine, to investigate a similar but more potent compound called N-acetylglucosamine (GlcNAc).

A large number of proteins in the body are modified by the attachment of sugar molecules to their surface through a process called glycosylation, and altered glycosylation has been implicated in some autoimmune diseases. Demetriou's team found that naturally occurring GlcNAc molecules attach to T-cell receptors and these GlcNAc "branches" form a lattice on the cell surface that prevents the receptors from clustering near where the antigens are located (see Diagram). Less clustering means less antigen binding, and less activation of Th1 cells, reducing the autoimmune reaction.

Mice given oral GlcNAc supplements had twice as much GlcNAc branching on their T-cell receptors as untreated mice. The researchers also found that T-cells engineered to cause the mouse equivalent of MS failed to do so if they had been incubated in GlcNAc first. A daily oral dose of GlcNAc also prevented type 1 diabetes in mice genetically engineered to develop the disease (*The Journal of Biological Chemistry*, DOI: 10.1074/jbc.M701890200).

T-cells engineered to cause the mouse equivalent of multiple sclerosis failed to do so if they had been incubated in GlcNAc

The researchers found that naturally occurring GlcNAc molecules attach to T-cell receptors and these GlcNAc "branches" form a lattice on the cell surface that prevents the receptors from clustering near where the antigens are located… less clustering means less antigen binding, and less activation of Th1 cells, reducing the autoimmune reaction

The Journal of Biological Chemistry, DOI: 10.1074/jbc.M701890200).

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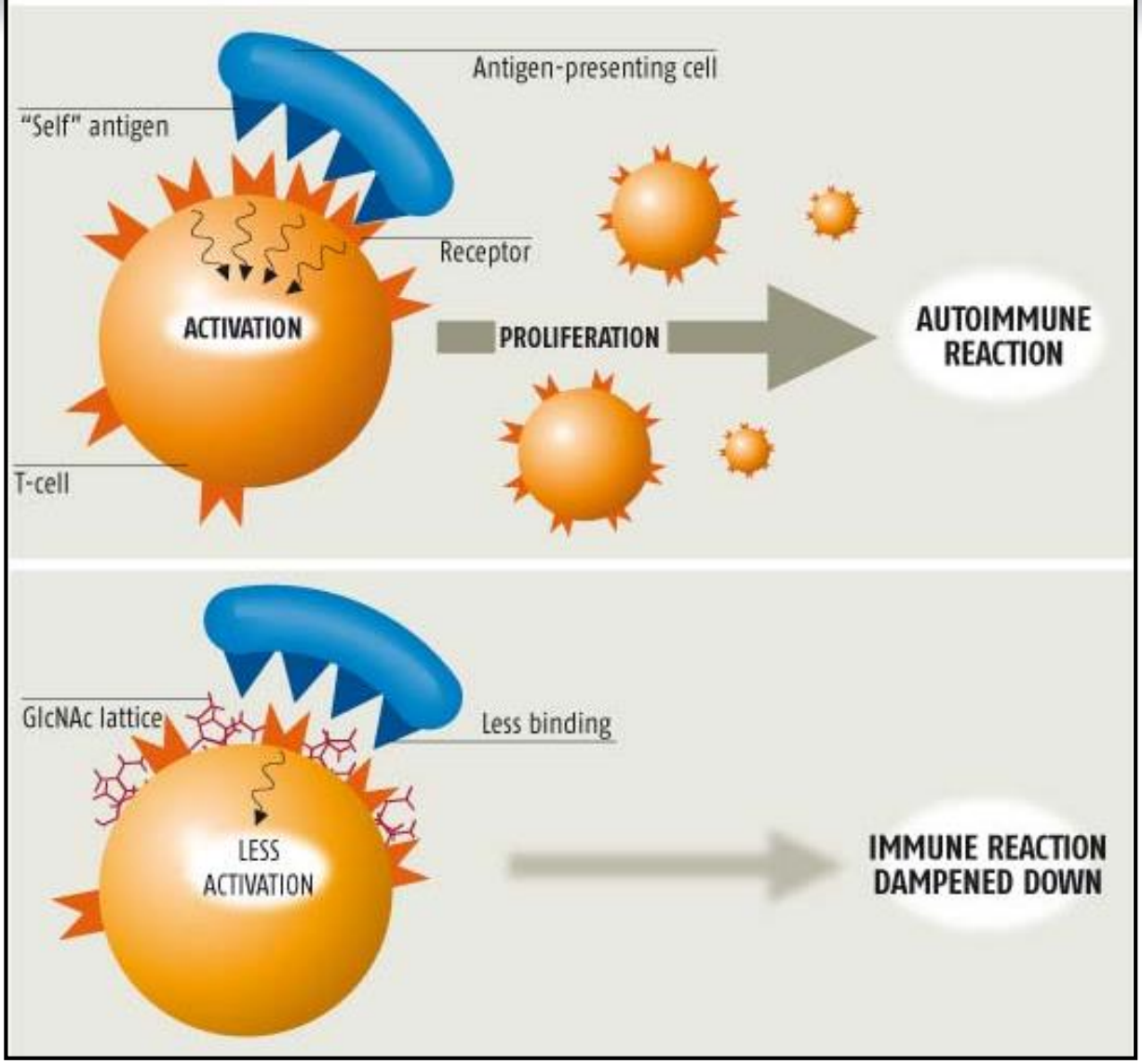
CROWD CONTROL

When a T-cell receptor binds to a "self" antigen, other receptors on the cell cluster around it and bind to more antigens. This results in a strong autoimmune response. In the presence of GlcNAc the clustering is blocked, resulting in less T-cell activation and a dampened immune response



SMALL INTESTINE

Zinc carnosine, a health food supplement that stabilises small bowel integrity and stimulates gut repair processes

A Mahmood, A J FitzGerald, T Marchbank, E Ntatsaki, D Murray, S Ghosh, R J Playford

