Chapter 19
Diet, Physical Activity, and Cancer Prevention

Elaine B. Trujillo, Sharon A. Ross, and Cindy D. Davis

Key Points

- Achieve and maintain a healthy weight throughout life; this is one of the most important ways to reduce cancer risk.
- Eat mostly foods of plant origin, including at least 2–2½ cups (14–20 oz or 400–575 g) of a variety of non-starchy vegetables and fruits. Eat whole grains and/or legumes with every meal, and limit refined starchy foods.
- Limit consumption of red meat to 18 oz (510 g) per week and limit processed meat consumption.
- Limit daily alcoholic drinks to two drinks a day for men and one for women.
- Minimize sedentary behavior and engage in regular physical activity of all types, including occupational, household, transport, and recreational for cancer prevention.
- Cancer survivors should follow the recommendations for cancer prevention regarding diet, body weight, and physical activity.

Keywords Cancer • Diet and prevention • Body mass index • Phytochemicals • Meat • Alcohol

Introduction

Cancer is a leading cause of death in the USA. *Cancer* is a general term that represents more than 100 diseases, each with their own etiology. Cancer risk is influenced by both genetic and environmental factors including dietary habits. While each type of cancer has unique characteristics, all cancers share one common feature, unregulated cell division. All cancers begin when a single cell acquires multiple genetic changes and loses control of its normal growth and replication processes. The cancer process, which can occur over decades, includes fundamental, yet diverse, wide cellular processes, such as cellular differentiation, cellular proliferation/signaling, and apoptosis [1]. These processes can be influenced by diet.

E.B. Trujillo, M.S., R.D.N. (✉) • S.A. Ross, Ph.D., M.P.H.
Division of Cancer Prevention, National Cancer Institute,
National Institutes of Health, Rockville, MD 20850, USA
e-mail: trujille@mail.nih.gov

C.D. Davis, Ph.D.
Office of Dietary Supplements, National Institutes of Health, Rockville, MD, USA

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Evidence continues to mount that altering dietary habits is an effective and cost-efficient approach for both reducing cancer risk and modifying the biological behavior of tumors [2]. The importance of diet was emphasized more than a quarter century ago when Doll and Peto [3] suggested that approximately 35% (10–70%) of all cancers in the USA might be attributable to dietary factors. In 2007, similar conclusions were reached by the World Cancer Research Fund/American Institute of Cancer Research (WCRF/AICR) in the most comprehensive evidence-based report on the role of food, nutrition, and cancer prevention; the report concluded that diet and physical activity were major determinants of cancer risk [2]. On a global scale, diet and physical activity could potentially prevent over three to four million cancer cases each year [2]. The WCRF/AICR provides an ongoing update of diet, nutrition, and physical activity and cancer risk through the Continuous Update Project [4].

The American Cancer Society's (ACS) latest annual report on cancer incidence, mortality, and survival indicates a 23% drop in the cancer death rate since its peak in 1991; overall, cancer incidence is stable in women and declining by 3.1% per year in men. This trend is thought to be due to steady reductions in smoking combined with advances in cancer prevention, early detection, and treatment of some of the leading causes of cancer death [5]. Greater attention to environmental factors, such as dietary habits and smoking, holds promise to make even greater reductions in cancer rates. Cancer is no longer being viewed as an inevitable consequence of aging. Only about 5–10% of cancers can be classified as familial. The capability of utilizing smoking cessation, food and nutrition strategies, and the promotion of physical activity suggests that cancer is a largely preventable disease.

