Breast Cancer Mortality and Diet in the United States

Sharon Parten Gaskill,1 William L. McGuire, Charles K. Osborne, and Michael P. Stern
Divisions of Clinical Epidemiology and Oncology, Department of Medicine, University of Texas Health Science Center at San Antonio, San Antonio, Texas 78284

ABSTRACT

Internationally, breast cancer mortality is correlated with intestinal lactase deficiency and dairy product consumption beyond childhood. Within the United States, age-adjusted breast cancer mortality is positively associated with consumption of milk, butter, and total milk fat in regional analyses, and it is associated with milk demand in state-based analyses. Breast cancer mortality is also positively associated with demand for total calories, protein, fat, beef, and table fats (butter and margarine), and it is negatively associated with egg demand. Only the associations with milk and egg demand, however, survive when the Southern states are eliminated from the analyses or when either age of first marriage or income is controlled. The associations with milk and egg demand persist despite multiple controls for other dietary and demographic variables, although the association with milk demand loses statistical significance in some second- and third-order partial correlations. The inverse correlation with egg demand is strong but in the opposite direction from what might have been expected from previous studies. The correlation between milk demand and breast cancer mortality, although weaker, is consistent with results from previous studies, and it suggests a possible special role for dairy products in the etiology of breast cancer.

INTRODUCTION

Previous epidemiological and laboratory studies have sought to identify elements of diet which may contribute to the initiation or promotion of breast cancer. The consumption of fat (1, 10, 15, 54), animal protein (18, 27, 32, 54), and sugar (1, 18, 26, 27), as well as total caloric intake (1, 10, 54), are among those dietary factors implicated by these studies. This paper explores the relationship between breast cancer mortality and the consumption of milk and other foods in the United States.

Our attention was first drawn to the possible relationship between milk consumption and breast cancer by the observation that, internationally, an inverse relationship exists between the prevalence of lactase deficiency and mortality from breast cancer. Lactase, the intestinal enzyme responsible for the digestion of the milk sugar lactose, is present in all mammals at birth; after weaning, however, lactase production usually declines so that the adult mammal is incapable of digesting lactose (43). Most human populations follow this same pattern, exhibiting low levels of intestinal lactase activity and of milk consumption after childhood (4, 43, 56). Exceptions to this pattern include populations of northwestern European stock (including the United States, Australia, and Canada) and scattered groups in other parts of the world, many of which have an ancient history of dairying (4, 43, 56). In these populations, the consumption of dairy products is often quite high (4, 6, 43, 56) as are breast cancer death rates (1, 10, 53, 54). Thus, internationally at least, lactase sufficiency and presumably dairy product consumption after childhood are positively associated with breast cancer mortality. Chart 1 illustrates this relationship. The prevalence of adult lactase sufficiency and mortality from breast cancer are both high in the northwestern European countries and in whites from the United States; in Asia, Africa, and Mexico, on the other hand, lactase production is rare after childhood, and breast cancer mortality is only a fraction of that of the northwestern Europeans. In blacks from the United States and Mexican Americans, the prevalence of adult lactase sufficiency has risen only modestly beyond that of the Bantu and of Mexicans; because the persistence of intestinal lactase is believed to be largely genetically determined (43, 55), this small increase is probably largely due to intermarriage. Nonetheless, with exposure to the dairying culture in the United States, these groups might be expected to have partially adopted the milk-drinking behavior of the dominant society (3, 24, 38, 65), and their death rates from breast cancer have shown striking increases.

These comparisons have suggested the possibility that milk consumption may contribute in some way to the initiation or development of breast cancer. Such an international association, however, might be confounded by other interpopulation differences, among them differences in other dietary patterns, levels of affluence, reproductive patterns, genetic predisposition, and social and cultural patterns. In order to measure and at least partially control for the effects of these other variables, we have examined the relationship between milk consumption and breast cancer mortality within a single country, the United States.

