The relation between total fat intake and risk of colon cancer has been well studied. In general, studies have found little or an inconsistent association between the two.1 In contrast with the results for total fat, little is known about the relation of individual fatty acids and colon cancer risk. A paper in this issue of the International Journal of Epidemiology addresses the association between specific dietary fatty acids and risk of colorectal cancer.2 The investigators examined this relationship among French-Canadian men and women in Montreal using a case-control design. Diet was assessed using food frequency questionnaires in addition to face-to-face interviews.

Before commenting on the findings regarding intake of specific dietary fatty acids and risk of colorectal cancer, several points are worth considering. Diet is not the only source for many fatty acids, which are also produced endogenously. Moreover, based on genetic and other nutritional differences, fatty acid metabolism may vary among individuals. Thus, isolating the effects of individual fatty acids of dietary origin on colon cancer is complex. In addition, certain methodological issues are important to consider. In general, case-control studies on diet and cancer may be prone to methodological bias because dietary information is collected after the diagnosis of cancer. One study found that subjects with colon cancer reported substantial dietary changes after the diagnosis;3 such changes could have distorted the reporting of past diet.

One of the main findings of Nkondjock and colleagues was that medium chain fatty acids from dairy products were related to reduced risk of colorectal cancer among women. Of the few studies that have examined medium chain fatty acids in relation to colon cancer risk,4–6 one investigation4 found no association and two reports5,6 observed an increased risk with individual medium chain fatty acids. Most studies that have evaluated various sources of fats in relation to risk of colon cancer have not found dairy fat to be related to colon cancer risk.1 Is it possible that other factors in dairy products may have accounted for the observed inverse associations between medium chain fatty acids and colorectal cancer risk? Epidemiological and other research shows that specific factors in dairy products, such as calcium or vitamin D, are inversely related to risk of colon cancer.7 Conceivably, such factors could have contributed to or accounted for the apparent protective effect. Unfortunately, the contributions of calcium and vitamin D to the reduced risk observed were not evaluated in the present study.

An additional finding of Nkondjock and colleagues was that alpha-linolenic acid (which was derived mainly from fats and oils in this population) was inversely associated with colorectal cancer risk among women. The apparent protective effect of alpha-linolenic acid on risk for colorectal cancer is supported by mechanistic studies showing that long-chain omega-3 fatty acids decrease prostaglandin E2 production in the colon by suppressing COX-2 induction, thereby altering proliferation in the colonic mucosa.11 However, three previous epidemiological studies4,9,10 found no association between alpha-linolenic acid and colon cancer risk. A particularly intriguing finding of Nkondjock et al., that requires confirmation in future studies, was that the omega-6 to omega-3 fatty acid ratio was positively associated with colorectal cancer risk among women.

The strongest relationship observed in the current study was the direct association between intake of arachidonic acid and risk of colorectal cancer in both genders. This observation is consistent with experimental studies showing that elevated levels of arachidonic acid are associated with increased production of prostaglandins,11 factors that play a causal role in colon carcinogenesis. The findings regarding arachidonic acid are also compatible with previous epidemiological studies suggesting that

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**Commentary: Can dietary fatty acids affect colon cancer risk?**

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intake of meat, particularly red meat, increases the risk of colon cancer.\textsuperscript{1} Alternatively, arachidonic acid may have reflected a correlated component of meat intake, such as haem iron or heterocyclic amines formed during cooking. Other fatty acids present in meat, such as palmitic acid or stearic acid, which have been hypothesized to be potentially mutagenic to colonocytes,\textsuperscript{12} were unrelated to risk.

Because unsaturated fatty acids are prone to oxidative modification, the availability of antioxidants such as vitamin C or carotenoids may mitigate their potential for oxidative damage.\textsuperscript{13} Thus, the investigators examined whether the association between polyunsaturated fatty acids and risk of colorectal cancer might be modified by intake of vitamin C or carotenoids. They found that intake of arachidonic acid was related to increased risk particularly among men with high intakes of vitamin C and among women and men with low intakes of carotenoids. Whether these findings reflect causality remains speculative despite the existence of several plausible metabolic pathways.

Interestingly, the relationships of most fatty acids with risk of colorectal cancer were stronger in women than in men. As Nkondjock and colleagues speculate, sex-specific differences in bowel transit time or bile acid production may have accounted for the gender-specific variations observed. Because smoking was much more prevalent among men than women in the study population, an alternative explanation is that smoking-related colon cancers among men may dilute the relative risks associated with intake of specific fatty acids if these cancers develop through a causal pathway independent of fatty acid intake. Another explanation is that women in this study provided more accurate dietary information. Despite the potential limitations in study design and the complexities in interpreting the findings, the results suggest several intriguing hypotheses that warrant further evaluation.

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