While considerable evidence points to diet as a critical factor in determining cancer risk, there are numerous inconsistencies in the literature. Much of this variation in response may relate to the genetic background of the individual which can markedly influence the response to specific foods [6]. By utilizing genetic information, we may be able to identify those individuals who must assure an adequate intake of a particular nutrient for cancer prevention. For example, dietary calcium can interact with a polymorphism in the vitamin D receptor (the *Fok 1* restriction site) to affect colon cancer risk. In this example, dietary calcium was not associated with colon cancer risk in individuals who were homozygous for the capital F genotype for the vitamin D receptor, but low dietary calcium was found to be associated with increased colon cancer risk with increased copies of the little f allele for the vitamin D receptor [6]. Selected polymorphisms may also be useful as surrogate markers for those who might be placed at risk from excessive exposures. However, the existence of about 30,000 genes and many million single nucleotide polymorphisms indicate that understanding individual responses to foods or components is extremely complicated.

Overweight and Obesity

The latest estimates from the Center for Disease Control and Prevention (CDC) show that obesity rates among adults rose to almost 38% in 2013/2014, up from 35% in 2011/2012 [7]. Excess body weight has been suggested as a risk factor for most, but not all, cancers [8]. On the other hand, overweight and obesity are protective against lung cancer, especially in current and former smokers [9]. In addition to differences in cancer etiology, the lack of an association across all cancers may reflect the imprecision in using body mass index (BMI) as a surrogate risk marker. BMI is the most common marker for overweight and obesity; overweight and obesity are defined as a BMI >25 and >30, respectively. BMI has been shown to correlate with direct body fat measures. However, in older persons or those who have muscle loss or wasting, BMI may indicate a lesser degree of body fatness than is actually the case and, conversely, BMI may reflect a higher degree of body fatness in persons with higher lean body mass.

The use of biomarkers of the metabolic syndrome holds promise for determining which shifts in body energetics are likely contributing to increased cancer risk or changes in the behavior of tumors [10]. Regardless, the WCRF/AICR panel judged the evidence as convincing that greater body fatness is a cause of cancers of the esophagus, pancreas, colorectum, postmenopausal breast, endometrium, and kidney [2, 4]. Greater body fatness is probably a cause of cancer of the gallbladder, both directly and indirectly, through the formation of gallstones [2]. Location of body fat also appears important since intra-abdominal visceral fat accumulation may be more detrimental than peripheral subcutaneous fat accumulations [8]. Hence, a high waist circumference may be especially hazardous.

Energy balance is often used to describe the complex interaction between diet, physical activity, and genetics on growth and body weight over an individual's lifetime. The influence of energy balance on cancer risk involves many potential interrelated mechanisms, including insulin resistance, altered sex hormone metabolism, and increased inflammation (Fig. 19.1).

Early in the twentieth century, research began to emerge that caloric restriction was an effective strategy for increasing longevity and decreasing cancer risk. Caloric restriction has several favorable effects on cancer processes including decreased mitogenic response, increased rates of apoptosis, reduced inflammatory response, induction of DNA repair enzymes, altered drug-metabolizing enzyme expression, and modified cell-mediated immune function [10]. At least parts of these anticancer properties associated with caloric restriction likely involve changes in the IGF-1 pathway [10]. Modalities for the treatment of the metabolic syndrome, such as bariatric surgery and metformin, also may mitigate cancer development through altering IGF-1 [11]. Attainment and maintenance of a healthy body weight throughout life may be one important way to protect against cancer and other common chronic diseases including hypertension and stroke, type 2 diabetes, and coronary heart disease.

