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Review

Role of nutritional factors in pathogenesis of cancer

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Abstract

Diet and nutrition are crucial factors throughout the complete life course in the promotion and upholding of good health. It has always been accepted that our defencelessness to infection and disease was influenced by diet and environmental as well as genetic factors. Nutrition is coming to the front position as a principle modifiable determinant of chronic disease, with scientific confirmation with time more supporting the view that alterations in diet have strong effects, equally positive as well as negative, on health throughout life. For the most part notably, nutritional adjustments may not only influence present health but also determine whether or not an individual will develop chronic non-communicable diseases like cancer. Diet is a blend of protective, mutagenic, and carcinogenic agents; the majority of them are metabolized by the enzymes of biotransformation process. Genetic polymorphisms that alter protein expression or else the function of these enzymes can change the risk of developing cancer. The scientific community has identified numerous naturally occurring materials in plant food with the power to resolve possible carcinogens. A few of these nutrients and natural phytochemicals look for toxins and usher them from the body before they can cause cell damage that may lead to cancer. Others give the impression to make it easier for the body to make repairs at the cellular level. At a standstill, others may help bring to an end cancer cells from reproducing. Even after a cell begins to experience damage that can lead to cancer, what you eat and drink, and how you live can still help short-circuit the cancer process. It is thought that a diet containing defensive micronutrients as well as carcinogens and mutagens may adapt the risk of cancer development, particularly in genetically susceptible individuals.

Key words: Nutritional factor; Dietary practices; Susceptibility; Cancer.

Introduction

Nutritional factors have been thought responsible for about 30 per cent of cancers in more developed countries, making nutrient secondary only to tobacco as a mendable cause of cancer (Doll, 1981). The share of diet-to-cancer risk in low-income countries has been considered to be lower, perhaps around 20 per cent (Miller, 2001). The relationship between nutritional factors and pathogenesis of cancer first established by an experimental study conducted in 1940s where sequential confinement of nutritional factors markedly reduced the incidence of cancer in mice (Tannenbaum, 1940). After 2 decades other advancement like development of cancer registries and research focused on effect of environmental factors on human health depicts larger picture about the geographical variations in cancer incidence which might be due to the differences in lifestyle and dietary habits (Doll, 1966; Doll, 1970; Armstrong, 1975). It is followed by prominent number of case-control studies in 1970s

and 1980s to identify nutritional risk factors with greater specificity. Food patterns and specific food components, macro- and micronutrients may all play etiological roles and their effects may also be modified by other lifestyle factors such as physical activity or childbearing patterns. It has been hypothesized that 30%–40% of different subtypes of cancer may preclude with a healthy lifestyle and dietary habits. In some studies, probable associations have suggested with a few nutritional factors, but have focused mostly on the potential increased risks linked with the consumption of eggs, meat, and dairy products and the promising drop in risk connected with high intake of fruit and vegetables (Wolk, 1996; Lindblad, 1997; Handa, 2002; Nicodemus, 2004). Obesity is substantially correlated with carbohydrate and an established risk factor for cancers of the oesophagus (adenocarcinoma) colorectum, breast, endometrium and kidney (International Agency for Research on Cancer, 2002; Key, 2004). Contribution to obesity by dietary carbohydrates after that they nearly without doubt also add to rising the risk for these meticulous cancer sites (van Dam, 2007).

Hormonal and reproductive factors are the established risk factors for breast cancer, and it is obvious that higher intake of sucrose or else higher glycemic load may increase risk leading to obesity which will in turn increase the endogenous oestrogen levels (Key, 2003). Some evidence has led to the suggestion that a high intake of dietary fibre might reduce the risk of breast cancer, colorectal cancer, and stomach cancer (Burkitt, 1969; De Stefani, 1999). Carbohydrates are not considered to be directly pertinent to the aetiology of few types of cancer like liver cancer, lung cancer, ovarian cancer, prostate cancer, and bladder cancer (Jain, 2000; Pandey, 2003; Zeegers, 2004; Chan, 2005). Experimental studies and epidemiological data both indicate that high-fat diets increase the risk of cancer at sites such as breast, colon, prostate and pancreas (Armstrong, 1975; Carroll, 1983; Prentice, 1990). However, these associations are due to correlations with intake of animal fat, not vegetable fat (Rose, 1986). Based on these epidemiological investigations and animal studies, dietary fat increasing has been hypothesized to act by excretion of bile acids, which can be converted to carcinogens or promoters. Dietary polyunsaturated vegetable oils promote tumorigenesis in animals whereas saturated fats and polyunsaturated fish oils either have little effect or are inhibitory. Omega-3 fat acids that are present in fish oils and in some vegetables may reduce the incidence of breast and colon cancer (Carroll, 1991). It seems that monounsaturated oils such as olive oil, behave in a neutral manner. There is much convincing evidence that a high consumption of protein sources such as red and processed meat is associated with increased colorectal cancer risk (World Cancer Research Fund and American Investigation of Cancer Research, 2007). Furthermore, in a controlled trial, a low protein–high protein weight-loss diet has been observed to reduce fecal cancer-protective metabolites and increase hazardous metabolites, which could increase the risk of colon cancer (Russell, 2007). A possible increased risk of respiratory cancer was observed with a tendency of an increased general cancer risk over a shorter time. So cancer is one of the most important diseases that affect people worldwide. Cancer usually is an environmental disease and strongly associated with nutritional factors and precipitated by genetic factors. In this review, we have discussed the role of dietary factors which could have a significant role as a promoter or inhibitor in pathogenesis of different subtypes of cancer worldwide.

Prevalence of cancer

Cancer accounts for approximately 13 per cent of all deaths each year with the most common lung cancer, stomach cancer, colorectal cancer, liver cancer, and breast cancer. In 2008, approximately 12.7 million cancers were diagnosed and 7.6 million people died of cancer worldwide. This makes cancer the leading cause of death in the developed world, and the second leading cause of death in the developing world (Jemal, 2011). According to National Institute of Cancer, a wing of National Institute of Health in 2016, a rough and ready 1,685,210 new cases of cancer will be identified in the USA and about 595,690 individuals will pass away from the disease. In 2016, the most common cancers are proposed to be bladder cancer, breast cancer, bronchus cancer, colon and rectum cancer, lung cancer, prostate cancer, melanoma of the skin, leukaemia, thyroid cancer, kidney and renal pelvis cancer, pancreatic cancer, and endometrial cancer.

The probability of developing cancer may either increase or decrease depending on what individuals eat and how often they exercise. Nutritional factors are estimated to account for approximately 30 per cent of cancers in industrialized countries, making diet secondary only to tobacco as a hypothetically avoidable cause of cancer. Research to date has revealed few explicit relationships between exact nutritional factors and cancer risk. Studies have investigated the definite role of diet in the progress of major cancers. In developing countries, 60 per cent of these cancers are attributed to a diet low in fruit, vegetables, and animal products. All the way through the world, consumption of thermally very hot drinks and food raises the risk of these cancers.

Alteration in diet possibly will play a significant role in the rising frequency of specific cancers. Conventional and industrial food processing methods as well as microbiological and chemical food contaminants are the factors that may add to the carcinogenicity of diets (Table 1) (Key, 2004).

Table 2 summarizes the association between food or nutrients and cancers, which are frequent or increasing and which have been suggested to be related to dietary habits in the earlier epidemiological studies (Tominaga, 1987).

Demographic details

Earlier it was believed that cancer is more of a developed world issue; however, ratio is changing with time, and at present, 57 per cent of all cancers (excluding non-melanoma skin cancer) occur in less developed countries and 43 per cent in more developed countries. The list for cancer occurrence and mortality is topped by lung cancer in the global population, and it has been the most common cancer since 1985, with 1.35 million cases found in 2002, representative of 12.4 per cent of all new cancers. It is right now one of the most fatal widespread cancers—average 5 year survivals in Europe is approximately 10 per cent, hardly better than (8%–9%) in developing countries and the most avoidable. Globally, in prevalence, stomach cancer ranks fourth; however, owing to its lethality, second among the causes of cancer death. China has the uppermost rates as well as 42 per cent of universal cases. Almost 23 per cent of all cancers among women are breast cancers, the most common cancer among women, with approximately 1.15 million cancer cases in 2002. Prevalence is greatly high in developed countries; more than half of all cases are diagnosed. The most lethal cancer is liver cancer, which is sixth in prevalence worldwide, and ranks third in death, which comes after lung and stomach cancers. The major risk factor for liver cancer is chronic infection with hepatitis B virus (HBV), and hepatitis C virus is as well a factor. Cervical cancer comes after breast cancer, the next most common cancer among women globally, and accounts for 15 per cent of cancer among women. Another more common cancer in developing countries is oesophagus cancer.

