WHAT IS METABOLIC ENDOTOXEMIA?

Metabolic endotoxemia is essentially an innate immune response that becomes a sub-clinical, persistent, low-grade inflammation because of increased, circulating endotoxins. - Primarily LPS.

- Metabolic endotoxemia is a condition that is estimated to affect approximately 33% of the western population.
- The conditions is characterized by increased serum endotoxin (typically lipopolysaccharide) concentration during the first five hours of the post-prandial period following consumption of a meal.
- Meals that are high in fat and dense in calories seem to impact the condition more so than low fat and low calorie meals.
- This increase in serum endotoxin concentration is followed by elevated inflammation that is marked by measurable increases in interleukin-6, interleukin-1-beta, interferon-gamma, triglycerides and post-prandial insulin.
- Chronic metabolic endotoxemia and the associated inflammation has been shown to have significant correlation to increases in the risk of developing a variety of chronic diseases.

To date, studies support a strong correlation between metabolic endotoxemia (ME) and the increased risk or onset of conditions such as cardiovascular disease, diabetes, obesity, hypogonadism, autoimmunity and even mood disorders such as anxiety and depression.
WHAT IS AN ENDOTOXIN?

AKA lipopolysaccharide (LPS)

- Inflammatory immunogens
- Component of gram-negative bacterial outer cell wall
  - Adhesin for colonization of host
  - Diversity of antigenic strains
- Circulates at low-grade levels in healthy individuals
- Toxicity mainly mediated by the lipid-A component

Structure of Lipopolysaccharide


http://caltagmedsystems.blogspot.com/2013/05/uscn-specialist-elisa-kit-manufacturer.html
TLR4 is an important signaling protein in innate immunity and is found on the surfaces of innate immune defense cells like Macrophages and dendritic cells.

Circulating LPS gets bound by a phospholipid transfer protein called LBP, which carries LPS to the CD14-TLR complex for examination.

Once LPS-LBP has bound to the CD14-TLR complex, it initiates an immune cascade that leads to the activation of NF-KB.

The activation of NF-KB leads to the increased expression of pro-inflammatory mediators TNFa, IL-1beta, IL-6 and MCP-1.

Innate immune cells that become activated by LPS and subsequently cause the chronic release of pro-inflammatory cytokines, exist in all parts of the body, including the blood-brain barrier.
CD14 Mutant Mice are Protected against LPS-induced Inflammation. mRNA Concentrations of IL-6, PAI-1, and IL-1 in Adipose Tissue 3 h after a Saline (control [CT]; n = 6) or an LPS (n = 6) Infusion in WT (A) and CD14 Mutant (B) Mice. *P < 0.05

Patrice D. Cani et al. Diabetes 2007;56:1761-1772
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CLINICAL MANIFESTATIONS OF LPS INDUCED CHRONIC IMMUNE ACTIVATION
THE METABOLIC SYNDROME

- Heart Disease
- Lipid Problems
- Hypertension
- Type 2 Diabetes
- Dementia
- Cancer
- Polycystic Ovarian Syndrome
- Non-Alcoholic Fatty Liver Disease
Changes in circulating endotoxin levels (A) and triglyceride levels (B) in NOC, IGT, Obese, and Type 2 Diabetic (T2DM) subjects.

Changes in circulating endotoxin levels (A) and triglyceride levels (B) in NOC, IGT (impaired glucose tolerance), obese, and type 2 diabetic (T2DM) subjects. Endotoxin and triglyceride levels were measured at baseline and then, after a high-SFA meal, at each hour postprandially over a 4-h duration. Each point on the graph represents the mean value for each cohort (± SEM).

Alison L. Harte et al. Dia Care 2012;35:375-382

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Increase in Endotoxin Levels Between the NOC Subjects and the Obese (A), IGT (B), And Type 2 Diabetic (T2DM) (C) Subjects from Baseline to 4 h after a High-fat meal.
High-fat Feeding Increased Endotoxemia and Changed Intestinal Microbiota.

