Epidemiological Correlations between Diet and Cancer Frequency

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Abstract

The literature concerning international correlations between dietary items and cancer frequency is reviewed. An updated correlation of the most recent data on cancer mortality and food consumption is made. Strong and consistent correlations are reported between death rates of cancers of the colon and breast and the per capita consumption of total fat and of nutrients derived from animal sources, especially beef, pork, eggs, and milk. Similar but less consistent correlations have been reported with cancers of the prostate, ovary, and endometrium. In addition, correlations between precursor lesions of coronary heart disease and colon cancer in New Orleans autopsy populations are reported. Some studies suggest that milk intake correlates better with atherosclerotic disease while beef intake correlates better with colon cancer. Negative correlations of colon cancer rates and vegetable consumption are reported. Colon cancer rates also show negative correlations with stool weight, irrespective of the type of vegetable responsible for the increased bulk. Epidemiological data are consistent with the hypothesis that excessive beef and low vegetable consumption are causally related to colon cancer. These food items probably do not have a direct carcinogenic role but rather provide a microenvironment favorable to the actions of carcinogens.

Introduction

This is an attempt to open a discussion on the subject of diet-cancer relationships based mostly on a brief review of correlation studies. In addition, brief mention is made of studies of the correlation between the precursor lesions of colon cancer and coronary heart disease.

Brief Review of Correlation Studies

The notion that nutrition and cancer might be interrelated is an old one. In modern times, one of its most articulate disciples has been Tannenbaum (41). His most prolific contributions are in the experimental field, but he also did some correlation studies, mostly based on the statistics of life insurance companies in which he found a positive association between overweight and several types of cancer. He simulated this human situation in numerous animal experiments and established firmly that excessive nutrition enhances cancer development and progression (42).

Intercountry data on dietary intake were utilized on a large scale for correlation studies with coronary heart disease before similar studies were done for neoplastic disease. An initial positive correlation between coronary heart disease and total fat intake was later found to be even stronger when saturated fats alone were considered (25). Many studies primarily concerned with cancer have also included coronary heart disease in their analysis because of its well-known correlation with certain neoplasms (47).

Cancer correlation studies were greatly facilitated by the pioneer work of Segi, who collected and adjusted the cancer death rate to its now widely used "world" population model (45). Lea (27) in 1967 correlated cancer death rates as adjusted for age by Segi with the availability of foods as proved by the FAO publications. He was impressed by the fact that neoplasms seem to fall into two groups. Group 1 was positively correlated with the ingestion of fat, sugar, animal protein, eggs, and milk. Prominent members of this group were cancers of the breast, ovary, large bowel, and prostate. Group 2 was formed principally by cancers of the stomach and liver and showed a negative association with such food items.

Wynder et al. (46, 47), while reporting on studies of analytical epidemiology of colon cancer, concluded that dietary factors and especially the high intake of fat appeared to be associated with the etiology of colon cancer. A positive correlation between death rates of colon cancer and myocardial infarction was reported, again pointing toward possibly related dietary etiologies for both diseases.

Carroll et al. (4) found a positive correlation between breast cancer death rates and the intake of fat and calories. They were of the opinion that fat intake was the most relevant parameter.

Gregor et al. (13) correlated food intake with death rates for gastrointestinal cancer in an effort to explain the negative correlation between death rates of gastric cancer and colon cancer. They reported that animal protein intake correlated positively with the death rate of colon cancer and negatively with gastric cancer. They corroborated previous findings by Dunn and Buell (9), who reached similar conclusions about the role of diet in gastrointestinal cancer while studying time trends in Japanese immigrants to California.

Hems (20) examined the relationship of dietary intake and breast cancer in the pre- and postmenopausal periods. He concluded that the intake of sugar and fat accounted for three-fourths of the intercountry variation in postmenopausal breast cancer, while for premenopausal cancer, genetic factors appeared to have a stronger influence.

Drasar and Irving (8) reexamined some of the mortality data and added studies of cancer incidence in 37 countries as correlated with the FAO dietary intake data. They found no correlation of dietary items with gastric cancer but a positive correlation between breast cancer and colon cancer rates and total fat, animal protein, eggs, and sugar. Correlations with other indicators of affluence were also positive, such as income, the number of automobiles, and television sets. No correlation with fiber intake was found.