MATERIALS AND METHODS

Data on weekly per capita consumption of various food items were collected by individual interview in the 1965–1966 Household Food Consumption Survey (60, 61). This survey provided information on food consumption in each of the 4 regions of the United States (excluding Alaska and Hawaii), South, West, North Central region, and Northeast (Chart 2). Because comparable consumption data were not available on a state-by-state basis, per capita food demand estimates for the 48 contiguous states and the District of Columbia were used for the more detailed, state-based analyses (49). The relationship between milk consumption and breast cancer mortality was therefore examined using 2 distinct sets of food data, per capita food consumption data for the 4 regions of the country and per capita food demand data for the individual states and Washington, D. C.

Age-adjusted breast cancer death rates among women were obtained for each state and the District of Columbia from the

1 To whom requests for reprints should be addressed, at Department of Medicine, University of Texas Health Science Center at San Antonio, 7703 Floyd Curl Drive, San Antonio, Texas 78284.

Received April 5, 1979; accepted June 1, 1979.
Vital and Health Statistics division of the USPHS for the period from 1969 to 1971 (63). In order to develop estimates of the breast cancer mortality in each of the 4 regions, the age-adjusted breast cancer death rate for each state was weighted by the state population; within each region, these weighted rates were then summed; finally, this sum was divided by the population of the entire region.

**Analysis by Region of the Relationship between per Capita Food Consumption and Breast Cancer Mortality.** Regional trends in food consumption were examined for all dairy products for which data were available and for certain other classes of food that were of particular interest. Because only 4 data points were available, no statistical tests were performed; instead, regional trends in the consumption of each food were examined for correspondence with regional breast cancer mortality trends (lowest in the South, rising through the West and North Central regions to a high in the Northeast).

**Analysis by State of the Relationship between per Capita Food Demand and Breast Cancer Mortality.** Per capita demand estimates for the 48 states and the District of Columbia were developed by Raunikar et al. (49) for a number of foods through the use of data on geographical and demographic variations in food consumption from the 1965–1966 Household Food Consumption Survey (60, 61) and from an intensive 5-year study of consumer behavior in Atlanta. Using these data, we developed estimates of fat intake by multiplying the demand for each food, expressed as a percentage of the national average, by the average daily fat intake in the United States obtained from that food (61) and then summing these food-fat products. The foods used in these calculations represent about 85% of the animal fat and 70% of the total fat in the American diet (61). Similar estimates were computed for protein intake, caloric intake, and meat intake for each state and Washington, D. C. Protein intake represents approximately 70% of the total protein in the diet of those in the United States, and meat intake accounts for about 85% of the meat in the diet (61). Caloric intake, however, represents only about 45% of the total caloric content of the American diet (61).
The following socioeconomic and demographic data for each state and the District of Columbia were obtained from the 1970 United States Census (58, 59): mean age of first marriage (as a rough predictor of age at first pregnancy) for women who were 30 to 49 years old in 1970; mean number of children even born to women who were 35 to 44 years old in 1970; median income in 1969 for a family of 4; percentage of the state population residing in urban areas in 1970; percentage of the population who were nonwhite in 1970; 1970 population density per square mile; and percentage of women ages 16 years or over who were employed in 1969. Percentage of the population who were Jewish (20) was included in some analyses because of the 2-fold risk of breast cancer among Jewish women compared with non-Jewish Caucasians (14). State mortality data were obtained as described above.

Pearson product-moment correlations were computed between age-adjusted breast cancer mortality and each of the food demand and demographic variables; the significance of each correlation was tested by comparing the quantity

\[ r \left( \frac{N-2}{1-r^2} \right)^{1/2} \]

with Student's t distribution with \( N - 2 \) d.f., using a 2-tailed test of significance. Partial correlations were computed for those foods found to have significant 0-order correlations with breast cancer; the significance of these correlations was tested by comparing the quantity

\[ r \left( \frac{DF - 1}{1-r^2} \right)^{1/2} \]

with Student's t, using a one-tailed test of significance.