Alison L. Harte et al. Dia Care 2012;35:375-382

©2007 by American Diabetes Association
I WAS HERE FIRST!
Metabolic Endotoxemia Impairs Adipocyte Morphology.

Alison L. Harte et al. Dia Care 2012;35:375-382
©2007 by American Diabetes Association
The present data suggest that an increased JNK activity in the hypothalamus underlies the development of insulin resistance during prolonged exposure to endotoxins. Our study reveals that weight gain is not mandatory for the development of hypothalamic insulin resistance and the blockade of proinflammatory pathways could be useful for restoring the insulin signaling during prolonged low-grade inflammation as seen in obesity.
Metabolic endotoxemia: a molecular link between obesity and cardiovascular risk

Ana Luisa Neves¹, João Coelho¹, Luciana Couto², Adelino Leite-Moreira¹ and Roberto Roncon-Albuquerque Jr³
Departments of ¹Physiology and Cardiothoracic Surgery ²General Practice, Faculty of Medicine, University of Porto, Al. Prof. Hernãni Monteiro; 4200-319 Porto, Portugal

Abstract
Obesity is associated with significantly increased cardiovascular (CV) risk and mortality. Several molecular mechanisms underlying this association have been implied, among which the intestinal barrier has gained a growing interest. In experimental models of obesity, significant alterations in the intestinal barrier lead to increased intestinal permeability,

Key Words
- endotoxemia
- obesity
- cardiovascular diseases
METABOLIC ENDOTOXEMIA AND ELEVATED LPS IN DISEASE

Metabolic Endotoxemia Initiates Obesity and Insulin Resistance
Patrice D. Cani, Jacques Amar, et al.
Diabetes 2007 Jul; 56(7): 1761-1772. https://doi.org/10.2337/db06-1491

Metabolic endotoxemia directly increases the proliferation of adipocyte precursors at the onset of metabolic diseases through a CD14-dependent mechanism

Lipopolysaccharide Causes an Increase in Intestinal Tight Junction Permeability in Vitro and in Vivo by Inducing Enterocyte Membrane Expression and Localization of TLR-4 and CD14

Elevated endotoxin levels in non-alcoholic fatty liver disease
Alison L Harte et al.
Journal of Inflammation 20107:15
Received: 3 September 2009 Accepted: 30 March 2010Published: 30 March 2010
METABOLIC ENDOTOXEMIA AND ELEVATED LPS IN DISEASE

**Induction of autoimmunity in good and poor responder mice with thyroglobulin and lipopolysaccharide.**
Esquivel PS, Rose NR, Kong YC.

**Immunomodulation of murine cytomegalovirus-induced myocarditis in mice treated with lipopolysaccharide and tumor necrosis factor.**
Lenzo JC, Fairweather D, Shellam GR, Lawson CM.

**Lipopolysaccharide injection induces relapses of experimental autoimmune encephalomyelitis in nontransgenic mice via bystander activation of autoreactive CD4+ cells.**
LPS disrupts ghrelin function which has a direct impact on appetite and mood, LPS can migrate to the blood-brain barrier and cause inflammation along with inhibition of dopamine receptors. Inflammation in the blood brain barrier leads to cognitive decline.

LPS can get into the amygdala and hippocampus which disrupts memory function. Elevated LPS in sensory neurons in the dorsal root stimulate nociceptors. LPS can increase the turnover of serotonin in the synapse and CNS reducing the concentration in those regions. Intra-cranially LPS causes microglial activation and neuronal loss. Chronic activation of the innate immune system in various tissues leads to the by-stander effect where self-tissues inadvertently become targeted by the immune system.