Table 1. Diet, nutrition, and cancer: levels of evidence.

Evidence	Decreased risk	Increased risk
Convincing	Physical activity (colon)	Overweight and obesity (oesophagus, colorectum, breast in post-menopausal women, endometrium, kidney) Atatoxin (liver) Chinese-style salted fish (nasopharynx)
Probable	Fruit and vegetables (oral cavity, oesophagus, colorectum)	Preserved meat (colorectum) Salt-preserved food and salt (stomach) Very hot drinks and food (oral cavity, pharynx, oesophagus)
Possible/insufficient	Fibre, soya, fish, carotenoids Vitamin B2, B6, folate, C, D, E Calcium, zinc, and selenium Non-nutrient plant constituents like flavonoids, isoflavones, lignans	Animal fat Heterocyclic amines Polycyclic aromatic hydrocarbons Nitrosamines

Table 2. Nutritional risk factors for selected cancers.

Site for cancer	High risk factors	Low risk factors
Stomach	Salty food Salted or dried fish Large amount of rice Hot drinks and food Irregular meals	Milk and dairy products Raw vegetables Fruit
Colorectum	High-fat diet Low-fibre diet Beer (rectal cancer) Cholesterol	Fibre-rich diet (grains and pulses) Good protein–rich diet (cheese, beaf)
Oesophagus	Alcoholic beverages Hot drinks and food Diet poor in protein, vitamins, and minerals	Vegetables and fruit Diet rich in good protein, vitamins, and minerals
Breast	High fat/calorie diet	–
Lung	Cholesterol	Green–yellow vegetables Carotene, vitamin A

Prevalence of colon as well as rectal cancers varies about 25-fold from the high-income plus high-incidence developed countries to Africa and Asia, where occurrence is smallest. Even though detailed explanations are indefinable, the difference is believed to be ecological, with the leading factors related to most important dietary components. Prostate cancer is comparatively common, more so in industrialized countries than in developing countries, 19 versus 5.3 per cent. Three-quarters of all prostate cancer cases are in men aged 65 and older (Institute of Medicine, 2007).

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Cancer of oral cavity and pharynx

Several studies confirmed dietary patterns particularly; food-intake patterns have a pertinent role in the possibility of oral as well as pharyngeal cancer. The oral cancer risk appeared to be reduced by about 50 per cent by the addition of one serving of fruit and vegetables per day, protection by fruit and vegetables mainly because of selected micronutrients, counting β-carotene, and other carotenoids (La Vecchia *et al.*, 1991; Zheng *et al.*, 1993). However, pre-cancerous lesions of the oral cavity induce alterations in food practices (e.g. lessened citrus as well as fruit consumption), which will so be the consequence, more willingly than the cause, of the disease. In US study, moreover, we found some direct linkage among meat, saturated fats, cholesterol intake, and risk of oral cancer, and from the study conducted in Northern Italy (La Vecchia *et al.*, 1991), a linkage was found with retinol, an indicator of meat intake. Direct associations were found with eggs, pork, and sausages, which may again imitate a hostile effect of cholesterol and animal fats (Franceschi *et al.*, 1991; Marshall and Boyle, 1996) and probably of carcinogens in broiled meat (de Meester and Gerber, 1995) but also will possibly be a common sign of a poorer diet. As in earlier studies (Marshall *et al.*, 1992; Marshall and Boyle, 1996), a small indication emerged for a link among bread and cereals and oral cancer. The nutritional epidemiology of oral cancer is also marked by two risk factors that appear far more powerful than nutrition: tobacco use and alcohol consumption (Marshall *et al.*, 1992). Overall, a high intake of fruit and vegetables probably reduces the risk of oral cancer, and consumption of very hot drinks and food, typically consumed in some cultures, probably increases the risk of cancers of the oral cavity and pharynx.

Gastrointestinal cancer

Gastrointestinal (GI) cancer refers to malignant conditions of the GI tract and accessory organs of digestion, including the oesophagus, stomach, pancreas, small intestine, rectum, and anus. Oesophageal cancer is among upper digestive tract cancers and mainly prevalent in developing and underdeveloped countries. There is much sufficient evidence which supports that the use of uncooked fruit and vegetables, mainly citrus fruit, might lessen the danger of oesophageal cancer (Ziegler *et al.*, 1981; Cheng *et al.*, 1992; Hu *et al.*, 1994). Nevertheless, lack of a considerable link between oesophageal cancer and cooked vegetables proposes that the defensive factors in vegetables cannot resist the heat involved in cooking. Furthermore, the stronger contrary relationship of oesophageal cancer risk with citrus, more willingly than other fruit, provides support to the theory that vitamin C might be playing a fundamental advantageous role as it slows down the formation of carcinogens and protects DNA from mutagenic attack (Ziegler *et al.*,1981; Tuyns *et al.*,1987, Hercberg *et al.*, 1998). Many studies support the fact that cereals may increase the risk of oesophageal cancer (Yu *et al.*, 1988; Tzonou *et al.*, 1996). Soup and very hot beverages are positively associated with oesophageal cancer risk because their high temperature could be responsible for precancerous lesions of the oesophagus and precipitate in the form of cancer (De Stefani *et al.*, 1990; Cheng *et al.*, 1992; Hu *et al.*, 1994). Several other studies showing an increased risk are mainly related to barbecued and fried meat (Yu *et al.*, 1988; De Stefani *et al.*,1999), suggesting that the cooking method could be involved in oesophageal carcinogenesis. Several studies suggested that vitamin A can play a vital role in defensive injured epithelial

cells in opposition to attack by carcinogens, and oesophageal epithelial cells are more susceptible to the deficiency in vitamin A (Poulain *et al.*, 2009). Some studies have provided sturdy confirmation that polyphenol derived from tea may possibly possess the bioactivity to have an effect on the development of different cancers (Khan and Mukhtar, 2007). Also the relationship between drinking different tea and their associated danger has been reported in some studies from diverse parts of the world (Castellsague *et al.*, 2000; Ganesh *et al.*, 2009; Ibiebele *et al.*, 2010; Li *et al.*, 2002). Among minerals, the anticancer role of selenium and zinc was the research focus, and some researchers reported that selenium and zinc were preventive factors for occurrence of oesophageal cancer (Cai *et al.*, 2006; Lu *et al.*, 2006; Wei *et al.*, 2004).

Evidence supports that gastric cancer has an environmental etiology, of which diet appears to be the most important component. Furthermore, a human model of gastric carcinogenesis has been developed and studied extensively based on a multistage process in which dietary constituents act on the mucosa at various stages, leading from superficial gastritis to carcinoma, and the role of *N*-nitroso compounds has been emphasized (Correa *et al.*, 1988).

A case–control study conducted in Spain suggests that higher intake of salt and smoked as well as pickled food may perhaps be linked with a higher danger of gastric cancer, and this relationship will possibly result in the intragastric formation of nitrosamines (Ramón *et al.*, 1993). Salt is not a directly acting carcinogen, although it is thought to raise the risk of gastric cancer all the way through direct damage to gastric mucosa, resulting in gastritis, increased deoxyribonucleic acid (DNA) synthesis, along with cell proliferation (World Cancer Research Fund 1997). Superficial gastritis can lead to chronic atrophic gastritis, which is considered to be a precursor lesion in the progress of gastric cancer (Nomura *et al.*, 1996). Frequent consumption of beans and vegetables is reciprocally associated with risk of gastric cancer, and fresh meats, dairy products, and fresh fish are positively associated with risk of gastric cancer, whereas frequent consumption of sweets was associated with 70 per cent increased risk of gastric cancer (Ward *et al.*, 1999). A diet rich in meat-derived food has been suggested to play a role in gastric carcinogenesis by several studies in Western populations (Buiatti *et al.*, 1989; Wu-Williams *et al.*, 1990; De Stefani *et al.*, 1998). The underlying mechanism for this association is unclear but may involve increased tolerance to DNA damage associated with reduced mismatch repair (MMR) genes activity (Buermeyer *et al.*, 1999).

