REVIEW

Nutrition and Cancer: A Critical Review

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INTRODUCTION

After several decades of relative neglect, attention is again being focused upon the role of diet in the development of cancer. A variety of studies in laboratory animals and in human populations suggest that factors such as dietary contents of fat, fiber, trace minerals (mainly selenium and zinc) and vitamins influence cancer incidence and development.

In recent years the involvement of nutrition with cancer is one of the most fascinating aspects of cancer research that remain largely unexplored. One of the main reasons for the increased interest in this area of research is the rapid increase in cancer death (now, in Europe and North America, approximately one in five persons dies from cancer). Because of the diversity in this area with regards to the many types of cancer and the variety of nutritional factors this study will be limited to nutrition and breast cancer, the effects of alcohol, and preventive measures. Epidemiological data will also be evaluated.

Dietary Factors and Breast Cancer

Breast cancer is the primary cause of deaths in women in Europe and in the USA. Among all forms of cancer, breast cancer is the most common form. Annually, an estimated 100,000 new cases are diagnosed in the USA. More than 35,000 deaths per year were attributed to this disease.

England, Holland and Denmark are among the countries with the highest breast cancer deaths (Table 1). The international pattern shows that Europe and the USA have the highest breast cancer death rates (average = 32/100,000) which is several times higher than the rate in Japan and developing countries (average = 4/100,000). One question raised by this international pattern is whether the variations are genetically or environmentally (mainly diet) related.

Although genetic factors may influence breast cancer, this influence was shown to represent a tiny fraction. Thus, the variations observed in international studies are mainly due to nutritional factors, life style and industrialisation. It has been shown that people who immigrated from a country with a low incidence to a country of high incidence of breast cancer have been seen to acquire the rates of their host (new) environment[1] For example, the Japanese who immigrated to the USA or Europe had this experience, as second generation had cancer rates approaching those of USA or Europe.

Now, it is generally accepted that breast cancer incidence is a multi-factorial disease: it is influenced by fat, selenium, oral contraceptives, alcohol, stress and smoking.[2] Evidence that dietary fat is a key determinant of risk is

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Table 1
Age-adjusted death rate per 100,000 people

Country	*Site of Cancer*				
	Stomach (men)	*Colon and rectum (men)*	*Prostate (men)*	*Uterus*	*Breast (women)*
Denmark	19	34	24	15	31
Holland	25	27	24	9	32
England	24	28	19	10	34
USA	7	27	23	8	27
Japan	66	16	4	9	6
Nicaragua	0.1	0.1	1	1	1
Thailand	2	2	0.2	4	2

From Wynder et al. Cancer campaign, Early diagnosis of breast cancer, Grundmann E, Beck L,eds. 1976:1-28

reinforced by a variety of epidemiologic studies. These studies show high correlations between incidence (and mortality) and fat consumption in various countries (as shown in figure 1): the higher the fat consumption results in higher rate of breast cancer deaths. It was shown also that cooking the fat (fried foods) increases the risk of breast cancer.[3] Advocates and promoters of the health food industry claim that fat from plant sources (such as margarines and oils) is of less risk as compared to fat from animal sources. This hypothesis has been proven to be wrong: in fact, experiments have shown that fats from plants (polyunsturated fats) were more effective tumour promoters than were fats from animal origin (saturated fats). This may be due to the formation of free radicals from diets high in polyunsaturated fatty acids.[4,5]