RESULTS

Relationship between Regional Food Consumption and Regional Breast Cancer Mortality

Regional age-adjusted annual breast cancer death rates per 100,000 women were lowest in the South and rose though the West and North Central regions to a high in the Northeast (Chart 3). Per capita consumption of selected food items is shown for each of these regions in order of ascending breast cancer mortality (Charts 4 to 10).

The consumption of the 4 major classes of dairy products, milk, cream and ice cream, cheese, and butter, is presented in Chart 4. Milk consumption, which accounts for the bulk of dairy product consumption, rose modestly but consistently from the South through the Northeast following the same general trend as did breast cancer mortality. Cream and ice cream, however, showed no such trend. Cheese consumption like breast cancer mortality showed a strong South-non-South gradient, but when the South was excluded cheese consumption declined as breast cancer mortality rose. The greatest percentage of increase was found in butter consumption which was almost 3 times as high in the Northeast as in the South; this trend suggested that milk fat could be a critical variable in the observed relationship between milk consumption and breast cancer mortality. When all 4 classes of dairy products were combined, a positive association was indeed seen between total milk fat consumption and breast cancer mortality. Total fat consumption, however, showed a slightly negative trend overall (Chart 5). When animal and vegetable fats were examined separately, no trend was seen in animal fat consumption; vegetable fat consumption actually declined as breast cancer mortality rose. When individual vegetable fats were examined, margarine and vegetable shortening both...
showed similarly negative trends (Chart 6). These results suggested that the trends observed in the consumption of milk, butter, and total milk fat were not simply part of an overall positive trend in fat consumption.

Neither total protein nor animal protein consumption showed consistent regional trends (Chart 7) although a generally positive South-non-South gradient could be observed due to the particularly low consumption of protein in the South; outside the South, however, protein consumption fell as breast cancer mortality increased. Total meat consumption showed a generally positive trend, although it actually peaked in the North Central region rather than in the Northeast where breast cancer mortality is highest. Beef consumption displayed a pattern similar to that of protein; pork consumption showed no consistent trend.

Egg consumption (Chart 8) showed a strong negative trend dropping steadily as breast cancer mortality rose.

The consumption of complex carbohydrates (estimated by total carbohydrates minus carbohydrates from sugar, sweets, and non-bread bakery products) declined consistently from the South to the Northeast (Chart 9), although the largest drop occurred from the South to the West. Unlike the other complex carbohydrates, bread showed a trend parallel to that of breast cancer mortality. The consumption of sugar and sweets, on the other hand, showed no clear geographical pattern. Alcohol consumption, although it did not rise consistently from the South to the Northeast, was over twice as high in the Northeast as in the South (Chart 10). Finally, total caloric intake (Chart 11) showed no strong regional trends.

In summary then, only milk, butter, total milk fat, and bread consumption increased consistently with regional breast cancer mortality; less consistent increases were seen in the consumption of meat and alcohol. The consumption of vegetable fats, eggs, and total complex carbohydrates declined consistently as mortality increased; less consistent declines appeared in total dietary fat. Neither total protein, nor animal protein, nor caloric intake displayed geographical trends in relation to breast cancer mortality.

Relationship between State Food Demand and State Breast Cancer Mortality

Zero-Order Correlations, 48 States and District of Columbia. Analyses of food demand estimates for the 48 contiguous states and the District of Columbia (Table 1) confirmed the
Table 1