<table>
<thead>
<tr>
<th>CONDITION</th>
<th>MECHANISM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin Resistance</td>
<td>LPS enters and causes inflammation in the enteric nervous system leading to a disruption in the gut-brain axis of communication.</td>
</tr>
<tr>
<td>Chronic Constipation</td>
<td>LPS enters the enteric nervous system and causes disruption in signals for gastric emptying and bowel motility.</td>
</tr>
<tr>
<td>Mood and Appetite Disorders</td>
<td>LPS disrupts ghrelin function which has a direct impact on appetite and mood,</td>
</tr>
<tr>
<td>Depression</td>
<td>LPS can migrate to the blood-brain barrier and cause inflammation along with inhibition of dopamine receptors.</td>
</tr>
<tr>
<td>Cognitive Decline</td>
<td>Inflammation in the blood brain barrier leads to cognitive decline.</td>
</tr>
<tr>
<td>Loss of Memory and Recall</td>
<td>LPS can get into the amygdala and hippocampus which disrupts memory function.</td>
</tr>
<tr>
<td>Depression</td>
<td>LPS can increase the turnover of serotonin in the synapse and CNS reducing the concentration in those regions.</td>
</tr>
<tr>
<td>Anorexia</td>
<td>The reduction of serotonin in the synapse and CNS is proposed as a possible mechanism for anorexia.</td>
</tr>
<tr>
<td>Anxiety</td>
<td>LPS disrupts key communication between the hypothalamic-adrenal-pituitary axis thereby increasing the expression of corticosteroid releasing hormone.</td>
</tr>
<tr>
<td>Chronic Pain</td>
<td>Elevated LPS in sensory neurons in the dorsal root stimulate nociceptors.</td>
</tr>
<tr>
<td>Parkinson’s</td>
<td>Intra-cranially LPS causes microglial activation and neuronal loss.</td>
</tr>
<tr>
<td>Hypogonadism (low testosterone)</td>
<td>Increased circulating LPS and the subsequent chronic immune activation has feedback inhibition of testosterone production. GELDING theory.</td>
</tr>
<tr>
<td>Autoimmunity</td>
<td>Chronic activation of the innate immune system in various tissues leads to the by-stander effect where self-tissues inadvertently become targeted by the immune system.</td>
</tr>
</tbody>
</table>
GUT PERMEABILITY – CHRONIC INFLAMMATION

Stress induces endotoxemia and increasing barrier permeability
Karin de Punder* and Leo Pruimboom

“Chronic non-communicable diseases (NCDs) are the leading causes of work absence, disability, and mortality worldwide. Most of these diseases are associated with low-grade inflammation.”

“In combination with modern life-style factors, the increase in bacteria/bacterial toxin translocation arising from a more permeable intestinal wall causes a low-grade inflammatory state. We support this hypothesis with numerous studies finding associations with NCDs and markers of endotoxemia, suggesting that this process plays a pivotal and perhaps even a causal role in the development of low-grade inflammation and its related diseases.”

GROUND ZERO OF MOST HEALTH DISORDERS
Intestinal inflammation alters VAN function which induces leptin and insulin resistance, leading ultimately to overeating and obesity.
GUT DYSBIOSIS AS ROOT CAUSE OF OBESITY

- LPS translocation
- Chronic inflammation
- Afferent nerve dysfunction
- Overeating feedback loop
THE GUT MICROBIOME IS A VAST ECOSYSTEM
HEALTHY GUT CHARACTERISTICS

- Increased microbial diversity
- Low levels of pathogens and toxins
- Thick mucosal barrier
- Strong epithelial tight junctions
- Low mucosal inflammation
GUT-DAMAGING FACTORS

- Antibiotics
- Excessive alcohol
- Smoking
- Stress
- Lack of sleep
- Intense exercise
- Artificial sweeteners
- Saturated fats
- Glyphosate
DISRUPTION OF GUT MICROBIOTA
"The disruption of gut microbiota has been implicated in many conditions and diseases, including obesity, inflammatory bowel disease, irritable bowel syndrome, type 2 diabetes, and colorectal cancer."