Gut 2007;56:168–175. doi: 10.1136/gut.2006.099929

See end of article for authors' affiliations

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Accepted 30 May 2006
Published Online First 15 June 2006

Background: Zinc carnosine (ZnC) is a health food product claimed to possess health-promoting and gastrointestinal supportive activity. Scientific evidence underlying these claims is, however, limited.
Aim: To examine the effect of ZnC on various models of gut injury and repair, and in a clinical trial.
Methods: In vitro studies used pro-migratory (wounded monolayer) and proliferation ([^{3}H]-thymidine incorporation) assays of human colonic (HT29), rat intestinal epithelial (RIE) and canine kidney (MDCK) epithelial cells. In vivo studies used a rat model of gastric damage (indomethacin/restraint) and a mouse model of small-intestinal (indomethacin) damage. Healthy volunteers (n = 10) undertook a randomised crossover trial comparing changes in gut permeability (lactulose:rhamnose ratios) before and after 5 days of indomethacin treatment (50 mg three times a day) with ZnC (37.5 mg twice daily) or placebo coadministration.
Results: ZnC stimulated migration and proliferation of cells in a dose-dependent manner (maximum effects in both assays at 100 μmol/l using HT29 cells), causing an approximate threefold increase in migration and proliferation (both p<0.01). Oral ZnC decreased gastric (75% reduction at 5 mg/ml) and small-intestinal injury (50% reduction in villus shortening at 40 mg/ml; both p<0.01). In volunteers, indomethacin caused a threefold increase in gut permeability in the control arm; lactulose:rhamnose ratios were (mean (standard error of mean)) 0.35 (0.035) before indomethacin treatment and 0.88 (0.11) after 5 days of indomethacin treatment (p<0.01), whereas no significant increase in permeability was seen when ZnC was coadministered.
Conclusion: ZnC, at concentrations likely to be found in the gut lumen, stabilises gut mucosa. Further studies are warranted.

Currently, there is much interest in the value of natural medicinal products, functional foods and "nutriceuticals" to prevent or treat illness. Unfortunately, current evidence of the scientific validity of many of these traditional and commercial compounds is severely limited.

One such product is zinc carnosine (ZnC), which is an artificially produced derivative of carnosine, where zinc and carnosine are linked in a one-to-one ratio to provide a polymeric structure. This product is currently marketed by several companies as a zinc dietary supplement with "added value for gastric health". Combining zinc with carnosine could theoretically provide added benefits over simple zinc supplementation as carnosine is a dipeptide (comprising β-alanine and L-histidine) that is naturally present in long-living cells such as muscle and nerves, where, among other actions, it probably has a role as an antioxidant.[1]

To examine further its potential biological actions in a scientific setting, we have performed a series of studies to analyse ZnC in regard to its effects on various mechanisms of gut integrity and repair using well-validated in vitro and in vivo models, and in a clinical trial.

MATERIALS AND METHODS

All chemicals were purchased from Sigma (Poole, Dorset, UK) unless otherwise stated. ZnC was provided by Lonza Nutrition (USA).

Ethics

All animal experiments were approved by local animal ethics committees and covered by the appropriate licences under the Home Office Animals Procedures Acts, 1986. The clinical trial was approved by a local ethics committee and conformed to national requirements.

Study series A: Effect of ZnC on in vitro models of repair

Background to methods

One of the earliest repair responses after injury to tissue is the migration of surviving cells over any denuded area to re-establish epithelial integrity. As it is extremely difficult to study this effect in a human or animal, cell culture models are commonly used as surrogate markers of this pro-migratory response.

Cell migration as a model of wound repair

Cell migration assays were performed using our previously published methods.[2] Two cell lines were assessed: the human colonic carcinoma cell line HT29 and the canine epithelial kidney cell line MDCK.

Cells were grown to confluence in six-well plates in Dulbecco's modified Eagle medium (DMEM) containing 10% fetal calf serum at 37°C in 5% CO_2 and were then serum starved for 24 h. The monolayers were then wounded by scraping a disposable pipette tip across the dishes, washed with fresh serum-free medium and cultured in serum-free medium in the presence of 1–1000 μM ZnC, equimolar zinc sulphate or equivalent bovine serum albumin (BSA) concentrations (to analyse non-specific protein effects). Additional monolayers

Abbreviations: ANOVA, analysis of variance; BrdU, bromodeoxyuridine; BSA, bovine serum albumin; DMEM, Dulbecco's modified Eagle medium; EGF, epidermal growth factor; HPLC, high-pressure liquid chromatography; NSAID, non-steroidal anti-inflammatory drug; RIE, rat intestinal epithelium; ZnC, zinc carnosine

In volunteers, indomethacin caused a threefold increase in gut permeability in the control arm; lactulose:rhamnose ratios were (mean (standard error of mean)) 0.35 (0.035) before indomethacin treatment and 0.88 (0.11) after 5 days of indomethacin treatment (p,0.01), whereas no significant increase in permeability was seen when ZnC was coadministered.

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Dig Dis Sci. 2012 Apr;57(4):1000-12. doi: 10.1007/s10620-011-1947-9. Epub 2011 Oct 26.

Glutamine and whey protein improve intestinal permeability and morphology in patients with Crohn's disease: a randomized controlled trial.

Benjamin J[1], Makharia G, Ahuja V, Anand Rajan KD, Kalaivani M, Gupta SD, Joshi YK.

Author information

Abstract

BACKGROUND: Increased intestinal permeability (IP) has been implicated in the etiopathogenesis, disease activity and relapse of Crohn's disease (CD). Glutamine, the major fuel for the enterocytes, may improve IP.

AIM: We evaluated the effect of oral glutamine on IP and intestinal morphology in patients with CD.

METHODS: In a randomized controlled trial, consecutive patients with CD in remission phase with an abnormal IP were randomized to a glutamine group (GG) or active control group (ACG) and were given oral glutamine or whey protein, respectively, as 0.5 g/kg ideal body weight/day for 2 months. IP was assessed by the lactulose mannitol excretion ratio (LMR) in urine, and morphometry was performed by computerized image analysis system.