Howell (22, 23) examined again the correlation between
colorectal cancer and diet by means of international dietary
data, data of a case-control study conducted by Haenszel (19),
and data on food consumption within the United States. Her
correlation studies were based on incidence and mortality rates
and again showed a positive association of colorectal cancer
frequently with fat and animal protein intakes. In her opinion,
correlation studies did not provide an adequate base to con-
cider one dietary component more suspect than the other. In
in-control studies, milk and eggs did not differentiate be-
tween cases and controls, and beef stood out as the food item
most consistently associated with colon cancer. Howell also
reported a strong negative correlation between rice consump-
tion and the colon cancer rate.

Enstrom (11) failed to find positive correlations between time
trends and socioeconomic class on the one hand and cancer
rates on the other. He based his analysis on data for United
States populations which have become homogeneous with
respect to diet and cancer rates.

Armstrong and Doll (1) took advantage of the available new
data on cancer incidence, refined statistical techniques, and
indicators of data reliability to critically reexamine the question
diet-cancer correlations. They found gastric cancer to be
negatively correlated with fat consumption; this negative as-
association explained formerly reported associations with protein
consumption. Meat and animal protein consumption was the
variable most highly correlated with colon cancer. Controlling
for this variable reduced substantially the correlations with
other variables, including total fat, whereas no other variable
reduced the correlation coefficient with meat to less than 0.70.

In the case of cancer of the breast, corpus uteri, and ovary, on
the other hand, total fat intake provided the highest and most
consistent correlation coefficients. Cereal and "pulses" showed
negative association with these 3 endocrine-related cancers. Total fat consumption was also found to be positively
correlated with cancer of the prostate, testes, kidney, and
nervous system, but some of these correlations were weak or
inconstant.

Leveille (28) examined the time trends of colon cancer and
food consumption in Connecticut from 1935 to 1965. He found
the by now well-known correlation with beef consumption and
also called attention to the fact that increases in fat and protein
in the diet are accompanied by other changes, notably by a
reduction in consumption of cereal and potatoes in the United
States. He found a very strong negative correlation between
colon cancer and cereals and potato consumption. Correlations
of this type have contributed to the present interest in studying
the possible role of fiber in preventing colon cancer (26)
originally proposed by Burkitt (3), based on observations of
high dietary fiber and low colon cancer frequency in Africa.

Hems (21) studied the correlation between diet and death
rates for breast cancer in 41 countries as well as the influence
of childbearing. He found a positive correlation with total fat,
animal protein, and animal calories, but, because these 3 items
were closely correlated with one another, it was not possible to
assign an etiological role to one of them independently of the
other. Differences in childbearing per se contributed little to
the international variation. He also reported a positive correla-
tion between breast cancer rates and heights of women in 29
countries. This confirmed previous results of case-control stud-
ies in Holland (7), Greece (43), Slovenia (37), and Brazil (33).
Since nutrition influences height, this could be an indirect
indication of nutrition, but genetic factors most probably also
have a strong influence on body height.

Gaskill et al. (14), based on a 1965 to 1966 household food
consumption survey, analyzed the data for the main regions of
the United States. They found again the positive association of
breast cancer rates and milk consumption. In addition, they
found a previously undetected negative correlation between
breast cancer rates and egg consumption. Egg consumption
could be an indicator of poor socioeconomic status at the
present time in the United States or could have some unknown
biological significance. The lack of consistency with other
international data should caution against assigning a causal
role to such a negative correlation. While consumption of eggs
has declined in the United States since 1939, the availability
of other dairy products and meat has increased remarkably (28).
This means that eggs are becoming relatively less important as
a source of energy, and the negative correlation may be an
expression of the excessive intake of other types of food.

Enig et al. (10) provided a critique of the fat-cancer hypo-
thesis and noted that the increase in fat consumption in the U.
S. has been mainly due to an increase in vegetable fat, mostly
containing trans-double bonds. They suggest that processed
vegetable fats should be investigated as possible etiological
agents. It should be noted that the marked increase in vege-
table fat consumption has been taking place without a marked
reduction in the consumption of other types of fat. This results
in an excessive overall fat intake and makes it difficult to assign
etiological roles to one particular type of fat to the exclusion
of the other.

Liu et al. (29) based their correlation analysis on estimates
of the contents of cholesterol, fatty acids, and fiber on the
items reported in the food consumption tables of FAO. They
found that the correlation of colon cancer rates with cholesterol
intake remained significant when adjustments were made for
fiber and other fats; adjusting for cholesterol, on the other
hand, decreased most of the other correlations to nonsignifi-
cant levels.