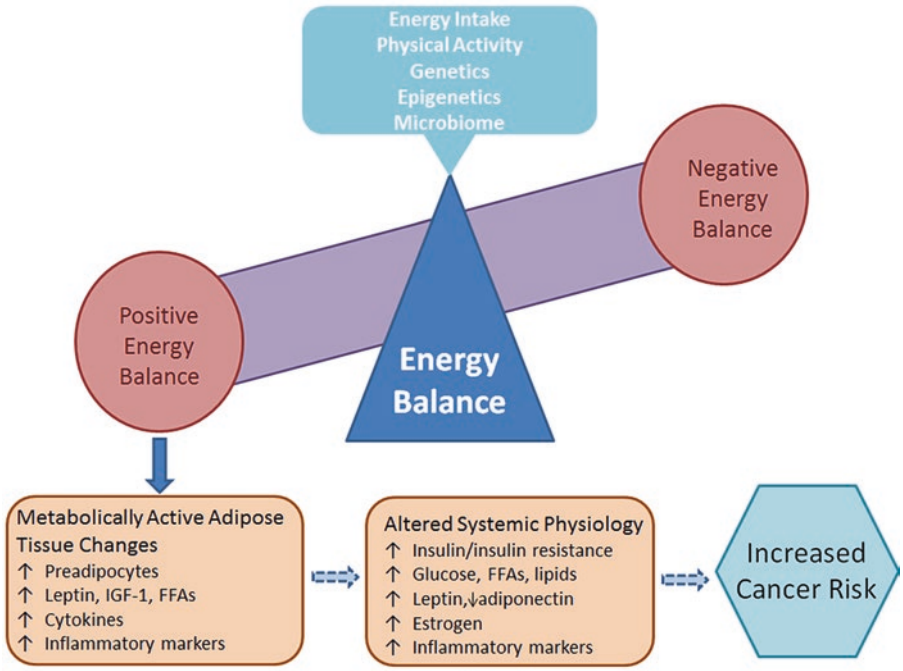

Fig. 19.1 Long-term positive energy balance due to excessive energy intake and/or low levels of energy expenditure can lead to obesity. The metabolic consequences of long-term positive energy balance and the accumulation of excessive body fat include increased IGF-1, insulin, and leptin concentrations. These effects can stimulate cellular proliferation, inhibit apoptosis, increase insulin resistance, alter steroid hormone metabolism, and stimulate inflammatory/oxidative stress processes, all of which can contribute to increased cancer risk [8]

A major challenge in understanding the complex relationship between obesity and cancer is determining which host characteristics are causative and which are associative. Recent research suggests that obesity is associated with alterations in the gut microbiome [12], but it is not yet clear whether these obesity-microbiome changes cause the increased cancer risk associated with obesity. The human gastrointestinal tract harbors trillions of microorganisms, most of which are commensal and have adapted over time to the milieu of the human colon. The mutualistic relationship between the intestinal microbiota, particularly bacteria, and their mammalian host is thought to be influenced, at least in part, by diet. Consumption of various nutrients and other food components affects the structure of the microbial community and provides substrates for microbial metabolism. Eating patterns modify microbial community structure, and microorganisms can also generate new compounds from food components. Some of these compounds are beneficial while others may be harmful. Many of the specific bacterial taxa, as well as microbially generated metabolites, may have a role in health and disease development including obesity and cancer.

Physical Activity

A key variable in the energy balance equation is energy expended via physical activity. Despite the numerous health benefits associated with physical activity, Americans are not incorporating enough physical activity into their daily routines. The CDC estimates that less than half of all adults meet the 2008 Physical Activity Guidelines and that less than three in ten high school students get at least 60 min of physical activity every day [13]. Overall, industrialization, urbanization, and mechanization have fostered a largely sedentary population in many parts of the world.

Regular, sustained physical activity protects against cancer of some sites independent of its effects on body fatness [2]. The WCRF/AICR panel found convincing evidence that physical activity protects against colon cancer [2, 4]. It probably also protects against endometrial and postmenopausal breast cancer; however, the evidence for premenopausal breast cancer is limited [2, 4]. Because physical activity promotes a healthy body weight, physical activity also likely protects against those cancers whose risk is increased by obesity.

Physical activity may influence cancer development through multiple, perhaps overlapping, biological pathways, several of which are mentioned in Fig. 19.1. Physical activity promotes regular bowel movements, which may decrease the time the colon is exposed to potential carcinogens. Additionally, physical activity causes changes in insulin resistance, metabolism, and hormone levels, which may help prevent tumor development, and alters a number of inflammatory and immune factors [14].