RESULTS: Patients (age 34.5 ± 10.5 years; 20 males) were assigned to the GG (n = 15) or ACG (n = 15). Fourteen patients in each group completed the trial. The LMR [median (range)] in GG and ACG at 2 months was 0.029 (0.006-0.090) and 0.033 (0.009-0.077), respectively, with P = 0.6133. IP normalized in 8 (57.1%) patients in each group (P = 1.000). The villous crypt ratio (VCR) [mean (SD)] in GG and ACG at 2 months was 2.68 (1.02) and 2.49 (0.67), respectively, (P = 0.347). At the end of 2 months LMR improved significantly in GG from 0.071 (0.041-0.254) to 0.029 (0.006-0.090) (P = 0.0012) and in ACG from 0.067 (0.040-0.136) to 0.033 (0.009-0.077) (P = 0.0063). VCR improved in the GG from 2.33 (0.77) to 2.68 (1.02) (P = 0.001), and in ACG from 2.26 (0.57) to 2.49 (0.67) (P = 0.009).

CONCLUSIONS: Intestinal permeability and morphology improved significantly in both glutamine and ACG.

JPEN J Parenter Enteral Nutr. 2015 May 13. pii: 0148607115587330. [Epub ahead of print]

Glutamine Restores Tight Junction Protein Claudin-1 Expression in Colonic Mucosa of Patients With Diarrhea-Predominant Irritable Bowel Syndrome.

Bertrand J[1], Ghouzali I[1], Guérin C[1], Bôle-Feysot C[1], Gouteux M[1], Déchelotte P[2], Ducrotté P[3], Coëffier M[4].

⊕ Author information

Abstract

BACKGROUND: Recent studies showed that patients with diarrhea-predominant irritable bowel syndrome (IBS-D) had an increased intestinal permeability as well as a decreased expression of tight junctions. Glutamine, the major substrate of rapidly dividing cells, is able to modulate intestinal permeability and tight junction expression in other diseases. We aimed to evaluate, ex vivo, glutamine effects on tight junction proteins, claudin-1 and occludin, in the colonic mucosa of patients with IBS-D.

MATERIALS AND METHODS: Twelve patients with IBS-D, diagnosed with the Rome III criteria, were included (8 women/4 men, aged 40.7 ± 6.9 years). Colonic biopsy specimens were collected and immediately incubated for 18 hours in culture media with increasing concentrations of glutamine from 0.6-10 mmol/L. Claudin-1 and occludin expression was then measured by immunoblot, and concentrations of cytokines were assessed by multiplex technology. Claudin-1 expression was affected by glutamine ($P < .05$, analysis of variance). In particularly, 10 mmol/L glutamine increased claudin-1 expression compared with 0.6 mmol/L glutamine (0.47 ± 0.04 vs 0.33 ± 0.03, $P < .05$). In contrast, occludin expression was not significantly modified by glutamine. Interestingly, glutamine effect was negatively correlated to claudin-1 (Pearson $r = -0.83$, $P < .001$) or occludin basal expression (Pearson $r = -0.84$, $P < .001$), suggesting that glutamine had more marked effects when tight junction protein expression was altered. Cytokine concentrations in culture media were not modified by glutamine treatment.

CONCLUSION: Glutamine increased claudin-1 expression in the colonic mucosa of patients with IBS-D. In addition, glutamine effect seems to be dependent on basal expression of tight junction proteins.

Immunology

Additional Tests			
	Result		Range
SIgA	**134**	**Low**	510-2040 ug/mL
Anti-gliadin	**9.3**	**High**	0.0-6.4 ug/mL
Elastase 1	**205**		>200 ug/ml
Lactoferrin	**16.2**	**High**	0.0-7.2 ug/mL
Occult blood	**Negative**		neg

SIgA

- The main antibody lining the gastrointestinal and respiratory tracts

Immunology

SIgA Low

- Chronic stress
- Immunocompromised
- Dysbiosis
- Immuno-compromised medications

SIgA High

- Immune response to pathogenic organisms in the GI tract
- Sensitivities to foods

Immunology

SIgA Low

- Probiotics *(S. boulardii, Bifidobacteria)*
- Colostrum
- Glutamine

SIgA High

- Remove pathogens, opportunistic bacteria, parasites, virus
- Rule of food sensitivities
- Elimination diet

Immunology

Additional Tests			
	Result		Range
SIgA	**134**	**Low**	510-2040 ug/mL
Anti-gliadin	**9.3**	**High**	0.0-6.4 ug/mL
Elastase 1	**205**		>200 ug/ml
Lactoferrin	**16.2**	**High**	0.0-7.2 ug/mL
Occult blood	**Negative**		neg

Anti-Gliadin Antibody (High)

- Gluten enteropathy or sensitivity in the colon
- Remove gluten
- Consider mucosal healing support [ie. GI Revive, Glutamine and/or AllerGzyme, Digestzymes (DPP-IV)]

