Inflamed, bothered and confounded

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Making the right choice to reduce inflammation. Hamburger (saturated fats-associated with elevated inflammation) vs. salmon burger (omega 3s-associated with decreased inflammation). (Image provided by Drs. Sandi Navarro and Emily White).

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Inflammation is the immune system's response to a stimulus. Inflammation can occur as a short-term response to infection and injury, aimed at removing the stimulating agent and repairing damaged tissue. Additionally, inflammation can occur as a prolonged and dysregulated response; such low-grade, systemic inflammation has been linked to chronic diseases such as type II diabetes, cardiovascular disease, and cancer. Commonly, epidemiologic and intervention studies use circulating biomarkers of inflammation to determine disease risk.

However, it is unclear whether certain factors (dietary, anthropometric, etc.) consistently associate with inflammation biomarkers (blood or urine measures that indicate inflammation) and how these factors vary by biomarker. Understanding this would allow researchers to properly account for confounders specific to the particular inflammation biomarker-disease association. To address this question Drs. Sandi Navarro, Emily White, and colleagues, examined the associations of 38 exposures, including demographic factors, anthropometric measures, history of chronic disease, medication use, dietary factors, and supplement use, with a panel of 8 inflammation biomarkers to identify similarities and differences in the associations with these biomarkers. The results from their study were recently published in *Cancer Epidemiology, Biomarkers & Prevention*.

Their analysis included 217 participants from the VITamins And Lifestyle (VITAL) biomarker study, a sub-study of the VITAL cohort, a prospective study of over 77,000 Western Washington residents, ages 50-76 years, focused on supplement use in relation to cancer incidence. "The VITAL database is a rich data source, containing information about a wide variety of characteristics and lifestyle factors – including diet, physical activity, health history, medication use, etc., through validated questionnaires." Dr. Navarro elaborates, "This allowed us to look at a large number of determinants

of inflammation while adjusting for other factors that may confound the relationship. We also looked at a panel of eight different blood biomarkers to learn whether the relationship between these factors and markers of inflammation are consistent."

Using age, sex, and body mass index (BMI) adjusted linear regression, the researchers examined 38 exposures (demographic and anthropometric measures, chronic disease history, medication, dietary factors, and supplement use) with 8 inflammation biomarkers: C-reactive protein (CRP), prostaglandin E2 metabolite (PGE-M), IL1b, IL6, IL8, TNFa, and the soluble TNF receptors (sTNFR) I and II.

From the linear regression analyses, increasing age was associated with higher concentrations of all biomarkers except IL1b. BMI was positively associated with CRP and sTNFR I and II. Saturated fat intake was associated with increased CRP, sTNFRII, TNFa, and IL1b, whereas eicosapentaenoic acid + docosahexaenoic acid (EPA + DHA) intake (diet or total) was associated with decreased CRP, TNFa, and IL1b. Results for sex were varied: CRP and IL6 were lower among men, whereas PGE-M and sTNFRI were higher. Higher CRP was also associated with smoking, hormone replacement therapy use, and Ɣ-tocopherol intake; lower CRP with physical activity, and intakes of dietary vitamin C and total fiber. They found strong correlations between concentrations of TNFa and the ILs (Pearson correlation coefficient, r ranging from 0.66– 0.80). sTNFRI and sTNFRII were only modestly correlated with one another (r = 0.50), while the remaining biomarkers were either weakly correlated or uncorrelated.

In summary, Dr. Navarro notes, "this is the first study to look at nearly 40 different demographic and lifestyle factors at the same time to determine what is associated with blood markers of inflammation. The most consistent factors linked with higher inflammation were increasing age, BMI and intakes of saturated fat, whereas higher intakes of EPA and DHA omega 3 fatty acids (like those found in fatty fish, e.g., salmon) were associated with lower levels of inflammation. Our results suggest that potential confounders vary in population studies, depending on the marker being measured. These results will help other investigators choose which factors should be considered when planning studies that include blood markers of inflammation."

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