ROLE OF DIET IN CANCER

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Cancer is an increasing health problem, not only for industrialized countries but also for most other parts of the world.

The large differences in cancer rates among countries, striking changes in these rates among migrating populations, and rapid changes over time within countries indicate that some aspect of lifestyle or environment is largely responsible for the common cancers in Western countries(1).

Stomach cancer is one of the most common cancers worldwide. Almost two-thirds of the cases occur in developing countries and 42% in China alone(1). The geographical distribution of stomach cancer is characterized by wide international variations; high-risk areas (Age adjusted incidence rate (ASR) in men, >20 per 100,000) include East Asia (China, Japan), Eastern Europe, and parts of Central and South America. Incidence rates are low (<10 per 100,000 in men in Southern Asia, North and East Africa, North America, and Australia and New Zealand). Patterns in women are broadly similar to those in men. When comparing incidence cases of stomach cancer in Hawaii Japanese and Caucasians by place of birth as obtained from the Hawaii Tumor Registry, Kolonel and colleagues found higher ASR among the Japanese migrants to Hawaii than the Japanese born in Hawaii, while the Caucasian migrants to Hawaii had lower rates than the Caucasians born in Hawaii (2). This result indicates the importance of early and different exposure to the risk of developing gastric cancer.

Animal studies have been extremely useful in providing hypotheses and supporting evidence. The ability of chronic caloric restriction to inhibit the formation of various tumors of the mouse has been long recognized (3). Later, it was demonstrated that the observed phenomenon is due to caloric restriction and not dietary fat content (4). Ideally, all diet and cancer-hypothesized relationships would be evaluated by randomized trials in humans, but in most instances such studies may never be feasible because of the need for large sample sizes, long (and uncertain) duration of follow-up, and high levels of compliance. So far prospective epidemiologic studies provide the best available evidence. These are less subject to serious problems of confounding that can make cross-cultural comparisons completely misleading, and they avoid the problem of recall bias that can affect typical case-control studies of diet.

The topic received great attention in a review conducted by the British epidemiologists Richard Doll and Richard Peto (5). These epidemiologists were asked to identify the causes of cancer mortality in the United States. Of course tobacco was high on the list at about 30% – causing about 30% of cancers. But what was surprising to many people was a 35% estimate for diet. However, there was a lot of uncertainty about that estimate. Doll and Peto also said it might be as little as 10% or as high as 70% of cancers that were related to diet – some exposures interact with each other. And proportions are impossible to quantify because not all avoidable causes are known. This conclusion set off a huge amount of investigation over the next two and a half decades.

Dietary fat has been hypothesized to be the key factor because national consumption is correlated with the international differences (6). However, detailed analyses in large prospective studies have not supported an important role of dietary fat. Instead, positive energy balance,

reflected in early age at menarche and weight gain as an adult, is an important determinant of breast and colon cancers, consistent with numerous studies in animals (7&8). As a contributor to positive energy balance, and possibly by other mechanisms, physical inactivity has also been shown to be a risk factor for these diseases and in part accounts for the international differences (9&10). Although the percentage of calories from fat in the diet does not appear related to risk of colon cancer, greater risks have been seen with higher consumption of red meat, suggesting that factors other than fat per se are important. in prospective trials (11). On the other hand, a long standing belief in the protective role of fruits and vegetables was not confirmed. Taken together, the evidence supports a role for the triad of diet, body mass index and exercise in carcinogenesis. The Women Health Initiative (WHI) study is A randomized, controlled, primary prevention trial conducted at 40 US clinical centers from 1993 to 2005 (12).

A total of 48 835 postmenopausal women, aged 50 to 79 years, without prior breast cancer, were randomly assigned to the dietary modification intervention group (40% [n = 19 541]) or the comparison group (60% [n = 29 294]). The intervention was designed to promote dietary change with the goals of reducing intake of total fat to 20% of energy and increasing consumption of vegetables and fruit to at least 5 servings daily and grains to at least 6 servings daily. Comparison group participants were not asked to make dietary changes. Surprisingly, that intervention did not result in a statistically significant reduction in invasive breast cancer risk over an 8.1-year average follow-up period. However, the non-significant trends observed suggesting reduced risk associated with a low-fat dietary pattern indicated that longer, planned, nonintervention follow-up may yield a more definitive comparison. That same study failed to confirm the protective effect of normal levels of vitamin D against colorectal cancer suggested previously by the nurses' health study (13). However, there were major limitations of that trial. Calcium and vitamin D was given as a combination. One of the limitations was just the fact that it was seven years, and that's quite a short time in the development of colorectal cancer. It may be almost wishful thinking to believe that something like vitamin D or calcium could have an effect that quickly. Also, 69% of the women in the study were taking calcium supplements on their own, in both the placebo group and the active group, which causes huge misclassification. The controversial result from one of the best well designed trials speaks for the complexity of conducting prospective trials to address the role of a single nutrient in cancer.

The evidence does not only support a role for the triad in carcinogenesis, but also in mortality from cancer (14). In a prospectively studied population of more than 900,000 US adults, increased body weight was associated with increased death rates for all cancers combined and for cancers at multiple specific sites, including esophagus, colon and rectum, liver, gallbladder, pancreas, and kidney; the same was true for death due to non-Hodgkin's lymphoma and multiple myeloma. The authors estimated that current patterns of overweight and obesity in the United States could account for 14 percent of all deaths from cancer in men and 20 percent of those in women. Even more interesting were data suggesting midrange intake of most major energy sources was associated with best survival after treatment of breast cancer, and extremes were associated with less favorable outcomes (15).

Recent data confirmed that vitamin E supplements, selenium supplements, or the 2 of them taken together did not reduce the risk of developing prostate cancer (16). If anything, there was a small trend towards an increase in the number of prostate cancer cases for the men randomized to take vitamin E, and a small increase in the number of cases of type II diabetes mellitus in men taking only selenium.

In light of the above discussion, moderation of diet (quantity and quality) seems the most reasonable approach to adopt throughout life.

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