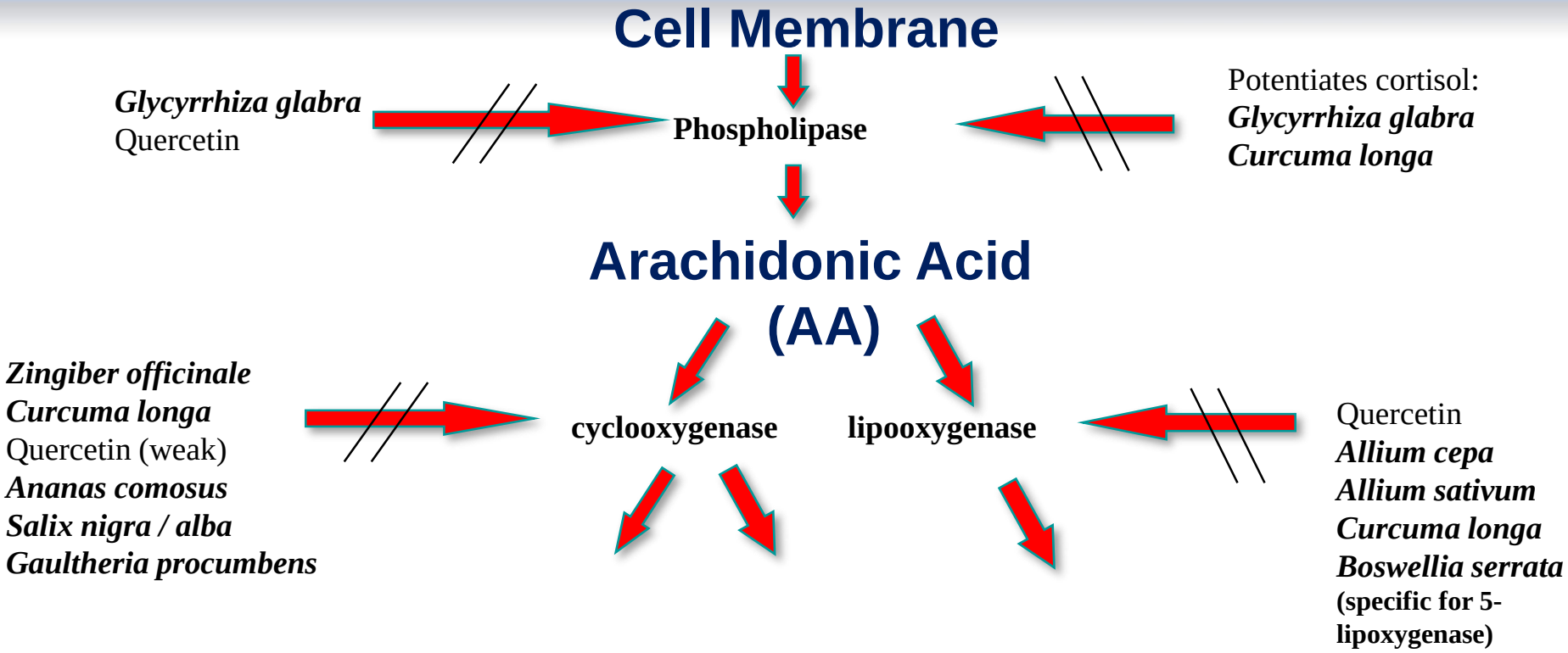
Inflammation

Additional Tests			
	Result		Range ug/g
Secretory IgA	**931**		510 - 2010
Anti-gliadin IgA	**105**	**High**	0 - 100
Elastase-1	**510**		>200
Calprotectin	**983**	**High**	<50
Fecal Occult Blood	**Negative**		Negative

Calprotectin

- A marker of neutrophil-driven inflammation
- Mucosal inflammation
- IBD (Crohn's, ulcerative colitis)
- Anti-inflammatory nutrients and botanicals (ie. GI repair nutrients, polyphenols, enzymes, curcumin, fish oil)

Botanical Modulation of Arachidonic Acid Cascade



Other Anti-Inflammatory Botanicals

Ananas comosus -- fibrinolysis, inhibits bradykinin, increases Series I Prostaglandins

Tanacetum parthenium -- inhibits platelet aggregation

Scutellaria baicalensis -- stabilizes mast cell membranes

Quercetin -- stabilizes mast cell membranes

Matricaria chamomilla -- unknown

Capsicum minimum -- depletes substance P

Ammi visnaga -- stabilizes mast cell membranes

Courtesy of: Eleanor Barrager, RD (Australia) and The Institute for Functional Medicine

β-Glucuronidase

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Additional Tests			
	Result		Range
Secretory IgA	**1491**		510 - 2010 ug/g
Anti-gliadin IgA	**209**	High	0 - 100 U/L
Elastase-1	**139**	Low	>200 ug/g
Calprotectin	**5**		<50 ug/g
b-Glucuronidase	**1892**	High	<1123 U/mL
Steatocrit	**33**	Very High	<15 %
Fecal Occult Blood	**Negative**		Negative

β-Glucuronidase

- an enzyme made by the body but mainly by intestinal bacteria.
- ↑ levels of β-glucuronidase may indicate an unfavorable environment in the gut.
- It is essential for detoxification
- excessive levels can promote the enterohepatic recirculation of toxins and hormones, which can ↑ carcinogens in the gut.
- ↑ levels have been observed in certain cancers.

β-Glucuronidase

- When levels are high, consider dietary, environmental, and gut health interventions to normalize gut microbiota and support detoxification pathways.
  - Probiotics
  - High fiber diet
  - Calcium D-Glucarate
  - Ascorbic acid (1500 mg/d)
  - Milk Thistle

Occult Blood

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Additional Tests			
	Result		Range
SIgA	**287**	**Low**	510-2040 ug/mL
Anti-gliadin	**1.4**		0.0-6.4 ug/mL
Elastase 1	**202**		>200 ug/ml
Lactoferrin	**46.6**	**High**	0.0-7.2 ug/mL
Occult blood	**Positive**		neg

Occult Blood (Positive)

- Upper GI bleed
  - Peptic ulcer, IBD, Parasite, Colon cancer, Hemmorrhoids
- Address GI dysfunction
- Rule of Iron deficiency anemia
- Anti-inflammatory diet
- Anti-inflammatory nutrients and botanicals