The WCRF/AICR recommends that individuals should be moderately physically active, equivalent to brisk walking for at least 30 min every day. As fitness improves, individuals should aim for at least 60 min of moderate activity, or 30 min of more vigorous physical activity, everyday [2].

Plant Foods

Evidence that plant foods protect against cancer comes principally from epidemiological, animal, and cell culture studies. Plant-based diets are high in nutrients and dietary fiber, low in energy density, rich in phytochemicals, vitamins, and minerals, and are associated with protection from various cancers. Phytochemicals refer to a variety of plant components that often perform important functions in the plant, such as providing color, flavor, or protection. The phytochemical composition of fruits and vegetables depends on the species and the subtype, as well as the environmental, cultivation, growing, harvesting, and storage conditions. Many of the health benefits, including cancer prevention, of diets rich in fruits and vegetables are due, in part, to the presence of multiple phytochemicals (Table 19.1).

Table 19.1 Selected dietary compounds and cancer risk

Phytochemical/nutrient	Dietary sources	Cancer effect [↑, ↓, I]	Potential cancer site[s]	Comments
Phytochemicals				
Allyl sulfur compounds	Onions, garlic, leeks, chives	↓	Stomach, CRC	Although compounds in garlic demonstrate anticancer activity, there is insufficient clinical evidence for recommending garlic supplements
Carotenoids	Citrus fruit, carrots, squash, pumpkin	↓	Mouth, pharynx, larynx, lung	
β-Carotene	Green leafy vegetables, carrots, pumpkin, sweet potatoes, squash, spinach, apricots, cantaloupe, pink grapefruit, green peppers	↓	Esophageal	
		↑	Lung	Evidence is from high-dose β-carotene supplements
Lycopene	Tomatoes, tomato products, guava, watermelon, pink grapefruit, apricots	**I**	Prostate	Epidemiological studies suggest that consuming foods containing lycopene decreases prostate cancer risk, interventional studies do not confirm the effect
Phytates, lignin, plant stanols, sterols	Whole grain and cereal products	↓	CRC, stomach	
Quercetin	Onion, red grapes, citrus fruit, broccoli	↓	Lung	
Soy isoflavones [genistein and daidzein]	Soybeans	**I**	Breast	Because of the potential to stimulate growth of estrogen-dependent human tumor cells [in animals], women on antiestrogen treatments should avoid soy isoflavone supplementation. No risk associated with soy isoflavones from food. Foods containing soy may decrease all-cause mortality in cancer survivors
Nutrients				
Calcium	Milk, cheese and other dairy products	↓	CRC	Milk [from cows] and supplemental calcium [1200 mg/day] probably decrease CRC risk; cheese may increase CRC risk
Folate	Vegetables [especially dark green leafy vegetables], fruits, and liver	↓	Pancreatic, esophageal, CRC	Folic acid is the supplemented form of folate and is added to bread and grain products to decrease occurrence of neural tube defects in newborns

(continued)

Table 19.1 (continued)

Phytochemical/nutrient	Dietary sources	Cancer effect [↑, ↓, I]	Potential cancer site[s]	Comments
n-3 Fatty acids	Fish [salmon, tuna]	**I for ↓**	CRC	Evidence refers to n-3 fatty acids from fish [DHA and EPA, not alpha-linolenic acid found in flax, soy, walnuts]
n-6 Fatty acids	Vegetable oils [corn, soybean, sunflower], salad dressings	**I for ↑**	Breast	WINS trial found that reducing dietary fat intake to 20% calories from fat with weight loss may reduce breast cancer recurrence, especially in women with ER disease
Selenium	Seafood, organ meats, muscle meats, cereals and other grains, dairy products, poultry, fish, eggs	↓	Prostate, stomach, lung, CRC	AICR CUP downgraded evidence for prostate cancer risk from strong to no conclusions
		↑	Prostate	SELECT trial found that high dose selenium supplements doubled the risk of developing high-grade cancer in men who started the trial with high selenium levels
Vitamin B6 [pyridoxine]	Fish, beef liver, organ meats, starchy vegetables, fruit [other than citrus], fortified cereals, beef, poultry	↓	Esophageal	
Vitamin C	Fruits and vegetables: citrus fruits, tomatoes and tomato juice, potatoes, red and green peppers, kiwifruit, broccoli, strawberries, Brussels sprouts, cantaloupe	↓	Esophageal	
Vitamin D	Fortified dairy products, eggs, mushrooms, fish	**I**		2014 US Preventive Services Task Force: no conclusions could be drawn regarding the benefits or harms for cancer prevention
		↓	CRC	
Vitamin E	Nuts, seeds, vegetable oils, green leafy vegetables, fortified cereals	↓	Esophageal, prostate	

