

Cancers of the Gut and Western Ills

In their well-known 1981 review on the causes of cancer in the United States, Doll and Peto* estimated that around one-third of deaths from cancer could be attributed to diet and were therefore, in principle, preventable. Epidemiological evidence continues to support this general conclusion, but in contrast to cardiovascular disease, for which the link to nutrition is now generally recognized, the relationship between diet and cancer has made much less impact on both policy-makers and the general public. One reason for this is the absence of any single hypothesis on which to build a dietary strategy for cancer prevention; this itself is a reflection of the complexity of human diets and the obvious fact that cancer is not a single disease. Although there has been huge progress in our understanding of the molecular basis of many cancers in recent years, most of the new knowledge has been deployed in the search for new therapies rather than to understand the role of nutrition in their causation. Nevertheless, the mechanisms linking diet to cancer can be understood and exploited for prevention as much as for treatment, and there are sound scientific and strategic reasons to focus such research on carcinomas of the alimentary tract.

The hypothesis that “overnutrition” increases the risk of bowel cancer is supported by studies within the populations of the developed world, where overconsumption of energy, low levels of physical activity, high body mass index, and abdominal obesity are strong independent risk factors for colorectal carcinoma, much as they are for insulin resistance and cardiovascular disease. A similar link to obesity has been established for esophageal adenocarcinoma, once the rarest form of cancer of the esophagus but now advancing rapidly throughout North America and Western Europe.

What do we know about the links between gut-related cancer progression and diet? Although mutagens are present in foods and feces at low concentrations, there is little evidence that the adverse effects of diet on alimentary cancers in the West are caused by food-borne carcinogens that can be identified and eliminated from the food chain. It seems more plausible that the Western gut becomes vulnerable to neoplasia because of adverse metabolic factors, such as pro-inflammatory agents produced by adipose tissue, and because of low intakes of anticarcinogens from plant foods. The chronic use of aspirin and other nonsteroidal anti-inflammatory drugs significantly reduces the risk of colorectal and esophageal cancers, perhaps by inhibiting the expression of the pro-inflammatory enzymes in precancerous tissues. Both diseases are also less common among consumers of diets rich in fruits and vegetables, which harbor a huge variety of biologically active secondary metabolites such as glucosinolates and flavonoids, which may act synergistically in the human diet.

There are profound and fascinating biological problems to be solved in the search for the links between nutrition and cancer, and the human digestive tract is likely to prove an immensely rewarding focus for future research. Meanwhile, carcinomas of the gut are among the most common causes of morbidity and death from cancer in the developed world. The role of weight, lack of exercise, and inadequate consumption of plant foods in their etiology needs to be more widely acknowledged and publicized.

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*R. Doll, R. Peto, *J. Natl. Cancer Inst.* **66**, 1191 (1981).

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