| Correlation of age-adjusted breast cancer mortality with demand for selected foods |
|---------------------------------|-----|----------------|-----|----------------|
|                                  | 48 contiguous states | 32 non-Southern |      | states         |
|                                  |        | states        |      |                |
| Milk                             | 0.506  | <0.001        | 0.489 | 0.005          |
| Table fats (primarily butter and | 0.370  | 0.009         | -0.005| 0.764          |
| margarine)                       |        |               |      |                |
| Beef                              | 0.282  | 0.050         | -0.420| 0.017          |
| Cheese                           | 0.238  | 0.100         | -0.564| <0.001         |
| Frozen desserts                  | 0.213  | 0.071         | -0.116| 0.526          |
| Poultry                          | 0.060  | 0.342         | 0.586 | <0.001         |
| Pork                             | -0.054 | 0.357         | 0.235 | 0.196          |
| Fish                             | -0.080 | 0.292         | 0.633 | <0.001         |
| Eggs                             | -0.608 | <0.001        | -0.676| <0.001         |
| Meat intake                      | 0.194  | 0.181         | 0.210 | 0.248          |
| Fat intake                       | 0.373  | 0.008         | -0.159| 0.385          |
| Protein intake                   | 0.438  | 0.002         | 0.044 | 0.810          |
| Caloric intake                   | 0.450  | <0.001        | 0.079 | 0.667          |

With regard to the other dietary components of interest, fat intake, caloric intake, protein intake, and the demand for table fats (butter and margarine) and beef were all found to be positively correlated with breast cancer mortality. For all items except table fats, a hybrid category, these results were unexpected since no positive trends had been seen for these variables in the regional data. Neither meat intake nor demand for poultry, pork, or fish showed any significant correlation with breast cancer mortality.
Egg demand, on the other hand, was again found to have a strong negative correlation with breast cancer mortality ($r = -0.608; p < 0.001$) consistent with the striking relationship seen in the 4-region food consumption data. In summary then, 0-order correlations with breast cancer mortality were negative for egg demand and positive for the demand for milk, table fats, and beef and for the intake of calories, protein, and fat.

Data from the 1970 census on the reproductive histories of adult women were consistent with previous epidemiological findings (Table 2) that breast cancer mortality in the state was positively correlated with the mean age of first marriage of women in the state ($r = 0.859; p < 0.001$) and negatively correlated with the mean number of children born to them. Significant positive correlations were also found with the following socioeconomic variables: median family income; percentage of the population residing in urban areas; population density; percentage of the population who were Jewish; and percentage of women who were employed. No relationship was found between breast cancer mortality and the percentage of the population who were nonwhite.

**Zero-Order Correlations, 32 Non-Southern States.** Regional data had revealed that the Southern states were often outliers from the rest in their consumption of such foods as beef, cheese, and protein. For this reason, data for the 32 non-Southern states were analyzed separately (Tables 1 and 2). With the Southern states eliminated, only 2 foods continued to show significant correlations in the same direction originally observed: milk ($r = 0.469; p < 0.01$) and eggs ($r = 0.676; p < 0.001$). Of the demographic variables, 5 remained significantly correlated with mortality from breast cancer when the Southern states were excluded; these were mean age of first marriage, median income, percentage of the population that is Jewish, population density, and number of children born.

**First-Order Partial Correlations, 48 States and District of Columbia.** When either age of first marriage or median income was controlled (Table 3), only 2 of the foods originally correlated with breast cancer mortality maintained significant correlations: milk, which continued to show a positive correlation; and eggs, which continued to show a negative correlation. None of the demographic variables originally correlated with breast cancer mortality showed significant positive correlations once age of first marriage was controlled. When median income was controlled, only age of first marriage and percentage Jewish continued to show a positive association with breast cancer mortality.

In further analyses (not shown), milk demand, egg demand, age of first marriage, and median income maintained significant correlations with breast cancer mortality despite controls for each of the other variables in Table 3.

