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# NUTRITION IN CANCER

**A graduation project submitted as part of the requirements for obtaining a Bachelor of Pharmacy degree .**

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# NUTRITION IN CANCER REVIEW

## INTRODUCTION :

The nutritional needs of a cancer patient depend on several factors, including the stage of the disease (i.e. treatment, recovery and living after recovery), the symptoms experienced, the type and frequency of the cancer treatment being used and the side effects associated with that treatment, and the effect of the specific cancer on food and nutrient ingestion, tolerance, and utilization. For many cancer patients, managing nutritional needs while living with advanced cancer becomes a particular challenge that needs to be overcome.

The onset of cancer is reported to cause profound metabolic and physiological changes which tend to increase the nutritional needs for protein, carbohydrate, fat, vitamins and minerals. Therefore, nutritional requirements are high during cancer treatment, and may lead to malnutrition. Malnutrition can be prevented simply by eating enough foods rich in nutrients and antioxidants. An adequate nutrient supply will assist the body in rebuilding damaged cells, and antioxidants may directly fight the cancer. [1]

In the early 1900s, the focus of diet research was on identifying and preventing nutrient-deficiency diseases. Later, the focus changed to identifying nutrient requirements. More recently, research has focused on the role of diet in maintaining health and reducing the risk of non communicable diseases such as cancer. Potentially, all types of dietary components have potential to affect health status, causing or preventing diseases . [2]

The last 30 years have seen an explosive increase in research on diet and cancer; although many topics have been examined, **three dominant themes have evolved.**

**The first was the dietary fat and cancer hypothesis**, the many prospective studies that have not found important associations between dietary fat and incidence of breast or other cancers strongly suggest that low fat diets adopted during mid-life will not provide a practical means of substantially reducing cancer risk Whether there may be effects of specific types or sources of fat has not been fully resolved; for example, the inverse associations of olive oil and risk of breast cancer seen in some case-control studies has yet to be examined in prospective studies. (3)

**A second major theme in research on diet and cancer has been the fruit and vegetable hypothesis**, where by increases in consumption would strongly reduce risks of many types of cancer.

In 1997, the World Cancer Research Fund and the American Institute for Cancer Research produced an extensive report stating that diets rich in fruits and vegetables "decrease the risk of many cancers" .

Some anticancer benefit of increasing fruits and vegetables may still exist, particularly among persons with very low intakes. Also, there may be modest benefits for specific foods and specific cancers; for example, for tomato products and prostate cancer. Some of the phytochemicals isolated from fruits and vegetables may also have anticancer roles in more concentrated forms. Further, evidence is strong that increasing fruit and vegetable consumption will reduce risk of cardiovascular disease , so that campaigns to promote consumption of these foods have a public health benefit even though the impact on cancer incidence is likely to be much smaller than anticipated. (4)

**The third general theme in nutrition and cancer research could be termed the energy balance hypothesis**, in which excessive energy

intake in relation to physical activity leads to overweight ,which increases the incidence of many cancers .

This hypothes is has been robustly supported by large numbers of both case-control and cohort studies.

Cancers increased by overweight and obesity include those of the breast (postmenopausal), endometrium, pancreas, colon, kidney, and esophagus (adenocarcinoma). [5]

## Review of the role of diet in the etiology of the major cancers

### *Cancers of the oral cavity, pharynx and oesophagus :

In developed countries, the main risk factors are alcohol and tobacco, and up to 75% of these cancers are attributable to these two lifestyle factors . [6]

The mechanism of the effect of alcohol on these cancers is not known, but may involve direct effects on the epithelium.[7]

In developing countries, around 60% of cancers of the oral cavity, pharynx and oesophagus are thought to be due to micronutrient deficiencies related to a restricted diet that is low in fruits and vegetables and animal products ; it should be noted, however, that the evidence for a protective effect of fruits and vegetables is largely derived from case-control studies and there are few data yet from prospective studies. [8]

There is also consistent evidence that consuming drinks and foods at a very high temperature increases the risk for these cancers. [9]

### *Nasopharyngeal cancer :

This is particularly common in Southeast Asia , and has been consistently associated with a high intake of Chinese- style salted fish, especially during early childhood . [10]

Chinese-style salted fish is a special product which is usually softened by partial decomposition before or during salting; other types of salted fish have been studied and not found to be convincingly associated with the risk for developing nasopharyngeal cancer . [11]