Cancer of the exocrine pancreas ranks fourth for cancer mortality in US men and women and is among the most rapidly fatal cancers worldwide (Surveillance, Epidemiology, and End Results Program, 1997). Thirty to fifty per cent of pancreatic cancers may be attributed to dietary factors (World Cancer Research Fund in association with the American Institute of Cancer Research, 1997). Dietary factors influence pancreatic cancer progression, which involves nutritional components affecting insulin insensitivity or else insulin-resistance pathways. Pancreatic exocrine cells are exposed to very high insulin concentrations, and facts indicate that insulin acts as a growth promoter and mutagen in the pancreas resulting in pancreatic tumour promotion. In response to high blood glucose concentrations, insulin is secreted into the blood, and the pancreas is exposed to a great deal of higher insulin concentrations; comparable to blood cancer risk, pancreatic cancer risk might increase as a result of nutritional factors that generate insulin spikes (Fisher *et al.*, 1996; Kazakoff *et al.*, 1996; Zagorsky *et al.*, 2005). A second main hypothesis linking dietary intake with pancreatic cancer suggests that dietary nutrients like β-carotene and total carotenoids, high serum α-tocopherol concentration, or vitamin C that reduce DNA damage or mutations by reducing oxidative stress and inflammation have inversely been associated with risk of pancreatic cancer (Lin *et al.*, 2005., Chan *et al.*, 2005., Stolzenberg-Solomon *et al.*, 2009). The defensive effect of nutrients linked with fruit and vegetables is also found, as the ingestion of most nutrients points out a dose-dependent risk reduction of pancreatic cancer growth. Antioxidants levels in serum have positively been associated with intake of fruit and vegetables, (Dauchet *et al.*, 2008), and these food items have been contrariwise related to pancreatic cancer risk (Inoue *et al.*, 2003; Nkondjock *et al.*, 2008). Non-enzymatic nutritional antioxidants (e.g. vitamin C and selenium) work jointly with enzymatic mechanisms to provide protection against oxidative stress (Maritim *et al.*, 2003). Various other nutritional factors like meat, dairy products, and eggs have also been investigated and encountered with elevated disease risks in some studies, although some studies reported null results (Mills *et al.*, 1988; Coughlin *et al.*, 2000; Stolzenberg-Solomon *et al.*, 2002; Michaud *et al.*, 2003). Increased risk has generally been attributed to the fat, saturated fat, or cholesterol content of meats and other animal products (Ghadirian *et al.*, 2003; Risch *et al.*, 2003; Vimalachandrac *et al.*, 2004; Food, nutrition and the prevention of cancer, 1997). Alternatively, meat preparation methods, such as grilling and frying, have been proposed as a source of carcinogens (World Cancer Research Fund 1997; Ghadirian *et al.*, 2003; Li *et al.*, 2004). Small intestine cancer is reasonably uncommon. Tobacco and alcohol consumption was unrelated to small intestine cancer risk; however, weekly or repeated consumption of red meat and monthly or more recurrent intake of salted or smoked food were related to 2- to 3-fold increases in risk. Nutritional factors are possibly concerned about the risk of small intestine cancer, although further research in other settings is requisite to make clear the determinants of these uncommon cancers (Chow *et al.*, 1993).

Colorectal cancer is a leading cause of death in the Western world. It is multifactorial in origin, combining genetic and environmental causes. Certain lifestyle factors, including nutrition, have been associated with a higher cancer risk. Newmark *et al.* (1984) studied the effect of dietary fat, phosphate, and calcium in colon cancer and suggested that increased dietary fat will endorse colon cancer by raising the free ionized fatty acid levels and bile acids in the colon contents. The annoying and toxic effects of the free acids in the presence of calcium ions on colon epithelial cells can be reduced by being converted to insoluble calcium soaps. Supplementary dietary calcium level to provide sufficient calcium and therefore to decrease the possible toxicity of dietary fat was considered (Newmark *et al.*, 1984). High consumption of vegetables and fruit and the avoidance of highly refined sugar containing food are likely to reduce the risk of colon cancer, although the responsible constituents remain unclear (Giovannucci *et al.*, 1994). An alternative hypothesis proposed by Giovannucci (1995) is that hyperinsulinemia promotes colon carcinogenesis. For colonic epithelial cells, insulin is an essential growth factor and is a mitogen of *in vitro* tumour cell development. The insulin/colon cancer theory is basically indirect and depends on the resemblance of factors which generate high insulin levels with those related to colon cancer risk supported by epidemiological study. The major determinants of insulin resistance and hyperinsulinemia are obesity, physical inactivity, and maybe a low dietary polyunsaturated fat-to-saturated fat ratio and come into view related to colon cancer risk. In the distal colon, elevated consumption of red meat raises the risk of colon cancer. Beef, pork, or lamb as a main dish is the particular food item most sturdily correlated with higher risk of colon cancer or adenoma. In the small intestine, fat from red meat may well be less

willingly digested or absorbed, possibly as a result of its high stearic acid content or because of its physical obstruction in muscle tissue, and consequently, more of it might reach the large bowel, persuade mitogenesis of adenoma and a few carcinoma cells, and accelerate growth. The hypothesis that fibre decreases the risk of colon cancer arose primarily from observations made by Burkitt in Africa (Burkitt *et al.*, 1974). Fibres are thought to lower the risk of colorectal cancer, either by altering the site of resistant starch fermentation from the proximal to the distal colon or by changing the absorption and metabolism of carcinogens in food (Govers *et al.*, 1999, Kestell *et al.*, 1999).

Cancer of respiratory organs

There are few observational studies of diet and lung cancer which suggest that increased intake of vegetables and fruit is associated with reduced risk in men and women; in various countries; in smokers, ex-smokers, and never-smokers; and for all histological types of lung cancer.

Slight protective effects were suggested for cruciferous vegetables and tomatoes, in addition to the strong protection afforded by carrot consumption. Prospective studies of blood β-carotene levels, debatably the best obtainable biomarker of vegetable and fruit intake, point out that low β-carotene level is prognostic of increased lung cancer prevalence. Although, in a randomized and placebo-controlled clinical trial in male smokers, lung cancer occurrence and total mortality were raised considerably among the men receiving β-carotene supplements owing to the exposure of heat and it turns into procarcinogen. If β-carotene can prevent lung carcinogenesis, which the trial cannot rule out, then the dosage, duration of use, method of administration, and/or subpopulation are critical. Several epidemiological studies have studied the relationship between dairy consumption and lung cancer risk, and produced inconsistent results. Few studies have been reported that intake of diary product may increase the risk of lung cancer (Axelsson *et al.*, 1996; Nyberg *et al.*, 1998). However, some studies are in contradicted farmer studies and found that dairy products were not significantly associated with lung cancer risk (Rachtan *et al.*, 2002; Van der Pols *et al.*, 2007). One study conducted in Missouri focused on non-smoking women with lung cancer, including a large number with adenocarcinoma, showed a strongly increasing trend in lung cancer risk with increased saturated fat consumption that may have been masked in earlier studies of lung cancer involving a high percentage of smokers (Michael *et al.*, 1993). Several observational epidemiological studies have indicated that diets high in fat, saturated fat, and cholesterol may increase the risk of lung cancer. The results showed a significant positive association between dietary cholesterol and the risk of lung cancer in men and women (Goodman *et al.*, 1988). A positive dose–response relation has been observed between the consumption of processed meats, dairy foods, eggs, and particular desserts, and the risk of lung cancer in men. Researchers also found a positive trend in the lung cancer risk in women with higher intake of some processed meats like bacon, spam, and desserts such as cakes and custard or cream pies. The dose–response association tended to be stronger among men who were intense smokers and also who were identified with squamous cell cancer of the lung (Goodman *et al.*, 1992). However, some data were inconsistent and concluded that there is no significant association between lung cancer and dietary cholesterol or saturated fat (Veierød *et al.*, 1997).