Case Studies

Using DFH Products and GI-MAP Testing

Case Study 1

Dr. Michael Jurgelewicz

A Case Study

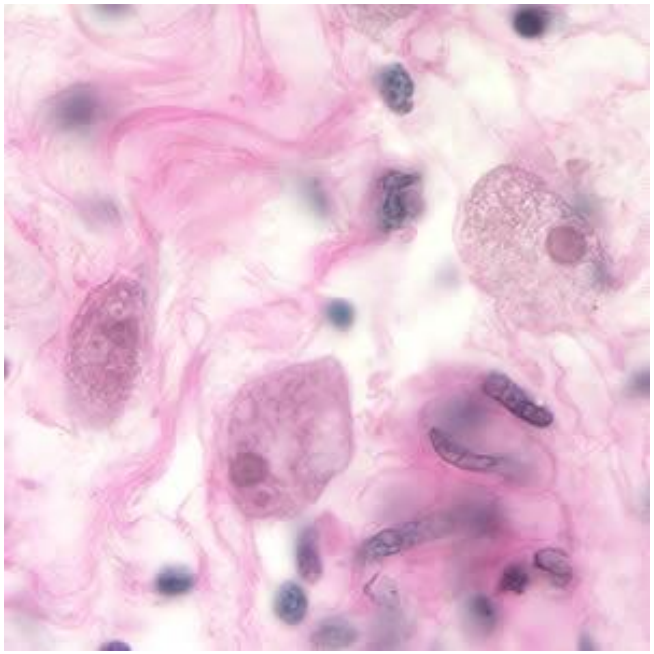
- History
  - 35-Year-Old Male
  - Lost 25 lbs without trying
  - Anxiety, Nervousness
  - Stomach Discomfort

	Patient:		Accession: 20150911-0006
	Collected:		Received: 09/11/2015
	DOB:		Completed: 09/17/2015

Ordered by: Michael Jurgelewicz, DC

Pathogens

Bacterial Pathogens	Result		Expected
Campylobacter	Negative		Neg
C. difficile Toxin A	Negative		Neg
C. difficile Toxin B	Negative		Neg
E. coli O157	Negative		Neg
Enterotoxigenic *E. coli* LT	Negative		Neg
Enterotoxigenic *E. coli* ST	Negative		Neg
Shiga-like Toxin *E. coli* stx1	Negative		Neg
Shiga-like Toxin *E. coli* stx2	Negative		Neg
Salmonella	Negative		Neg
Shigella	Negative		Neg
Vibrio cholera	Negative		Neg
Yersinia enterocolitica	Negative		Neg
Parasitic Pathogens			
Cryptosporidium	Negative		Neg
Entamoeba histolytica	Positive		Neg
Giardia	Negative		Neg
Viral Pathogens			
Adenovirus 40	Negative		Neg
Adenovirus 41	Negative		Neg
Norovirus GI	Negative		Neg
Norovirus GII	Negative		Neg
Rotavirus A	Negative		Neg
H. pylori			
Helicobacter pylori	2.5 E5	High	<7.0 E3
Virulence Factor, cagA	Negative		Neg
Virulence Factor, vacA	Negative		Neg
Normal Bacterial Flora			
Bifidobacter	1.6 E10		>8.9 E9
Enterococcus	5.3 E5		1.2 E4 - 3.1 E6
E. coli	7.1 E6		1.0 E4 - 7.6 E7
Lactobacillus	4.1 E9		1.0 E6 - 5.8 E9



Accession: 20150911-0006

Opportunistic Bacteria			
Potential Autoimmune Triggers	Result		Range
Citrobacter spp.	5.6 E3		<1.0 E4
Klebsiella pneumoniae	1.1 E3		<7.2 E3
Proteus spp.	<dl		<6.2 E3
Proteus mirabilus	<dl		<1.0 E3
Yersinia enterocolitica (from pg 1)	Negative		Neg
Additional Dysbiotic/Overgrowth Bacteria			
Morganella morganii	<dl		<1.0 E3
Pseudomonas spp.	5.2 E2		<2.5 E3
Pseudomonas aeruginosa	<dl		<1.0 E3
Staphylococcus spp.	4.3 E2		<1.0 E4
Streptococcus spp.	<dl		<1.0 E3
Parasites			
Blastocystis hominis	Negative		Neg
Dientamoeba fragilis	Negative		Neg
Endolimax nana	Positive		Neg
Entamoeba coli	Negative		Neg
Chilomastix mesnelli	Negative		Neg
Pentatrichomonas hominis	Negative		Neg
Microsporidia spp.	Negative		Neg
Fungi/Yeast			
Candida albicans	1.8 E3		<5.0 E3
Candida spp.	Negative		Neg
Cyclospora cayetanenensis	Negative		Neg
Geotricum spp.	Negative		Neg
Trichosporon spp.	Negative		Neg
Additional Tests			
	Result		Range
SIgA	5529	High	510-2040 ug/mL
Anti-gliadin	1		0.0-6.4 ug/mL
Elastase 1	**Pending		>175 mcg/g
Lactoferrin	23.4	High	0.0-7.2 ug/mL
Occult blood	Negative		neg

Accession: 20150911-0006

Antibiotic Resistance Genes	Phenotype	Genotype	Expected
H. pylori			
Clarithromycin	**Negative**	**Negative**	Neg
Fluoroquinolones	Positive	Positive	Neg

Phenotype; refers to resistance genes of the antibiotic/class that can be found on the genome of the positive organism.

Genotype; refers to resistance genes of the antibiotic/class that are not found on the genome of the positive organism but are found on genomes of bacteria of the microbiome.

Treatment Program

Gastrointestinal Support

- Comprehensive blend of botanical extracts used as natural antimicrobials, 2 capsules TID on an empty stomach
- *S. boulardii* 10 billion CFUs, 1 capsule BID with meals

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Patient:		Accession: 20151214-0007
Collected: 12/10/2015		Received: 12/14/2015
DOB:		Completed: 12/21/2015