### *Stomach cancer :

Stomach cancer was estimated to account for 876,000 cases and 647,000 deaths in 2000. [12]

Substantial evidence, mainly from case-control studies, suggests that risk is increased by high intakes of some traditionally preserved salted foods, especially meats and pickles, that risk is decreased by high intakes of fruits and vegetables, perhaps due to their vitamin C content. [13]

### -Meat

International correlation studies show a strong association between per capita consumption of meat and colorectal cancer mortality [14], and several mechanisms have been proposed through which meat may increase cancer risk. Mutagenic heterocyclic amines and polycyclic aromatic hydrocarbons can be formed during the cooking of meat at high temperatures[15], and nitrites and their related compounds found in smoked, salted and some processed meat products may be converted to carcinogenic N-nitroso compounds in the colon. [16]

### -Fat

As with meat, international correlation studies show a strong association between per capita consumption of fat and colorectal cancer mortality .[14]

Possible mechanisms proposed to explain such an association are that a high fat intake may increase the levels of cytotoxic free fatty

acids or secondary bile acids in the lumen of the large intestine. However, the results of observational studies of fat and colorectal cancer have, overall, not been supportive of an association with fat intake, especially after adjusting for total energy intake. [17]

### -Fruits, vegetables and fibre

Many case-control studies of colorectal cancer have observed moderately lower risk in association with high consumption of dietary fibre, and/or fruits and vegetables. [18] [19]

### -Folate

Some recent prospective studies have suggested that a methyl-deplete diet (i.e. a diet low in folate and methionine and high in alcohol) is associated with an increased risk of colon cancer. [20]

Also , use of folic acid- containing multiple vitamin supplements has been associated with lower risk of colon cancer.[21]

A diminished folate status may contribute to carcinogenesis by alteration of gene expression and increased DNA damage [22] [23] and chromosome breakage [24]

The finding that a common polymorphism in the methylenetetrahydrofolate reductase gene involved in folic acid metabolism may also be associated with colorectal cancer strengthens the hypothesis that dietary folate may be an important factor in colorectal carcinogenesis.[25]

### -Calcium

Another promising hypothesis is that relatively high intakes of calcium may reduce the risk for colorectal cancer, perhaps by forming complexes with secondary bile acids in the intestinal lumen or by inhibiting the hyper proliferative effects of dietary haem.[26]

Several observational studies have supported this hypothesis and two trials have suggested that supplemental calcium may have a modest protective effect on the recurrence of colorectal adenomas. [27] [28] [29]

### *Cancer of the liver :

Excessive alcohol consumption is the main diet-related risk factor for liver cancer in Western countries, probably via the development of cirrhosis and alcoholic hepatitis. [30]

### *Cancer of the pancreas :

Cancer of the pancreas was estimated to account for 216,000 cases and 214,000 deaths in 2000 and is more common in Western countries than in developing countries. Some studies have suggested that risk is increased by high intakes of meat, and reduced by high intakes of vegetables, but these data are not consistent and come mostly from case-control studies. [31]

### *Lung cancer :

Lung cancer is the most common cancer in the world.Heavy smoking increases the risk by around 30-fold, and smoking causes over 80% of lung cancers in Western countries. following the observation that, after allowing for smoking, increased lung cancer risk was associated with a low dietary intake of vitamin A .[32]

The possible effect of diet on lung cancer risk remains controversial. Several recent observational studies have continued to observe an association of fruits and vegetables with reduced risk, but this association has been weak in prospective studies. This apparent relationship may be partly due to residual confounding by smoking, since smokers generally consume less fruits and vegetables than non-smokers, but there may also be some protective effect of these

foods. In public health terms, however, the overriding priority is to reduce the prevalence of smoking .[33] [34]

### *Breast cancer :

Breast cancer is the second most common cancer in the world and the most common cancer among women.

Breast cancer was estimated to account for 1,105,000 cases and 373,000 deaths in women in 2000 .differences in dietary habits and physical activity may also contribute to breast cancer incidence .