Skin cancer and diet

In USA, skin cancer is the most common form of cancer which affects nearly one in five Americans (Skin cancer facts, 2014). In current years, skin cancer has been diagnosed greater than all other types of cancers combined, including basal cell carcinoma (BCC), squamous cell carcinoma (SCC), along with cancer of melanocytes (Siegel *et al.*, 2012; Actinic keratosis, 2014; Skin cancer facts, 2014). For skin cancer, there are numerous entrenched risk factors and a dietary factor is one of them. Evidence also supported that nutritional interventions may well benefit people who are at high risk of skin carcinoma. Researchers prove that people who consumed higher levels of fruit and vegetables had a 54 per cent reduced risk of SCC (Ibiebele *et al.*, 2007). Reduction in the risk was related to consumption of green leafy vegetables. Reduced risk of melanoma has been observed with high intake of vitamins A, C, D, α- and β-carotene, cryptoxanthin, lutein, and lycopene compared with low intake (Millen *et al.*, 2004). Regular eating (more than three servings per week) of celeriac and pomegranates was linked with a considerably reduced risk of BCC and SCC (de Vries *et al.*, 2012). Abundant nutrients like vitamins C and E are present in plants acting as antioxidants and so may possibly help us to guard against skin cancer. Vitamin C acts by scavenging free radicals to restore the activity of other antioxidants, resulting in enhancement of the immune system, and hydroxylates lysine as well as proline in the synthesis of connective tissues proteins, which may modify tumour development. An intracellular antioxidant vitamin E prevents lipid peroxidation (McNaughton *et al.*, 2005). The variant of vitamin A, retinoic acid, is important in skin cell proliferation, differentiation, and maintenance and will possibly lessen the quantity of ultraviolet (UV) light reaching the underlying layers of the skin by raising epidermal thickness with the intention that taking carotenoid through food has been shown to reduce the danger of skin cancer (Siegel *et al.*, 2012). Researchers established that UV light–induced erythema was appreciably decreased by photoprotective effect observed in the combination of carotenoids and α-tocopherol (Stahl *et al.*, 2000). In a similar study, β-carotene supplementation or mixture of carotenoids daily for 12 weeks was shown together to have photoprotective effects by reducing erythema induced by UV in human skin and gives defence against exposure to UV radiation (Heinrich *et al.*, 2003). Carotenoids may slow down skin carcinogenesis due to their antioxidant abilities; β-carotene improves immune system functioning, whereas provitamin A carotenoids could stop skin cancer through its conversion to retinoids (McNaughton *et al.*, 2005). Conversely, there are a few concerns in relation to the safety of enormously high doses of carotenoid supplementation, owing to higher lung cancer occurrence and mortality among smokers taking supplemental β-carotene (Omenn *et al.*, 1996). Numerous epidemiological studies have suggested that extreme use of red meat such as beef, pork, and lamb, and processed meats including bacon, sausage, and hot dogs is connected with higher rate of cancer and danger of all-cause mortality. Some carcinogens present in meat, which may increase the risk of cancer, comprise heterocyclic amines, polycyclic aromatic hydrocarbons, and nitrates as well as nitrites (used as preservatives) (Kushi *et al.*, 2012). A diet rich in high fat influences DNA damage, decreased cell apoptosis, increased inflammatory cytokines in the skin, and oxidative stress, and it also enhances skin carcinogenesis influencing the composition of cell membrane lipids and intercellular communication. A high-fat diet and high intake of red meat as well as processed meats are connected with skin cancer (McNaughton *et al.*, 2005).

Breast cancer

Breast cancer is one of the most common cancers and the leading cause of cancer death among females, accounting for 23 per cent of all cancer cases and 14 per cent of the cancer deaths all over the world (Ferlay *et al.*, 2010). However, breast tumours may differ

clinically and biologically by hormone receptor status and menopausal status. Dietary factors have long been thought to play a major role in the development of breast cancer; it stands out among the modifiable risk factors and has thus been investigated in numerous studies mostly with a focus on specific nutrients or components. Vegetables and fruit intake has been hypothesized to decrease breast cancer risk. Studies have been inconsistent. A case–control study which examined the relationship between diet, particularly vegetables and fruit, and breast cancer concluded that intake of vegetables shows a reduced risk of premenopausal breast. Evaluated components found collectively in vegetables can have a synergistic effect on the risk of breast cancer (Freudenheim *et al.*, 1996). A meta-analysis was carried out, in order to summarize published data on the relationship between breast cancer, fruit and vegetable consumption and/or the intake of beta-carotene and vitamin C. This analysis confirms the association between intake of vegetables and, to a lesser extent, fruits and breast cancer risk from published sources. Increasing vegetable consumption might reduce the risk of breast cancer (Gandini, 2000). In a case–control study of diet and breast cancer estimated by menopausal status, it was observed that a significant reduction in breast cancer risk is associated with higher dietary intake of total lignan precursors, at least among premenopausal women (McCann, 2004). Another case–control study carried out in Uruguay evaluated the protective effect associated with vegetables and fruit on nutrients and bioactive substances present in plant food in breast cancer cases. The results related to vegetable and nutrient intake were consistent with antioxidant and antiestrogenic effects. This may be arbitrated, among other nutrients, by intake of dietary fibre and lycopene (Ronco *et al.*, 1999). An analytical study has been accomplished to assess and measure the effect of eating of olive oil, margarine, and a variety of food groups on the breast cancer risk. Majority of macronutrients are not showing noteworthy relations with breast cancer risk, although vegetables and fruit are contrariwise, considerably, and strongly associated with this risk. Evidence also supported that ingestion of olive oil decreases the risk of breast cancer, whereas margarine ingestion shows to be related to high risk for the disease (Trichopoulou *et al.*, 1995). A Chinese study was conducted to examine the association between vegetables and fruit intake and breast cancer risk, which encountered an inverse association between the consumption of vegetable, fruit, and antioxidant nutrients and breast cancer risk and depicted a protective role of vegetables and fruit in breast cancer (Zhang *et al.*, 2009). Furthermore, few data are inconsistent and did not significantly correlate nutritional factors with breast cancer. A pooled analysis of cohort studies suggested that consumption of fruit and vegetables during adulthood or pre-menopausal state is not significantly associated with breast cancer risk and did not identify any fruit and vegetable subgroup or specific fruit or vegetable that had stronger and statistically significant associations with breast cancer risk compared with the associations observed for total consumption of fruit and vegetables (Smith-Warner, 2001). In a randomized trial of 7.3 year follow-up period of a nutritional intervention with which to attain a considerable change of diet that is rich in vegetables, fruit, and fibre and low in fat, the risk of developing further breast cancer events and survival was not changed in women treated earlier for early stage disease. In repetition, no major benefit was observed, in general, among population subgroups characterized by demographic characteristics, baseline diet, or initial tumour types (Pierce *et al.*, 2007). A prospective multicentre study on dietary questionnaire carried out between the ages of 25 and 70 years including both pre- and post-menopausal women observed no association of risk with either total consumption of vegetables and fruit or with vegetable subgroups (Van Gils *et al.*, 2005). In a population of fairly young, pre-menopausal women, ingestion of red meat was linked with an elevated risk of hormone receptor–positive breast cancer but not with hormone receptor–negative cancer risk (Cho *et al.*, 2006). A meta-analysis of 31 case–control and cohort studies establishes a 17 per cent increase in risk related to the highest category of meat intake (Boyd *et al.*, 2003). On the other hand, a pooled study of the raw data from eight potential cohort studies conducted in North America, Canada, and Western Europe was not capable to reveal such association (Missmer *et al.*, 2002). A case–control analysis of Chinese women in Shanghai establishes that the optimistic association with red meat ingestion was mainly limited to those who used deep-frying cooking methods, predominantly between those who deep-fried food to the "well done" stage, in pan drippings and in meat surfaces that show a brown or black crust (Dai *et al.*, 2002), suggestive of an effect of heterocyclic amines or other carcinogens produced at high temperatures. Nonetheless, the Nurses' Health nested case–control analysis showed no increase in risk with cooking method or meat eating even for the use of charred meat more than once in a week in rapid acetylators (Gertig *et al.*, 1999).

