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Diet and Breast Carcinoma in Multiethnic Populations

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There is accumulating evidence implicating a role for diet in many cancers and other chronic diseases. However, the extent to which dietary factors are related to the risk of breast carcinoma and may explain in part some of the racial/ethnic differences observed in breast carcinoma incidence rates is not known. In the last 20 years, a large number of studies (conducted primarily among white women in the U.S. or elsewhere in the West) have investigated the role of diet, in particular dietary fat, in the etiology of breast carcinoma. However, to my knowledge few U.S. studies regarding diet and breast carcinoma have included nonwhite women.[1-4]

This review first will describe some of the racial/ethnic differences in dietary habits. Second, it will review the role of selected dietary factors (e.g., fat, specific fatty acids, fried meat/heterocyclic amines [HAs], and alcohol) that have been hypothesized to increase the risk of breast carcinoma. Third, the current study will review the role of protective factors including fruits and vegetables and phytoestrogens and the risk of breast carcinoma.

Racial/Ethnic Differences in Nutrient Intake

A large number of studies have examined trends in dietary patterns in the U.S. population in the last 20 years. Before describing results from selected studies, it is important to note that differences in dietary trends reported in different studies may arise due to several reasons. They include differences in the methods used to assess diet as well as differences in the distribution of participants based on various characteristics (e.g., age, gender, social class, place of residence in the U.S., and place of origin in the host country) that may influence dietary habits**.**

Three recent studies, conducted between 1976–1980,[5] 1985–1986,[6] and in 1987 and 1992,[7] allowed comparison of fat intake among African-American, Latino, and white women in the U.S. (Table 1). In the 1970s–1990s,[5–7] the intakes of total fat and saturated fat in African-American and white women were similar. However, the intake of total and saturated fat was lower in Latino women compared with white and African American. In all three studies, the intake of cholesterol was highest in African-American women, intermediate in Latino women, and lower in white women.[5-7]

Data regarding intake of micronutrients[6,7] and fruits and vegetables[8,9] also are available in these national surveys (Table 2). Earlier survey results suggest higher intakes of fruits and vegetables[8] and fiber[6] in white women compared with African-American and Latino women but in more recent studies, intakes of fruits and vegetables[9] and specific micronutrients (i.e., fiber, carotene, vitamin C, and folate) were higher among Latino women compared with white and

TABLE 1
Intake of Total and Saturated Fat (in Percent Calories) and Cholesterol among White, African-American, and Latino Women

Reference		Block et al.[5]	Thompson et al.[6]	Norris et al.[7]
Survey		NHANES II, 1976–1980	USDA, 1985–1986	NHIS, 1992
	By race			
% fat calories	Wh	36.0	36.7	36.3
	AA	35.8	36.0	37.0
	Lat	NA	33.9	33.1
% saturated fat calories	Wh	12.5	13.4	12.6
	AA	12.3	12.5	12.9
	Lat	NA	12.3	12.2
Cholesterol intake (mg)	Wh	271	271	190
	AA	302	313	267
	Lat	NA	283	275

NHANES: National Health and Nutrition Examination Survey; USDA: U.S. Department of Agriculture; NHIS: National Health Interview Survey; Wh: white; AA: African-American; Lat: Latino; NA: not available.

African-American women. However, in all racial/ethnic groups, intake of fruits and vegetables remains considerably lower than the U.S. Department of Agriculture (USDA)'s daily recommended number of servings of vegetables (i.e., three or more servings) and fruits (i.e., two or more servings).[8]

A recent survey shows interesting secular trends in dietary patterns in different racial/ethnic groups, suggesting important influences of socioeconomic status and other factors.[10] These investigators reported reductions in intake of fat in all socioeconomic groups in both whites and African-Americans. The intake of fruits and vegetables among whites also decreased regardless of socioeconomic status but increased among African-Americans of high socioeconomic status. In the same study, consumption of grains and legumes increased over time among whites of medium and high socioeconomic status and declined among African-Americans of low socioeconomic status (dietary intakes of Latinos were not included in this study).[10,65,66]