### -Alcohol

The only other established dietary risk factor for breast cancer is alcohol. There is now a large amount of data from well-designed studies which consistently shows a small increase in risk with increasing consumption, with about a 7% increase in risk for an average of one alcoholic drink every day.[35]

The mechanism for this association is not known, but may involve increases in estrogen levels[36]; alternatively, some recent studies suggest that the adverse effect of alcohol may be exacerbated by a low folate intake .[37]

### *Other dietary factors

The results of studies of other dietary factors including meat, dairy products, fruits and vegetables, fibre and phyto- estrogens are inconsistent. [28] [29] [38] [39]

### *Cancer of the cervix :

Cancer of the cervix was estimated to account for 471,000 cases and 233,000 deaths in women in 2000. Fruits, vegetables and related nutrients such as carotenoids and folate tend to be inversely related with risk, but these associations may be largely due to confounding

by papillomavirus infections, smoking and other factors. Further research is needed, particularly on the possible role of folate deficiency.[28] [29]

### *Cancer of the ovary :

Cancer of the ovary was estimated to account for 192,000 cases and 114,000 deaths in women in 2000[12] , Risk is reduced by high parity and by long-term use of combined oral contraceptives.[40]

Some studies have suggested that risk is increased by high intakes of fat or dairy products, and reduced by high intakes of vegetables, but the data are not consistent and more prospective data are required to examine these possible association.[28]

### *Prostate cancer :

Prostate cancer was estimated to account for 543,000 cases and 204,000 deaths in 2000[12] .Diets high in red meat, dairy products and animal fat have frequently been implicated in the development of prostate cancer, although the data are not entirely consistent[28][41] Randomized controlled trials have provided substantial, consistent evidence that supplements of b-carotene do not alter the risk for prostate cancer[42] but have suggested that vitamin E [42] and selenium[43] might have a protective effect. Lycopene, primarily from tomatoes, has been associated with a reduced risk in some observational studies, but the data are not consistent.[44]

### *Bladder cancer :

Cancer of the urinary bladder was estimated to account for 336,000 cases and 132,000 deaths in 2000.[12]

. Smoking , increases the risk for bladder cancer.[6]

. Studies suggest that high intakes of fruits and vegetables may reduce risk, but this is not established and more prospective data are needed [28][45] [46]

## *Kidney cancer :

Cancer of the kidney was estimated to account for 189,000 cases and 91,000 deaths in 2000.[12]

Overweight/obesity is an established risk factor for cancer of the kidney, and may account for up to 30% of kidney cancers in both men and women100. There are only limited data on the possible role of diet in the etiology of kidney cancer, but some studies have observed an increase in risk with high intakes of meat and dairy products and a reduced risk with high intakes of vegetables.[28]

## connection between vitamin D and cancer risk :

Early epidemiologic research showed that incidence and death rates for certain cancers were lower among individuals living in southern latitudes, where levels of sunlight exposure are relatively high, than among those living at northern latitudes. Because exposure to ultraviolet light from sunlight leads to the production of vitamin D, researchers hypothesized that variation in vitamin D levels might account for this association.[47]

Experimental evidence has also suggested a possible association between vitamin D and cancer risk. In studies of cancer cells and of tumors in mice, vitamin D has been found to have several activities that might slow or prevent the development of cancer, including promoting cellular differentiation, decreasing cancer cell growth, stimulating cell death (apoptosis), and reducing tumor blood vessel formation (angiogenesis).[48] [49]

## vitamin D can help to reduce the risk of cancer in people :

A number of epidemiologic studies have investigated whether people with higher vitamin D intakes or higher blood levels of vitamin D have lower risks of specific cancers. The results of these studies have been inconsistent, possibly because of the challenges in carrying out such studies.[50]

Several randomized trials of vitamin D intake have been carried out, but these were designed to assess bone health or other non-cancer outcomes. Although some of these trials have yielded information on cancer incidence and mortality, the results need to be confirmed by additional research because the trials were not designed to study cancer specifically. [51]

The cancers for which the most human data are available are colorectal, breast, prostate, and pancreatic cancer. Numerous epidemiologic studies have shown that higher intake or blood levels of vitamin D are associated with a reduced risk of colorectal cancer.[52]

In contrast, the Women's Health Initiative randomized trial found that healthy women who took vitamin D and calcium supplements for an average of 7 years did not have a reduced incidence of colorectal cancer . Some scientists have pointed out that the relatively low level of vitamin D supplementation (10 µg, or 400 IU, once a day), the ability of participants to take additional vitamin D on their own, and the short duration of participant follow-up in this trial might explain why no reduction in colorectal cancer risk was found. Evidence on the association between vitamin D and the risks of all other malignancies studied is inconclusive.[53] [54]

## The nutritional requirements in cancer patients :

The energetic requirements of cancer patients, in principle, and if individualized measures (indirect calorimetry) are not performed, should be considered similar to those of healthy people (25–30 kcal/kg/day).[55]

