

## COMMENTS AND RESPONSES

### **Comment on: Lassenius et al. Bacterial Endotoxin Activity in Human Serum Is Associated With Dyslipidemia, Insulin Resistance, Obesity, and Chronic Inflammation. Diabetes Care 2011;34: 1809–1815**

**L**assenius et al. (1) have shown that high serum endotoxin activity is associated with components of metabolic syndrome. An important observation in their analysis is that most diabetic patients with high serum lipopolysaccharide (LPS) activity had elevated serum triglyceride and low HDL cholesterol concentrations and that serum LPS activity correlated positively with C-reactive protein, a marker for low-grade inflammation. The data presented is impressive; however, the source of endotoxemia was not clearly postulated. Also the exact composition of the diet consumed by the subjects was not mentioned. We think this information is significant because research has shown that certain diets induce inflammation and LPS production.

Our studies showed that a high-fat, high-carbohydrate meal (HFHC, 910 calories) induces an increase in plasma concentrations of LPS and lipopolysaccharide-binding protein (LBP) and in the expression of Toll-like receptor (TLR)-4, TLR-2, and suppressor of cytokine signaling 3 (SOCS-3) mRNA and protein. The HFHC meal also results in the induction of a comprehensive oxidative and inflammatory stress response characterized by an increase in reactive oxygen species (ROS) generation and nuclear factor- $\kappa$ B binding activity in

both mononuclear cells (MNCs) and polymorphonuclear leukocytes (PMNLs), as well as increases in p47<sup>phox</sup> expression and plasma MMP-9 concentrations (2). The induction of SOCS-3 postprandially may contribute to the pathogenesis of leptin and insulin resistance because SOCS-3 is known to interfere with insulin and leptin signal transduction. It is also of interest that saturated fat (cream) intake leads to an increase in LPS and LBP, the increased expression of TLR-4 and SOCS-3, as well as other proinflammatory changes, whereas glucose intake induces only oxidative stress, inflammation, and SOCS-3 expression but not endotoxemia or an increase in TLR-4 expression (3). It would, therefore, appear that fats are potentially more injurious than glucose and possibly other carbohydrates.

A diet rich in fruit and fiber, consistent with the recommendations of the American Heart Association, does not induce an increase in LPS or any of the above mentioned inflammatory changes (2). We have also observed that the intake of orange juice along with a HFHC meal prevents the increase in LPS, TLR-4, TLR-2, ROS generation, and other inflammatory responses in MNCs and in plasma (4). Interestingly, a supplement containing resveratrol and muscadine polyphenols also suppresses the increase in oxidative stress, LPS and LBP concentrations, and expression of TLR-4, CD14, interleukin-1 $\beta$ , and SOCS-3 in MNC after a HFHC meal, demonstrating its acute antioxidant and anti-inflammatory effects in humans in the postprandial state (5).

In conclusion, there are food products that are proinflammatory and induce an increase in LPS, which lead to the induction of molecules that interfere with insulin and leptin signal transduction and thus promote insulin resistance. Such postprandial inflammation may also contribute to the pathogenesis of atherosclerosis and cardiovascular disease. On the other hand, our data point to the presence of anti-inflammatory foods that can potentially prevent these processes. These observations are of potential relevance in the prevention of diabetes and its atherosclerotic complications and will eventually contribute to the incorporation of anti-inflammatory meals into our lifestyle and eating habits.

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DOI: 10.2337/dc11-1862

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**Acknowledgments**—P.D. is supported by the National Institutes of Health (grants R01-DK069805 and R01-DK075277) and the American Diabetes Association (grant 708CR13).

No potential conflicts of interest relevant to this article were reported.

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