Reviews in Oncology 3 (1990) 1
(in Acta Oncologica Vol. 29, Fasc. 1)

FROM THE DEPARTMENT OF PREVENTIVE MEDICINE AND BIOSTATISTICS, UNIVERSITY OF TORONTO, TORONTO, ONTARIO, CANADA.

DIET AND CANCER

A review

A. B. MILLER

Abstract

Diet is one of the major causes of cancer. The epidemiologic data on which this conclusion is based has been derived from analytic epidemiologic studies, buttressed by descriptive (ecologic) epidemiology and studies in experimental animals. Although the evidence is not entirely consistent, high dietary fat intake appears to be a major cause of breast cancer, and more consistently, of colorectal cancer, and probably prostate cancer as well. Obesity is an important cause of endometrial cancer, and increases the risk of breast cancer in postmenopausal women, though increasingly there is evidence that suggests that obesity is protective for breast cancer in premenopausal women. There is inconsistent evidence that dietary fibre is protective for colerectal cancer, though good evidence that vegetable consumption is protective. Several studies have pointed to a protective effect of betacarotene for lung cancer, but betacarotene may be acting as an indicator of other protective factors in diet. Recommendations for dietary modification, congruent with recommendations for the prevention of cardiovascular and other chronic diseases, are now appropriate.

Key words: Breast cancer, colorectal cancer, diet, endometrial cancer, epidemiology, prevention, prostate cancer, stomach cancer.

Of the known causes of cancer, dietary factors collectively contribute to a large proportion of potentially preventable cancers. Estimates have varied, but tend to be around 30–35%, though the evidence is not precise and several years ago Doll & Peto suggested a range of 10–70% (1). The importance of dietary factors seems almost as great in developing countries as it increasingly appears to be so for the technically advanced countries, though most, but not all of the data has been derived from the latter. The stage has now been reached where appropriate and acceptable recommendations can be made on optimal dietary patterns. Such recommendations can be designed not only to reduce the incidence of cancer of most sites, but to prevent adverse changes in the rates of all cancers. At the same time these recommendations are compatible with those made for the prevention of other dietary associated diseases, especially cardiovascular disease. Recently a committee of the US National Research Council has produced recommendations directed to this end (2). These will be reviewed at the end of this paper. In the main part of the paper, however, I shall review the scientific basis for the recommendations, concentrating on that derived from epidemiology.

Dietary fat

Of all dietary factors believed to affect cancer incidence, dietary fat has perhaps attracted most interest. This is in part due to the strong correlations noted in international data between the incidence of or mortality from certain cancer sites and estimated population intake of dietary fat (3), and in part because of observations from animal experimental models. The international correlation studies (ecologic studies) connot be used to infer causality, but they are useful in raising hypotheses. They may also provide some indication of the range of an effect, which may be difficult to determine within a country if dietary patterns are relatively homogeneous. Although for both mammary cancer and colon cancer in rodents strong associations have been noted with high fat in the diet, perhaps particularly with regard to colorectal cancer, the animal models have been developed specifically to explore mechanisms potentially relevant to the fat hypothesis and therefore cannot be used to confirm the validity of that hypothesis (4).

In the absence of human intervention studies, most emphasis has to be placed on the results of analytic epidemiology, namely case-control and cohort studies. In case-control studies dietary histories of newly diagnosed cases are compared with those from comparable controls,

preferably drawn from the same population as the cases. In cohort studies, dietary data are collected from an identified group or cohort, usually with a self-administered questionnaire, and the cohort is followed to determine the subsequent incidence of cancer. Unfortunately, many of the reported studies were based on inadequate dietary methodology, often with a very indirect assessment of dietary fat intake. Further, all the case-control studies provide estimates of fat intake which relate to current or recent diet, and which therefore only imperfectly, if at all, reflect diet at the relevant time period for cancer induction.

Breast cancer

For breast cancer, the ecologic studies have shown strong associations with dietary fat (3). One recent study of international data has shown that the effect is largely restricted to fat calories, calories from protein, carbohydrate and alcohol having no significant effect (5). Much of the other positive evidence associating dietary fat with increased risk comes from case-control studies, though in many the associations have been weak. Some of these studies collected data only on fat containing foods, such as a study in Seventh-Day Adventists in California (6), a study in Canada in which increasing risk with increasing consumption of whole milk, beef and a protective effect from fish consumption was found (7), and a study in France where increased risk from consumption of full cream milk and cream was found (8). In other studies it was possible to characterise respondents in terms of dietary fat intake. Two such studies have been performed in Canada. In the first, suggestive associations were found with total fat intake (9). In the second, increasing risk with increasing consumption levels of beef, pork, animal fat and animal protein were found, with suggestive dose-response relationships (10). Although this study can be criticised on methodological grounds, because the control group was interviewed by a completely different team at a different time period, it is not clear why this should have been a source of systematic bias. A large study in Israel pointed to the importance of dietary pattern (11). Risk was increased in those with a high consumption of fat and protein and a low consumption of fibre, whereas risk was lowest in those with a low consumption of fat and protein, and a high consumption of fibre. A study in Italy showed a significant increased risk with increasing total and saturated fat consumption (12). Positive associations were also found with consumption of diary products, particularly those rich in fat, such as high-fat cheese and whole milk. These associations were characterised by significant dose-response trends and were not modified by adjustment for total calorie intake or for other risk factors for breast cancer. In the Netherlands a case-control study also found elevated risk for high fat consumption (13). In general the level of increased risk found in these studies was of the order of 1.5 to 2.0, though risks >3.0 in the highest quartile or quintile relative to the lowest were found in the studies in Italy (12) and the Netherlands (13). Some other case-control studies, however, have been entirely negative, including studies in New York State (14) and Australia (15). A large cohort study of American nurses was also negative (16). However, the difference in intake between the upper and the lower quintiles of fat intake in this study could not be expected to demonstrate more than a relative risk of 1.4 if the international correlation studies are a guide. With this weak risk anticipated, and the possibility of measurement error from a self-administered questionnaire, it is perhaps not surprising that such a study should be negative.