The Role of Fiber

Several investigators have noted a negative correlation be-
tween fat and fiber intake. Simultaneously with an increase in
fat consumption, there has been a decrease in the consumption
of fruits and vegetables in the United States (28). This trend is
generally observed as the level of affluence of the population
under study increases. Direct correlations of cancer rates with
dietary fiber have not been consistently found (8). However,
the calculation of "fiber" component of diet, based on inter-
national data, is far from satisfactory. It is well known that there
is a great variation in the type of vegetables consumed in
different countries, and their content of fiber is either unknown
or inaccurately estimated. While the definition fiber is still
controversial and the characterization of different types of fiber
is under investigation, it remains true that populations with low
colon cancer rates have bulkier diets than do those with high
rates. Two independent studies in Hawaii (15) and Scandinavia
(24) have shown that the daily stool weight is greater in low-
risk populations. This strengthens the observation made by
Leveille that changing the energy intake from vegetable to
animal sources is a characteristic of populations at high risk
for cancer of certain organs, especially breast and colon. This
is well illustrated by a recent dietary survey conducted by Fajardo (12) in rural areas of Colombia with very low incidence of breast and colon cancer; in a typical village (Guaitirilla), 82.5% of the calories and 76.4% of the protein came from vegetable sources.

**Updated Correlations**

In order to take a closer look at the role of vegetables in cancer risk, we calculated single (Pearson) and rank (Spearman) correlation coefficients for disease rates (38, 39) as compared to dietary information (13). The most recent available cancer rates as age-adjusted by Segi were utilized for 1973 and matched with diet data as published by FAO for the years of 1964 to 1966. This allows an 8- to 9-year lapse between dietary data and cancer rates to partially accommodate the well-known latency period needed for the development of neoplastic processes. In a total of 41 countries, mortality data and detailed information for most dietary items were available. The only exception was the data on beans which appeared as a separate item in only 15 of the countries under study. Data were available from Mauritius, Canada, Costa Rica, Cuba, Dominican Republic, El Salvador, Mexico, Nicaragua, United States, Uruguay, Venezuela, Hong Kong, Israel, Japan, Singapore, Austria, Belgium, Bulgaria, Czechoslovakia, Denmark, Finland, France, West Germany, Greece, Hungary, Iceland, Ireland, Italy, Luxembourg, The Netherlands, Norway, Poland, Portugal, Rumania, Spain, Sweden, Switzerland, England, Yugoslavia, Australia, and New Zealand.

Correlation coefficients were calculated for males for cancers of the oral cavity, esophagus, stomach, intestines, and prostate (1973). Rates for breast and cervix were calculated for females. Additionally, rates for tuberculosis, infectious and parasitic diseases, and arteriosclerotic heart diseases were calculated for males (1960 to 1961). Since body size is related in part to nutrition, correlations were calculated with body height. The latter data were available only for women in 27 of the countries under study (32).

Table 1 shows the correlation coefficients that were significant at the 0.05 level. No significant correlations were found for cancer of the oral cavity, esophagus, stomach, or cervix; for tuberculosis; or for infectious diseases. The only exception was a weak (0.42) correlation between esophageal cancer and rice consumption. There were also significant correlations between the following diseases and cancer sites: oral cavity and esophagus (0.78); stomach and arteriosclerotic heart disease (−0.47); intestine and breast (0.90); intestine and prostate (0.73); intestine and arteriosclerotic heart disease (0.48); breast and prostate (0.77); breast and arteriosclerotic heart disease (0.41); prostate and arteriosclerotic heart disease (0.46).

Our findings confirmed what previous investigators have pointed out; diseases which have a better correlation with dietary data are cancers of the intestine, breast, and prostate and arteriosclerotic heart disease. Their correlations with total fat intake and with sources of animal protein and fat, well shown in Table 1, have also been extensively discussed by previous investigators. The same diseases correlate well with the physical quality of life index and with the gross national product, indicating that they are diseases of affluence. Affluence seems to bring with it dietary changes which result in an excessive consumption of animal proteins. Leveille has calculated that the excess protein intake in the United States is more than double the recommended dietary allowances (28).

Table 1 emphasizes the negative correlations of the diseases under study with the consumption of rice, corn, and beans, which may suggest a protective role for these food items. As stated previously, the excessive intake of animal protein (mostly meat) in affluent societies takes place simultaneously with a decrease in the consumption of vegetables (28). This makes it possible at the present time to determine if the "protective" effect of rice, corn, and beans is by direct action or if it is merely a sign of the damage caused by excessive meat. The question may never be resolved, but its resolution becomes somewhat academic when one thinks that, in the past, dietary changes in human populations simultaneously have reduced starchy foods and increased meat consumption. This may indicate that disease prevention could be accomplished by reversing both trends simultaneously. The role of starchy vegetables may be to satisfy the appetite and, therefore, limit the excessive meat intake. Most habits are not suppressed but rather replaced.