Protein requirements should be between 1 (minimum) and 1.2–1.5 g/kg/day and if there is protein catabolism it could be increased to 2 g/kg/day . In patients with acute or chronic renal failure, the protein supply should not exceed 1.0 or 1.2 g/kg/day, respectively.[56]

Another subject that need to be taken into account are the water and sodium needs of patients, which should be below normal (30 ml/kg/day for water and 1 mmol/kg/day for sodium) in the case of peritoneal carcinomatosis if there is obstruction or ascites for avoiding overload or third space.[55]

Regarding other components, especially vitamins and trace elements, if there are no specific deficits it is not recommended to supplement in amounts higher than the recommended daily doses (RDD).[55]

## Dietary factors which convincingly increase risk :

- An aspect of diet clearly related to cancer incidence is consumption of **alcoholic beverages,** which convincingly increases the risk of cancers of the oral cavity, pharynx, larynx, esophagus, liver and breast (and probably colorectum).

Recent studies suggest that the excess risk of breast and colon cancer associated with alcohol consumption may be concentrated in persons with low folate intake.[57]

- **Aflatoxin** : Food contaminated with aflatoxin convincingly increases the risk of liver cancer. However, this contamination

occurs mainly in areas where hepatitis viruses are a major cause of liver cancer, and the importance of aflatoxin in the absence of hepatitis virus infections (for example, after immunisation) is not clear.[57]

- **Chinese-style salted fish** : High intake of Chinese-style salted fish, predominantly consumed in some Asian populations, convincingly increases the risk of nasopharyngeal cancer.[58]

## *Specific Nutrients and Selective Nutritional Supplementation Linked to Cancer Prevention/Recurrence:*

*Evidence supports a relationship between colorectal cancer and prebiotic, probiotic, symbiotic, and dysbiotic bacteria . Many practitioners and patients may not be aware of the existence and role of "prebiotics." Prebiotics are fermentable ingredients that specifically target components of the indigenous microbiota known to be beneficial. They are short-chain low-digestible carbohydrates (LDCs) metabolized by gut microbiota and are used as an energy source, immune system enhancers, or facilitators of mineral uptake.*

*Intake of foods containing LDCs can improve the state of health and may prevent diseases such as certain forms of cancer. The combination of pro- and prebiotics has excellent potential to effectively help the restoration of immune system function to more physiological states.*

***Probiotics** may suppress the growth of bacteria that convert pro carcinogens into carcinogens, thereby reducing the amount of carcinogens in the intestine .Since cancers of the gastrointestinal tract may account for 25% of all cancers and for 9% of cancer deaths worldwide, we can see how the exogenous administration of synergistic bacterial strains (probiotics) has been more frequently suggested to influence various processes associated with an increased cancer risk.[59]*

*So far, **mechanisms** that could explain the preventive action of probiotics against colorectal cancer onset may **include** :*

***(a)** binding and degradation of potential carcinogens .*

***(b)** quantitative, qualitative, and metabolic alterations of the intestinal microflora*

***(c)** production of anti-tumorigenic or anti mutagenic compounds*

***(d)** competition with putrefactive and pathogenic microbiota*

***(e)** enhancement of the host's immune response*

***(f)** direct effects on cell proliferation*

***(g)** improvement of the host's immune response*

***(h)** anti proliferative effects via regulation of apoptosis and cell differentiation*

***(i)** fermentation of undigested food*

***(j)** inhibition of tyrosine kinase signaling pathways .*

*Particularly meaningful to patients in treatment regimens that include radiation therapy (RT) to the abdominal region for cervical, ovarian, prostate, sigmoid, or colorectal cancer is the potential therapeutic benefit from probiotics.[60]*

***Omega-3 Fatty Acids :***

*There is accumulating evidence that the use of omega-3 fatty acids has the potential as anticancer compounds. How they interact with the cancer process is becoming clearer as investigations unfold. "Diets rich in omega-3 polyunsaturated fatty acids (ω3-PUFAs) such as alpha-linolenic acid, eicosapentaenoic acid, and docosahexaenoic acid are associated with a **decreased** incidence*

*and severity of several chronic diseases including cardiovascular disease (CVD) and cancer" .*

*The inflammation contributes to tumor initiation, progression, and growth. Omega-3 fatty acids have known* ***anti-inflammatory effects****, and their role in cancer prevention and in cancer treatment is becoming better defined. ω3- PUFAs such as eicosapentaenoic acid (EPA) and polyphenols such as curcumin and resveratrol have been demonstrated to have* ***anti colorectal cancer activity*** *in preclinical models.*