These national dietary surveys do not include sufficient numbers of other racial/ethnic groups (e.g., Asian-Americans, Native Hawaiians, and Native Americans) to allow separate comparisons in these groups. Data from a large (> 200,000 participants) multiethnic cohort of adult men and women (living primarily in Hawaii and Los Angeles County) allowed comparison of dietary patterns of whites, African-Americans, Latinos, Japanese, and Native Hawaiians.[11] From 1993–1996, participants entered the cohort by completing a detailed self-administered mailed questionnaire that elicited a quantitative food frequency history. Analysis of the baseline dietary characteristics shows that compared with fat intake in white women (as percent calories from fat), fat intake was lower in Japanese-American women, higher among Latino and African-American women, and comparable in Hawaiian women.[11] Similar to findings of the 1992 National Health Interview Survey (NHIS),[7] intake of fiber, carotene, vitamin C, and folate also was higher among African-American and Latino women compared with white women in this cohort.[11] Compared with white women, Hawaiian-American women also showed higher intakes of these micronutrients whereas Japanese-American women showed comparable intakes of carotene and vitamin C but lower intakes of fiber and folate.[11] Two food groups of particular interest in the etiology of breast carcinoma showed marked racial/ethnic differences. Intake of legumes was at least twice as high among Latino women (67 g per day) compared with white women and the intake of tofu (a main source of isoflavones) was at least 4 times higher among Japanese-American women (24 g per day) compared with white women.[11]

Dietary Fat

Dietary fat has been the major focus in the search for dietary causes of breast carcinoma for more than 20 years, but its significance remains controversial. In a meta-analysis of 7 large prospective studies covering close to 5000 breast carcinoma cases, the risk of breast carcinoma appeared to be unrelated to the intake of dietary fat.[12] A recent update based on 14 years of follow-up of the Nurses' Health Study also showed no association between dietary fat and breast carcinoma risk in this cohort.[13] Meta-analyses of case–control studies found some support for an association between dietary fat and breast carcinoma,[14,15] but these results have been questioned because of the potential for recall bias in case–control studies.[16] However, published cohort and case–control studies contain little data regarding subjects with extremely low fat intakes (i.e., < 2% of women in the pooled cohort studies consumed < 20% of calories from fat[13]). This figure is likely to be lower after correction of measurement error in the diet histories.[17,18]

One of the difficulties in interpreting the findings of the published epidemiologic studies is that few have considered the relative levels of fatty acids that contribute to the total amount of fat consumed.[19] There is some suggestion that the recent increase of breast carcinoma cases in Japan[20] and the historic international differences in breast carcinoma incidence rates[21] may be related to differences in the

TABLE 2
Intake of Fruits and Vegetables and Various Micronutrients among White, African-American, and Latino Women

Study	Diet variable: Fruits/vegetables	Whites	African-American	Latino
Patterson et al.[8] (NHANES II, 1976–1980)	% consumed			
	2+ servings fruit/day	32%	24%	NA
	3+ servings vegetable/day	25%	18%	NA
	2+ fruit & 3+ vegetables/day	9%	5%	NA
Patterson et al.[9] (NHIS, 1987)	Fruits (per week)[a]	9.0	9.4	10.5
	Vegetables (per week)[a]	13.6	12.2	17.0
		3.2	3.1	3.9
	Micronutrients-daily mean			
Thompson et al.[6] (USDA, 1985–1986)	Fiber (g)	11.1	8.5	9.2
Norris et al.[7] (NHIS, 1992)	Fiber (g)	8.9	9.1	11.7
	Carotene (mg)	2392	2941	2774
	Vitamin C (mg)	118	139	148
	Folate (μg)	224	230	268

NHANES: National Health and Nutrition Examination Survey; NA: not available; NHIS: National Health Interview Survey; USDA: U.S. Department of Agriculture.
[a] Median levels.