"Intelligent modulation of the intestinal community is a topic that had gained considerable interest and has the possibility to be extremely beneficial for human health."
While some results related to dysbiosis in IBD are different between studies owing to variations of sample type, method of investigation, patient profiles, and medication, the most consistent observation in IBD is reduced bacterial diversity, a decrease of Firmicutes, and an increase of Proteobacteria."

“A number of trials have shown that therapies correcting dysbiosis are promising in IBD.”
"A. muciniphila is inversely associated with obesity, diabetes, cardiometabolic diseases and low-grade inflammation."

"Nowadays, A. muciniphila is widely considered as a novel potential candidate to improve metabolic disorders associated with obesity, diabetes, liver diseases and cardiometabolic disorders. Indeed, its administration has been shown to profoundly reduce the development of such diseases."
"The abundance of *F. prausnitzii* was decreased in IBD patients compared with healthy controls."

"In summary, our meta-analysis and systematic review suggest a possible **protective benefit of *F. prausnitzii*** against the development of IBD. Therefore, further treatment such as probiotics or prebiotics to increase the levels of *F. prausnitzii* in IBD are lead to attempts."
DYSFUNCTION OF MUCOSAL BARRIER
Three studies now characterize how gut epithelial barrier dysfunction is involved in IBD, autoimmune disease, and systemic infection.

Pathogenic bacteria can induce intestinal barrier defects and translocate to lymph nodes and liver, triggering systemic autoimmune disease, such as systemic lupus erythematosus (SLE).
The results show that intestinal mucosal dysfunction characterized by an increased translocation of gram-negative enterobacteria (leaky gut) plays a role in the inflammatory pathophysiology of depression.
In the pathophysiology of GERD, abnormal exposure of the esophagus to luminal contents leads to chronic mucosal inflammation that is characterized by the release of IL-8 specifically, as well as other proinflammatory mediators, from the esophageal mucosa.

Hydrogen ions and gastric pepsin exert a corrosive effect on the surface of the esophageal mucosa and degrade junctional proteins, thereby destroying epithelial barrier function with the consequent induction of intramucosal inflammation.
“Early HIV infection is consistently associated with a rapid, dramatic, and largely irreversible depletion of mucosal CD4+ memory T-cells, particularly those expressing the HIV coreceptor CCR5.”

“In conclusion, further studies are needed to solve the complex riddle of how the interaction between primate lentiviruses and the host mucosal immune system leads to the severe mucosal immune dysfunction associated with progression to AIDS.”
Identification of gut microbiome signatures associated with longevity provides a promising modulation target for healthy aging

Fanli Kong\(^{a,b,c}\#\), Feilong Deng\(^{a,c}\#\), Ying Li\(^{c}\), and Jiangchao Zhao\(^{a}\)

\(^a\)Department of Animal Science, Division of Agriculture, University of Arkansas, Fayetteville, AR, USA; \(^b\)College of Life Science, Sichuan Agricultural University, Ya'an, Sichuan, China; \(^c\)Farm Animal Genetic Resources Exploration and Innovation Key Laboratory of Sichuan Province, Sichuan Agricultural University, Chengdu, Sichuan, China

**ABSTRACT**
The world population is aging, which poses a significant burden to the economy and health care system. As people age, so do their gut microbiomes. Age-related changes in gut microbiome have been reported, including decreased microbial diversity and increased Proteobacteria. Recently, we characterized the gut microbiome of a group of long-living (≥ 90 years old) Chinese people. Interestingly, the diversity of their gut microbiome was greater than that of a young adult control group. We also identified several potentially beneficial bacteria enriched in the long-living Chinese group. These results were validated using data from an independent Italian cohort that included a group of long-living individuals. Other recent studies have found similar results. Here, we provide a summary of these discoveries and discuss their implications in healthy aging.
TOTAL GUT RESTORATION