Cervical cancer

Globally, in women, cervical cancer is the second most frequent cancer between the age of 15 and 44 years and most general in developing countries (Parkin *et al.*, 2001). Human papillomaviruses (HPV) make up to 83 per cent of all cervical cancer cases and recognized as an essential but not as an enough cause for cervical cancer. The risk of developing cervical cancer in combination with HPV may influence endogenous as well as exogenous co-factors (Bosch *et al.*, 2002; Castellsague *et al.,* 2003; Munoz *et al.,* 2004). Some dietary factors could be involved as co-factors in cervical carcinogenesis, but evidence is inconclusive. Only a small number of case–control and cohort studies looked at the role of diet intake as a cofactor for cervical cancer or as a risk factor for HPV persistence (Garcı´a-Closas *et al.*, 2005; World Cancer Research Fund and American Investigation of Cancer Research, 2007). In a recent comprehensive review, an international expert committee concluded that there is limited evidence suggesting that carrot intake may protect against cervical cancer (World Cancer Research Fund and American Investigation of Cancer Research, 2007).

Prostate cancer

Incidence and mortality rates vary widely across populations, with the highest rates in North America and Northern Europe, intermediate rates in Southern Europe and Latin America, and the lowest rates in Asia and Africa. Higher ingestion of animal protein may increase the occurrence of prostate cancer by enhancing growth hormone activity (Sato, 1963). Ecological studies suggested that milk drinking is strongly linked with both occurrence and mortality from prostate cancer (Ganmaa *et al.*, 2002; Colli and Colli, 2006). Evidence also suggests that a higher intake of dairy protein might increase the risk of prostate cancer by increasing the production of insulin-like growth-factor-I (IGF-I), which can consecutively endorse the progress of prostate cancer (Allen *et al.*, 2007). It has been hypothesized that higher intake of calcium, mainly from dairy products, may possibly increase the risk by suppressing the synthesis of 1,25-dihydroxyvitamin D, which has an anti-tumour effect on human prostatic cells *in vitro* (Giovannucci, 1998). Most mysteriously, many meats are cooked at elevated temperatures, for instance, by pan frying, grilling, or barbecuing resulting in the

formation of heterocyclic amines, a potent carcinogen in animals (Sugimura *et al.*, 2000). On the other hand, green vegetables demonstrated a defensive role in violent prostate cancer. An inverse relationship with green–yellow vegetables has been observed in the study conducted in Japan (Ohno, 1988); one more study conducted in Canada established an inverse relationship with green vegetables, cruciferous vegetables, and tomatoes (Jain, 1999); a study conducted in the USA reported a converse association with carrots (Schuman, 1982); and an inverse association with carrots, cabbage, and spinach was found in the study conducted in South Africa (Walker, 1992).

Conclusion

The etiology and pathogenesis of cancer is a multifaceted interplay mechanism of genetic and environmental factors. Nutritional intake and nutrient supplements are considered to be important environmental factors, so scientists have reported that dietary and nutrients might play a significant role in cancer development. In addition, many studies have reported the close link of the quantity and quality of dietary nutrients with cancer occurrence and pathogenesis. There is a noticeable difference in cancer development with the similar dietary intake among individuals. This could be explained by the dissimilarity in their genetic polymorphisms, which leads to materializing the concept of nutrigenomics and nutrigenetics which may explain the association of specific nutrient intake with genetic variations on cancer pathogenesis.

References

Key, T. J., Schatzkin, A., Willett, W. C., Allen, N. E., Spencer, E. A., Travis, R. C. (2004). Diet, nutrition and the prevention of cancer. *Public Health Nutrition*, 7: 187–200.

Skin Cancer Foundation (2014). *Actinic Keratosis*. http://www.skincancer.org/skin-cancer-information/actinic-keratosis. Accessed January 26.

Allen, N. E., *et al.* (2007). Serum insulin-like growth factor (IGF)-I and IGF-binding protein-3 concentrations and prostate cancer risk: results from the european prospective investigation into cancer and nutrition. *Cancer Epidemiology, Biomarkers & Prevention: a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology*, 16: 1121–1127.

Armstrong, B., Doll, R. (1975). Environmental factors and cancer incidence and mortality in different countries, with special reference to dietary practices. *International Journal of Cancer*, 15: 617–631.

Axelsson, G., Liljeqvist, T., Andersson, L., Bergman, B., Rylander, R. (1996). Dietary factors and lung cancer among men in west sweden. *International Journal of Epidemiology*, 25: 32–39.

Bosch, F. X., Lorincz, A., Muñoz, N., Meijer, C. J., Shah, K. V. (2002). The causal relation between human papillomavirus and cervical cancer. *Journal of Clinical Pathology*, 55: 244–265.

Boyd, N. F., Stone, J., Vogt, K. N., Connelly, B. S., Martin, L. J., Minkin, S. (2003). Dietary fat and breast cancer risk revisited: a meta-analysis of the published literature. *British Journal of Cancer*, 89: 1672–1685.

Buermeyer, A. B., Deschênes, S. M., Baker, S. M., Liskay, R. M. (1999). Mammalian DNA mismatch repair. *Annual Review of Genetics*, 33: 533–564.

Buiatti, E., *et al.* (1989). A case-control study of gastric cancer and diet in italy. *International Journal of Cancer*, 44: 611–616.

Burkitt, D. P. (1969). Related disease–related cause? *Lancet (London, England)*, 2: 1229–1231.

Cai, L., *et al.* (2006). Dietary selenium intake, aldehyde dehydrogenase-2 and X-ray repair cross-complementing 1 genetic polymorphisms, and the risk of esophageal squamous cell carcinoma. *Cancer*, 106: 2345–2354.

Carroll, K. K. (1991). Dietary fats and cancer. *American Journal of Clinical Nutrition*, 53(4 Suppl): 1064S–1067S.

Carroll, M. D., Abraham, S., Dresser, C. M. (1983). Data from the National Health Survey. Vital and Health Statistics series 11, no. 231. DHHS Publ. No. (PHS) 83-1681. *Dietary Intake Source Data: United States, 1976–1980*. Hyattsville, MD: National Center for Health Statistics, Public Health Service, U.S. Department of Health and Human Services.

Castellsagué, X., Muñoz, N., De Stefani, E., Victora, C. G., Castelletto, R., Rolón, P. A. (2000). Influence of mate drinking, hot beverages and diet on esophageal cancer risk in south america. *International Journal of Cancer*, 88: 658–664.

Castellsague´, X., Mun˜oz, N. (2003). Cofactors in human papillomavirus carcinogenesis—role of parity, oral contraceptives, and tobacco smoking. *Journal of the National Cancer Institute. Monographs*, 31: 20–28.

Chan, J. M., Gann, P. H., Giovannucci, E. L. (2005). Role of diet in prostate cancer development and progression. *Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology*, 23: 8152–8160.

Chan, J. M., Wang, F., Holly, E. A. (2005). Vegetable and fruit intake and pancreatic cancer in a population-based case-control study in the san francisco bay area. *Cancer Epidemiology, Biomarkers & Prevention: a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology*, 14: 2093–2097.

Cheng, K. K., Day, N. E., Duffy, S. W., Lam, T. H., Fok, M., Wong, J. (1992). Pickled vegetables in the aetiology of oesophageal cancer in hong kong chinese. *Lancet (London, England)*, 339: 1314–1318.

Cho, E., *et al.* (2006). Red meat intake and risk of breast cancer among premenopausal women. *Archives of Internal Medicine*, 166: 2253–2259.