**Higher-Order Partial Correlations, 48 States and District of Columbia.** Finally, second- and third-order correlations were calculated controlling for all possible combinations of either 2 or 3 of the following variables: age of first marriage; median income; percentage urban; population density; percentage Jewish; and intake of protein, meat, fat, and calories. In each of the 120 partial correlations thus calculated (not shown), milk demand remained positively correlated with breast cancer mortality; in all but 15 cases, these correlations were statistically significant ($p < 0.05$). Fourteen of the 15 exceptions involved combinations including protein, fat, and/or caloric intake. Because each of these variables is highly correlated with milk demand ($r = 0.811, 0.859$, and $0.717$, respectively), we examined their first-order partial correlations with breast cancer mortality controlling for milk demand; none was significant [protein ($r = 0.125; p = 0.451$), fat ($r = -0.075$), calories ($r = 0.034$)]. In the 15th case, however, the third-order correlation between milk demand and breast cancer mortality, although it remained positive, was reduced to statistical insignificance ($r = 0.194; p = 0.098$) by simultaneously controlling age of first marriage, median family income, and percentage urban population. The negative correlation observed between egg demand and breast cancer mortality remained statistically significant throughout the entire battery of partial correlations.
**Correlation of breast cancer mortality, milk demand, and egg demand with mortality from cancers of other sites**

Zero-order correlations between age-adjusted breast cancer mortality, milk demand, and egg demand and age-adjusted mortality from cancer of other sites (63) were computed for the 48 contiguous states and the District of Columbia.

<table>
<thead>
<tr>
<th>Site of cancer</th>
<th>Breast cancer</th>
<th>Milk demand</th>
<th>Egg demand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovaries</td>
<td>0.591*</td>
<td>0.615*</td>
<td>-0.223</td>
</tr>
<tr>
<td>Rectum</td>
<td>0.857*</td>
<td>0.571*</td>
<td>-0.600*</td>
</tr>
<tr>
<td>Colon</td>
<td>0.880*</td>
<td>0.509*</td>
<td>-0.553*</td>
</tr>
<tr>
<td>Breast</td>
<td>0.596*</td>
<td>0.393*</td>
<td>0.001</td>
</tr>
<tr>
<td>Testes</td>
<td>-0.064</td>
<td>0.393*</td>
<td>0.001</td>
</tr>
<tr>
<td>Digestive organs</td>
<td>0.830*</td>
<td>0.290*</td>
<td>-0.486*</td>
</tr>
<tr>
<td>Intestines</td>
<td>0.252*</td>
<td>0.252*</td>
<td>-0.280</td>
</tr>
<tr>
<td>All sites</td>
<td>0.675*</td>
<td>0.002</td>
<td>-0.308*</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.465*</td>
<td>-0.085</td>
<td>-0.274</td>
</tr>
<tr>
<td>Respiratory organs</td>
<td>0.283*</td>
<td>-0.292*</td>
<td>0.012</td>
</tr>
<tr>
<td>Prostate</td>
<td>0.037</td>
<td>-0.464*</td>
<td>-0.057</td>
</tr>
<tr>
<td>Cervix</td>
<td>-0.282*</td>
<td>-0.713*</td>
<td>0.181</td>
</tr>
</tbody>
</table>

* p < 0.001.  
* p < 0.01.  
* p < 0.05.

**Relationship between Milk and Egg Demand and Mortality from Cancer of Other Sites**

Examination of the relationship between milk and egg demand and mortality from cancer of other sites (Table 4) revealed significant positive correlations between milk demand and mortality from cancer of the ovaries, rectum, colon, and testes and significant negative correlations between milk demand and cancer of the cervix, prostate, and respiratory organs. In the case of egg demand, no significant positive associations were found with cancer of any site. Significant negative correlations were found between egg demand and cancer of the rectum, colon, and stomach and cancer of all sites.

**DISCUSSION**

Hems (27) has suggested that individual risk of breast cancer may depend upon 2 factors: diet, which varies markedly among nations and is primarily responsible for the international variation observed in breast cancer mortality; and reproductive history, which, given the dietary practices of a specific population, modulates individual risk of breast cancer within that population. The preeminence of the effect of age of first marriage in our data for the United States and the failure to find associations between breast cancer mortality and such variables as dietary fat intake or total caloric intake are consistent with Hems’ explanation. The variation in diet from one state to another within the United States may be inadequate for one to detect significant differences in a specific dietary component, particularly in one that is difficult to measure with accuracy or for which only incomplete data are available. If this is the case, however, then it seems noteworthy that, despite these problems, the consumption of both milk and eggs showed significant correlations with breast cancer mortality.