(continued)

Table 19.1 (continued)

Phytochemical/nutrient	Dietary sources	Cancer effect [↑, ↓, I]	Potential cancer site[s]	Comments
Macronutrients				
Fat	Dietary fats from plant and animal foods	↑	Lung, postmenopausal breast, CRC	Total fat may increase risk of lung and postmenopausal breast; animal fat may increase risk of CRC
Fiber	Whole grains, fruits, vegetables, legumes	↓	CRC, breast	Fiber may decrease all-cause mortality for cancer survivors
Sugar	Sugar in foods [juices, milk, honey, syrups, high-fructose corn syrup], sugars added to foods [sugar-sweetened beverages, baked goods, cereals, canned products]	↑	CRC	
Specific foods/beverages				
Alcohol	Beers, wines, spirits/liquors	↑	CRC, mouth, pharynx, larynx, esophageal, postmenopausal breast, liver	
		↓	Kidney	Alcohol intakes up to 30 g/day [about two drinks]
Coffee	Coffee beverages from ground, roasted coffee beans	↓	Endometrial, liver	
Legumes	Beans, lentils, peas, peanuts	↓	Prostate, stomach	
Processed meat	Ham, bacon, hot dogs, pastrami, salami, sausages	↑	CRC, esophageal, lung, stomach, prostate	Convincing for CRC
Red and processed meat	Beef, lamb, pork, goat	↑	CRC, stomach, esophagus, lung, pancreas, endometrial	Convincing for CRC
Salt and salty foods	Added table salt, salt-preserved foods [salted meat, fish, vegetables], salty processed foods [chips, nuts, snack foods]	↑	Stomach	

↑ increased cancer risk, ↓ decreased cancer risk, *I* inconclusive effects on cancer risk, *CRC* colorectal cancer, *ER* estrogen receptor, *DHA* docosahexaenoic acid, *EPA* eicosapentaenoic acid
Source: Refs. [2, 4, 15, 16, 28–30]

Vegetables, particularly the non-starchy vegetables, and fruits may be protective for a variety of cancers, notably stomach, colorectal, mouth, pharynx, larynx, lung, esophageal, and pancreatic [2]. While these relationships are based on the epidemiologic literature, there are a number of limitations that are specific to the analysis of dietary intake of fruit and vegetables, including: most studies of consumption of dietary fruit and vegetables have been conducted in populations with relatively homogeneous diets; smokers consume less fruit and vegetables than nonsmokers; fat intake inversely correlates with fruit and vegetable intake in the United States; and studies using self-reporting tend to overreport vegetable and fruit consumption. Thus, many uncertainties exist about the relationship between plant-based diets and cancer prevention.

The magnitude of the response to vegetables and fruits and other dietary components is probably influenced by many factors, including individual genetic background and a host of environmental factors, as well as the type, quantity, and duration of consumption of these foods, and interactions among food components. The allium family, which contains about 500 food species including garlic, onion, leeks, and chives, illustrates the complexity of food. The allyl sulfur compounds within the allium family are thought to contain anticancer properties. However, these foods also contain many other potentially protective constituents, including amino acids, carbohydrates, and flavonoids. Similarly, other foods contain multitude phytochemicals that make drawing conclusions about the health benefits of a single compound in a food difficult.

