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BACKGROUND PAPER NUTRITION AND CANCER

Americans are properly concerned and curious over research reports associating nutrition--our eating habits---with either real or suspected risks of developing cancers. Just what might be the roles of fats and fibers, vitamins and food additives, alcohol and nitrites, or methods of cooking foods such as hamburgers?

Prudence, for personal guidance, calls for knowing the facts in this area of very complex research. Some evidence is based upon laboratory experiments; some upon observations of human populations (epidemiology); some still is surmise. And, as with any subject, misunderstandings or exaggerations can creep in through word-of-mouth repetition.

This report seeks to put in focus some of the major questions in the public mind concerning diet and causation of cancer.

CANCER INCIDENCES

A first consideration is to appreciate that cancers, by all present understanding, do not spring forth overnight, any more than the "sudden" heart attack does. Cancer results from a long-term process, and has many causative factors, some of them probably working in tandem. What influence our diet plays would involve not only what we habitually are eating now, but also what we were consuming, or not consuming, 20 years ago or more.

In the last 20 years, by American Cancer Society statistics, stomach cancer has declined in incidence in both men and women in this country.

NUTRITION AND CANCER

There are various theories as to why this encouraging development came about, but no general agreement about them. One theory is that vitamin C may protect against formation of suspected cancer-causing agents, nitrosamines, in the stomach. With modern national distribution of foods, most of us now get a steady rather than seasonal intake of vitamin C from lettuce, tomatoes, orange juice and other sources. Increasing refrigeration of foods has almost paralleled the decline in stomach cancer. One hunch is that before better refrigeration, there was more partial fermentation of some foods, making them less wholesome, and perhaps involving formation of nitrosamines. Other specialists say they simply have no ideas to account for the decline. Lung cancer, attributed primarily to cigarette smoking, is rampant now among men and women alike. After it as the main cancer killers come cancer of the large bowel (colon-rectum), prostate gland and pancreas in men, and in women cancer of the breast and large bowel. Except for an increase in cancer of the pancreas, attributed in part to cigarette smoking, all these forms of cancer have struck at about the same incidence level for the last 50 years. So it seems logical that whatever causes them has been operating for all that time, without much success yet in identifying them.

IMPACT OF DIET

A few cancer specialists estimate that 40 to 45 percent or more of all cancers in this country appear linked in some degree to diet and nutrition. But others of equal expertise think this estimate is far too high, or at least that suspected links are far from proven. They do not see justification yet for changing American diets.

IMPACT OF DIET

The clear challenge is for research to identify, clearly, any diet habits or nutrients that may be responsible for inducing or promoting cancers. Guilty or suspect nutrients then could be omitted, or protective nutrients perhaps added.

One basis advanced for a high estimate of 45 percent of cancers being linked to diet is to ascribe deaths from breast cancer, the large bowel, ovary, prostate and endometrium as being associated with diet. High fat diet and low intake of vitamin C are given as the suspected causes.

Elements or events in our environment are blamed by some researchers as being causative factors in 80 to 90 percent of all human cancers. (This doesn't mean the causes have been identified, and therefore could be corrected.) "Of all the potential environmental factors, diet and nutrition appear linked to 40 percent of all cancers in males, and 60 percent in females," says Dr. Gio Gori of the National Cancer Institute. The estimates are based partly on epidemiological studies of students, migrants, and special populations such as Seventh Day Adventists whose diet differs significantly from the typical American intake.

Expressing another view, Dr. Warren Winkelstein, Jr., dean of the School of Public Health, University of California, Berkeley, says lung cancer could be reduced drastically if people would act upon the knowledge that cigarette smoking is a main cause, but "beyond that, however, we lack sufficient knowledge regarding the prevention of the major cancers."

HIGH FAT DIETS

Americans typically consume diets high in animal fats, including meats, butter, eggs, whole milk and cheeses, getting about 40 percent of their calories from fats. High-fat diets, especially in saturated fats and cholesterol, have long been blamed for promoting atherosclerosis, the clogging of vital arteries that underlies most heart attacks and strokes.

Now the high-fat diet stands accused of playing significant roles in breast cancer and cancers of the prostate and colon. To summarize some key points of evidence presented by Dr. Ernst Wynder and Dr. John Weisburger of the American Health Foundation:

The Japanese consume a diet with fats supplying only 15 to 20 percent of calories. Japanese women living in Japan have had a low incidence of breast cancer, although the rate has risen recently as the diet came to include more fats. Japanese women who migrate and adopt a Western or American style diet higher in fats have shown a rising incidence in breast cancer.