RECONDITION | REINFORCE | REBUILD
RECONDITION the gut with probiotics

REINFORCE beneficial changes with Precision Prebiotics

REBUILD intestinal mucosa with amino acids
• Obesity is associated with **low microbial diversity** in the gut
• **To revitalize a garden:** remove the weeds and fertilize the plants
• Bacillus spores do this by:
  • modulating the microbiota through quorum sensing
  • increasing short-chain fatty acid production by 40%
  • encouraging the growth of keystone bacteria like *Akkermansia muciniphila*, *Faecalibacterium prausnitzii*, and *Bifidobacteria*

100% spore-based Bacillus probiotics have been clinically shown to improve leaky gut by 60% in just 30 days. This unique all-spore formula effectively **RECONDITIONS** the gut by increasing microbial diversity and encouraging the growth of key health-promoting, commensal gut bacteria.
Effects of Bacillus subtilis on Epithelial Tight Junctions of Mice with Inflammatory Bowel Disease.

Gong Y1, Li H1, Li Y1.

"B. subtilis intake up-regulated expression of TJ proteins (claudin-1, occludin, JAM-A, and ZO-1), for improved barrier function, and down-regulated cytokine expression (IL-6, IL-17, IL-23, and TNF-α) to reduce intestinal epithelial damage."

Histological alterations of intestinal villi in chickens fed dried Bacillus subtilis var. natto.

Samanya M1, Yamauchi KE.

"These birds had a tendency to display greater growth performance and intestinal histologies, such as villus height, cell area and cell mitosis, than the controls."

Bacillus subtilis Protects Porcine Intestinal Barrier from Deoxynivalenol via Improved Zonula Occludens-1 Expression

Min Jeong Gua, Sun Kwang Songa, Sung Moo Park

"B. subtilis may have potential to enhance epithelial barrier function and to prevent the cells from DON-induced barrier dysfunction."
Prospective Study

Oral spore-based probiotic supplementation was associated with reduced incidence of post-prandial dietary endotoxin, triglycerides, and disease risk biomarkers

Brian K McFarlin, Andrea L Henning, Erin M Bowman, Melody M Gary, Kimberly M Carbajal

Brian K McFarlin, Andrea L Henning, Erin M Bowman, Melody M Gary, Applied Physiology Laboratory, University of North Texas, Denton, TX 76203, United States

Brian K McFarlin, Andrea L Henning, Kimberly M Carbajal, Department of Biological Sciences, University of North Texas, Denton, TX 76203, United States

Author contributions: McFarlin BK designed the study, collected data, interpreted findings, and prepared manuscript; Henning AL, Bowman EM, Gary MM and Carbajal KM collected data, interpreted findings, and prepared manuscript.

Institutional review board statement: The study was reviewed

licensors by nc/4.0

Manuscript source: Invited manuscript

Correspondence to: Brian K McFarlin, PhD, FAcSM, FTOS, Associate Professor, Applied Physiology Laboratory, University of North Texas, 1921 West Chestnut Street, PEB Room 209, Denton, TX 76203, United States. brian.mcfarlin@unt.edu

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First decision: March 13, 2017
The effect of 30-days of probiotic supplementation on post-prandial responses to a high-fat meal: Pilot Study

Principal Investigator: Brian K. McFarlin, PhD, FACSM, FTOS  University of North Texas

![Graph showing endotoxin levels at different feeding times.](chart.png)
The effect of 30-days of probiotic supplementation on post-prandial responses to a high-fat meal: Pilot Study

Principal Investigator: Brian K. McFarlin, PhD, FACSM, FTOS  University of North Texas
The effect of 30-days of probiotic supplementation on post-prandial responses to a high-fat meal: An Expanded Pilot Study

Principal Investigator: Brian K. McFarlin, PhD, FACSM, FTOS University of North Texas

- Spore Treatment Group: 45% Reduction
- Placebo Treatment Group: 32% Increase
- Over 60% Difference between the groups
The effect of 30-days of probiotic supplementation on post-prandial responses to a high-fat meal: An Expanded Pilot Study