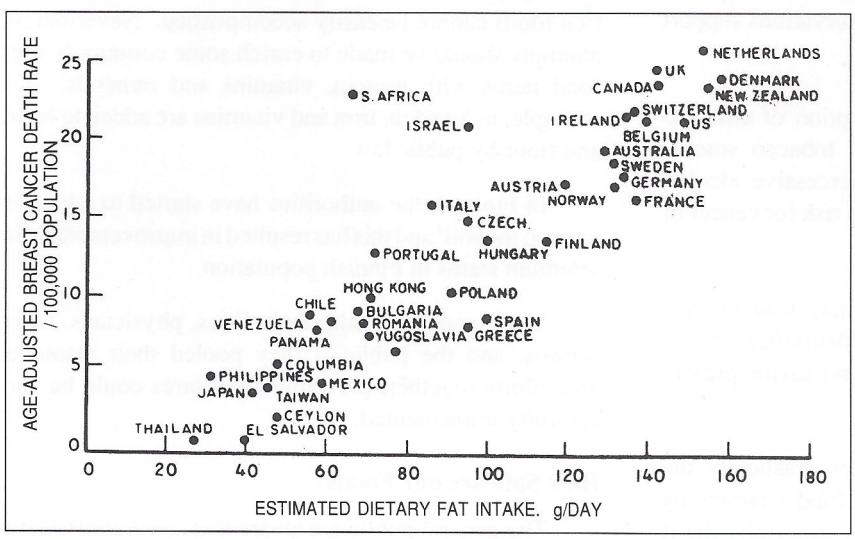

Figure 1 *Positive correlation between per capita consumption of dietary fat and age-adjusted mortality from breast cancer.*

One of the most interesting nutritional factors involved in cancer is selenium. Selenium is a mineral which is found in microamounts in foods. Foods such as grains, oysters, garlic, liver, kidney and meat are rich sources of selenium.

However, the level of selenium in animal meats (including liver and kidney) depends on the level of selenium in the plants consumed which in turn depends on the level of selenium in the soil.

Some ares in this world were exposed to geographical changes in the past which affected the level of selenium in the soil. Denmark, Holland, Australia and some areas in the USA have low selenium in their soils and, thus, the levels of selenium in the plants and animal meats are low as compared to areas of high selenium. For example, wheat grown in Australia contains about 0.1 gram of selenium per kilogram while wheat grown in North Dakota (a high selenium area in the USA) contains 1.1 grams of selenium per kilogram (more than 10 times).

Studies in many research centres in many countries have shown that cancer risk is high among people who consume low selenium in their diet. Human body needs about 50-200 micrograms of selenium per day. Numerous studies in experimental animals confirmed the effect of selenium in the development and promotion of breast cancer. It seems that low selenium intake combined

Table 2
Classification of risk factors in cancer

Factors	*Very high risk*	*High risk*	*Moderate risk*	*Low risk*
High fat diet (specially fried food)	yes	yes	yes	no
Low selenium intake	yes	yes	no	no
Long use of birth control pill	yes	yes	no	no
High alcohol consumption*	yes	yes	no	no
Did not breast feed*	yes	no	no	no
Severe stress and depression*	yes	no	no	no
Smoking*	yes	no	no	no

*Promotion factors

with high fat intake would increase the risk of cancer. This is logical because selenium can inhibit (or at least reduce) the production of carcinogens/free radicals (cancer-causing substances) from fats. In other words, selenium can counteract the carcinogenic effects of fat.

To briefly summarise the relative effects of many factors in the incidence of breast cancer, the risk can be classified into 4 types (Table 2) along with the factors involved in each. This classification is from a nutritionist point of view.

Alcohol-Cancer-Diet Interrelationship

There appears to be no experimental or epidemiological evidence justifying alcohol as a carcinogen by itself. This applies only to moderate alcohol consumption. However, alcohol plays an indirect role in the development of cancer in human. The following observations support this hypothesis:

First: Alcohol facilitates the absorption of environmental carcinogens such as tobacco smoke. This explains the fact that excessive alcohol drinking increases a smoker's risk for cancer of the upper alimentary tract.

Second: Excessive alcohol drinking may lead to liver damage and thus affect the "detoxification" of environmental carcinogens and toxins present in foods.

Third: Alcohol consumption reduces drastically the absorption and utilisation of food vitamins by the body. Vitamin deficiency especially the B group makes the epithelial cells susceptible to cancer formation.

Fourth: Alcohol consumption reduces the absorption and utilisation, by the body, of trace minerals (mainly zinc and selenium). Zinc deficiency has been shown to impair the immune response[6,7] in human.

Preventive Measures

Preventive measures in the field of nutrition may be difficult to implement because they often involve social habits not easily broken or socio-economic problems not easily changed. This is an area that should be of particular concern to health authorities.