Colorectal cancer

For colorectal cancer, although there have been negative studies, the evidence is becoming more consistent. A case-control study on Seventh-Day Adventists showed that meat of any type, beef products, beef hamburger and lamb increased risk (6). In a study of Bay area blacks, the highest risk was found in those with a high consumption of saturated fat containing foods and a low consumption of fibre (17). A study in Canada showed a dose-response relationship, strongest for saturated fat and colon and rectal cancer in both sexes. The risk in the highest saturated fat intake category relative to the lowest was of the order of 2.5 (18). Similar findings were seen in a recent study in Western New York (19), and in the large cohort study of American nurses (20). In a study in the Marseilles region of France, there was no evidence of increased risk from dietary fat, though oils, especially olive oil, were protective (21). In two studies in Australia (22, 23), both dietary fat and sources of animal protein, appeared to increase risk. In a large cohort study in Japan high meat consumption, presumably indicative of high fat consumption, was associated with increased risk of colon cancer (24).

Other cancers

For other cancers, there is less evidence. Some studies suggest increased risk from fat intake for prostate cancer, while a few suggest similar effects for pancreas, kidney and even lung cancer (25). For prostate cancer, one of the largest case-control studies, conducted in Hawaii, found a dose-response gradient in risk of prostate cancer associated with saturated fat intake in men age 70 years and older (26). In contrast, a much smaller study conducted in American blacks (who have a higher incidence of prostate cancer than whites) found increased risk associated with fat intake only for those under the age of 50 (27). A further American study of whites found elevated risk associated with increasing consumption of animal fats, with no apparent differential effect by age (28). For ovarian cancer there has been one positive (29) and one negative (30) study.

Calorie intake, energy expenditure and obesity

In general, the studies that have evaluated nutrients have failed to find a specific effect of calorie intake over and above the effect of other nutrients such as dietary fat. Many studies have investigated associations between various measures of weight and risk of specific cancers, and these to some extent may represent the effects of increased caloric intake, though it is increasingly clear from studies of obese individuals that in those constitutionally predisposed to obesity, a balance has to be maintained between food intake and energy utilisation in the activities of daily life (2).

Weight

Positive associations have been reported between excess weight and cancers of the gallbladder, biliary duct, endometrium, ovary, breast, and cervix in women, and cancers of the colon and prostate in men. The associations for ovary, cervix and colon have not been consistent, but the remaining sites are generally considered to be causally associated with obesity.

In the American Cancer Society cohort study conducted between 1960 and 1972, positive associations were reported between excess weight and cancers of the gallbladder, biliary duct, endometrium, ovary, breast, and cervix in women, and cancers of the colon and prostate in men (31). A substantial increase in risk for cancer of the endometrium with increasing weight or other measures of obesity has been a consistent finding in other studies, for example in case-control studies in Northern Italy (32) Denmark (33), and the United States (34). Studies of breast cancer have also offered evidence for an association between weight indices and increased risk. The effect has primarily been observed in postmenopausal women (35–37). Associations have either been absent, or negative in premenopausal women. Thus, in a recent cohort study, Willett et al. (38) found a significant inverse relationship between the body mass index (BMI) and age-adjusted relative risks of breast cancer in 121 964 US nurses aged 30–55. In a study in Israel (37), risk was increased in postmenopausal women past the age of 60 with an elevated body mass index, but decreased in those who had lost weight during their adult life. There is some evidence that for both these sites adipose tissue is acting as an estrogen producing organ.

Some studies have suggested that height rather than weight may be the better predictor of breast cancer risk (39, 40). Nutritional status during adolescence may therefore be a critical variable.

Concerning other sites, case-control studies of ovarian cancer have obtained weakly positive (30) and weakly negative (41) associations with weight. Others have reported that increased weight is associated with risk of cancer of the prostate (42, 43).

Increased risk of various cancers associated with measures of decreased weight, for example, cancer of the esophagus (44) and cancers of the lung (31) has also been reported, but these are probably indicators of impaired nutritional status reflecting social factors, or tobacco or alcohol use.

Caloric intake

A few studies have estimated total caloric intake in relation to cancer risk. Four case-control studies of colorectal cancer, one in Canada (18), one in Australia (22), one in the United States (45) and one in Belgium (46) reported differing results. Cases reported a greater caloric intake than controls in the Canadian, Australian and US studies but the opposite was found in the Belgian study. A reanalysis of the Canadian data (47) reaffirms that the risk in this study is associated with saturated fat intake for both males and females, and that the relative risks associated with caloric intake are very close to unity.

Energy expenditure

Two studies have indirectly examined the role of energy expenditure in relation to risk of colon cancer. In both it was reported that colon cancer cases had more sedentary occupations than controls (48, 49), but this was not found for rectal cancer in one (48). In addition, a follow-up of college alumnae produced evidence suggesting that the cumulative incidence of breast and female reproductive system cancers was less in former college athletes than in non-athletes (50). This effect may be due to suppression of ovarian function in athletes, however, rather than a direct effect of energy expenditure.