**Relationship between Breast Cancer Mortality and the Consumption of Dairy Products**

In international studies (1, 54), breast cancer mortality has been associated with the consumption of milk, and in studies conducted within a single country (34, 57), it has been associated with the consumption of milk, butter, cheese, and other dairy products. The consumption of non-milk dairy products, particularly butter and cheese, has also been associated with increased breast cancer risk in a case-control study (48) and a prospective incidence study (34).

Our analyses provide some support for these associations and suggest that the positive association between milk consumption and breast cancer mortality (a) may be related to milk fat and (b) may be independent of other dietary and demographic variables. Milk demand remained positively associated with breast cancer mortality when any of a large number of dietary and demographic variables was controlled. Only in a few cases, when milk demand was simultaneously controlled for certain combinations of these variables, did the strength and significance of its association with breast cancer mortality weaken appreciably. This is not surprising, however, since these variables are themselves closely associated with milk demand. Nonetheless, these results could be interpreted as an indication that milk consumption is no more than a marker for a high-risk lifestyle (e.g., late first pregnancy, high income, living in a city, or eating a diet high in protein, fat, or calories). The perseverance, however, of a positive relationship, despite multiple controls for these highly intercorrelated variables, suggests that the association between milk consumption and breast cancer mortality may be of fundamental biological significance.

**Relationship between Breast Cancer Mortality and the Consumption of Other Foods**

Previous studies have found a strong correlation between fat intake and the development of mammary tumors in rats (10–12), and international comparisons (10, 12, 18, 26, 27, 39, 54) have suggested that this association exists in women as well. Within a single country, however, the association between fat intake and breast cancer incidence and mortality has not been well established (34, 57). Data from case-control (13, 44, 48) and prospective incidence (34) studies have been suggestive but inconclusive. They typically have implicated selected high-fat foods including dairy products, as a rule, but have not made a strong case for an association between breast cancer and total fat intake. In our own analyses of state-based data, we initially found a positive correlation between fat intake and breast cancer mortality. However, when we controlled for other dietary and demographic variables, the correlation disappeared, but only within the various states, these latter 2 variables may be of fundamental importance than dietary fat in the development of breast cancer.

The consumption of protein, particularly animal protein, has been associated with breast cancer mortality in international studies (1, 10, 18, 27, 32, 54), although animal studies have not provided strong support for this association (10). Within a single country (Japan), meat consumption has been associated with increased risk of breast cancer in 2 prospective incidence studies (34), and pork consumption has been associated with increased breast cancer mortality in a 12-district study (57). Unfortunately, other key variables such as reproductive history, economic status, and degree of westernization typically were...
not controlled in these studies, so that their results, although suggestive, remain inconclusive. In our data for the United States, pork demand showed no relationship with breast cancer mortality. Only weak positive associations were observed between breast cancer mortality and the consumption of protein, meat, and beef, and these were obliterated either when age of first marriage or median income was controlled or when the Southern states were excluded from the analyses.

Like fat intake, total caloric intake has been correlated with the incidence of both spontaneous and induced mammary tumors in rats and mice (10, 19, 45) and has shown a positive correlation with breast cancer mortality in international studies (1, 54). Within a single human population, however, only a weak association has been found between the 2 (34, 44). We found no correlation between total caloric intake and breast cancer mortality in our regional analyses and only a weak association, which did not survive detailed examination, in our state-based data.