Table 1 also shows a positive correlation between body height and cancer of the colon, breast, and prostate. This has been well described previously for breast cancer (7). Table 1 also shows height to be correlated with affluence and with sources of animal protein and fat as well as negatively correlated with the consumption of rice and corn. It would be reasonable to assume that a reduction in protein intake and an increase in the consumption of starchy vegetables might in the long run affect the average height of the population, a probably very unpopular result. On the other hand, it is hard to believe that an unlimited excess of protein consumption will result in unlimited increases in the height of the individuals in the community. The ideal situation should supply adequate energy sources to satisfy the growing needs of the body and less than excessive nutrition after full growth has been achieved. This should be a high priority challenge for our society at the present time.

**Table 1**

**Significant (p < 0.05) Pearson’s correlation coefficients**

Age-adjusted mortality rates (38) are correlated with per capita consumption of dietary item (13) and height.

<table>
<thead>
<tr>
<th>Gross national product</th>
<th>Wheat</th>
<th>Rice</th>
<th>Maize</th>
<th>Beans</th>
<th>Cattle meat</th>
<th>Pork</th>
<th>Eggs</th>
<th>Milk</th>
<th>Oil and fat</th>
<th>Animal proteins</th>
<th>Fat</th>
<th>Calories</th>
<th>Proteins</th>
<th>Fat</th>
<th>Female height</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>0.67</td>
<td>−0.34</td>
<td>−0.67</td>
<td>−0.68</td>
<td>0.54</td>
<td>0.60</td>
<td>0.75</td>
<td>0.48</td>
<td>0.64</td>
<td>0.82</td>
<td>0.49</td>
<td>0.74</td>
<td>0.74</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td>Breast (female)</td>
<td>0.66</td>
<td>0.34</td>
<td>−0.50</td>
<td>−0.66</td>
<td>0.58</td>
<td>0.62</td>
<td>0.75</td>
<td>0.55</td>
<td>0.64</td>
<td>0.84</td>
<td>0.48</td>
<td>0.75</td>
<td>0.75</td>
<td>0.63</td>
<td></td>
</tr>
<tr>
<td>Prostate</td>
<td>0.64</td>
<td>−0.58</td>
<td>−0.53</td>
<td>−0.66</td>
<td>0.47</td>
<td>0.48</td>
<td>0.48</td>
<td>0.52</td>
<td>0.51</td>
<td>0.44</td>
<td>0.76</td>
<td>0.52</td>
<td>0.72</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td>Atherosclerotic heart disease</td>
<td>0.52</td>
<td>−0.40</td>
<td>0.48</td>
<td>0.46</td>
<td>0.59</td>
<td>0.48</td>
<td>0.48</td>
<td>0.51</td>
<td>0.48</td>
<td>0.74</td>
<td>0.51</td>
<td>0.73</td>
<td>0.73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td>0.70</td>
<td>−0.42</td>
<td>−0.66</td>
<td>0.71</td>
<td>0.64</td>
<td>0.48</td>
<td>0.56</td>
<td>0.47</td>
<td>0.69</td>
<td>0.61</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
The Milk versus Meat Controversy

Since milk, beef, pork, and eggs are the prominent sources of animal protein and fat in most wealthy societies, special attention should be given to these items. Table 1 shows positive correlations of all of these items with the diseases under consideration. The correlation coefficient between atherosclerotic heart disease and egg consumption in our tabulations was weakly positive (0.35) and not significant (p = 0.08). It should be noted, however, that the recent drop in coronary heart disease death rates in the United States has followed a decrease in the consumption of eggs and an increase in the consumption of vegetable fat, and the possible causal linkage between the 2 events should be considered. The fact that cancer rates have not dropped simultaneously with heart disease may indicate differences in either the pathogenesis or the etiology which should be investigated further. Most countries have similar patterns of consumption of animal fat and meat, and this accounts for the positive correlations with both items, which are practically impossible to separate in tabulations of data from all countries. A few countries have definite preferences for their source of animal protein, and this provides some opportunity for limited discriminatory analysis (2). One such contrasting pattern is provided by Argentina and Finland, as shown in Table 2, which shows data on daily (1964 to 1966) per capita consumption of milk and meat (3) as well as the truncated (ages 35 to 64 years) annual death rates (Finland, 1960 to 1961; Argentina, 1962 to 1964) for coronary disease and cancer of the colon and breast (36, 39, 40). The high milk intake of the Finns is better reflected in their high heart disease rates, while the high beef intake of the Argentinians is better reflected in their high colon cancer rate. The rates of breast cancer, however, are high in both countries, probably indicating that either source of animal protein and fat may influence its development. A similar situation seems to exist for prostatic carcinoma; truncated rates for ages 35 to 74 years are 24.7 for Argentina and 17.7 for Finland.