Laboratory findings support the suspicion of fats as a factor. Breast cancers, whether spontaneous or induced by chemicals, occur more frequently in animals fed diets rich in fats. The increased risk relates to increased production of prolactin, a hormone. Animals given anti-prolactin do not show an increase in tumors, Dr. Wynder reports.

Prolactin and estrogen may be potential tumor promoters. They and other types of lipids or fats are found in the breast fluid of non-lactating woman. This fluid is in intimate contact with the ductal cells from which most breast cancers arise.

"We are suggesting that this ductal fluid contains specific carcinogens the nature of which remains to be identified, and potential tumor promoters such as prolactin and estrogens." Breast fluid "tends to reflect a woman's eating and social habits" (nicotine appears in breast fluid five minutes after a woman smokes a cigarette,) and the amount of secretion "has been reported to correspond to breast cancer rates in high and low rate countries."

Adopting the so-called "prudent" diet lower in fats and cholesterol might protect women against breast cancer, Dr. Wynder says, as well as helping to keep arteries and hearts healthier.

Other studies indicate high fat diets may increase risks of cancer of the prostate and large bowel. Rats given a chemical that induces bowel cancer develop more of such tumors when they are also fed a high fat diet, Dr. Weisburger reports. High fat diets may stimulate greater production of bile acids which might be promoting agents for bowel cancer. These hypotheses are being investigated more fully.

FIBER IN FOODS

Americans and other Westerners consume a good deal of refined foods, sugar and white bread, protein, with usually not a great deal of cereals or foods supplying bulk to the intestines. Many Africans such as the Bantus, and people in other areas of the world, depend more upon rice and unrefined cereals, thus consuming much more "bulk."

Westerners have a high incidence of cancer of the colon or bowel, while the Bantus and others do not. An indicated conclusion is that food choice (or necessity may spell the difference. But how and why? A British physician, Dr. Dennis P. Burkitt, theorizes that bulky, undigested food residues make quicker passage through the intestines, thus reducing the time in which bacteria or other cancer-causing substances could be in contact with intestinal tissues. Studying Bantus, Dr. Burkitt was impressed with their low incidence of appendicitis as well as bowel cancer, a benefit he thinks stems from high fiber content in their diet. (Fiber is defined as the residue of plant cells after digestion by alimentary enzymes).

If--as mentioned above---bile acids or their breakdown products might be involved in causing cancer, the high fiber diet with its larger bulk would decrease the time such agents could be in contact with intestinal tissues.

THREE "N'S"

Three "N's"--- nitrites, nitrates and nitrosamines---are suspects in the diet-cancer complex.

Nitrites are substances used in cured meats, fish and other products to prevent growth of organisms causing botulism or food poisoning, and also to add attractive red coloring in products such as bacon. Nitrates are natural chemicals in many common vegetables, such as celery, spinach and beets. They can be changed to nitrites by saliva.

In the stomach, nitrites can react with secondary amines to form nitrosamines.

These are chemicals known to be strong cancer-producers in various animal species, at low doses. They might therefore also cause cancers in humans, but this point has not yet been proved. Nor is it known whether nitrosamines might have additive or promoting effects when combined with other chemical agents.

Sodium nitrite added to bacon can be transformed into nitrosamines during frying. Because of uncertainty over effects of nitrosamines, and to play on the safer side, the Department of Agriculture ruled that effective June 15, 1978, bacon could contain no more than 120 parts per million of sodium nitrite, compared with the 200 that had been permitted before. Later the allowable dose is to be reduced to 40 parts per million.

FOOD ADDITIVES

More than 1,300 food additives now are officially approved for use as colors, flavors, preservatives, thickeners and other agents for keeping foodstuffs fresh, attractive, storable, and other purposes, says a U.S. Senate Report on Dietary Goals for the United States. All "are considered safe by the FDA (Food and Drug Administration) based on varying degrees of testing, review of scientific literature, expert opinion, and long-term usage."

As watchdog, the FDA occasionally takes some off the list. A recent example was withdrawal of Red Dye No. 2 used for coloring foods like maraschino cherries. There is sentiment to substitute "natural" vegetable dyes for synthetic dyes first introduced several decades ago. Some specialists also feel that additives should be held to a "necessary" minimum, because they might possess additive or synergistic effects.