Internationally, intake of highly refined carbohydrates, particularly sugar, has been positively associated with breast cancer mortality (1, 8, 18, 26, 27). Within a single nation, bread consumption more frequently has been associated with breast cancer incidence and mortality than has sugar consumption (34, 48). Similarly, in our own regional food consumption analyses, bread was the only nondairy food to show a regional consumption pattern comparable to that of breast cancer mortality. The consumption of sugar and sweets showed no such pattern. The consumption of total complex carbohydrates, bread notwithstanding, has been negatively correlated with breast cancer mortality in both international and intranational studies (34, 55) and in our regional data as well. Alcohol consumption, on the other hand, has been positively associated with breast cancer mortality within the United States in previous studies (7, 65) and in our regional data. Previously reported correlations between each of these foods and breast cancer typically lacked appropriate controls for confounding variables. Because no state demand data were available for these foods, such potentially confounding variables could not be controlled in our analyses for these foods either.

The finding of a strong inverse association between egg consumption and breast cancer mortality was both unexpected and intriguing. Previous international studies had found a positive correlation between egg consumption and breast cancer mortality (1, 54), and a prospective incidence study in Japan had shown a striking association between egg use and risk of breast cancer (34). In a study of 12 districts of Japan, however, egg consumption was found to be negatively associated with breast cancer mortality (57), and our own analyses have revealed a strong inverse correlation between egg consumption and breast cancer mortality within the United States. Because previous studies failed to control for either income or reproductive history in their reported analyses, their results may have been confounded. Indeed, one possible explanation for the dramatic negative correlation between egg consumption and breast cancer mortality found in our data might be that egg consumption in this country happens to be a particularly sensitive marker for the low-risk lifestyle. According to this interpretation, the woman who consumes eggs heavily would tend to be of relatively low income with an early first pregnancy, low consumption of dairy products, and so on. The strength and persistence of this association, however, despite multiple controls for key dietary and demographic variables, suggest that such an explanation may be inadequate and that this association deserves further careful study.

Possible Biological Mechanisms

Dairy Product-Breast Cancer Association

If a biological link does indeed exist between the consumption of individual dairy products or milk fat itself and the development of breast cancer, possible explanations might include the following.

1. Increased Total Fat Intake. Of the nutrients previously associated with increased risk of breast cancer, total fat intake has probably received the widest attention. Possible mechanisms for this relationship include an increased production of carcinogenic estrogens and other carcinogens within the intestine (see Paragraph 2), an increase in the total amount of body fat with consequently increased peripheral production of estrogen (15, 16), lowered age of menarche (22, 36) which has been associated with an increased risk of breast cancer (16, 23), and changes in plasma hormone profiles in a direction favorable to the development of breast cancer (5, 12, 32, 33) either through one of the above mechanisms or independently. This explanation of the dairy product-breast cancer association is weakened, however, by the failure of intranational studies (including ours) to find a strong association between total fat intake and breast cancer risk in women.

2. Modification of the Composition of the Intestinal Flora. It has been shown that certain anaerobic intestinal bacteria can produce both estrogens and carcinogens from metabolic derivatives of cholesterol, bile acids, and other steroids (17, 29–31, 67). It has also been shown that diet can modify the concentration of some strains of these bacteria within the intestine (21, 50, 51). It is possible that milk consumption, either by increasing the concentration of substrate (cholesterol derivatives, bile acids, and steroids) or by modifying the floral environment, may contribute to the production of carcinogenic estrogens and other carcinogens within the intestine.

Ingestion of Some Hormonal Factor in Milk. Rodent and perhaps human breast tissue is influenced by a variety of hormones including estrogen, progesterone, glucocorticoids, insulin, prolactin, thyroid hormone, and possibly others including a whole array of recently identified serum polypeptide growth factors (47). Plant estrogens have also been found to be biologically active in human breast cancer cells in vitro and to markedly enhance tumor cell proliferation (42). Many of these factors are known to be secreted into bovine milk. In addition, a mitogenic factor capable of stimulating DNA synthesis and cell division in vitro has recently been isolated from human milk (37). The concentration of these substances in bovine milk and their potential effect on tumorigenesis in humans remain to be defined. Whether they enter the bloodstream of the human milk drinker in any significant quantities is not known.

