

NUTRITION and CANCER

Prof. Dr. Meral Aksoy

Department of Nutrition and Dietetics, Hacettepe University

Cancer is the common name given to various severe diseases, which have many causes of origination. The habitual use of alcohol and tobacco, environmental pollution, sexual behavior, types of occupation, geophysical factors, certain infections, medications, genetic susceptibility and nutritional habits are among the causes of the disease. According to the World Health Organization (WHO) data of 2005, 13% of the world mortality rates are caused by cancer. The most frequently observed cancer types in males are respectively lung, stomach, prostate, colon/rectum and liver cancers, whereas breast, cervix, colon/rectum, lung and stomach cancers are the most frequently observed types in turn in females according to the 2000 data of WHO (1). According to the Ministry of Health data, this ranking is quite similar with the cancer types in Turkey. In Turkey, bronchus/lung cancer, stomach cancer, lymphoma, prostate, cancer and larynx cancer are respectively the most frequently observed types in males, whereas breast, uterus, bronchus/lung, stomach cancers, and lymphoma are respectively the most frequently observed types in females (2).

Cancer ranks second in the list of most frequent diseases in Turkey. The correlation of the disease, which has many causes, with nutrition is 35% unless environmental conditions are taken into consideration and, according to various references, the correlation reaches to 75% if environmental conditions are taken into account (3). Nowadays, the impact of nutrition on the genetic structure is also considered within this interaction. Such impact is being discussed both in terms of the origination of the disease and in terms of the methods of treatment. Mostly air, water and soil pollution, and food of plant and animal origin, which are grown, processed, stored and prepared for consumption under these conditions, can be mentioned among environmental factors. Furthermore some consider the habits of tobacco and alcohol use within this group.

Sufficiency and equilibrium of energy intake and physical exercise: The research conducted on test animals for years demonstrated that restraining energy intake reduces spontaneous tumor formation and development. Since it is not ethical to restrain energy intake after tumor formation in human beings it is not much possible to show this effect. Nevertheless epidemiologic studies show that certain cancer types such as breast, prostate, lung, ovary, colon/rectum and renal cancers are observed

more frequently in fat persons. A reason of these factors is the increased fat tissue in obese persons and due to this, the inability especially in women to remove estrogen metabolites from the environment as required. It is detected that high Body Mass Index (VKG - BMI) value in puberty increases the mortality risk because of breast and prostate cancer in advanced ages (4). The insufficiency of daily exercise in such persons also increases the cancer risks for all types mentioned above.

Carbohydrates, the blood glucose level and cancer: Our main source of energy is the carbohydrates. The consumption of carbohydrates is greater, because they are tasty and can be converted to energy quickly. Nevertheless the refined and low energy carbohydrates cause obesity and insulin resistance, and also their immoderate consumption is a risk factor in illness according to some references. In a long-term prospective study, it was showed that hunger hyperglycemia and/or diabetes increase cancer risk (5). The fasting blood sugar exceeding 90 mg/dl increases the risk, while it being over 145 mg/dl makes the interaction more explicit. The increase in risk affects the pancreas most, which is followed by the esophagus, liver, gall tract, colon, rectum, and cervix cancers. There are researchers, who support that hyperglycemia should be assessed separately since it is not only observed in fat persons besides others, who argue that hyperglycemia, insulin resistance and obesity should be taken into consideration together. On the other hand research demonstrated that without the presence of diabetes, the high rate of glycemic load in the diet increases the risk of pancreas cancer in males and colon/rectum cancer in females if food rich in fructose, glucose and refined carbohydrates are excessively consumed (6). Although it is known that the diet fibers reduce especially the risk of colon and rectum cancer (7), it was showed that bran does not have preventive effect (8). Nonetheless it is known that diet fibers increase the feces volume, water absorption, excretion of foreign substances (especially by binding bile acids), reduce the passage duration of feces from the intestines, alter the microorganism configuration and structure short-chain fatty acids by diluting the feces; hence, based on all these activities it is argued that diet fibers have preventive effect (9).

The amount and types of fat in the diet: Fats are the highest energy giving substances among food. The fat store of our body could also be assumed as an energy store. Therefore persons who consume too much fat and do not get sufficient exercise increase their risk of disease by getting fat. Some epidemiological and experimental studies pointed out that fat consumption rich in unsaturated fatty acids (butter, solid margarines, tallow, etc.) increases colon, rectum, pancreas, renal cancer risks, as well as the risk of breast and endometrium cancers in postmenopausal women (9). In countries such as Greece and Spain where olive oil, which has high oleic acid content, is consumed more, the breast cancer incidence is lower. It was found that the tumor stimulating effect