Correlations between Precursor Lesions

Colon cancer and coronary heart disease are the end points of prolonged, seemingly independent pathological processes. Stages previous to the final result can be identified and quantified in autopsy populations following methodology described previously (5–31). We have estimated the area of the aorta involved by atherosclerosis as well as the prevalence of colorectal polyps in 847 autopsies in New Orleans. Table 3 gives the prevalence of adenomatous polyps in males for categories of atherosclerotic involvement of the aorta. These categories were defined for each age group according to previous investigations (31), and the ones represented in Table 3 represent a summary for all ages.

In New Orleans men, greater involvement with atherosclerosis is associated with higher polyp prevalence. This indicates that, in these populations, the factors responsible for both lesions are either the same or similar in distribution. Given previously discussed dietary associations, the latter explanation is favored, namely, that both dairy products and beef are excessively consumed by New Orleans populations (35). It is suggested that applying these techniques to populations with contrasting dietary habits, such as Argentina and Finland, might throw additional light on the subject. From their recent work on atherosclerosis, Strong and collaborators have reported that, in the last 15 years, there has been a decrease in the involvement of the aorta and coronary arteries by atherosclerosis. This correlates well with the decline in coronary heart disease death rates that has been observed in the country. No similar decrease has been observed in colon cancer death rates or in the prevalence of colonic polyps. This suggests that dietary changes may be taking place which tend to lower coronary heart disease rates but do not affect colon cancer rates.

Case-Control Studies

A thorough discussion of the results of case-control studies will not be attempted. They have been summarized recently (17, 44). Several of them, conducted in populations at high risk to colon cancer, have not found an association with meat or other suspect dietary items (17). This does not negate the role of animal proteins and fat, because there is, in effect, an overmatching due to the fact that most members in our community eat excessive amounts of beef. It should also be remembered that at least 50% of people in the United States over 60 years of age, when colon cancer is more frequent, carry adenomatous polyps in their colon. This means that at least one-half of the controls will be carriers of a lesion which is considered a precursor of colon cancer. This may explain why, in populations with more variability in meat intake, positive associations between colon cancer and beef are found (19).

It should also be kept in mind that dietary items probably are not direct carcinogens but rather are promoters of the action of a carcinogen. Our epidemiology techniques take into account only the final product. In the absence of an initiator, no degree of promotion will lead to cancer. In such circumstances, case-control studies may give contradictory results.

At least 2 case-control studies have shown an inverse association of colon cancer rates and fiber in the diet (16, 34). This has led to the very interesting speculations about the role of certain indole-containing cruciferous plants in the induction of presumably protective enzymes in the tissues (17). Population data suggest that greater stool bulk correlates negatively with colon cancer rates, irrespective of the type of vegetable responsible for the greater bulk (15, 24).
This brief review suggests that the best hypothesis available for testing today is that colon cancer is related to consumption of excessive animal fat and protein, especially beef, and insufficient consumption of vegetables to increase food bulk. Since changes to reverse these trends in adults do not appear to be hazardous, intervention trials should be considered seriously. The biggest difficulty is with the end point for evaluation of the results, but recent progress in endoscopic techniques and mutagenesis assays offers alternatives to cancer as an end point.

Conclusions

I would like to propose that: (a) total fat and animal protein strongly correlate internationally with arteriosclerotic heart disease, colon cancer, and breast cancer; (b) similar but less consistent correlations are found with cancer of the ovary, endometrium, and prostate; (c) fat versus protein-independent effects are difficult to discriminate in interpopulation correlations; (d) the available data suggest that fat correlates better with arteriosclerotic heart disease, and meat correlates better with colon cancer; (e) the fiber issue has not been resolved by interpopulation correlation studies, but greater food bulk shows a good inverse correlation with colon cancer rates; (f) meat consumption appears to be excessive in the United States when compared to other countries and when compared to nutritional requirements; and (g) high meat and low bulk appeared together in United States diets. They probably should be reduced together in attempts to prevent the disease and reverse the trends of high cancer rates.

References


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