High-fat diet is associated with endotoxemia and low-grade inflammation

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Endotoxin (lipopolysaccharide [LPS]) is located at the outer membrane of the Gram-negative bacteria such as *Escherichia coli, Salmonella, Shigella, Pseudomonas, Neisseria, Haemophilus influenzae, Bordetella pertussis* and *Vibrio cholerae*, and is regarded as one of the potent virulence factors of these bacterial species. In the circulation system, 80–97% of it is bound to the lipoproteins. The subclinical elevation in circulating endotoxin level is known as the metabolic endotoxemia. This elevation is not overtly apparent in a clinical setting but is being investigated as a significant potential etiology for several chronic diseases. The effect of high doses of LPS (10-200 ng/ml) on inflammation is well known, but the research is still going on about the effect of very low doses of LPS (1-100 pg/ml) on inflammatory and metabolic alterations.

A small but significant increase in pro-inflammatory cytokines and chemokines may occur with a persistent exposure to very low doses of LPS. Thus, this metabolic endotoxemia may lead to the chronicity of low-grade inflammation observed in many of the disease pathologies including type 2 diabetes mellitus, atherosclerosis, Parkinson's disease and cancer metastasis. This model may explain the development of low-grade, chronic inflammation, at least in part due to the lack of an appropriate counter response through the inadequate expression of anti-inflammatory mediators and negative feedback loops.[1]

One of the prominent and emerging sources of metabolic endotoxemia is the consumption of high-fat diets, which may facilitate the gut absorption of endotoxin and change the gut flora that allows the endotoxin to enter systemic circulation.[2-5] It may be possible that the altered gut populations affect the amount of lipid absorbed by the gut, therefore allowing greater amounts of LPS into circulation. Moreover, the risk of LPS "leaking" into the bloodstream may also be increased by the differences in gut bacterial population dynamics and the general increase in bacterial load.

One recent study showed that just eating a high-fat "Western-style" diet for one month produced a dramatic 71% increase in

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plasma levels of endotoxin activity in comparison to a "prudent-style" diet.[6] This study revealed that the Western-style diet might contribute to endotoxemia by altering the gastrointestinal barrier function or the composition of the microbiota.[6] The effect of high-fat diet on metabolic endotoxemia seems to be reversible by the study, but one question arises. Could the development of metabolic endotoxemia by high-fat diet be prevented by antibiotics or probiotics? In fact, the therapeutic approaches aimed at reducing the translocation of endotoxin from the gut to the circulation need to be explored with regard to the possible prevention of several chronic diseases, which occur in the context of the chronic low-grade inflammation.

Keywords: High-fat diet; metabolic endotoxemia; low-grade inflammation

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