Principal Investigator: Brian K. McFarlin, PhD, FACSM, FTOS

University of North Texas
The effect of 30-days of probiotic supplementation on post-prandial responses to a high-fat meal: An Expanded Pilot Study
Principal Investigator: Brian K. McFarlin, PhD, FACSM, FTOS University of North Texas

SNEAK PREVIEW

<table>
<thead>
<tr>
<th>Time</th>
<th>1-OH</th>
<th>1-3H</th>
<th>1-5H</th>
<th>2-OH</th>
<th>2-3H</th>
<th>2-5H</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spores</td>
<td>150.0</td>
<td>160.0</td>
<td>170.0</td>
<td>180.0</td>
<td>190.0</td>
<td>200.0</td>
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<tr>
<td>Placebo</td>
<td>140.0</td>
<td>150.0</td>
<td>160.0</td>
<td>170.0</td>
<td>180.0</td>
<td>190.0</td>
</tr>
</tbody>
</table>

MCP-1 (pg/mL)
The effect of 30-days of probiotic supplementation on post-prandial responses to a high-fat meal: An Expanded Pilot Study

Principal Investigator: Brian K. McFarlin, PhD, FACSM, FTOS University of North Texas

<table>
<thead>
<tr>
<th>Variable</th>
<th>Spore-based Probiotic</th>
<th>30-d Supplementation</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre 3-h 5-h</td>
<td>Pre 3-h 5-h</td>
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<tr>
<td>Endotoxin</td>
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<td>Triglycerides</td>
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<tr>
<td>Ghrelin</td>
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<tr>
<td>MCP-1</td>
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<tr>
<td>IL-12p70</td>
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<td>IL-1beta</td>
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<td>IL-6</td>
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<td>IL-8</td>
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<td>Glucose</td>
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<td>Insulin</td>
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<td>Leptin</td>
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<td>GM-CSF</td>
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<td>IL-4</td>
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<td>IL-5</td>
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<td>IL-10</td>
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<td>IL-13</td>
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<tr>
<td>TNF-alpha</td>
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</tbody>
</table>

Variables Significantly Affected by Probiotic

Variables Not Significantly Affected by Probiotic
The gut microbiome is a dynamic ecosystem that is constantly changing. Building a diverse, healthy garden requires the proper fertilizer. Most prebiotics can feed both harmful and beneficial bacteria. A precision prebiotic can selectively feed important keystone strains, like Akkermansia muciniphila, Faecalibacterium prausnitzii, and Bifidobacteria, which are associated with reduced risk of chronic disease.

Clinically-tested, non-digestible oligosaccharides can increase microbial diversity and selectively feed beneficial bacteria. These functional fibers REINFORCES the beneficial microbial changes created by Bacillus spores to promote a strong and diverse microbiome.
MICROBIAL CHANGES FROM OLIGOSACCHARIDES

- FOS ↑ *F. prau* by 100% in 4 weeks
- FOS ↑ *A. mucin* by 8,000% in 5 weeks
- GOS ↑ *Bifido* by 67% in 1 week
- XOS ↑ *Bifido* by 21% in 4 weeks
PROBIOTIC ONLY

RECONDITION the gut

SYNBIOTIC

REINFORCE beneficial changes

**F. prausnitzii - Donor 1**

**Faecalibacterium - Lumen - Donor 1**

**Lactobacillus - Donor 1**

**Lactobacillus - Lumen - Donor 1**
Akkermansia Below Detection Level
Spore treatment significantly increased butyrate concentrations during the final weeks of treatment. An increase of 3.9 mM (70.2%) in the AC, 2.8 mM (24.1%) in the TC and 3.6 mM (28.4%) in the DC was observed.
• A thick, gel-like mucus layer protects the intestinal lining from damage
• Many chronic diseases are linked to the breakdown of the intestinal mucosa
• Butyrate increases mucin production by up-regulating MUC2 genes
• **Bacillus spores and 4 amino acids** can rebuild this intestinal barrier
• through the modulation of tight-junction proteins and butyrate-producing microbiota

These key amino acids can increase mucin production by 95% in order to **REBUILD** a healthy mucosal barrier. IgG immunoglobulins can also be useful in fending off inflammatory toxins and pathogens while the intestinal mucosa regenerates.