Ordered by: Michael Jurgelewicz, DC

Pathogens		
Bacterial Pathogens	Result	Expected
Campylobacter	**Negative**	Neg
C. difficile Toxin A	**Negative**	Neg
C. difficile Toxin B	**Negative**	Neg
E. coli O157	**Negative**	Neg
Enterotoxigenic *E. coli* LT	**Negative**	Neg
Enterotoxigenic *E. coli* ST	**Negative**	Neg
Shiga-like Toxin *E. coli* stx1	**Negative**	Neg
Shiga-like Toxin *E. coli* stx2	**Negative**	Neg
Salmonella	**Negative**	Neg
Shigella	**Negative**	Neg
Vibrio cholera	**Negative**	Neg
Yersinia enterocolitica	**Negative**	Neg
Parasitic Pathogens		
Cryptosporidium	**Negative**	Neg
Entamoeba histolytica	**Negative**	Neg
Giardia	**Negative**	Neg
Viral Pathogens		
Adenovirus 40	**Negative**	Neg
Adenovirus 41	**Negative**	Neg
Norovirus GI	**Negative**	Neg
Norovirus GII	**Negative**	Neg
Rotavirus A	**Negative**	Neg
H. pylori		
Helicobacter pylori	**<dl**	<7.0 E3
Virulence Factor, cagA	**Negative**	Neg
Virulence Factor, vacA	**Negative**	Neg

Retest 3 months later

RA Case Study

Dr. Michael Jurgelewicz

A Case Study

- History
  - 51- Year-Old Female
  - c/o Joint pain
  - DX with RA in 1996

Medications

- Enbrel
- Previously taking Plaquenil and Celebrex

Initial Laboratory Results
Laboratory tests ordered and rationale

1. Multiprofile panel: A comprehensive assessment including organic acids and oxidative stress markers; assists in detecting individual etiopathologenic factors and in individualizing treatment plans.

2. Food-specific IgG antibodies: Food reactions have been associated with inflammation. Multiple IgG reactions suggest intestinal hyperpermeability. Removing offending foods may reduce inflammation.

3. Stool test: Assessment of GI microbial status and GI function. GI imbalances have been identified as involved in the pathogenesis of food sensitivities, food allergies, and autoimmune disorders.

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EDITORIAL

THE IMMUNOLOGY OF GLUTEN SENSITIVITY BEYOND THE INTESTINAL TRACT

A. VOJDANI, T. O'BRYAN[1] and G.H. KELLERMANN[2]

Immunosciences Lab., Inc., Beverly Hills, CA; [1]Davis Parkway, Wauconda, IL; [2]NeuroScience, Osceola,

Received October 16, 2007 – Accep

Celiac disease and gluten-sensitive enteropathy are ter process affecting the small bowel. However, evidence has b that gluten sensitivity or celiac disease can exist even i many organs. Based on overwhelming evidence, immuno in the joint, the heart, thyroid, bone, and, in particular, t I. When blood samples of patients with celiac disease ar antigens, in addition to gliadin antibody, a significant perce against transglutaminase, heat shock protein, collagen, th (transglutaminase), myelin basic protein, cerebellar and s patients with celiac disease may result in neuroimmune dis population, the incidence of various autoimmune disorder 30-fold in patients with celiac disease. Therefore, immune or celiac disease, in addition to gliadin and transglutami against thyroglobulin, thyroid peroxidase, heat shock pr protein, cerebellar peptide and synapsin. This novel lab autoimmunity may enable clinicians to detect markers o of gluten sensitive and celiac disease patients and implem significant improvement and control of associated diseases.

Gluten sensitivity, celiac disease (CD) and gluten-sensitive enteropathy are terms that have been used synonymously to refer to a disease process affecting the small bowel and characterized by gastrointestinal symptoms and malabsorption. However, since 1966 scientific evidence has been accumulated demonstrating that gluten sensitivity can exist even in the absence of enteropathy. For example, patients with dermatitis herpetiformis and presentation of blistering skin do not have any gastrointestinal symptoms but have elevated gliad a glu CD the c as fa this p tissue to vi based pathogenesis involving organs other than gut and skin, many scientists have begun to re-evaluate

Key words: celiac disease, gluten sensitivity, enteropathy, synapsin, autoimmune disease

The gut-joint axis: cross-reactive food antibodies in rheumatoid arthritis

Patients with rheumatoid arthritis (RA) often feel there is an association between food intake and rheumatoid disease severity. In a recent study of this putative immunological link between gut immunity and RA, food IgG, IgA and IgM antibodies were measured in serum and perfusion fluid from the jejunum of 14 RA patients and 20 healthy controls to determine the systemic and mucosal immune response. The antigens originated from cow's milk (α-lactalbumin, β-lactoglobulin, casein), cereals, hen's egg (ovalbumin), cod fish and pork meat. In the intestinal fluid of many RA patients, all three immunoglobulin classes showed increased food specific activities, including gliadin antibodies (3).

It is well-known that some 80% of untreated RA patients have been shown to have reduced maximum gastric acid output leading to a marked reduction in dietary protein degradation, which contributes to enhanced food immunoreactivity (4-5).

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Patient:	Accession:	
	20160701-0017	
Collected: 06/29/2016	Received: 07/01/2016	
DOB:	Completed: 07/21/2016	

Ordered by: Michael Jurgelewicz, DC

Pathogens

Bacterial Pathogens	Result		Expected
Campylobacter	Negative		Neg
C. difficile Toxin A	Negative		Neg
C. difficile Toxin B	Negative		Neg
E. coli O157	Negative		Neg
Enterotoxigenic *E. coli* LT	Negative		Neg
Enterotoxigenic *E. coli* ST	Negative		Neg
Shiga-like Toxin *E. coli* stx1	Negative		Neg
Shiga-like Toxin *E. coli* stx2	Negative		Neg
Salmonella	Negative		Neg
Shigella	Negative		Neg
Vibrio cholera	Negative		Neg
Yersinia enterocolitica	Negative		Neg
Parasitic Pathogens			
Cryptosporidium	Negative		Neg
Entamoeba histolytica	Negative		Neg
Giardia	Positive		Neg
Viral Pathogens			
Adenovirus 40	Negative		Neg
Adenovirus 41	Negative		Neg
Norovirus GI	Negative		Neg
Norovirus GII	Negative		Neg
Rotavirus A	Negative		Neg

H. pylori			
Helicobacter pylori	2.1 E4	High	<7.0 E3
Virulence Factor, cagA	Negative		Neg
Virulence Factor, vacA	Positive		Neg