Common green, yellow, red, and orange vegetables and fruits contain a variety of carotenoids, including lutein, zeaxanthin, cryptoxanthin, lycopene, β-carotene, and α-carotene. Carotenoid intake is associated with reduced risk of cancer of the mouth, pharynx, larynx, and lung [2]. Although epidemiological studies reported that high intakes of β-carotene-rich fruits and vegetables or high plasma concentrations of the β-carotene are inversely associated with lung cancer risk [2], in two randomized intervention trials, the intake of β-carotene supplements were found to have adverse effects. The α-Tocopherol β-Carotene Study (ATBC) and the β-Carotene and Retinol Efficacy Trial (CARET) showed increased lung cancer incidence in high-risk subjects (active smokers) [15, 16]. Unlike β-carotene supplements, β-carotene-rich vegetables and fruits contain many other compounds that may be protective against cancer, which may explain the variability seen in these studies. In fact, β-carotene may simply be a marker for the actual protective substances in vegetables and fruit. Alternatively, the protective effect at dietary intake amounts of carotenoids may be lost or reversed at the pharmacological levels found in supplements. The ATBC and CARET studies illustrate that consumption of supplements for cancer prevention might have unexpected adverse effects in certain populations and that definitive evidence for safety and efficacy is required before dietary supplementation guidance can be proposed.

Folate, an essential B vitamin found in dark green leafy vegetables, legumes, and fruits, serves as an example for the importance of diet–gene interactions. The mechanisms by which folate can modulate carcinogenesis are related to the sole biochemical function of folate—mediating the transfer of one-carbon moieties. In this role, folate is an important factor in DNA synthesis, stability, integrity, and repair. Evidence from cell culture, animal, and human studies indicates that folate deficiency is associated with DNA strand breaks, impaired DNA repair, and increased mutations. Folic acid, the supplement form of this vitamin, can correct some of the defects induced by folate deficiency. Epidemiologic and intervention studies support the role of folate in reducing the risk of colorectal cancer [2]. However, a common polymorphism in methylenetetrahydrofolate reductase (MTHFR) can potentially modify the effect of folate on colorectal cancer risk. Several MTHFR genes appear to influence colorectal cancer risk. MTHFR 677C>T has been studied extensively and is most strongly related to colorectal cancer risk, though not for risk of colorectal adenoma [17]. Furthermore, other MTHFR polymorphisms, combined with low plasma folate levels, may increase colorectal cancer risk [18]. Possibly 50–100 genes, either directly or indirectly, are involved with folate metabolism, which illustrates the complexity of diet–gene interactions. Not all individuals respond identically to folate

and other bioactive food components. A further understanding of the genetics of folate metabolism will clarify the optimal quantity of folate intake at a population and potentially individual level.

Whole grain intake also has been linked to a reduction in cancer risk, particularly those of the colon/rectum and stomach. Benefits attributed to whole grain consumption are observed at relatively low intakes (between two and three servings per day). However, in some Western countries, typical consumption of whole grain foods is less than one serving per day. Brown rice, bulgur, pearl barley, whole grain corn, whole oats, whole rye, and whole wheat are widely available whole grains in the USA. Unraveling the effects of grains is complicated by the fact that individuals consuming enhanced quantities of whole grains and cereal fibers have better health status, lower BMIs, lower intakes of alcohol and red meat, smoke less, and are more physically active [19]. Several compounds, including phytate, phytoestrogens such as lignan, plant stanols, and sterols, and several vitamins and minerals, present in whole grains may contribute to the observed lower risk of cancer. Additionally, the high fiber content of whole grains, and also of fruit and vegetables, is satiating and therefore helps prevent overconsumption of energy and may explain in part their anti-carcinogenic properties.