Carbohydrates

There is little epidemiological evidence to support a role for carbohydrates *per se* in the etiology of cancer. Part of the difficulty is that carbohydrates are often considered in epidemiology studies as just one component of total energy and not analyzed separately.

There have been several international correlation studies that evaluated the potential role of sugar and sometimes carbohydrates in the etiology of some cancers. Armstrong & Doll (3) found a positive correlation between sugar intake and mortality of cancer of the colon, rectum, breast and ovary; and incidence of cancer of the corpus uterus. Similar positive correlations were found for incidence or mortality of cancer of the prostate, kidney, and nervous system, and incidence of cancer of the testicles; there was an inverse correlation for incidence of liver cancer. For pancreatic cancer there was a positive correlation between sugar intake and mortality. For most of the sites reported particularly colon, rectum, and breast, the positive correlations with fat intake were greater than for sugar intake.

Other investigators had similar findings (51, 52). However, subsequently, Carroll (53) found that while breast cancer mortality is positively correlated with the percent of calories derived from dietary fat, it varies inversely with the percent of calories from carbohydrate. Hems & Stuart (54) also found an inverse relationship between breast cancer incidence and starch intake.

Hakama & Saxen (55) found a strong correlation with the per capita intake of cereal used as flour and mortality from stomach cancer. The possible association between carbohydrate intake and gastric cancer was further evaluated by Modan et al. (56) who found that high starch foods were consumed more frequently by cases than by controls. Similarly, in a case-control study of diet and stomach cancer in Canada, a trend of increasing risk with consumption of carbohydrate as a whole was found though the odds ratio for each increase of 100 g a day of carbohydrate was only 1.53 (57).

In two case-control studies of colorectal cancer using essentially the same dietary instrument, the effect of monosaccharides has been evaluated. In a study conducted in Marseilles (21) there appeared to be no evidence of increasing risk with increasing consumption of monosaccharides. However, in a study conducted in Belgium (46) mono and disaccharide intake showed increasing risk of both colon and rectal cancer with increasing consumption levels. The relative risk for the highest compared to the lowest consumption level was 1.7 for colon cancer and 2.4 for rectal cancer.

Protein

A direct effect of dietary protein on cancer risk has been difficult to assess in epidemiologic studies due to the high correlation between fat and protein intake in the western diet (3, 18, 58).

Colorectal cancer

Large bowel cancer incidence and mortality are positively associated with total per capita protein intake, and especially with animal protein (3, 59). In a more recent report (60), this association held for underdeveloped but not developed countries. Comparisons between two Scandinavian populations or among regional populations in Britain, did not find significant associations of large bowel cancer with dietary protein (61–63).

Four case-control studies have assessed protein intake in relation to risk of cancer of the large bowel. Jain et al. (18) found that both colon and rectal cancer cases had a significantly higher protein consumption than neighborhood controls, but they found a stronger association for dietary fat. Potter & McMichael (22) found that dietary protein was the most consistent risk factor for cancers of the colon and rectum among both sexes in a population-based case-control study in South Australia. In another population-based case-control study in Australia (23) protein intake was associated with colorectal cancer risk in univariate analyses, but there was no clear dose-response gradient and protein was not a significant variable in the multivariate analyses. A case-control study of colorectal cancer in the Marseilles region of France found a protective effect of protein intake, with a significant linear trend, on colorectal cancer, but this trend was no longer significant when the subsites of colon and rectum were examined separately (21).

Reports on two cohort studies do not support an association between dietary protein and colon cancer risk (64, 65). Neither found a difference between colon cancer cases and controls in their intake of animal or vegetable protein.

Several epidemiological studies, both correlational and case-control, reported positive associations between meat consumption (an important fat as well as protein source in western diets) and colon or rectal cancer risk (66, 67), though in other reports, no association with meat intake was found (68, 69). In one of these, it was clear that saturated fat intake was the critical risk factor for colon cancer (67).

Breast cancer

Ecologic correlation studies have shown strong positive associations between dietary protein intake, particularly animal protein, and breast cancer incidence or mortality (3, 51, 58, 70–72). In the study by Armstrong & Doll (3) and in a further analysis by Hems (73), the association of breast cancer with dietary fat was stronger than with protein.

Some case-control studies have looked at dietary protein in relation to breast cancer risk. Phillips (6) found an association between breast cancer risk and consumption of high fat foods but not with protein sources in particular. In a study in Canada, similar associations between breast cancer risk and estimated level of consumption of both animal fat and animal protein were found (10). In a case-control study in Israel, increased risks were associated with animal protein, but no clear dose-response trend was found (11). Similar associations with fat were stronger.

In case-control studies in Hawaii and Japan, dietary intake was compared between breast cancer cases and hospital and neighborhood controls (74, 75). Although cases as a group consumed somewhat more animal protein than controls, there was no clear trend of increasing risk with increasing animal protein intake in either study.

Breast cancer mortality was positively associated with meat consumption in a cohort of approximately 140 000 women in Japan (76). The death rate for women over age 60 who ate meat daily was more than double that for women who ate meat less frequently. However, breast

cancer mortality in a cohort of US Seventh-Day Adventists was not significantly increased with greater consumption of meat (77).

