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High dietary intake of linoleic acid more than doubles the risk of ulcerative colitis

A high dietary intake of linoleic acid—an essential n-6 polyunsaturated fatty acid found in red meats, polyunsaturated margarines and various cooking oils—more than doubles the risk of developing incident ulcerative colitis, according to the results of a new multicenter European study.

Linoleic acid is converted to arachidonic acid, which is incorporated into the colonocyte cell membrane; once released from the cell membrane, arachidonic acid is metabolized to proinflammatory eicosanoids (including prostaglandin E_2, leukotriene B_4 and thromboxane A_2). These proinflammatory eicosanoids are present in the colonic mucosa of patients with ulcerative colitis. High levels of dietary linoleic acid have, therefore, been hypothesized to stimulate the development of ulcerative colitis. "There is experimental work supporting the hypothesis," says Andrew Hart from the University of East Anglia, UK, who is one of the study authors, "but very limited epidemiological work and no previous cohort study, hence this work."

In this study, the authors employed a prospective cohort design to reduce the potential for both recall bias and selection bias and, therefore, to "…produce the most accurate information on whether a high dietary intake of linoleic acid could lead to the development of ulcerative colitis."

Dietary information was gathered from participants recruited into the European Prospective Investigation into Cancer and Nutrition (EPIC) study via country-specific food frequency questionnaires (FFQs). These data were then used to calculate nutrient intake (frequency of consumption × fatty acid content [as reported in national food content databases]). All of the centers involved validated the FFQ data against 24 h recall questionnaires.

The participants were then followed up to identify any incident cases of ulcerative colitis—any participants who had ulcerative colitis at recruitment or who developed ulcerative colitis within

18 months of recruitment were excluded to try to make sure that the data provided were a true reflection of dietary intake before symptoms developed. The results were analyzed using a nested case–control method, in which every case was matched with four controls who were randomly selected from the same center and were of the same gender, a similar age and recruited into the EPIC study at a similar time.

FFQ data were available for 203,193 participants who were recruited into the EPIC study. Ulcerative colitis developed in 126 participants. The median time from recruitment to a diagnosis of ulcerative colitis was 4.0 years and the median age at diagnosis was 60.0 years.

Most significantly, the risk of developing ulcerative colitis was more than doubled for the highest quartile of dietary linoleic acid intake (odds ratio [OR] 2.49, 95% CI 1.23–5.07, $P = 0.01$) when adjusted for center, gender, age at recruitment, energy intake and cigarette smoking. The authors suggest that "if the association is a causative one then 30% of all cases could be attributed to such higher intakes". There was also a statistically significant increase in the risk of developing ulcerative colitis across the quartiles of dietary linoleic acid intake (OR 1.32 per quartile increase, 95% CI 1.04–1.66, $P = 0.02$).

An association was also found between the development of ulcerative colitis and increased dietary intake of docosahexaoenoic acid, a fatty acid that is found in fish oil. This association was, however, a negative one (OR 0.23, 95% CI 0.06–0.97, $P = 0.05$), which means that docosahexaoenoic acid has a protective effect.

To complement the questionnaire-based data obtained in this study, the authors are now performing studies using biomarkers of linoleic acid intake. "If a causal link [between high dietary intake of linoleic acid and the development of ulcerative colitis] is confirmed," explains Hart, "then reducing the amount of linoleic acid in the diet may help prevent ulcerative colitis." In addition, the authors are looking into the possibility that symptoms can be prevented and the quality of life improved in patients with ulcerative colitis if it is recommended that they lower their dietary intake of linoleic acid.

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