While man is adding chemicals to his foods, it should be kept in mind that "Natural foods contain thousands of different chemicals, practically none of which have been tested for safety by the standard procedures used for food additives," says Dr. Thomas J. Jukes of the Division of Medical Physics, University of California, Berkeley. "Many of these substances are well known to be toxic at levels only moderately higher than those reaching the consumer. Some examples are solanine (present in potatoes), antithyroid substances that are present in members of the cabbage and mustard family (such as broccoli and radishes), tannin in Tea and coffee, and arsenic in shrimp."

ARTIFICIAL SWEETENERS

Cyclamates and saccharin both became banned as artificial sweeteners in soft drinks and other products after experiments showed that high doses caused bladder cancers in laboratory rats. Saccharin received a legislative reprieve, at least temporarily, after public protests that it was to be taken off the market. There are scientific and economic reasons for using such animals and extremely high doses of an agent as a test system. But it is also criticized as being more suggestive than positive in terms of human meanings. To some critics, it overlooks the possibility that the human body, evolved over so many thousands of years, may have defensive mechanisms against very small amounts daily or occasionally of a carcinogen, while the rat was being overwhelmed by massive doses over a short period of time.

AFLOTOXINS

These are cancer-causing chemicals produced by fungi growing on peanuts, corn and soybeans, and some other crops. For Americans at least, sanitary and protective measures in processing such foods prevent the growth of dangerous molds on peanuts and other foods. Most people throw moldy food away. Afloxin in this country would be an unusual cause of cancer, says Dr. Gori of NCI.

VITAMINS

An easy but dangerous belief is that if something is good for you, then more must be better. Applied to vitamins, this can be hazardous. Too much vitamin A or D, for example, may cause headaches, blurred vision, injury to the nervous system, and other effects, says the National Nutrition Consortium. One vitamin may block the body's utilization of another vitamin.

Anyone consuming a really balanced diet receives all the vitamins normally needed for good health. There is no anti-cancer magic in any vitamin, although interesting research is going on using retinoids, synthetic analogs of vitamin A, to prevent development of cancer of the breast, lung and bladder in experimental animals.

ALCOHOL

Among other of its influences, alcohol is an irritant to the mucosa or lining of the throat, esophagus and stomach. If combined with the physical and chemical insults from tobacco smoke, alcohol may well promote cancers in these areas. The evidence for this is mostly observational. Studies have not been made comparing groups of people---those who neither smoke nor drink; those who use alcohol but not tobacco; those who smoke but don't drink, and those who use alcohol plus cigarettes.

COOKING

Methods of preparing foods can affect their nutritional value, safety (as in killing bacteria) or possibly by creating hazardous substances. In Iceland, the wood smoking of fish to preserve this food creates benzpyrene, a cancer-causing chemical in animals. Iceland has a high rate of stomach cancer, but whether benzpyrene is responsible is not established.

Recently a Washington University team reported that some conventional ways of cooking hamburgers created substances that are mutagenic --- meaning they cause genetic changes --- in salmonella, a type of bacteria responsible for food poisoning. This test is regarded as a screen for substances that might be cancer-causing in animals, and possibly hence in humans. The mutagens were found in fried hamburgers, but not those cooked in a microwave oven, or broiled.

The researchers said their findings should be regarded as a warning that these substances represent a risk of unknown magnitude to the people who are exposed to them."

To others, the evidence on hamburgers is very slim and preliminary, if not premature for public announcement at this state of investigation.

Dr. Arthur C. Upton, director of the National Cancer Institute, says

mutagenicity--the ability to produce genetic changes in some organism---cannot be relied upon as a predictor of cancer "because the correlation between mutagenicity and carcinogenesis isn't perfect. I think we must acknowledge that the cancer process is in fact a multi-causal, multi-factorial, multi-stage process leading ultimately to a malignancy, but beginning with a sort of genetic determinant in the cell that can be influenced by environment."

"Two or more carcinogens acting in combination may be mutually inhibitory, additive, or multi-placative in their effects," and metabolic differences among individuals may be important also,

Research efforts are steadily being increased to pinpoint what influences food and nutrition may have in promoting or inducing cancer, or possibly in conferring protection against some forms of malignancy. The field obviously is very complex.

As a measure of response to the challenge, the ACS in fiscal year 1977 devoted more than 13 percent of its total research grants budget---more than \$4,000,000 in 78 grants---directly or indirectly related to nutrition and cancer. The NCI is spending \$6,996,000 for fiscal year 1978 and \$7,465,000 for FY 1979 on various aspects of nutrition research.

The ACS and NCI are co-sponsors of a National Conference on Nutrition in Cancer scheduled in Seattle, Washington, June 29-July 1, 1978.