Other cancers

In a study of diet and esophageal cancer in Calvados (France) Tuyns et al. (78) found that animal proteins and fresh meats were protective. Separating the effect of specific nutrients was difficult because of intercorrelation between individual intake of most nutrients, though intake of specific foods were not so highly inter-correlated.

Pancreatic cancer has been associated with dietary protein intake in several geographic correlational analyses (3, 79, 80). High frequency of meat consumption has also been associated with risk for this cancer in some case-control studies (81, 82) but not others (83, 84). Hirayama (24) observed a marked increase in pancreatic cancer mortality among daily meat eaters who also smoked cigarettes in a prospective cohort of 265 000 adults in Japan.

Prostate cancer was positively correlated with protein intake (animal as well as total) in several ecological analyses (3, 58, 79). While one case-control study in American blacks found a nonsignificant increase in protein intake by cases at all ages (27), Graham et al. (28), studying white Americans, found a statistically significant trend in risk associated with higher frequency of consumption of meats and fish (protein intake *per se* was not estimated) only in men 70 years or older.

Dietary fibre

Most of the methodological problems discussed above for epidemiological studies of dietary fat apply also to studies of dietary fibre. In addition the methodology for assessment of dietary fibre has undergone marked changes in the past decade, without any final conclusion as to what constitutes dietary fibre, or in some instances, the components of dietary fibre that are potentially relevant in cancer etiology. Thus dietary data bases, especially in the past, were often inadequate to provide estimates of dietary fibre intake, studies purporting to support the 'dietary fibre hypothesis' being dependant on indexes of 'fibre-rich foods'.

Most of the studies relate to colorectal cancer and, with few exceptions, no association has been found for dietary fibre *per se* in case-control studies (85). In particular, no evidence of decreased risk was found for increased fibre intake in studies in Canada (67), Australia (22) and the United States (19), and only a weak association in a further study in the United States (45). However, a protective effect was found in one study in Australia (23), and in a study in Belgium (46). Nevertheless in a study in France, where protective effects were found for vegetable intake, it was the fibre poor vegetables that showed the strongest protective effect (21). Ecologic studies have given inconsistent results (61, 62, 85). In view of the methodologic difficulties, it would seem prudent neither to conclude that current results reflect the absence of a true association between dietary fibre intake and colorectal cancer, nor that a truly protective effect of dietary fibre has just not been detectable by the studies performed to date. Animal studies have not been helpful in clarifying the possible relationship between fibre ingestion and colorectal cancer (4).

There have been only a few studies that have evaluated the possible effect of dietary fibre on other cancer sites. One study of stomach cancer found a protective effect (57), though it seems possible that this was explained, at least in part, by a protective effect of vitamin C in fibre rich fruits and vegetables. One study of breast cancer, showed that a dietary pattern combining high fibre consumption with low fat intake resulted in the lowest risk (11).

Fruit and vegetable intake

In a case-control study of colorectal cancer, evidence was found of a protective effect of cabbage and of other vegetables of the *brassica* genus (86). The protective effects seemed to be particularly related to the frequent ingestion of raw vegetables, especially cabbage, brussels sprouts, and broccoli. An inverse association for cabbage consumption in a case-control study of colorectal cancer was also found in Japan (87). These associations were interpreted as a possible effect of inhibition of the microsomal monooxygenase system and thus inhibition of the activation of chemical carcinogens (88). In a subsequent case-control study of colorectal cancer, we found only weak evidence of a protective effect of such vegetables after taking account of saturated fat intake, and then only in females, without a dose-response relationship (67).

In several studies of lung cancer, evidence of a protective effect of consumption of vegetables has been found (89–91). These studies have generally been interpreted as providing evidence for a protective effect of betacarotene. However, it is possible that other factors found in the vegetables may be responsible for some of the protective effect. Indeed, in a large cohort study in Japan, a protective effect of green-yellow vegetable consumption was found for several cancers, including cancers of the stomach and colon, as well as for lung cancer (91).

In summary, there is consistent evidence of protective effects of fruit and vegetables consumption against several cancers. Although much of this effect could be due to components of dietary fibre (for colorectal cancer), vitamin C (for stomach cancer), and betacarotene (for lung cancer), the possibility remains that other protective factors in vegetables may be responsible for at least part of the protective effects.

Alcohol

Associations between alcohol drinking and certain types of cancer have been observed for many years. Increased mortality from oropharyngeal cancer has been observed among persons in occupations involving high alcohol consumption, as well as among alcoholics, whereas alcohol abstainers such as Seventh-Day Adventists and Mormons in the US have decreased risks. Most analyses showed multiplicative interactions between alcohol and tobacco (92).

Many studies have also shown an association between heavy alcohol drinking and laryngeal cancer. In nearly all the analyses, alcohol and tobacco were found to interact in a multiplicative fashion (93).

A high prevalence of alcoholism has been generally found among patients with esophageal cancer. In a series of studies conducted in France, the joint effect of alcohol and tobacco was multiplicative with a very high risk among persons who both drank and smoked heavily (94). In a case-control study of black men in Washington, DC, the risk was more pronounced among consumers of hard liquor than among consumers of beer (95).

An association between beer sales and rectal cancer in 41 states in the US and in 24 countries has been found (96). Although two studies in brewery workers were not consistent, several case-control studies have found associations between beer drinking and rectal cancer (92).

Some studies have suggested an association between cancers of the stomach and pancreas and alcohol consumption. However, most studies have not confirmed these associations.

