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How to Reduce Metabolic Endotoxemia

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Approximately 50 percent of the Western population suffers from a condition known as metabolic endotoxemia (ME). The condition is characterized by increased serum endotoxin concentration during the first five hours of the post-prandial period. This increase in serum endotoxin concentration then triggers systemic inflammation, resulting in elevated interleukin-6, interleukin-1-alpha, interferon-gamma, triglycerides and post-prandial insulin levels, many of which have a strong correlation to a variety of chronic diseases.[1]

Current studies demonstrate a strong correlation between ME and the risk or onset of conditions such as cardiovascular disease, diabetes, obesity, hypogonadism, autoimmunity, and even mood disorders such as anxiety and depression.[2-8]

An Innate Immune Response

ME is an innate immune response that results in subclinical, persistent, low-grade inflammation due to elevated circulating endotoxins. The primary endotoxin of concern is lipopolysaccharide (LPS), a major component of the outer cell membrane of gram-negative bacteria residing in the gut. In fact, the majority of the microbes in the digestive tract are gram-negative bacteria, including clostridium sp., enterococcus sp., escherichia sp., and bacteroides sp.

Trillions of commensal bacteria in the gastrointestinal tract contain LPS, and when these bacteria lyse, they release LPS into the intestinal lumen. This process happens quite frequently, as many bacteria die off during a meal, but LPS remains harmless inside the intestinal lumen. It is not until LPS reaches the brush border and enters circulation that it begins to trigger low-grade inflammation.

Once inside the circulatory system, LPS can trigger innate immune activation and subsequent inflammation anywhere in the body. LPS can delay gastric emptying, slow bowel motility, disrupt ghrelin function, inhibit testosterone production, reduce serotonin, and so much more.

Metabolic endotoxemia could very well be the primary driver of most chronic illnesses plaguing the Western world. The causes of ME do not appear to be genetic or congenital, but rather a result of lifestyle choices.[9]

Reducing ME Risk: Dietary Choices

Fortunately, there are some basic lifestyle choices that can help reduce the risk and incidence of ME. Minimizing alcohol consumption, cessation of smoking, expanding the diversity of dietary macronutrients, and reducing saturated fat intake can all have a drastic impact on ME.

New research indicates that meals high in saturated fat appear to be more damaging to the gut than meals high in unsaturated fat.[10] When commensal gut bacteria use saturated fatty acids to form their outer membranes, they produce a more toxic form of LPS. In fact, coconut oil appears to be the most potent stimulator of LPS toxicity in the gut.

However, unsaturated fatty acids appear to produce a neutral form of LPS. Furthermore, omega-3 fatty acids appear to protect the intestinal lining by reducing the amount of LPS released into

circulation.[11]

In addition to the above lifestyle modifications, ME can also be contained by increasing secretory immunoglobulin A levels, strengthening the mucosal barrier, and modulating the immune system.

Secretory immunoglobulin A (sIgA) is the first line of defense against free LPS liberated in the lumen of the intestines. sIgA has the capability to bind and neutralize LPS in the lumen and mucosa itself. Nutrients that have been shown to have a positive impact on the production and secretion of IgA are essential omega fatty acids, glutathione, glycine, glutamine, phosphatidylcholine, vitamin C, zinc and colostrum.

The mucosa is a key barrier that protects LPS from entering into the basolateral layer. When the mucosa suffers from inadequate production of mucin and inadequate viscosity, it fails to perform its barrier function and thus allows for the migration of LPS. Increasing mucin production can help restrict the movement of LPS toward the intestinal epithelial.

Nutrients that have been shown to support increased mucin production are L-threonine, L-serine, L-proline, and L-cysteine.

The Value of Probiotic Spores

One of the best ways to modulate the microbiome and protect against conditions such as ME is with spore-based probiotics.[12-13] It is clear dysbiosis drives ME; thus, a healthy microbiome has the capability to protect the body from the damaging effects of ME.

The major issue with most probiotics is that they do not survive gastric passage to enter the small or large intestines intact and viable. However, probiotic spores have the capability to survive the harsh gastric passage and enter the intestines completely viable. To date, bacterial spores are the only strains that have been shown to treat metabolic endotoxemia.

Probiotic spores were the subject of a university, double-blind, and placebo-controlled trial to evaluate the ability of the spores to reduce or prevent ME.[14] In addition to assessing changes in dietary endotoxemia, the researchers also measured transient changes in cardiovascular disease (CVD) risk factors, other novel disease risk biomarkers, and the immune system itself, following a high-fat challenge meal.

Healthy volunteers were screened for an endotoxic response to the challenge meal. If they showed the response, they were enrolled into the study and randomized into either the placebo group or treatment group. They consumed the placebo or treatment product for 30 days, with no other interventions or lifestyle changes.

After the 30 days, they reported back to the lab for their "post-treatment" response and received a second challenge meal. All the same bloodwork was run to access their levels of endotoxemia. The data showed a clear shift to a protective microbiome after just 30 days of supplementation with the spores. The post-test challenge in the treatment group showed a drastic reduction in endotoxemia. Interestingly, the placebo group progressively worsened.

These probiotic spores are likely the most promising therapy for metabolic endotoxemia, as no other probiotics or compounds have demonstrated this effect. Collectively, the findings of this study demonstrate a significant blunting of metabolic endotoxemia, triglycerides, and systemic inflammatory markers IL-6, IL-8, MCP-1, IL-1ß and IL-12 following a 30-day period of probiotic supplementation.

This study is the first to demonstrate that a short-term probiotic intervention can alter dietary endotoxemia in human subjects.

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