Just as individual foods are complex, containing multiple phytochemicals that may affect health and disease risk, the diet and dietary pattern is also complex and may affect disease risk. Individuals eat varying quantities, proportions, and combinations of foods and beverages at different frequencies. How various dietary patterns affect disease risk is an emerging area of nutrition research.

The Dietary Patterns Methods Project (DPMP) analyzed the association of select dietary patterns as characterized by dietary quality indices and mortality outcomes using three large cohort studies in the USA. Using four dietary indices commonly used in the USA, the Healthy Eating Index 2010, the Alternative Healthy Eating Index 2010, the alternate Mediterranean Diet score, and the Dietary Approaches to Stop Hypertension score, the DPMP found that high dietary quality scores were associated with a 19–24% and a 11–23% lower cancer mortality in men and women, respectively [20].

Several leading organizations provide public guidance on the optimal diet for cancer prevention. According to the WCRF/AICR, the ACS, and the World Health Organization, a cancer prevention diet is plant-based and includes vegetables and fruits, legumes, whole grains, and nuts [2, 21, 22]. Specifically, the guidelines include consuming 2–2½ cups (14–20 oz or 400–574 g) of a variety of non-starchy vegetables and fruits daily, and foods prepared with whole grains instead of refined grains [2, 21, 22].

Meat Intake

Meat, including all animal flesh apart from fish and seafood, can be classified as red or white. White meat is generally poultry and usually has more white than red muscle fibers. Red meat is unprocessed mammalian muscle meat, including beef, veal, pork, lamb, mutton, horse, or goat meat. Processed meat refers to meats preserved by smoking, curing, salting, or addition of chemical preservatives [2]. In 2015, the International Agency for Research on Cancer (IARC) concluded that there is sufficient evidence to conclude that processed meat is carcinogenic in humans; they classified the consumption of processed meat as a Group 1 carcinogen. These conclusions were based on the weight of evidence for colorectal cancer. A positive association was also found between the consumption of processed meat and stomach cancer. In regard to red meat consumption, the IARC found limited evidence for carcinogenicity; consumption of red meat was classified as Group 2A, probably carcinogenic to humans [23].

A range of mechanisms may account for the observed relationship between meat consumption and colorectal cancer risk. Cooking methods may foster the formation of carcinogens including polycyclic aromatic hydrocarbons (PAHs) and heterocyclic amines (HCAs) [23]. The formation of PAHs and HCAs is dependent on cooking time and temperature; the amounts of these compounds are increased

in meats that are cooked at high temperatures until well done [24]. PAHs are formed from the pyrolysis of fats that occurs when fat drips from meat onto hot coals, forming smoke that is redeposited on the meat surface. HCAs are formed during high-temperature cooking by the reaction between creatinine or creatinine, amino acids, and sugars found in muscle meats [24]. In view of the possible role of PAHs and HCAs in human carcinogenesis, minimizing exposure, such as by avoiding overheating and overcooking, seems prudent.

Nitrites and nitrates are often used as preservatives in meats and add the red-pink color to cured meats. These additives are not carcinogenic, but they can interact with dietary substances such as amines or amides to produce *N*-nitroso compounds which are carcinogenic to humans [24]. Several naturally occurring foods and their constituents, including tea, garlic, and cruciferous vegetables, may inhibit the formation of endogenous nitrosamines. This reduction in carcinogen formation may contribute to the generally protective effect of fruit and vegetables on cancer risk.

Iron deficiency is the most common and widespread nutritional deficiency in the world. Heme iron from animal sources is better absorbed than iron from plant sources, and thus animal food is important in minimizing iron deficiency. However, heme iron can act as a catalyst in the formation of *N*-nitroso compounds in the gut and may increase cell proliferation in the mucosa [24]. Environmental pollutants, such as some heavy metals, polychlorinated dibenzo-*p*-dioxins, and dibenzofurans, dioxin-like polychlorinated biphenyls, and others contained in raw or unprocessed meat, may play a role in carcinogenesis [25]. Genetic mutations and diet–gene interactions with red meat intake also may make individuals and/or populations susceptible to increased cancer risk, particularly colorectal cancer.