In North America and western Europe, cirrhosis of the liver is mainly related to alcohol consumption. There is a firm association between cirrhosis of the liver and primary liver cancer (PLC). However, not all studies of alcoholics have shown an increased risk of PLC. Evidence on viral hepatitis and PLC in the alcoholic is also accumulating (2, 92).

In many studies which have evaluated an association, it has been found that there appears to be an increased risk of breast cancer in relation to alcohol consumption (97). In several of the positive studies risk appears to be associated with moderate alcohol consumption. However, in many of these studies, nutritional variables could not be fully evaluated. It is therefore possible that increased alcohol consumption may be a marker of other factors which increase the risk of breast cancer.

In summary, of all dietary factors shown to increase the risk of cancer, the evidence is strongest for alcohol. Although the largest risks relate to cancers shown to be increased by a joint exposure to cigarette smoking (especially oral cavity, pharyngeal and esophageal cancer, and the parts of the extrinsic larynx directly exposed to alcohol) the evidence is now conclusive that alcohol alone increases the risk of these cancers. Alcohol consumption is also causally related to primary liver cancer. However, the role of alcohol in increasing the risk of colon, rectal and breast cancer is still uncertain. The associations noted for the latter sites may reflect confounding with other causal factors.

Other dietary factors

A host of studies have evaluated the effect of various vitamins, minerals, beverages and other dietary components on the risk of a number of cancer sites (98). Although many have concluded that specific dietary factors (for example betacarotene or vitamin C) may be protective against cancers such as lung (89, 99, 100) and stomach (57), the evidence is not conclusive. A major difficulty is that the majority of the studies with significant findings were derived from an incomplete assessment of dietary intake, and therefore the investigators were unable to evaluate the possibility that the dietary factor considered was confounded by another more relevant dietary factor. Indeed those few studies that have included complete dietary assessment have in general failed to show that the specific micronutrient under consideration (for example betacarotene or vitamin C) made an independent contribution once other factors were taken into account (98).

Of the other dietary factors that could be considered, only for aflatoxin is there conclusive evidence of increase in cancer risk (though only for liver cancer) (98). There is however some epidemiological evidence that excess nitrite and or salt consumption will increase the risk of stomach cancer (57), while as yet undefined micronutrient deficiencies probably increase the risk of esophageal cancer.

Dietary recommendations

The Committee on Diet and Health of the National Research Council (2), having carefully reviewed the evidence associating dietary factors with the risk of chronic diseases, including cancer, concluded that a number of recommendations were appropriate for the general population. Although the evidence for these was greater for heart disease than cancer, a number can be expected to reduce cancer incidence, and some were largely adopted on the basis of data on cancer. These can be summarised as follows:

1. Reduce fat intake to between 25 and 30% of total calories with no more than 10% of total calories from saturated fats, 6–8% as polyunsaturated fats, and the remainder as monounsaturated fats.
2. Consume a variety of green and yellow vegetables and tubers, citrus fruits and whole grains and cereals.
3. Adjust exercise and food intake to maintain healthy body weight.
4. Limit the use of salt and the consumption of salty, salt- or nitrite-preserved and pickled foods.

5. If you drink alcoholic beverages, limit consumption to no more than the equivalent of two small drinks daily.
6. Minimize contamination of foods with carcinogens from any source.

The implementation of such recommendations is likely to require concerted action on several fronts. These include increasing the knowledge of the public through public education, obtaining the cooperation of the food producing, manufacturing and distributing industries to ensure that the public has the necessary choices available, and some actions from governments. Government support of the food industry can have adverse consequences. For example government grants or subsidies have sometimes been made to promote the development of animal husbandry, encourage high fat content of meat, and encourage the provision of high fat milk and cream, even to schools. Indeed, the agricultural policies of the EEC have for some time encouraged the production of fat and alcohol. An increase in fat intake and particularly in saturated fat resulting from such policies may specifically effect areas of Southern Europe where some dietary associated cancers are much lower in incidence than in Northern or Western Europe. On the other hand, the recently observed increase in alcohol consumption in Central and Northern Europe may lead to an increase in the incidence of cancers of the upper digestive tract in these areas. There is, therefore, a risk of a major increase in incidence of dietary associated cancers in Europe, other than the decline in stomach cancer already observed. National government policies should be directed to reducing dietary fat and alcohol consumption, and supporting prudent dietary recommendations such as those summarised above.