- SBI increases intestinal mucosal CD4+ lymphocytes
- Improves duodenal function
- Promotes intestinal repair in HIV enteropathy


- SBI heals gastric mucosa in pediatric UC case study
- Decrease in pediatric UC activity index


- Binds and neutralizes several toxins from C. difficile strains, including hypervirulent strains
MUCIN BUILDING BLOCKS

Specific Amino Acids Increase Mucin Synthesis and Microbiota in Dextran Sulfate Sodium–Treated Rats

Magali Faure,* Christine Mettraux,* Denis Moennoz,* Jean-Philippe Godin,* Jacques Vuichoud,* Florence Rochat,* Denis Brequilé,* Christiane Obled,† and Irène Corthész-Theulaz*

*Nestlé Research Center, Nutrition and Health Department, Lausanne, Switzerland and †Unité de Nutrition et Métabolisme Protéique, INRA, Theix, France

ABSTRACT During the anabolic response associated with inflammation, mucin synthesis and colonic protection may be compromised by the limited availability of specific amino acids. We therefore determined the effect of dietary amino acid supplementation on the microbiota, mucin status, and mucosal damage in dextran sulfate sodium (DSS)-treated rats. From 8 d before to 28 d after colitis induction, male Sprague-Dawley rats (10 mo old, n = 8/group) were fed a control diet supplemented or not with 2 different doses of an amino acid cocktail containing L-threonine, L-serine, L-proline, and L-cysteine. All diets were isonitrogenous (adjusted with L-alanine). The higher dose of amino acids increased the number of Muc2-containing goblet cells in the surface epithelium of the ulcerated area, stimulated mucin production in the colon, and restored the mucin amino acid composition and mucosal content to healthy, control values. The colonic mucin synthesis rate was specifically stimulated by 95%, whereas the protein turnover was unchanged. All bacterial populations, markedly altered by the DSS treatment, were promoted. In conclusion, in inflammatory situations, an increase in threonine, serine, proline, and cysteine dietary supply can promote mucin synthesis, reestablish the gut microbiota, and thus favor colonic protection and mucosal healing. J. Nutr. 136: 1558–1564, 2006.

KEY WORDS: mucin • amino acids • protein synthesis • intestine • rats

L-threonine, L-serine, L-proline & L-cysteine increased colonic mucin synthesis by 95%

- Reduce intestinal inflammation by inhibiting activation of NF-kB cascade
- Block JNK stress-activated pathways
- Protect against experimental colitis
- Reduce risk of IBD


- Increased butyrate production by 21%
- Reduced fecal calprotectin levels by 22%
TOTAL GUT RESTORATION

RECONDITION

REBUILD

REINFORCE
CONCLUSION

- Metabolic endotoxemia is the #1 cause of morbidity and mortality worldwide.
- Metabolic Endotoxemia leads to conditions like obesity, heart disease, autoimmunity, diabetes, etc.
- Metabolic Endotoxemia is a feature of a dysbiotic gut, which leads to leptin and insulin resistance.
- Bacillus spores reduce post-prandial endotoxemia and key biomarkers for cardiovascular disease, diabetes and neurodegeneration, i.e. IL-6, IL-1b, and INF-g with NO dietary changes or other therapies.
- Bacillus spores also reduce triglycerides, post-prandial insulin and improve satiety.
- Bacillus spores RECONDITION the gut microbiome.
- Non-digestible oligosaccharides REINFORCE microbiological changes.
- Key amino acids can REBUILD the intestinal mucosal barrier.