Ingestion of an Oncogenic Virus in Milk Which Is Trophic to the Human Breast. Murine milk contains an oncogenic virus (mouse mammary tumor virus) which is responsible for breast cancer in mice (40), and morphologically similar particles have been identified in human milk (40), although the biological significance of these latter particles is unknown. It is conceiv-
able that bovine milk might contain an oncogenic virus responsible for human breast cancer. Milk from cows with bovine leukemia is known to contain an oncogenic virus which is infectious for several species (2, 9). If bovine milk does contain such a virus, its tropism to the breast might be expressed only towards the sexually mature organ. Such a phenomenon would be analogous to the tropism of the mumps virus to the mature testis only and would be compatible with evidence suggesting that the period from menarche to first pregnancy is a period of heightened susceptibility to the causative agent of breast cancer (14, 41).

**Increased Exposure to Contaminants Found in Milk.** Several hormonal substances have been used as growth promotants for cattle. These include diethylstilbestrol, melengestrol acetate, and zeronol, a derivative of the potent phytoestrogen zearalenone (46). Antimicrobial agents are also commonly administered to food animals (28, 64), and pesticides and industrial contaminants, including heavy metals, may inadvertently make their way into animal feed (46, 68). A number of these substances have been detected in animal tissues and bovine milk (28, 46, 68). It is possible that regular consumption of milk or milk products by providing chronic exposure to low doses of these substances may increase breast cancer risk.

**Egg-Breast Cancer Association**

Because cholesterol derivatives may serve as substrate for the production of estrogens and carcinogens within the intestine, it might have been expected that egg consumption would be positively rather than negatively correlated with breast cancer mortality. The possibility remains, of course, that the negative correlation observed in our data is entirely spurious, seriously confounded by other dietary and demographic variables. If, however, egg consumption does impart some protection against breast cancer, one possible mechanism for this effect, which is consistent with our data, is that egg consumption modifies the fecal flora environment in a direction unfavorable to the production of carcinogens. If this were true, one would expect to see a negative correlation between egg demand and cancer of the intestines, colon, and rectum, as well as cancer of certain target organs (e.g., the breast and uterus in the case of carcinogenic estrogens), and possibly cancer of all sites. We found exactly these results. Egg demand was significantly negatively correlated with cancer of the intestines, colon, rectum, breast, uterus, and all sites combined. In addition, egg consumption was negatively correlated with gastric cancer which has been postulated to be associated with the colonization of the stomach by nitrosamine- or other carcinogen-producing bacteria (17). These various findings could theoretically be related by the presence of some bacteriostatic substance in eggs. Several antibacterial proteins have, in fact, been isolated from egg white [e.g., lysozyme, conalbumin, and avidin (25)], and it is possible that one of these proteins or some other component of eggs may inhibit the growth of carcinogen-producing bacteria within both the stomach and the gut.

Hopefully, ongoing case-control studies will provide further data with which to evaluate the observed associations between breast cancer mortality and the consumption of milk and eggs. Because the years between menarche and first pregnancy appear to comprise a critical period in the development of breast cancer (14, 40, 41), it may be important to examine food consumption patterns during these years. Data on calcium intake from the Health and Nutrition Examination Survey of 1971–1974 (62) would suggest that a major decline in milk consumption occurs between ages 11 and 22 so that even in a population in which most individuals consume milk during childhood, there may be considerable variation in milk-drinking behavior during adolescence and young adulthood, a period of major theoretical interest. Data on the consumption of eggs and dairy products during these years and on breast cancer status later in life would help to clarify the significance of the associations reported in this paper.

**ACKNOWLEDGMENTS**

We are grateful to Dr. R. Raunikar, Dr. J. C. Purcell, and Dr. J. C. Elrod of the College of Agriculture, University of Georgia, for their help in providing state-based food demand estimates and to Ellen Bystrom for her assistance in the preparation of the manuscript.

**REFERENCES**


Breast Cancer Mortality and Diet in the United States


Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/39/9/3628

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.