Normal Bacterial Flora			
Bifidobacter	1.6 E10		>8.9 E9
Enterococcus	7.3 E4		1.2 E4 - 3.1 E6
E. coli	5.9 E6		1.0 E4 - 7.6 E7
Lactobacillus	6.4 E5	Low	1.0 E6 - 5.8 E9

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6/29/2016

Accession: 20160701-0017

Opportunistic Bacteria			
Potential Autoimmune Triggers	Result		Range
Citrobacter spp.	<dl		<1.0 E4
Klebsiella pneumoniae	<dl		<7.2 E3
Proteus spp.	<dl		<6.2 E3
Proteus mirabilus	<dl		<1.0 E3
Yersinia enterocolitica (from pg 1)	Negative		Neg
Additional Dysbiotic/Overgrowth Bacteria			
Morganella morganii	<dl		<1.0 E3
Pseudomonas spp.	<dl		<2.5 E3
Pseudomonas aeruginosa	<dl		<1.0 E3
Staphylococcus spp.	3.8 E4	High	<1.0 E4
Streptococcus spp.	8.1 E3	High	<1.0 E3

Parasites			
Blastocystis hominis	Positive		Neg
Dientamoeba fragilis	Positive		Neg
Endolimax nana	Positive		Neg
Entamoeba coli	Negative		Neg
Chilomastix mesnelli	Negative		Neg
Cyclospora cayetanensis	Negative		Neg
Pentatrichomonas hominis	Negative		Neg

Fungi/Yeast			
Candida albicans	<dl		<5.0 E3
Candida spp.	Low		Neg
Geotricum spp.	Negative		Neg
Microsporidia spp.	Negative		Neg
Trichosporon spp.	Negative		Neg

Additional Tests			
	Result		Range
SIgA	3512	High	510-2040 ug/mL
Anti-gliadin SIgA	92.8	High	0.0-6.4 ug/mL
Elastase 1	166	Low	>200 ug/ml
Lactoferrin	4.4		0.0-7.2 ug/mL
Occult blood	Negative		neg

