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Age is the strongest predictor of breast cancer risk, but other factors like family history, age at menarche and first birth, number of breast biopsies and age at biopsy, finding of atypical hyperplasia, alcohol consumption, and vitamins A, C, and E intake may influence breast cancer risk. (6) Human ecological studies have shown that breast cancer is more common in North America, Australia, and Western Europe relative to South and Central America, Asia, and Africa. The higher national per capita fat consumption in "western" countries was postulated as a possible cause of the observed increased incidence of breast cancer. Migration studies of Asian-American women show that Asian-American women born in the West have a 60% higher breast cancer risk than Asian-American women born in the East. Furthermore, breast cancer risk doubled after a decade of living in the West in Asian-American women who had immigrated from East to West. (14) In animal studies, high-fat diets increased susceptibility to mammary tumors in rodents. (7) These observations seem to indicate that there may be a positive correlation between dietary fat intake and breast cancer.

Case-Control Studies

Many case-control studies have been conducted to test the hypothesis that dietary fat intake is positively correlated with breast cancer incidence. Case-control studies are retrospective studies in which a population of subjects diagnosed with breast cancer is identified and compared with a selected control population. The dietary histories of the cases and the controls are collected and analyzed. In general, case-control studies demonstrate a small, but statistically significant positive association between dietary fat intake and breast cancer risk. A case-control study in Hawaii demonstrated that saturated fat was weakly associated with breast cancer in Japanese and Caucasian women, and that Caucasians consumed more saturated fat and had a higher attributable risk factor. (5) A case-control study in Singapore indicated that in premenopausal women, high intakes of polyunsaturated fats, -carotene, soya protein were associated with a low risk of breast cancer; high red-meat intake was associated with high risk. In postmenopausal women, no dietary effects were observed. (10) A recent case-control study in two cities in China found only a modest, non-significant association between breast cancer and all components of dietary fat (saturated, polyunsaturated, and monounsaturated). Crude fiber, carotene, and vitamin C in green vegetables were strongly inversely correlated with breast cancer risk. (13) A couple of case-control studies done in Greece and Spain demonstrated a statistically significant inverse relationship between monounsaturated fat intake (olive oil) and breast cancer risk. (9), (11) While case-control studies demonstrate a general trend towards a small positive correlation between dietary fat and breast cancer, they have been criticized because they fail to account for recall bias. Recall bias is the overestimation of previous dietary fat intake once a diagnosis of breast cancer has been made. Cohort studies, on the other hand, because of their structure do not have this problem with recall bias. (3) In case-control studies, the selection of an appropriate control is also of great importance, because an inappropriate control group may fail to demonstrate a difference that is there, or may conversely demonstrate a difference that is not really there but an artifact of the study design.

Cohort Studies

Cohort studies are prospective studies; a population is selected for study, dietary assessment is carried out, and cases of breast cancer that are later diagnosed are compared with individuals not diagnosed with breast cancer. A number of cohort studies have been carried out, ranging from the Adventist Health Study to the Nurses' Health Study (in which 89,494 nurses were followed for 8 years). (7, 12) While the cohort size in these studies is large, the number of diagnosed breast cancer cases is small (for example, 1439 cases in the Nurses' Health Study). Cohort studies have, on the whole, found no positive association between dietary fat intake and breast cancer risk. However, a small, non-significant inverse association was found between monounsaturated fat intake (olive oil) and breast cancer risk. (12) Further, the National Breast Screening Study in Canada found that there was an increased risk of dying of breast cancer with higher intakes of dietary fat before diagnosis. (8) Cohort studies have been criticized for having too small a sample size (of diagnosed cases of breast cancer) to be able to detect any statistically significant association. The recent pooled analysis by Hunter, Spiegelman, et. al. is an attempt to answer this criticism--by pooling data from seven cohort studies, they hoped to increase the power of their calculations. Their pooled analysis also demonstrated no statistically significant association.

Can the findings from cohort and case-control studies be reconciled?

The lack of agreement may be due to the different methodology used in the case-control and the cohort studies. Factors like the time period of reference, quantification of serving sizes, inclusion/exclusion of particular food items, handling of fats and oils in food preparation, food composition data, use of interviewers to administer the dietary assessment or self-administration are all likely to influence the findings of epidemiologic studies. (5) Bias in selection that affects both exposure and disease risk can also influence findings; most of the cohort studies have been carried out in North America where the range of dietary fat intake may be too narrow to detect any associations. (2) Methodological problems concerning the validation of methods of dietary measurement (food frequency questionnaire, diet history, 24-hour recall), and the validation of methods for adjusting the measured intakes for energy (which the animal studies demonstrated to be important as both calories and fat intake have an effect on mammary tumorigenesis) may also influence the findings. (2)

The best way to resolve the discrepancies in findings may be to move from observational studies to experimental studies. Controlled clinical trials of dietary modification may offer new insight into the question. There is evidence that diet alters estrogen concentrations, pharmacokinetics, and metabolism in healthy women. (1) The pilot study of the Women's Health Trial involved 73 healthy postmenopausal women who ate a low-fat diet for 10 to 22 weeks; serum estradiol levels were reduced significantly (17%). (4) It is believed that diet influences breast cancer risk by altering the endogenous hormone milieu; decreased fat intake (along with an increase in dietary fiber) may lower sex hormones and their interaction with the estrogen receptor. (1, 4) The National Cancer Institute is currently sponsoring 2 full-scale dietary-modification trials with breast cancer-related endpoints. The Women's Health Initiative is designed to study whether a low-fat diet will reduce breast cancer incidence. The Women's Intervention Nutrition Study is designed to study whether a reduction in dietary fat will decrease breast cancer recurrence and increase survival.

The findings from these large-scale multi-center studies should provide some answers to the question of whether dietary fat is associated with breast cancer risk. However, the studies still rely on a food frequency questionnaire to assess dietary status. It has been demonstrated that recall bias exists in cohort studies; with all the attention low-fat diets have received in relation to colon cancer and cardiovascular disease, as well as breast cancer, the subjects in the clinical trial are most likely aware of the hypothesized relation between dietary fat and breast cancer risk. This awareness may influence their dietary recall. An objective biological marker of dietary fat status would be an ideal marker for these types of clinical trials, but no such marker is currently available.

The original ecological studies demonstrated higher incidences of breast cancer in western countries. While diet may be involved, it is also possible that other lifestyle or environmental factors also play a role. A great deal more research needs to be done before it can be definitely concluded whether dietary fat is associated with breast cancer risk.

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