intake of specific fatty acids, specifically the ratio of intake of n-6 to n-3 polyunsaturated fatty acids. An increasing ratio of omega-3 fatty acids to total omega-6 fatty acids in adipose tissue fatty acids has been associated with a trend toward a decreasing risk of breast carcinoma in one study.[22] To my knowledge the effect of this ratio of fatty acids on the risk of breast carcinoma was not investigated in previous studies that determined levels of fatty acids in gluteal, abdominal, and mammary adipose tissues.[23-25]

A high intake of meat,[26-29] particularly red[30-34] and fried meats,[31,35,36] may be associated independently with an increased risk of breast carcinoma. Meat consumption may play a role in breast carcinoma development as a source of dietary fat, animal protein, mutagens, and/or carcinogens such as HAs.[37] HAs are formed in the browned and charred surface of meats. Several of the commonly found HAs (including IQ, MeIQ, PhIP, and MeIQx) have been shown to induce mammary gland tumors in rat models.[38]

De Stefani et al.[39] attempted to assess the relation between dietary intake of HA and risk of breast carcinoma directly. An index of HA exposure was calculated based on self-reported frequency of intake of specific foods of interest and the amounts of HAs reported for these foods in the literature. Statistically significant increasing trends of breast carcinoma risk were found with increasing levels of IQ, MeIQx, and PhiP exposure.[39] Zheng et al.[40] assessed HA exposure by asking subjects to report their preference for level of meat doneness with the aid of a series of color photographs that represented increasing levels of doneness of three meats (hamburger, beefsteak, and bacon). In this study, women who consumed these three meats consistently cooked very well done had a statistically significant four times higher risk compared with women who consumed the meats cooked as rare or medium. However, consumption of meats and other concentrated sources of HAs was not found to be associated with the risk of breast carcinoma in another study.[41]

Intake of foods rich in HAs (i.e., fried fish, fried chicken, bacon, and processed meats) varies by racial/ethnic groups; it is highest in African-Americans, intermediate in whites, and lowest in Latinos and Asians.[9,11,42] Urinary excretion of MeIQx, which is associated positively with intake frequencies of bacon, pork/ham, and sausage/luncheon meats has been found to be 1.3–3.0-fold higher in African-Americans than in Asians and whites, respectively.[42] Studies in multiethnic populations with a diverse intake of foods rich in HAs will provide important insights regarding its role in the development of breast carcinoma.

Alcohol

A large number of epidemiologic studies have investigated the association between alcohol intake and breast carcinoma risk. In a meta-analysis of 38 epidemiologic

studies, strong evidence of a positive dose-response relation between alcohol consumption and the risk of breast carcinoma was found. Daily consumption of 1 alcoholic drink was associated with an 11% increase (95% confidence interval [95% CI], 7–16%) in the risk of breast carcinoma compared with nondrinkers.[43] Similar conclusions were reached in a meta-analysis of 6 prospective studies, each of which included at least 200 incident breast carcinoma cases.[44] The source of the alcohol did not appear to influence the risk estimates greatly.[44]

Alcohol use is more prevalent among white women (56% consumed alcohol at least 6 times per year) than among African-American women (44%) and Latino women (47%).[9] The extent to which the higher intake of alcohol among white women may explain in part their higher rate of breast carcinoma is not known. It also is not known whether the effect of alcohol on the risk of breast carcinoma is similar in women of different racial/ethnic backgrounds.

Vegetables, Fruits, and Foods Rich in Phytoestrogens

With the generally inconsistent data regarding the role of fat in the development of breast carcinoma, the focus on diet has shifted to investigations of dietary factors that may protect against breast carcinoma. Several reviews conducted in the early 1990s suggested that a high intake of vegetables and fruits[45,46] and foods rich in phytoestrogens[47] may protect against breast carcinoma. A large number of anticarcinogenic agents present in these food sources are potential candidates.[45] This discussion will focus on two specific components, fiber and phytoestrogens, that are of specific interest in studies of multiethnic populations. Intake of fiber (i.e., from legumes) is particularly high among Latinos[9,11,48] and may explain in part their lower rates of breast carcinoma. Soy foods, a main source of isoflavones (one class of phytoestrogens), have been a staple in the Asian diet[47] and may have a role in conferring the lower risk of breast carcinoma observed in Asia.