What should be of concern to governments, control agencies and local health authorities is the implementations of strict laws and preventive measures in addition to public education. It is obvious that a recommendation to raise a population intake of proteins, minerals and vitamin-rich foods cannot be easily accomplished. Nevertheless, attempts should be made to enrich some commonly used food items with protein, vitamins and minerals. For example, in Sweden, iron and vitamins are added to bread and flour by public law.

In Finland, the authorities have started to add selenium to the soil[8] and this has resulted in improvement in the selenium status in Finnish population.

In general, the health authorities, physicians, nutritionists, and the public, if they pooled their resources and efforts together, preventive measures could be successfully implemented.

How Safe are our Foods?

The general public are aware that some constituents of foods and beverages may increase the risk of cancer. Their fears are associated more with man-made chemicals

than the naturally occurring constituents of food. The production, processing and preservation of food involves the use of hundreds of chemicals of which a number of them are now known to cause cancer in human. In this article I discussed the issue of HOW WE EAT and its relationship with cancer. However, the issue of HOW SAFE ARE OUR FOODS? is a different topic which deserves subsequent discussion in the future.

Validity of Epidemiological Data related to the Nutrition - Cancer Interrelationship

The major strength of epidemiological studies is that their focus on human populations circumvents two important limitations of laboratory research. First, since humans are observed directly, the results do not have to be extrapolated from one species to another.

Second, since the levels and patterns of exposure studied are those that actually occur among people, interpolation to low doses from the artificially high exposure levels frequently required in laboratory research can also be avoided. In addition, since the varieties of human experience produce a wide range of exposures to a given risk factor, epidemiological investigations are often able to examine directly the effects of different levels of exposure (ie. dose-response).

On the other hand, epidemiological studies present some special difficulties. To begin with, such research is limited by its need to rely primarily on observational data, because it is difficult and often unethical to conduct experiments (ie. intervention studies) on groups of humans. Furthermore, observational epidemiological studies are open to errors or bias. For example, persons who agree to participate in such studies or who are selected as participants by the investigator (eg. hospitalised patients) may not comprise truly representative groups of subjects and may yield misleading findings.

Unlike studies of cancer among smokers and non-smokers, dietary studies are confronted with the inherent difficulty of determining reasonably precise exposures. For example, the degree to which cases have been exposed to a particular dietary component may not be sufficiently different from that of controls to demonstrate any effect. Furthermore, it is often difficult to determine the specific dietary constituents to which study participants have been exposed.

Another difficulty inherent in epidemiological studies of diet and cancer is the long latency period between first exposure and overt manifestation of illness. In case-control studies, this delayed onset makes it necessary for investigators to learn what the subject are during some period beginning long before the study began, or to assume that recent intake reflect past exposures. In prospective cohort studies, the investigator must collect current dietary data and either wait (for up to 20 to 30 years) for the disease to appear or identify sufficiently large groups of subjects for whom there are adequate retrospective dietary data.

Accuracy in the measurement of both the exposure and the outcome variables is especially difficult to attain in the studies of diet and cancer. For example, the frequent dependence on recall data from interviewed subjects virtually guarantees imprecise measurement of dietary exposure, which might mask small but real differences between cases and controls. Correlation studies may suffer from differences among countries such as completeness of cancer reporting, diagnostic practices, and terminology. Furthermore, because cancer incidence (occurrence) data are frequently not available for such studies, reliance must be placed on mortality data instead. Since mortality reflects survival as well as incidence, it is not an ideal measure for cancer aetiology, particularly for sites where survival rates are high and have notable international variation. These and other considerations make it specially difficult to identify subtleties in the relationship between the degree of exposure and risk of disease.

Most of these deficiencies in epidemiological studies of diet and cancer are likely to result in non-differential misclassification, thereby reducing the likelihood that a given study will be able to demonstrate true differences that exist between the groups compared. Therefore, the results of epidemiological studies may often be assumed to represent conservative estimates of the true risk for cancer associated with the dietary exposures of interest.

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