Meat can be a valuable source of many nutrients, including protein, iron, zinc, selenium, and vitamins B_6 and B_{12}. Therefore, consumption of red meat in moderation can be part of a healthy diet. Cancer prevention guidelines include moderate consumption of red meat, if eaten at all, and suggest limiting intake to less than 18 oz (510 g) per week. Very little, if any, processed meat is recommended [2, 21].

Alcohol

Dietary alcohol (ethanol) has been classified by the IARC as a human carcinogen [26]. It is both a source of dietary energy and a drug, and can therefore influence both mental and physical performance. The WCRF/AICR panel judged that there is convincing evidence that alcoholic drinks increase cancer of the mouth, pharynx and larynx, esophagus, colorectum (men), and breast [2, 4]. Alcoholic drinks are probably also a cause of liver and colorectal cancers in women [2, 4]. Conversely, evidence suggests that moderate alcohol intake may decrease the risk of kidney cancer [2, 4]. The type of beverage consumed does not appear to influence risk and thus total alcohol appears to be the primary agent leading to the transformation of cells to neoplastic lesions.

Acetaldehyde, the first and most toxic metabolite of alcohol metabolism, is particularly damaging to cells. It reacts with DNA in experimental animals to form cancer-promoting compounds [27]. In addition, highly reactive, oxygen-containing molecules formed during alcohol metabolism can damage DNA, thus promoting tumor development. Experimentally, chronic alcohol consumption has been reported to promote tumor proliferation via increased vascular endothelial growth factor expression and tumor angiogenesis [27]. Considerable evidence also points to the ability of alcohol to alter retinoid metabolism and thus interfere with differentiation. A change in DNA methylation may be an overarching factor accounting for changes in multiple cancer-related processes [27]. The response to alcohol may depend on multiple factors including smoking, adequacy of the diet, and genetic susceptibility. A true understanding of the effect of dietary alcohol may be clouded because of the compounds found in alcohol, which can both promote and potentially suppress tumorigenesis.

Conclusions

Accumulating evidence continues to demonstrate that food can have a profound effect on cancer risk and tumor behavior. The overall response is likely dependent on literally thousands of bioactive components that occur in food and their interactions with other environmental factors, the gut microbiota, and the consumer's genetics. These effects, which may be inhibitory or stimulatory depending on the specific bioactive food component, are mediated through diverse biological mechanisms. The identification and elucidation of the specific molecular sites for food components is critical for identifying those who will benefit maximally or be placed at risk from excess exposure. Until this information is available it remains prudent to eat a variety of foods and to maintain a healthy weight through controlling caloric intake and exercise.

Expanding knowledge about the physiological consequences of nutrigenomics—which includes nutrigenetic (genetic profiles that modulate the response to food components), nutritional transcriptomics (influence of food components on gene expression profiles), and nutritional epigenomics (influence of food components on DNA methylation and other epigenetic events and vice versa)—should help identify those who will and will not respond to particular dietary interventions. New reports are constantly surfacing that population studies are underestimating the significance of diet in overall cancer prevention and therapy and that subpopulations may be particularly sensitive to subtle changes in eating behaviors. To identify those who will benefit most from dietary change, more attention needs to be given to the identification of three types of biomarkers: (1) those reflecting exposures needed to bring about a desired response; (2) those which indicate a change in a physiologically relevant biological process which is linked to cancer; and (3) those which can be used to predict a personalized susceptibility based on nutrient–nutrient interactions and gene–nutrient interactions.

As the science of nutrition unfolds, a clearer understanding will surely emerge about how food components modulate cancer, and how the food supply might be modified through agronomic approaches and/or biotechnology. While the challenges to unraveling the relationships between diet and cancer prevention are enormous, so is the societal and health benefits that will occur because of these discoveries.

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Suggested Further Reading

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