There is compelling rationale to suspect that fiber may play a role in breast carcinoma development. Subjects consuming high fiber diets have been found to have increased elimination of estrogen by the fecal route and reduced intestinal reabsorption of estrogen.[49] Reductions in serum estradiol levels have been associated with increases in fiber intake in some dietary intervention studies.[50,51] Supportive evidence of a protective effect of dietary fiber against breast carcinoma also has been reported in 1 of 4 cohort[52-55] studies and more than a dozen case–control studies.[14 and 56]

Phytoestrogens are estrogenic compounds found in plants. There are two main classes of phytoestrogens relevant in the human diet: isoflavones and lignans. The most significant source of isoflavones in the diet is soybeans whereas a large number of seeds, grains, and legumes are rich in lignans.[57] There is accumulating evidence from in vitro and animal studies that soy intake may influence the risk of breast carcinoma[57] but to my knowledge there still are few studies regarding this association in humans.[58] Since 1990, four case–control studies conducted in Asia or among Asian-Americans have evaluated the association between self-reported soy intake and risk of breast carcinoma. Results from these studies are mixed. In a large and well conducted study in China that considered many potential dietary and nondietary confounders in its analysis, there was no association observed between intake of soy and risk of breast carcinoma in both premenopausal and postmenopausal women.[59] In Singapore, premenopausal women reporting high soy intake ($\geq$ 55 g of soy per day) showed a significant 60% reduced risk compared with women with a lower soy intake ($<$ 20.3 g per day).[33,60] In Japan, compared with premenopausal women with less than weekly intake, frequent weekly consumers ($\geq$ 3 times/week) of bean curd were found to have a 30% reduced risk of breast carcinoma.[61] In both the Singapore and Japanese studies, the risk of breast carcinoma in postmenopausal women was not influenced by soy intake. Among Asian-Americans, intake of tofu was associated with a lower risk of breast carcinoma both overall and separately in premenopausal and postmenopausal women.[62] Similar results were obtained after adjustment for relevant menstrual and reproductive factors and selected dietary factors. Analysis by migration status showed a statistically significant protective effect of soy among immigrants but not in Asian-Americans born in the U.S.[62]

Two other studies comparing urinary excretion of phytoestrogens (as a marker of dietary intake) in breast carcinoma patients and healthy control women provided additional support for the phytoestrogen hypothesis.[63,64] In an Australian study, the risk of breast carcinoma was reduced by 50% ($P = 0.009$) for women whose urinary excretion of equol (an isoflavone metabolite) was above the baseline level. Breast carcinoma risk also was reduced by 70% for those women with the highest excretion levels of enterolactone (a lignan) compared with those women with the lowest excretion levels ($P = 0.01$).[63] However, it cannot be determined whether the effect of equol and enterolactone was adjusted for each other. In a study conducted in China,[64] women in the upper two tertiles of urinary isoflavone levels showed a statistically nonsignificant 50% reduction in the risk of breast carcinoma compared with those in the lowest tertile. Risk was lowest

(relative risk, 0.14; $P < 0.05$) for those displaying high excretion levels of both total isoflavones and phenols (a surrogate marker of fruit and vegetable intake).[63]

Multiethnic populations have a wide range of fat intake and great diversity in food sources of fat[11] and may be particularly suited for studying the role of specific types of fat and particularly the balance of specific fat components. There also are well established differences between racial/ethnic groups in the intake of specific vegetables, fruits, legumes, and soy.[9,11] Investigations in these populations present excellent opportunities to investigate the relation between specific micronutrients and food sources and breast carcinoma risk. Although to my knowledge there currently are few published studies regarding diet and breast carcinoma in multiethnic populations, several large, well–designed, case–control and cohort studies conducted in African-Americans, Latinos, and Asian-Americans are in progress. Results from these studies should help to bridge some of the gaps in our understanding of the role of diet and breast carcinoma.

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