Chow, W. H., Linet, M. S., McLaughlin, J. K., Hsing, A. W., Chien, H. T., Blot, W. J. (1993). Risk factors for small intestine cancer. *Cancer Causes & Control*, 4: 163–169.

Colli, J. L., Colli, A. (2006). International comparisons of prostate cancer mortality rates with dietary practices and sunlight levels. *Urologic Oncology*, 24: 184–194.

Correa, P. (1988). A human model of gastric carcinogenesis. *Cancer Research*, 48: 3554–3560.

Coughlin, S. S., Calle, E. E., Patel, A. V., Thun, M. J. (2000). Predictors of pancreatic cancer mortality among a large cohort of united states adults. *Cancer Causes & Control: CCC*, 11: 915–923.

Dai, Q., Shu, X. O., Jin, F., Gao, Y. T., Ruan, Z. X., Zheng, W. (2002). Consumption of animal foods, cooking methods, and risk of breast cancer. *Cancer Epidemiology, Biomarkers & Prevention*, 11: 801–808.

Dauchet, L., *et al.* (2008). Relationships between different types of fruit and vegetable consumption and serum concentrations of antioxidant vitamins. *The British Journal of Nutrition*, 100: 633–641.

de Meester, C., Gerber, G. B. (1995). The role of cooked food mutagens as possible etiological agents in human cancer. A critical appraisal of recent epidemiological investigations. *Revue D'epidemiologie Et De Sante Publique*, 43: 147–161.

De Stefani, E., Boffetta, P., Deneo-Pellegrini, H., Mendilaharsu, M., Carzoglio, J. C., Ronco, A. (1999). Carbohydrates and risk of stomach cancer in uruguay. *International Journal of Cancer*, 82: 618–621.

De Stefani, E., Boffetta, P., Mendilaharsu, M., Carzoglio, J., Deneo-Pellegrini, H. (1998). Dietary nitrosamines, heterocyclic amines, and risk of gastric cancer: a case-control study in uruguay. *Nutrition and Cancer*, 30: 158–162.

De Stefani, E., Muñoz, N., Estève, J., Vasallo, A., Victora, C. G., Teuchmann, S. (1990). Mate drinking, alcohol, tobacco, diet, and esophageal cancer in uruguay. *Cancer Research*, 50: 426–431.

de Vries, E., *et al.*; EPIDERM Group. (2012). Known and potential new risk factors for skin cancer in European populations: a multicentre case-control study. *The British Journal of Dermatology*, 167 Suppl 2: 1–13.

Doll, R., Payne, P., Waterhouse, J. (1966). *Cancer Incidence in Five Continents: A Technical Report*. Springer, Berlin.

Doll, R., Payne, P., Waterhouse, J. (1970). *Cancer Incidence in Five Continents*. Springer, Berlin.

Doll, R., Peto, R. (1981). The causes of cancer: quantitative estimates of avoidable risks of cancer in the United States today. *Journal of the National Cancer Institute*, 66: 1191–1308.

Ferlay, J., Shin, H. R., Bray, F., Forman, D., Mathers, C., Parkin, D. M. (2010). Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *International Journal of Cancer*, 127: 2893–2917.

Fisher, W. E., Boros, L. G., Schirmer, W. J. (1996). Insulin promotes pancreatic cancer: evidence for endocrine influence on exocrine pancreatic tumors. *The Journal of Surgical Research*, 63: 310–313.

Franceschi, S., *et al.* (1990). Smoking and drinking in relation to cancers of the oral cavity, pharynx, larynx, and esophagus in northern italy. *Cancer Research*, 50: 6502–6507.

Freudenheim, J. L., *et al.* (1996). Premenopausal breast cancer risk and intake of vegetables, fruits, and related nutrients. *Journal of the National Cancer Institute*, 88: 340–348.

Gandini, S., Merzenich, H., Robertson, C., Boyle, P. (2000). Meta-analysis of studies on breast cancer risk and diet: the role of fruit and vegetable consumption and the intake of associated micronutrients. *European Journal of Cancer (Oxford, England: 1990)*, 36: 636–646.

Ganesh, B., Talole, S. D., Dikshit, R. (2009). Tobacco, alcohol and tea drinking as risk factors for esophageal cancer: a case-control study from Mumbai, India. *Cancer Epidemiology*, 33: 431–434.

Ganmaa, D., Li, X. M., Wang, J., Qin, L. Q., Wang, P. Y., Sato, A. (2002). Incidence and mortality of testicular and prostatic cancers in relation to world dietary practices. *International Journal of Cancer*, 98: 262–267.

Garcı´a-Closas, R., Castellsague´, X., Bosch, X., Gonza´lez, C. A. (2005). The role of diet and nutrition in cervical carcinogenesis: a review of recent evidence. *International Journal of Cancer*, 117: 629–637.

Gertig, D. M., *et al.* (1999). N-acetyl transferase 2 genotypes, meat intake and breast cancer risk. *International Journal of Cancer*, 80: 13–17.

Ghadirian, P., Lynch, H. T., Krewski, D. (2003). Epidemiology of pancreatic cancer: an overview. *Cancer Detection and Prevention*, 27: 87–93.

Glade, M. J. (1991). *Food, Nutrition, and the Prevention of Cancer: A Global Perspective*. World Cancer Research Fund, Washington, DC.

Goodman, M. T., Hankin, J. H., Wilkens, L. R., Kolonel, L. N. (1992). High-fat foods and the risk of lung cancer. *Epidemiology (Cambridge, Mass.)*, 3: 288–299.

Goodman, M. T., Kolonel, L. N., Yoshizawa, C. N., Hankin, J. H. (1988). The effect of dietary cholesterol and fat on the risk of lung cancer in hawaii. *American Journal of Epidemiology*, 128: 1241–1255.

Handa, K., Kreiger, N. (2002). Diet patterns and the risk of renal cell carcinoma. *Public Health Nutrition*, 5: 757–767.

Heinrich, U., *et al.* (2003). Supplementation with beta-carotene or a similar amount of mixed carotenoids protects humans from UV-induced erythema. *The Journal of Nutrition*, 133: 98–101.

Hercberg, S., Galan, P., Preziosi, P., Alfarez, M. J., Vazquez, C. (1998). The potential role of antioxidant vitamins in preventing cardiovascular diseases and cancers. *Nutrition (Burbank, Los Angeles County, California)*, 14: 513–520.

Hu, J., *et al.* (1994). Risk factors for oesophageal cancer in Northeast China. *International Journal of Cancer*, 57: 38–46.

Ibiebele, T. I., van der Pols, J. C., Hughes, M. C., Marks, G. C., Williams, G. M., Green, A. C. (2007). Dietary pattern in association with squamous cell carcinoma of the skin: a prospective study. *The American Journal of Clinical Nutrition*, 85: 1401–1408.

Ibiebele, T. I., Taylor, A. R., Whiteman, D. C., van der Pols, J. C.; Australian Cancer Study. (2010). Eating habits and risk of esophageal cancers: a population-based case-control study. *Cancer Causes & Control: CCC*, 21: 1475–1484.

Inoue, M., *et al.* (2003). Epidemiology of pancreatic cancer in Japan: a nested case-control study from the hospital-based epidemiologic research program at Aichi Cancer Center (HERPACC). *International Journal of Epidemiology*, 32: 257–262.

Institute of Medicine. (2007). The cancer burden in low- and middle-income countries and how it is measured. In: Sloan F. A., Gelband H. (eds.) *Committee on Cancer Control in Low- and Middle-Income Countries*. National Academies Press, US, Washington (DC).

International Agency for Research on Cancer. (2002). Overweight and lack of exercise linked to increased cancer risk. In: Vainio H., Bianchini F. (eds.) *IARC Handbooks of Cancer Prevention*, vol. 6. World Health Organisation, Geneva.

Jain, M. G., Rohan, T. E., Howe, G. R., Miller, A. B. (2000). A cohort study of nutritional factors and endometrial cancer. *European Journal of Epidemiology*, 16: 899–905.