of fatty acids such as W-3 is lower compared to that of polyunsaturated fats. Among possible reasons of this finding we can refer to the fact that both w-3 and w-6 fatty acids are related to the synthesis of phospholipids, thereby to the cell membrane structure, that w-3 intake increases the glycemic index and prevents aberrant crypt foci (ACF) formation together with the oleic acid in the early stage. The ratio of w-6 to w-3 fatty acids in the diet is an important factor, and it is suggested that this ratio is kept at the lowest level. Among food of animal origin especially sea products (salmon, sardines, and mackerel) are those that include high amount of W-3 fatty acids, while among food of plant origin, green-leave vegetables, especially purslane, is rich in it. Eicosapentaenoic acid (**EPA**) and docosahexaenoic acid (**DHA**), which are considered in this group, are important. Conjugated linoleic acid (**CLA**), in turn, exists in the meat of ruminant animals, milk and milk products. This acid regulates immune response and reduces the fat tissue. Although they are of plant origin, it is suggested to reduce the consumption of trans-fatty acids taken from margarines. Excessive saturated fatty acid and w-6 intake is considered as a risk, since it changes the phospholipid structure of the membrane. There is not much disadvantage in the intake of saturated fatty acids, unless the daily energy requirement is exceeded and unsaturated fatty acids are consumed excessively. Fats, especially phospholipids, are essential for the membrane structure, the central nervous system and brain functions, and the immune system, which plays a crucial part in diseases. Thus, fat consumption should be balanced. If they are consumed excessively, they may stimulate disease by indirectly affecting the endocrine system, female sex hormones such as estrogen and prolactine and male sex hormones such as androgen (10, 11).

The activity of diet proteins: The research on high protein diets with various amounts of protein provided different results. It is detected that for the relationship between the risk of pancreas cancer and meat consumption, which is rich in proteins, especially the effect of processed meat (such as sausages, salami, etc.) is high (12). It was observed that the consumption of pork increases the risk by 50% compared to other red meat, whereas no such risk is found for poultry and fish meat. It should be noted that saturated fat intake with the meat can also be a factor. It is indicated that the consumption of beef, pork and mutton increases non-Hodgkin lymphoma risk; the increase in the relative risk is 2.2 times more in case red meat consumption is more than once a week. Similarly, a correlation between renal cell cancer risk and consumption of food rich in proteins is found, a risk that changes in parallel with the amount of protein intake. On the other hand, limited protein and energy intake causes a decline in the insulin growth factor (**IGF**). In hunger, despite the increase in growth hormone (**GH**), IGF-I declines due to the resistance in the liver, and vice versa in excess intake of protein. Such increase is also observed in intake of other proteins of animal origin and in parallel to VKG. Glutamine, the most abundant free amino acid in the body, is essential for the growth of normal and neoplastic cells. Methionine, in

turn, takes part in the synthesis of deoxyribonucleic acid (**DNA**) as it is important in the transport of monocarboxy particles (methyl donor). It is observed that the growth of the primary cultures of some cancer types depends on methionine. Branched-chain amino acids (leucine, isoleucine and valin) take part in the protection of the fatless mass of the body and in the regulation of the protein metabolism of skeletal muscles. A reduction in their intake causes increase of oxidation and disorder of amino acid metabolism.

Vitamins and Minerals: For a long time, the preventive activity of vitamins, which have antioxidant functions, has been stressed. The results of various researches did not provide results as expected (13). Nowadays, it has been suggested that excess intake of antioxidants would attract oxidized substances, and the importance of maintaining the *oxidant/antioxidant* balance is emphasized. One of the functions of **vitamin A** is formation and protection of epithelial tissue. The insufficiency of the vitamin leads to degeneration of tissue cells, consequently the risk of esophagus, urinary tracts, skin, stomach, nasopharynx and lung cancers emerge. It is observed, in turn, that the use of vitamin A and its derivatives reduces the growth of certain tumors. The incidence of lung, stomach, esophagus and oral cavity cancers is found to be lower in those who consume food rich in carotene, which is the precursor of vitamin A. Another antioxidant, **vitamin C**, increases the resistance of the person due its functions in the immune system and the connective tissue. It inhibits the mutagenicity, which might occur due to both the preparation of food, especially while cooking by coal grill, and within the organism itself. Along with vitamin **E**, it can prevent the formation of carcinogenic nitrosamines. It is indicated that the daily intake of vitamins E and C at a sufficient level reduces disease risk by 30%. In case of its insufficiency, the risk of esophagus, stomach, larynx and cervix cancers increases. The intake of vitamin C and the precursor of vitamin C, i.e. B-carotene, reduce the risk of stomach cancer because of *H. pylori* (14). Especially food rich in vitamin content, such as lemon juice, have preventive effect on stomach cancers. Recent studies focus on genetic variation and folic acid. While the colon and lymph cancer risks of C677T variant carriers in the 5-10 Methyltetrahydrofolate reductase gene is higher, the adult lymph cancer risk is higher in the carriers of A1298C variant of the same enzyme. Consumption of food rich in folic acid would have a preventive effect on the carriers of these variants (15). Since **riboflavin** prevents epithelial tissue atrophy and regulates the intestine flora and the enzyme activity of the liver, it is argued that it might have a preventive effect on colon and liver cancers. The insufficiency of **choline**, which is a lipotropic substance, increases liver cancer risk. Research on thiamine (**B₁**) showed that tumor formation increases in its insufficiency, and its sufficiency has a preventive effect.