*In* ***breast cancer****, higher intake of* ***omega-3 fatty acids*** *has been linked to* ***decreased*** *inflammation and decreased fatigue in breast cancer survivors .*[61]

*The relationship between specific* ***fatty acids*** *and prostate cancer survival remains a field with need for more research. Dietary intake of 14 fatty acids was analyzed in a population-based cohort of 525 Swedish men with prostate cancer.*

*Among all men, those with the highest omega-3 and total marine fatty acid intakes were 40% less likely to die from prostate cancer.*[62]

***The coffee and Cancer :***

*Because smokers also tend to be coffee drinkers, it is difficult to completely account for tobacco use in studies of coffee and strongly tobacco-related cancers. These issues can be addressed by examining risk in non-smokers, or with detailed statistical adjustment for smoking. For example, early research suggested that coffee increased the risk of bladder cancer, but the true causal factor was later found to be smoking.*

***- The effect of coffee in lowering cancer risk :*** *Recent studies find that coffee may lower the risk of several types of cancer, including head and neck, colorectal, breast, and liver cancer, although the*

*potential beneficial effects of coffee are not completely understood. Hundreds of biologically active compounds including caffeine, flavonoids, lignans, and other polyphenols are found in roasted coffee. These and other coffee compounds have been shown to increase energy expenditure, inhibit cellular damage, regulate genes involved in DNA repair, have anti-inflammatory properties and/or inhibit metastasis, among other activities. There is also evidence that coffee consumption is associated with lower risk of insulin resistance and type 2 diabetes, which have been linked to higher risks of colorectal, liver, breast and endometrial cancer incidence and/or mortality.*[63]

***- Acrylamide and its link to cancer :***

*Coffee can contain acrylamide, a chemical that is also used in certain industrial processes and has been commercially available since the 1950s. In addition to coffee, acrylamide is also found in French fries (frying causes acrylamide formation), toasted bread, snack foods, like potato chips and pretzels, crackers, biscuits, cookies and cereals, and in tobacco products. Acrylamide is classified by IARC as a "probable carcinogen," based primarily on genotoxicity experiments in animals. In 2002, Swedish scientists discovered that acrylamide could be formed from asparagine (an amino acid) and sugar during high-heat cooking. This discovery led to intensified research into the association between acrylamide intake from diet and cancer risk in humans. In 2011 and 2014, two large studies summarized the evidence in humans and found no association between dietary acrylamide and risk of several cancers.*[64]

## *Conclusions :*

Developing a healthier diet with the addition of specific supplements designed to reduce oxidative stress and inflammation should be an important part of an overall of cancer patient care. It is interesting to note that the cancer diagnosis is frequently a motivator for improving diet and nutrition.

A study of 1,560 patients with breast cancer found that intake of fruit and vegetables, whole grains, and lean sources of protein increased significantly after diagnosis, while consumption of high-fat, high-sugar products, red meat, some alcoholic drinks, and refined grains significantly decreased.

The importance of this study is that people can truly alter their dietary and nutritional habits when enough motivating factors are present. This is encouraging data that supports the importance of modifying diets for patients care. Sometimes, patients and their families also feel more positively, with a stronger sense of control over their circumstances, when they know they are engaged in behaviors that could benefit their overall health outcome.

We strongly believe that physicians should be encouraged to find occasions to impart appropriate nutritional, physical activity, and weight management guidance to their patients whenever possible. The appropriate teaching, offered with physician authority combined with an attitude of caring, when given at the right time, can have a life changing effect for a patient .

The majority of cancer fighting nutrients should be obtained via a wholesome diet. Nutrient-dense foods contain substantial amounts of key nutrients in relation to the dietary energy they provide .

Nutrient dense calories include fruits, vegetables, nuts, and select high quality dairy products and meats . Furthermore, vegetarian diets are associated with lower risk for cancer .

The evidence is mounting that diets based upon these foods can be beneficial to patients with cancer in survivorship and possibly for prevention of metastases or recurrences.

In conclusion, it is important to consider the diet and nutritional planning for patients in the palliative care setting, focusing on foods and supplements that provide cancer fighting nutrients, reduce oxidative stress and inflammation can help overall quality of life, and have a beneficial effect on their cancer and other medical conditions.[65] [66] [67]

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