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6/29/2016

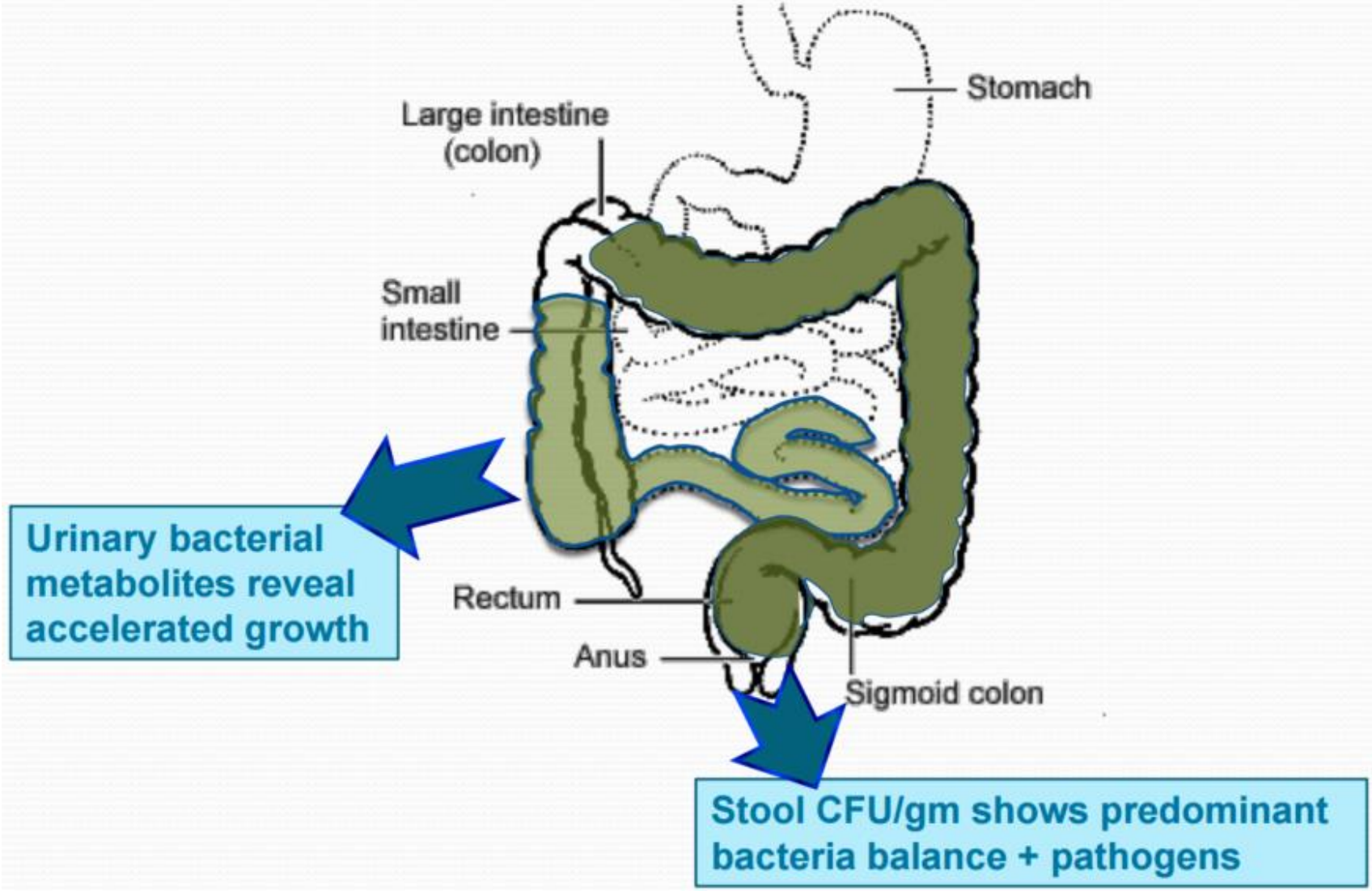
7/15/2016

Organix® Comprehensive Profile - Urine

Methodology: LC/Tandem Mass Spectroscopy, Colorimetric

Ranges are for ages 13 and over

		Results ug/mg creatinine		Quintile Ranking (1st / 2nd / 3rd / 4th / 5th)	95% Reference Range
Compounds of Bacterial or Yeast/Fungal Origin					
Bacterial - general					
36.	Benzoate	<DL*		0.6	<= 9.3
37.	Hippurate	205		548	<= 1070
38.	Phenylacetate	0.28	H	0.11	<= 0.18
39.	Phenylpropionate	<DL*			<= 0.06
40.	p-Hydroxybenzoate	0.7		1.1	<= 1.8
41.	p-Hydroxyphenylacetate	12		19	<= 34
42.	Indican	72	H	64	<= 90
43.	Tricarballylate	<DL*		0.73	<= 1.41
L. acidophilus / general bacterial					
44.	D-Lactate	5.7	H	1.9	<= 4.3
Clostridial species					
45.	3,4-Dihydroxyphenylpropionate	<DL*			<= 0.05
Yeast / Fungal					
46.	D-Arabinitol	27		36	<= 73


Stomach
Large intestine
(colon)
Small
intestine
Urinary bacterial
metabolites reveal
accelerated growth
Rectum
Anus
Sigmoid colon
Stool CFU/gm shows predominant
bacteria balance + pathogens

Treatment Program

Dietary Intervention

- Follow a gluten free diet. Avoid processed foods.

Gastrointestinal Support

- Comprehensive blend of botanical extracts used as natural antimicrobials, 2 capsules TID on an empty stomach
- Full spectrum digestive enzyme including betaine HCL, 1 capsule TID with meals
- *Saccharomyces boulardii* 10 billion CFUs, 1 capsules BID with meals

After 1 month

- Remove antimicrobials

	Patient:	Accession:
		20160929-0005
	Collected: 09/28/2016	Received: 09/29/2016
	DOB:	Completed: 10/14/2016

Ordered by: Michael Jurgelewicz, DC

Pathogens		
Bacterial Pathogens	Result	Expected
Campylobacter	**Negative**	Neg
C. difficile Toxin A	**Negative**	Neg
C. difficile Toxin B	**Negative**	Neg
E. coli O157	**Negative**	Neg
Enterotoxigenic *E. coli* LT	**Negative**	Neg
Enterotoxigenic *E. coli* ST	**Negative**	Neg
Shiga-like Toxin *E. coli* stx1	**Negative**	Neg
Shiga-like Toxin *E. coli* stx2	**Negative**	Neg
Salmonella	**Negative**	Neg
Shigella	**Negative**	Neg
Vibrio cholera	**Negative**	Neg
Yersinia enterocolitica	**Negative**	Neg
Parasitic Pathogens		
Cryptosporidium	**Negative**	Neg
Entamoeba histolytica	**Negative**	Neg
Giardia	**Negative**	Neg
Viral Pathogens		
Adenovirus 40	**Negative**	Neg
Adenovirus 41	**Negative**	Neg
Norovirus GI	**Negative**	Neg
Norovirus GII	**Negative**	Neg
Rotavirus A	**Negative**	Neg
H. pylori		
Helicobacter pylori	**<dl**	<7.0 E3
Virulence Factor, cagA	**Negative**	Neg
Virulence Factor, vacA	**Negative**	Neg
Normal Bacterial Flora		
Bifidobacter	**2.4 E10**	>8.9 E9
Enterococcus	**6.7 E5**	1.2 E4 - 3.1 E6
E. coli	**6.1 E6**	1.0 E4 - 7.6 E7
Lactobacillus	**2.8 E7**	1.0 E6 - 5.8 E9

9/28/2016

Accession: 20160929-0005

Opportunistic Bacteria			
Potential Autoimmune Triggers	Result		Range
Citrobacter spp.	<dl		<1.0 E4
Klebsiella pneumoniae	<dl		<7.2 E3
Proteus spp.	<dl		<6.2 E3
Proteus mirabilus	4.1 E2		<1.0 E3
Yersinia enterocolitica (from pg 1)	Negative		Neg
Additional Dysbiotic/Overgrowth Bacteria			
Morganella morganii	<dl		<1.0 E3
Pseudomonas spp.	<dl		<2.5 E3
Pseudomonas aeruginosa	<dl		<1.0 E3
Staphylococcus spp.	<dl		<1.0 E4
Streptococcus spp.	<dl		<1.0 E3
Parasites			
Blastocystis hominis	Negative		Neg
Dientamoeba fragilis	Negative		Neg
Endolimax nana	Negative		Neg
Entamoeba coli	Negative		Neg
Chilomastix mesnelli	Negative		Neg
Cyclospora cayetanensis	Negative		Neg
Pentatrichomonas hominis	Negative		Neg
Fungi/Yeast			
Candida albicans	<dl		<5.0 E3
Candida spp.	Negative		Neg
Geotricum spp.	Negative		Neg
Microsporidia spp.	Negative		Neg
Trichosporon spp.	Negative		Neg
Additional Tests			
	Result		Range
SIgA	1249		510-2040 ug/mL
Anti-gliadin SIgA	109	High	<100 U/mL
Elastase 1	209		>200 ug/ml
Calprotectin	33		<50 ug/g
Occult blood	Negative		neg

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9/28/2016

Treatment Program

Dietary Intervention

- Continue on a gluten free diet. Avoid processed foods.

Gastrointestinal Support

- Full spectrum digestive enzyme including betaine HCL, 1 capsule TID with meals
- *Saccharomyces boulardii* 10 billion CFUs, 1 capsules BID with meals

Don’t Get Hung Up on Labels

- Irritable Bowel Syndrome
- Hashimoto’s
- Rheumatoid Arthritis
- Autoimmune Diseases
- Crohn’s
- Ulcerative colitis
- Etc.

Fix what you find and maximize the GI environment!