Jain, M. G., Hislop, G. T., Howe, G. R., Ghadirian, P. (1999). Plant foods, antioxidants, and prostate cancer risk: findings from case-control studies in canada. *Nutrition and Cancer*, 34: 173–184.

Jemal, A., Bray, F., Center, M. M., Ferlay, J., Ward, E., Forman, D. (2011). Global cancer statistics. *CA: A Cancer Journal for Clinicians*, 61: 69–90.

Kazakoff, K., *et al.* (1996). Effects of voluntary physical exercise on high-fat diet-promoted pancreatic carcinogenesis in the hamster model. *Nutrition and Cancer*, 26: 265–279.

Key, T. J., Allen, N. E., Spencer, E. A., Travis, R. C. (2003). Nutrition and breast cancer. *Breast (Edinburgh, Scotland)*, 12: 412–416.

Key, T. J., Schatzkin, A., Willett, W. C., Allen, N. E., Spencer, E. A., Travis, R. C. (2004). Diet, nutrition and the prevention of cancer. *Public Health Nutrition*, 7: 187–200.

Khan, N., Mukhtar, H. (2007). Tea polyphenols for health promotion. *Life Sciences*, 81: 519–533.

Kushi, L. H., *et al.*; American Cancer Society 2010 Nutrition and Physical Activity Guidelines Advisory Committee. (2012). American Cancer Society guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. *CA: A Cancer Journal for Clinicians*, 62: 30–67.

La Vecchia, C., Negri, E., D'Avanzo, B., Boyle, P., Franceschi, S. (1991). Dietary indicators of oral and pharyngeal cancer. *International Journal of Epidemiology*, 20: 39–44.

Li, D., Xie, K., Wolff, R., Abbruzzese, J. L. (2004). Pancreatic cancer. *Lancet (London, England)*, 363: 1049–1057.

Li, K., Yu, P., Zhu, Y. F. (2002). Relationship between Congou tea and esophageal cancer in Chaoshan region of Guangdong, China. *Chinese Journal of Disease Control Prevention*, 6: 47–49.

Lin, Y., Tamakoshi, A., Hayakawa, T., Naruse, S., Kitagawa, M., Ohno, Y. (2005). Nutritional factors and risk of pancreatic cancer: a population-based case-control study based on direct interview in japan. *Journal of Gastroenterology*, 40: 297–301.

Lindblad, P., Wolk, A., Bergström, R., Adami, H. O. (1997). Diet and risk of renal cell cancer: a population-based case-control study. *Cancer Epidemiology, Biomarkers & Prevention: a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology*, 6: 215–223.

Lu, H., *et al.* (2006). Dietary mineral and trace element intake and squamous cell carcinoma of the esophagus in a Chinese population. *Nutrition and Cancer*, 55: 63–70.

Maritim, A. C., Sanders, R. A., Watkins, J. B. 3rd. (2003). Diabetes, oxidative stress, and antioxidants: a review. *Journal of Biochemical and Molecular Toxicology*, 17: 24–38.

Marshall, J. R., Boyle, P. (1996). Nutrition and oral cancer. *Cancer Causes & Control*, 7: 101–111.

Marshall, J. R., *et al.* (1992). Smoking, alcohol, dentition and diet in the epidemiology of oral cancer. *European Journal of Cancer. Part B, Oral Oncology*, 28B: 9–15.

McCann, S. E., Muti, P., Vito, D., Edge, S. B., Trevisan, M., Freudenheim, J. L. (2004). Dietary lignan intakes and risk of pre- and postmenopausal breast cancer. *International Journal of Cancer*, 111: 440–443.

McNaughton, S. A., Marks, G. C., Green, A. C. (2005). Role of dietary factors in the development of basal cell cancer and squamous cell cancer of the skin. *Cancer Epidemiology, Biomarkers & Prevention: a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology*, 14: 1596–1607.

Michael, C. R., Charles, C. B., Christine, S., Ross, C. B. (1993). Saturated fat intake and lung cancer risk among nonsmoking women in Missouri. *Journal of the National Cancer Institute*, 85: 1906–1916.

Michaud, D. S., Giovannucci, E., Willett, W. C., Colditz, G. A., Fuchs, C. S. (2003). Dietary meat, dairy products, fat, and cholesterol and pancreatic

cancer risk in a prospective study. *American Journal of Epidemiology*, 157: 1115–1125.

Millen, A. E., *et al.* (2004). Diet and melanoma in a case-control study. *Cancer Epidemiology, Biomarkers & Prevention: a Publication of the American Association for Cancer Research, Cosponsored by the American Society of Preventive Oncology*, 13: 1042–1051.

Miller, A. B. (2001). Diet in Cancer Prevention. http://www.who.int/ncd/cancer/publications/abstracts/abs9810_05 (accessed 2001).

Mills, P. K., Beeson, W. L., Abbey, D. E., Fraser, G. E., Phillips, R. L. (1988). Dietary habits and past medical history as related to fatal pancreas cancer risk among adventists. *Cancer*, 61: 2578–2585.

Missmer, S. A., *et al.* (2002). Meat and dairy food consumption and breast cancer: a pooled analysis of cohort studies. *International Journal of Epidemiology*, 31: 78–85.

Muñoz, N., *et al.* (2004). Against which human papillomavirus types shall we vaccinate and screen? The international perspective. *International Journal of Cancer*, 111: 278–285.

Newmark, H. L., Wargovich, M. J., Bruce, W. R. (1984). Colon cancer and dietary fat, phosphate, and calcium: a hypothesis. *Journal of the National Cancer Institute*, 72: 1323–1325.

Nicodemus, K. K., Sweeney, C., Folsom, A. R. (2004). Evaluation of dietary, medical and lifestyle risk factors for incident kidney cancer in postmenopausal women. *International Journal of Cancer*, 108: 115–121.

Nkondjock, A., Krewski, D., Johnson, K. C., Ghadirian, P.; Canadian Cancer Registries Epidemiology Research Group. (2005). Dietary patterns and risk of pancreatic cancer. *International Journal of Cancer*, 114: 817–823.

Nomura, A. (1996). Stomach cancer. In: Schottenfeld D., Fraumeni J. F. Jr (eds.) *Cancer Epidemiology and Prevention*. Oxford University Press, New York, NY, pp. 707–24.

Nyberg, F., Agrenius, V., Svartengren, K., Svensson, C., Pershagen, G. (1998). Dietary factors and risk of lung cancer in never-smokers. *International Journal of Cancer*, 78: 430–436.

Ohno, Y., Yoshida, O., Oishi, K., Okada, K., Yamabe, H., Schroeder, F. H. (1988). Dietary beta-carotene and cancer of the prostate: a case-control study in kyoto, japan. *Cancer Research*, 48: 1331–1336.

Omenn, G. S., *et al.* (1996). Risk factors for lung cancer and for intervention effects in CARET, the beta-carotene and retinol efficacy trial. *Journal of the National Cancer Institute*, 88: 1550–1559.

Pandey, M. (2003). Risk factors for gallbladder cancer: a reappraisal. *European Journal of Cancer Prevention: the Official Journal of the European Cancer Prevention Organisation ((ECP))*, 12: 15–24.

Parkin, D. M. (2001). Global cancer statistics in the year 2000. *The Lancet. Oncology*, 2: 533–543.

Pierce, J. P., *et al.* (2007). Influence of a diet very high in vegetables, fruit, and fiber and low in fat on prognosis following treatment for breast cancer: the women's healthy eating and living (WHEL) randomized trial. *JAMA*, 298: 289–298.

Poulain, S., Evenou, F., Carré, M. C., Corbel, S., Vignaud, J. M., Martinet, N. (2009). Vitamin a/retinoids signalling in the human lung. *Lung Cancer (Amsterdam, Netherlands)*, 66: 1–7.

Prentice, R. L., Sheppard, L. (1990). Dietary fat and cancer: consistency of the epidemiologic data, and disease prevention that may follow from a practical reduction in fat consumption. *Cancer Causes & Control: CCC*, 1: 81–97; discussion 99.