REFERENCES

1. Doll R, Peto R. The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. J Natl Cancer Inst 1981; 66: 1119–308.
2. Committee on Diet and Health. Diet and Health. Implications for reducing chronic disease risk. National Research Council. Washington, DC: National Academy Press, 1989.
3. Armstrong B, Doll R. Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. Int J Cancer 1975; 15: 617–31.
4. Hill MJ. Experimental studies of fat, fibre and calories in carcinogenesis. In: Miller AB, ed. Diet and the aetiology of cancer. Berlin: Springer-Verlag, 1989, pp 31–8.
5. Prentice RL, Kakar F, Hursting S, et al. Aspects of the rationale for the women's health trial. J Natl Cancer Inst 1988; 80: 802–14.
6. Phillips RL. Role of life-style and dietary habits in risk of cancer in Seventh-Day Adventists. Cancer Res 1975; 35: 3513–22.
7. Hislop TG, Coldman AJ, Elwood JM, et al. Childhood and recent eating patterns and risk of breast cancer. Cancer Detect Prev 1986; 9: 47–58.
8. Le MG, Moulton LH, Hill C, Kramer A. Consumption of dairy procedure and alcohol in a case-control study of breast cancer. J Natl Cancer Inst 1986; 77: 633–6.
9. Miller AB, Kelly A, Choi NW, et al. A study of diet and breast cancer. Am J Epidemiol 1978; 107: 499–509.
10. Lubin JH, Burns PE, Blot WJ, et al. Dietary factors and breast cancer risk. Int J Cancer 1981; 28: 685–9.
11. Lubin F, Wax Y, Modan B. Role of fat, animal protein, and dietary fiber in breast cancer etiology: a case-control study. J Natl Cancer Inst 1986; 77: 605–12.
12. Toniolo P, Riboli E, Protta F, et al. Calorie-providing nutrients and risk of breast cancer. J Natl Cancer Inst 1989; 81: 278–86.
13. van't Veer P, Kok FJ, Brants HAM, et al. Dietary fat and the risk of breast cancer. Int J Epidemiol 1989, (in press).
14. Graham S, Marshall J, Mettlin C, et al. Diet in the epidemiology of breast cancer. Am J Epidemiol 1982; 116: 68–75.
15. Rohan T, McMichael AJ, Baghurst PA. A population-based case-control study of diet and breast cancer in Australia. Am J Epidemiol 1988; 128: 478–89.
16. Willett WC, Stampfer MJ, Colditz GA, et al. Dietary fat and the risk of breast cancer. N Eng J Med 1987; 316: 22–8.
17. Dales LG, Freidman GD, Ury HK, et al. A case-control study of relationships of diet and other traits to colo-rectal cancer in American blacks. Am J Epidemiol 1979; 109: 132–44.
18. Jain M, Cook JM, Davis FG, et al. A case-control study of diet and colo-rectal cancer. Int J Cancer 1980; 26: 757–68.
19. Graham S, Marshall J, Haughey B, et al. Dietary epidemiology of cancer of the colon in Western New York. Am J Epidemiol 1988; 128: 490–503.
20. Stampfer MJ, Willett WC, Colditz GA, et al. A prospective study of diet and colon cancer in a cohort of women. Fed Proc 1987; 46: 883.
21. Macquart-Moulin G, Riboli E, Cornee J, et al. Case-control study on colo-rectal cancer and diet in Marseilles. Int J Cancer 1986; 38: 183–91.
22. Potter JD, McMichael AJ. Diet and cancer of the colon and rectum. J Natl Cancer Inst 1986; 76: 557–69.
23. Kune S, Kune GA, Watson LF. Case-control study of dietary etiological factors: the Melbourne colo-rectal cancer study. Nutr Cancer 1987; 9: 21–42.
24. Hirayama T. A large scale cohort study on the relationship between diet and selected cancers of digestive organs. In: Gastrointestinal cancer, endogenous factors. Banbury report 7. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory, 1981; 409–29.
25. Wahrendorf J. Dietary fat, dietary cholesterol and obesity as risk factors for colorectal cancer kidney cancer and other tumours. In: Miller AB, ed. Diet and the aetiology of cancer. Berlin: Springer-Verlag, 1989: pp 13–9.
26. Kolonel LN, Yoshizawa CN, Hankin JH. Diet and prostatic cancer; a case-control study in Hawaii. Am J Epidemiol 1988; 127: 999–1012.
27 Heshmat MY, Kaul L, Kovi J, et al. Nutrition and prostate cancer: a case-control study. Prostate 1985; 6: 7–17.
28. Graham S, Haughey B, Marshall J, et al. Diet in the epidemiology of carcinoma of the prostate gland. J Natl Cancer Inst 1983; 70: 687–92.
29. Cramer DW, Welch WR, Hutchison GB, et al. Dietary fat in relation to ovarian cancer risk. Obstet Gynecol 1984; 63: 833–8.
30. Byers T, Marshall J, Graham S, et al. A case-control study of dietary and non-dietary factors in ovarian cancer. J Natl Cancer Inst 1983; 71: 681–6.
31. Lew EA, Garfinkel L. Variations in mortality by weight among 750000 men and women. J Chron Dis 1979; 32: 563–76.
32. La Vecchia C, Decarlia A, Fasoli M, et al. Nutrition and diet

