

# For Better and for Worse, Diet Shapes Inflammatory Potential

**This review, authored by omega-3 expert Philip Calder, chromosome researcher Michael Fenech, and a team of nutritionists, microbiologists, and public health specialists, examines the origins of low-grade inflammation, commonly seen in obesity and during aging. At the population level, this chronic, ‘sterile’ form of inflammation correlates with relatively recent historical changes in the composition of human diets, and it often leads to immunometabolic consequences that can profoundly impact healthspan.**

Inflammation is both friend and foe, as these researchers note: necessary for immunosurveillance and protection yet, in modern times, apt to predispose many individuals to complex chronic illness. This expert team further states that “An unresolved inflammatory response is likely to be involved from the early stages of disease development.” Low-grade inflammation is particularly central to common age-related neurodegenerative and cardiometabolic conditions, and dietary habits—which are often formed by early-life experiences—can profoundly influence whether inflammation persists or resolves.

Relative to many other food components, dietary fats have outsized influence over body weight, fat mass, cell membrane function, and inflammation signaling. Many saturated fats (though not those from tropical plants such as coconut or palm) are known for proinflammatory influence, and substituting monounsaturated for them in diets is an accepted means of alleviating this metabolic stress. Omega-3 fats and their metabolites have emerged as a realistic means of actively recalibrating the immune response towards resolution, with downstream benefits to vascular function, metabolic flexibility, and long-term immune regulation.

This team notes that greater dietary fiber intakes and lower glycemic loads better reflect our ancestral diets, and these strategies are a major means of limiting postprandial glucose excursions, insulin resistance, and chronic immune activation. Plant flavonoids also offer distinct



advantages for immunomodulation through their salutary effects on cell signaling, mitochondrial function, genetic expression, and suppression of microglial activation, which is implicated in cognitive impairment.

This review is the collaborative result of an International Life Sciences Institute (ILSI) workshop on meaningful approaches for evaluating inflammatory status and addressing the chronic low-grade inflammation seen in aging, obesity, and comorbid conditions.

#### According to these experts:

**“It is not unreasonable to speculate that the adverse impact of the energy-dense, nutrient poor Western-style diet on [the] human gut microbiota and immune system, which have both been finely tuned and honed by high-fibre, high-polyphenol traditional diets over the millennia, may therefore be an important contributor to the environmental stimuli that trigger and progress autoimmune conditions.”**

#### Review Summary

Significant findings from this expert collaboration include:

- Postprandial inflammation may contribute significantly to dyslipidemia and chronic inflammation, with high-fat meals and dietary saturated fats of particular concern.
- In the elderly, reduced gut abundance of bifidobacteria has been seen to encourage lipopolysaccharide (LPS) endotoxemia by facilitating increased gut permeability. Fatty diets and Proteobacteria (often found to be abundant in gut dysbiosis) are sources of LPS, which these authors describe as an important trigger for low-grade inflammation and metabolic disease.
- Microglia are crucial immune-active neurons in the brain, and are typically long-lived. Their repeated activation can ‘prime’ them for an exaggerated immune response, resulting in a constellation of neuroinflammatory symptoms and disorders. LPS have been found to contribute to microglial priming.
- The researchers cite recent evidence suggesting that dietary flavonoids may inhibit microglial activation to help mediate immune balance within the central nervous system.
- Numerous clinical and epidemiologic studies have found that dietary intakes of flavonoids or flavonoid-rich foods have been associated with lower circulating levels of inflammation markers including C-reactive protein (CRP), interleukin-6, tumor necrosis factor (TNF), RANTES, and others. Flavonoids have also been seen to inhibit or downregulate multiple key inflammatory signaling networks.
- In considering systemic inflammation, the authors point out communications between the central nervous and immune systems, with neuronal, hormonal, immune, and metabolic networks coordinating intensively in shaping the chronic immune response. They stress



that these interactions can profoundly influence long-term cognition as well as energy metabolism and immunity.

- Maternal undernutrition, overnutrition, and obesity can each increase risk for immunometabolic, lung, and developmental disorders in their children, demonstrating the importance of nutrient density in perinatal diets.
- The most common hepatic disorder in Western countries is non-alcoholic fatty liver disease, usually diet-related. NAFLD involves hepatic lipid accumulation and decreased oxidation of fats for energy, progressing to a proinflammatory sequence of heightened oxidative stress, lipotoxicity, and cell senescence that can lead to cirrhosis and fibrosis.

Evaluation and monitoring of valid biomarkers of function of cells, tissues, and organs in advance of clinical symptoms is increasingly urgent. This team states that, as one example, morbidly obese individuals show marked variability in their expression of inflammation and dysglycemia. These experts foresee a future in which tissue-specific -omics profiling involving clusters of biomarkers will enable clinicians to better manage health through a fuller spectrum of wellness and disease.

### **NUTRITION CONCLUSION**

**This team concludes that “There is a substantial amount of evidence to suggest that many foods, nutrients, and non-nutrient food components modulate inflammation both acutely and chronically.”**

**They emphasize the value of bioactive flavonoids, dietary fiber, prebiotics, and omega-3 fats—especially from an early age—in modifying the modern propensity towards chronic inflammation and cardiometabolic health issues.**