Rachtan, J. (2002). Dietary habits and lung cancer risk among polish women. *Acta Oncologica (Stockholm, Sweden)*, 41: 389–394.

Ramón, J. M., Serra, L., Cerdó, C., Oromí, J. (1993). Dietary factors and gastric cancer risk. A case-control study in spain. *Cancer*, 71: 1731–1735.

Risch, H. A. (2003). Etiology of pancreatic cancer, with a hypothesis concerning the role of N-nitroso compounds and excess gastric acidity. *Journal of the National Cancer Institute*, 95: 948–960.

Ronco, A., De Stefani, E., Boffetta, P., Deneo-Pellegrini, H., Mendilaharsu, M., Leborgne, F. (1999). Vegetables, fruits, and related nutrients and risk of breast cancer: a case-control study in Uruguay. *Nutrition and Cancer*, 35: 111–119.

Rose, D. P., Boyar, A. P., Wynder, E. L. (1986). International comparisons of mortality rates for cancer of the breast, ovary, prostate, and colon, and per capita food consumption. *Cancer*, 58: 2363–2371.

Russell, W. R., *et al.* (2011). High-protein, reduced-carbohydrate weight-loss diets promote metabolite profiles likely to be detrimental to colonic health. *The American Journal of Clinical Nutrition*, 93: 1062–1072.

Sato, T. (1963) Chronic diseases suspected to arise through the enhanced activity of growth hormone by excessive intake of animal protein. IV. The cancer and the hypertrophy of the prostate. *The Bulletin of the Institute of Public Health*, 12: 222–228.

Schuman, L. M., Mandel, J. S., Radke, A., Seal, U., Halberg, F. (1982). Some selected features of the epidemiology of prostatic cancer: Minneapolis-St. Paul, Minnesota case-control study, 1976–1979. In: Magnus K. (ed.), *Trends in Cancer Incidence: Causes and Implications*. Hemisphere Publishing Corp, Washington, DC. pp. 345–354.

Siegel, R., *et al.* (2012). Cancer treatment and survivorship statistics, 2012. *CA: A Cancer Journal for Clinicians*, 62: 220–241.

Skin cancer facts. (2014). Skin Cancer Foundation. http://www.skincancer.org/skin-cancer-information/skin-cancer-facts. Accessed January 3, 2017.

Smith-Warner, S. A., *et al.* (2001). Intake of fruits and vegetables and risk of breast cancer: a pooled analysis of cohort studies. *JAMA*, 285: 769–776.

Stahl, W., Heinrich, U., Jungmann, H., Sies, H., Tronnier, H. (2000). Carotenoids and carotenoids plus vitamin E protect against ultraviolet light-induced erythema in humans. *The American Journal of Clinical Nutrition*, 71: 795–798.

Stolzenberg-Solomon, R. Z., Pietinen, P., Taylor, P. R., Virtamo, J., Albanes, D. (2002). Prospective study of diet and pancreatic cancer in male smokers. *American Journal of Epidemiology*, 155: 783–792.

Stolzenberg-Solomon, R. Z., *et al.* (2009). Vitamin E intake, alpha-tocopherol status, and pancreatic cancer in a cohort of male smokers. *The American Journal of Clinical Nutrition*, 89: 584–591.

Sugimura, T. (2000). Nutrition and dietary carcinogens. *Carcinogenesis*, 21: 387–395.

Surveillance, Epidemiology, and End Results Program. (1997). *SEER Cancer Statistics Review, 1973–1994: tables and graphs*. National Cancer Institute, Bethesda, MD.

Tannenbaum, A. (1940). Initiation and growth of tumors; introduction: effects of underfeeding. *American Journal of Cancer*, 39: 335–50.

Tominaga, S., Kato, I. (1987). Diet and cancer. *Asian Journal of Medicine*, 30: 268–74.

Trichopoulou, A., *et al.* (1995). Consumption of olive oil and specific food groups in relation to breast cancer risk in Greece. *Journal of the National Cancer Institute*, 87: 110–116.

Tuyns, A. J., Riboli, E., Doornbos, G., Péquignot, G. (1987). Diet and esophageal cancer in calvados (France). *Nutrition and Cancer*, 9: 81–92.

Tzonou, A., *et al.* (1996). Diet and risk of esophageal cancer by histologic type in a low-risk population. *International Journal of Cancer*, 68: 300–304.

van Dam, R. M., Seidell, J. C. (2007). Carbohydrate intake and obesity. *European Journal of Clinical Nutrition*, 61 Suppl 1: S75–S99.

van der Pols, J. C., Bain, C., Gunnell, D., Smith, G. D., Frobisher, C., Martin, R. M. (2007). Childhood dairy intake and adult cancer risk: 65-y follow-up of the Boyd Orr cohort. *The American Journal of Clinical Nutrition*, 86: 1722–1729.

van Gils, C. H., *et al.* (2005). Consumption of vegetables and fruits and risk of breast cancer. *JAMA*, 293: 183–193.

Veierød, M. B., Laake, P., Thelle, D. S. (1997). Dietary fat intake and risk of lung cancer: a prospective study of 51,452 norwegian men and women. *European Journal of Cancer Prevention: the Official Journal of the European Cancer Prevention Organisation ((ECP))*, 6: 540–549.

Vimalachandran, D., Ghaneh, P., Costello, E., Neoptolemos, J. P. (2004). Genetics and prevention of pancreatic cancer. *Cancer Control: Journal of the Moffitt Cancer Center*, 11: 6–14.

Walker, A. R., Walker, B. F., Tsotetsi, N. G., Sebitso, C., Siwedi, D., Walker, A. J. (1992). Case-control study of prostate cancer in black patients in Soweto, South Africa. *British Journal of Cancer*, 65: 438–441.

Ward, M. H., López-Carrillo, L. (1999). Dietary factors and the risk of gastric cancer in Mexico City. *American Journal of Epidemiology*, 149: 925–932.

Wei, W. Q., *et al.* (2004). Prospective study of serum selenium concentrations and esophageal and gastric cardia cancer, heart disease, stroke, and total death. *The American Journal of Clinical Nutrition*, 79: 80–85.

Wolk, A., Lindblad, P., Adami, H. O. (1996). Nutrition and renal cell cancer. *Cancer Causes & Control*, 7: 5–18.

World Cancer Research Fund and American Investigation of Cancer Research. (2007). *Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective*. American Investigation of Cancer Research, Washington, DC.

World Cancer Research Fund in association with the American Institute of Cancer Research. (1997). *Food, Nutrition, and Cancer Prevention: A Global Prospective*. American Institute of Cancer Research, Washington, DC.

Wu-Williams, A. H., Yu, M. C., Mack, T. M. (1990). Life-style, workplace, and stomach cancer by subsite in young men of Los Angeles County. *Cancer Research*, 50: 2569–2576.

Yu, M. C., Garabrant, D. H., Peters, J. M., Mack, T. M. (1988). Tobacco, alcohol, diet, occupation, and carcinoma of the esophagus. *Cancer Research*, 48: 3843–3848.

Zagorsky, J. L. (2005). Health and wealth. The late-20th century obesity epidemic in the U.S. *Economics and Human Biology*, 3: 296–313.

Zeegers, M. P., Kellen, E., Buntinx, F., van den Brandt, P. A. (2004). The association between smoking, beverage consumption, diet and bladder cancer: a systematic literature review. *World Journal of Urology*, 21: 392–401.

Zhang, C. X., Ho, S. C., Chen, Y. M., Fu, J. H., Cheng, S. Z., Lin, F. Y. (2009). Greater vegetable and fruit intake is associated with a lower risk of breast cancer among Chinese women. *International Journal of Cancer*, 125: 181–188.

Zheng, W., *et al.* (1993). Serum micronutrients and the subsequent risk of oral and pharyngeal cancer. *Cancer Research*, 53: 795–798.

Ziegler, R. G., Morris, L. E., Blot, W. J., Pottern, L. M., Hoover, R., Fraumeni, J. F. Jr. (1981). Esophageal cancer among black men in Washington, D.C. II. Role of nutrition. *Journal of the National Cancer Institute*, 67: 1199–1206.