in the etiology of endometrial cancer. Cancer 1986; 57: 1248–53.
33. Jensen H. Relationship of premorbid state of nutrition to endometrial cancer. Acta Obstet Gynecol Scand 1986; 65: 301–6.
34. Henderson BE, Casagrande BE, Pike MC, et al. The epidemiology of endometrial cancer in young women. Br J Cancer 1983; 47: 749–56.
35. Paffenbarger RS, Kempert JB, Chang HG. Characteristics that predict risk of breast cancer before and after the menopause. Am J Epidemiol 1980; 112: 258–68.
36. Talamini R, La Vecchia C, Decarli A, et al. Social factors diet and breast cancer in a northern Italian population. Br J Cancer 1984; 49: 723–9.
37. Lubin F, Ruder AM, Wax Y, et al. Overweight and changes in weight throughout adult life in breast cancer etiology. A case-control study. Am J Epidemiol 1985; 122: 579–88.
38. Willett WC, Browne ML, Bain C, et al. Relative weight and risk of breast cancer among premenopausal women. Am J Epidemiol 1985; 122: 731–40.
39. Tulinius H, Sigfusson N, Sigvaldason H, et al. Relative weight and human cancer risk. Int Cong Ser 1985; 685: 173–89.
40. de Waard F, Baanders-van Halewijn EA. A prospective study in general practice on breast-cancer risk in postmenopausal women. Int J Cancer, 1975; 14: 153–60.
41. Tzonou A, Day NE, Trichopoulos D, et al. The epidemiology of ovarian cancer in Greece: a case-control study. Eur J Cancer Clin Oncol 1984; 20: 1045–52.
42. Talamini R, La Vecchia C, Decarli A, et al. Nurtition, social factors, and prostatic cancer in a northern Italian population. Br J Cancer 1986; 53: 817–21.
43. Snowdon DA, Phillips RL, Choi W. Diet, obesity, and risk of fatal prostate cancer. Am J Epidemiol 1984; 120: 244–50.
44. Ziegler RG, Morris LE, Blot WJ, et al. Esophageal cancer among black men in Washington, DC. II. Role of nutrition. J Natl Cancer Inst 1981; 67: 1199–206.
45. Lyon JL, Mahoney AW, West DW, et al. Energy intake; its relationship to colon cancer risk. J Natl Cancer Inst 1987; 78: 853–61.
46. Tuyns AJ, Haelterman M, Kaaks R. Colorectal cancer and intake of nutrients; oligosaccharides are a risk factor, fats are not. A case-control study in Belgium. Nutr Cancer 1987; 10: 181–96.
47. Howe GR, Miller AB, Jain M. Re: 'Total energy intake: implications for epidemiologic analyses' by Willett and Stampfer (letter). Am J Epidemiol 1986; 124: 157–9.
48. Vena JE, Graham S, Zielezny M, et al. Lifetime occupational exercise and colon cancer. Am J Epidemiol 1985; 122: 357–65.
49. Garabrant DH, Peters JM, Mack TM, et al. Job activity and colon cancer risk. Am J. Epidemiol 1984; 119: 1005–14.
50. Frisch RE, Wyshak G, Albright NL, et al. Lower prevalence of breast cancer and cancers of the reproductive system among former college athletes compared to non-athletes. Br J Cancer 1985; 52: 885–91.
51. Hems G. The contributions of diet and childbearing to breast-cancer rates. Br J Cancer 1978; 37: 974–82.
52. Carroll KK. Dietary factors in hormone-dependent cancers. In: Current concepts in nutrition. Vol. 6, Nutrition and Cancer. New York: John Wiley & Sons, 1977, pp 25–40.
53. Caroll KK. Experimental studies on dietary fat and cancer in relation to epidemiological data. In: Ip C, Birt DF, Rogers AE, Mettlin C, eds. Prog Clin Biol Res, Vol 222, Dietary Fat and Cancer. New York: Alan R Liss Inc, 1986, pp 231–48.
54. Hems G, Stuart A. Breast cancer rates in populations of single women. Br J Cancer 1975; 31: 118–23.
55. Hakama M, Saxen EA. Cereal consumption and gastric cancer. Int J Cancer 1967; 2: 265–8.
56. Modan BW, Barrell V, Lubin F, et al. The role of starches in the etiology of gastric cancer. Cancer 1974; 34: 2087–92.
57. Risch HA, Jain M, Choi NW, et al. Dietary factors and the incidence of cancer of the stomach. Am J Epidemiol 1985; 122: 947–57.
58. Kolonel LN, Hankin JH, Lee J, et al. Nutrient intakes in relation to cancer incidence in Hawaii. Br J Cancer 1981; 44: 332–9.
59. Gregor O, Toman R, Prusova F. Gastrointestinal cancer and nutrition. Gut 1969; 10: 1031–4.
60. Thind IS. Diet and cancer—an international study. Int J Epidemiol 1986; 15: 160–3.
61. Bingham S, Williams DRR, Cole TC, et al. Dietary fibre and regional large-bowel cancer mortality in Britain. Br J Cancer 1979; 40: 456–63.
62. International Agency for Research on Cancer Intestinal Microecology Group. Dietary fibre, transit-time, faecal bacteria, steroids and colon cancer in two Scandinavian populations. Lancet 1977; 2: 207–11.
63. Jenson OM, MacLennan R, Wahrendorf J. Diet, bowel function, fecal characteristics, and large bowel cancer in Denmark and Finland. Nutr Cancer 1982; 4: 5–19.
64. Garland C, Shekelle RB, Barrett-Connor E, et al. Dietary vitamin D and calcium and risk of colorectal cancer: a 19-year prospective study in men. Lancet 1985; 1: 307–9.
65. Stemmermann GN, Nomura AMY, Heilbrun LK. Dietary fat and the risk of colorectal cancer. Cancer Res 1984; 44: 4633–7.
66. Berg JW. Can nutrition explain the pattern of international epidemiology of hormone-dependent cancers? Cancer Res 1975; 35: 3345–50.
67. Miller AB, Howe GR, Jain M, et al. Food items and food groups as risk factors in a case-control study of diet and colo-rectal cancer. Int J Cancer 1983; 32: 155–61.
68. Enstrom JE. Colorectal cancer and consumption of beef and fat. Br J Cancer 1975; 32: 432–9.
69. Kolonel LN. Fat and colon cancer: how firm is the epidemiologic evidence? Am J Clin Nutr 1987; 45: 336–41.
70. Gaskill SP, McGuire WL, Osborne CK, et al. Breast cancer mortality and diet in the United States. Cancer Res 1979; 39: 3628–37.
71. Gray GE, Pike MC, Henderson BE. Breast-cancer incidence and mortality rates in different countries in relation to known risk factors and dietary practices. Br J Cancer 1979; 39: 1–7.
72. Knox EG. Foods and diseases. Br J Prev Soc Med 1977; 31: 71–80.
73. Hems G. Associations between breast cancer mortality rates, child-bearing and diet in the United Kingdom. Br J Cancer 1980; 41: 429–37.
74. Hirohata T, Shigematsu T, Nomura AMY. Occurrence of breast cancer in relation to diet and reproductive history: a case-control study in Fukuoka, Japan. Natl Cancer Inst Monogr 1985; 69: 187–90.
75. Hirohata T, Nomura AMY, Hankin HJ, et al. An epidemiologic study on the association between diet and breast cancer. J Natl Cancer Inst 1987; 70: 595–600.
76. Hirayama T. A large scale cohort study on cancer risks by diet with special reference to the risk reducing effects of green-yellow vegetable consumption. In: Hayashi Y,

Nagao M, Sugimura T, et al, eds. Diet, Nutrition and Cancer. Tokyo: Japan Scientific Societies Press, 1986; pp 41–53.
77. Mills PK, Annegers JF, Philips RL. Animal product consumption and subsequent fatal breast cancer among Seventh-Day Adventists. Am J Epidemiol 1988; 127: 440–53.
78. Tuyns AJ, Riboli E, Doornbos G, et al. Diet and esophageal cancer in Calvados (France). Nutr Cancer 1987; 9: 81–92.
79. Boing H, Martinez L, Frentzel-Beyme R, et al. Regional nutritional pattern and cancer mortality in the Federal Republic of Germany. Nutr Cancer 1985; 7: 121–30.
80. Lea AJ. Neoplasms and environmental factors. Ann R Coll Surg Engl 1967; 41: 432–8.
81. Ishii K, Nakamura K, Ozaki H, et al. [In Japanese]. [Epidemiological problems of pancreas cancer]. Jpn J Clin Med 1968; 26: 1839–42.
82. Mack TM, Yu MC, Hanisch R, et al. Pancreas cancer and smoking, beverage consumption, and past medical history. J Natl Cancer Inst 1986; 76: 49–60.
83. Gold EB, Gordis J, Diener MD, et al. Diet and other risk factors for cancer of the pancreas. Cancer 1985; 55: 460–7.
84. Norell SE, Ahlbom A, Erwald R, et al. Diet and pancreatic cancer: a case-control study. Am J Epidemiol 1986; 124: 894–902.
85. Jensen OM. Dietary fibre, carbohydrate and cancer: epidemiologic evidence. In: Miller AB, ed. Diet and the aetiology of cancer. Berlin: Springer-Verlag, 1989, pp 21–29.
86. Graham S, Dayal H, Swanson M, et al. Diet in the epidemiology of cancer of the colon and rectum. J Natl Cancer Inst 1978; 61: 709–14.
87. Haenszel W, Locke FB, Segi M. A case-control study of large bowel cancer in Japan. J Natl Cancer Inst 1980; 64: 17–22.
88. Wattenberg LW. Inhibitors of chemical carcinogens. In: Burchenal JH, Oettgen HF, eds. Cancer: Achievements, Challenges and Prospects for the 1980s. Vol 1. New York: Grune and Stratton, 1981, pp 517–39.
89. Ziegler RG, Mason TJ, Stemhagan A, et al. Carotenoid intake, vegetables, and the risk of lung cancer among white men in New Jersey. Am J Epidemiol 1986; 123: 1080–93.
90. MacLennan R, Da Costa J, Day NE, et al. Risk factors for lung cancer in Singapore Chinese, a population with high female incidence rates. Int J Cancer 1979; 20: 854–60.
91. Hirayama T. Nutrition and cancer—a large scale cohort study. In: Knudsen I, ed. Genetic toxicology of the diet. New York: Alan R Liss Inc, 1986, pp 299–311.
92. Jensen OM, Miller AB. Alcohol. In: Miller AB. ed. Diet and the aetiology of cancer. Berlin: Springer-Verlag, 1989, pp 65–70.
93. Burch JD, Howe GR, Miller AB, Semincew R. Tobacco, alcohol, asbestos and nickel in the etiology of cancer of the larynx. A case-control study. J Natl Cancer Inst 1981, 67: 1219–24.
94. Tuyns AJ, Pequignot G, Jensen OM. Le cancer de l'oesophage en Ille-et-Villaine en fonction des niveaux de consommation d'alcool et de tabac. Des risques qui se multiplient. Bull Cancer 1977; 64: 45–60.
95. Pottern LM, Morris LE, Blot WJ, et al. Esophageal cancer among black men in Washington DC. I. Alcohol, tobacco and other risk factors. J Natl Cancer Inst 1981; 67: 777–83.
96. Breslow NE, Enstrom JE. Geographic correlations between cancer mortality rates and alcohol-tobacco consumption in the United States. J Natl Cancer Inst 1974; 53: 631 9.
97. Graham S. Alcohol and breast cancer. N Eng J Med 1987; 316: 1211–3.
98. Miller AB. Vitamins, minerals and other dietary factors. In: Miller AB, ed. Diet and the aetiology of cancer. Berlin: Springer-Verlag, 1989, pp 39–54.
99. Shekelle RB, Lepper M, Lui S, et al. Dietary vitamin A and risk of cancer in the Western Electric Study. Lancet 1981; 2: 1185–9.
100. Byers TE, Graham S, Haughey BP, et al. Diet and lung cancer risk: findings from the Western New York diet study. Am J Epidemiol 1987; 125: 351–63.