There is also a view that the supplemental intake of thiamine and/or with enriched food plays a part in the formation of cancers.

Being an activator of many enzymes, **zinc** is claimed to have a preventive effect from colorectal cancers. For the zinc level of the tissue in persons with high esophageal cancer risk is low, it is argued that zinc might have a preventive effect. Moreover the antioxidant activity of the mineral, its binding effect on certain carcinogens and effect on membrane permeability are signified as its preventive effect from other diseases. It is demonstrated that **copper** intake at a low level with the diet reduces the feces water level and increases free radicals and alkaline phosphatase. These are accepted as risk factors for colon cancer. It is argued that **selenium** reduces disease risk, for it prevents peroxidation together with vitamin E and glutathione, takes part in detoxification and binds nitrates in the soil so as to ensure the amount of nitrate in plants to remain within the normal range. Its insufficiency can cause liver necrosis and hepatocellular carcinoma. There are 25 different selenoprotein gene codes in the genome of the mammals. One or more selenium molecule is detected in each of these genes. It is argued that these molecules have a preventive role on cancer. Moreover, the studies carried out showed that it reduces the prostate cancer risk by 30%. The insufficiency of selenium causes oxidative stress, which could be corrected by supplementing vitamin E. High **iodine** deficiency or its high dose intake, might cause thyroid cancer by leading to goiter. While in regions of endemic goiter due to chronic iodine deficiency follicular histological thyroid type is observed, in regions of endemic goiter due to excess iodine intake, papillary histological type is more frequently observed. Iron deficiency, which is critical for nutrition, has been associated with the cancers of the upper digestive system. On the one hand iron is preventive due to its role in the immune system, on the other hand, free **iron** (especially iron used in the enrichment of food) becoming pro-oxidant (ferric oxide) carries a high carcinogenic risk. Nevertheless, the intake and absorption of the mineral of plant origin is difficult. The iron, which is taken by the diet and could not be absorbed, increases the formation of free iron in the colon and causes mucosal cell damage. The hem iron is discovered to be active in the formation of heterocyclic amines and the proliferation of the epithelial tissue. To have transferrin saturation over 60% and daily iron intake over 18 mg by the diet are identified as risk factors for cancer. The view suggesting that **calcium** increases prostate cancer risk could not be proved, but it is suggested that sufficient and balanced intake of it with vitamin D₃ reduces colon/rectum cancer risk (16). The preservative effect of the combined intake of vitamin D and calcium becomes more evident in persons who have polymorphic alleles in the receptors of vitamin D.

Sulphur and food with sulphur content are important for protection from diseases, due to the fact that it is both antioxidant and takes part in detoxification and phase II enzymes. The mineral affects ACF formation even at the beginning stage, and allyl sulphur compounds are prominent in phase I and phase II reactions. Compared to mono sulphide compounds, disulphide compounds are more effective in reactions. The intake of nickel with food, drinks and by respiration, and the presence of various forms of it render the identification of its impact on diseases difficult. The water soluble mineral, which is taken by water (the C₁ class) is admitted as carcinogenic. It is detected that the blood lead level is higher in malignant cases than benign cases, and there is accumulation of lead in tumors.

Other substances in non-nutritional food: In this category, we have the substances present in the structure of food, which are not food themselves, but have benefits and functions like food, and called “**food for functional, health, medical, regulatory, special nutrition or pharmacological purposes**”. The biologically active compounds of plant origin are called “**phytochemicals**”. There are 8000 varieties of these in our food. Their functions are to counteract the effects of oxidant radicals, activate the enzymes taking part in detoxification, stimulate the immune system, take part in gene expression related to apoptosis, and regulate the hormone metabolism, and anti-bacterial and anti-viral effects. As these are abundant in raw fruits and vegetables, it is associated with the low esophagus, oral cavity, pancreas, stomach, colon, rectum and lung cancer incidences in persons who consume plenty of fruits and vegetables. The preventive effect of soy bean on breast cancer has attracted attention, and the researches carried out showed that isoflavones such as *genistein*, *daitzin*, *glycitin* in it include plant estrogens. When such phytoestrogens present both in the soy bean and the flax seed function as estrogen agonists, it has an estrogenic effect; and when these function as estrogen antagonists, in turn, they are bound to estrogenic receptors and suppress the effect of estrogen. It is suggested that isoflavones have a preventive effect on those who have high hormone related cancer risks such as breast, endometrium and prostate cancers. But, taking these at pharmacological doses may cause endometrium hyperplasia.

It is noticed that *epigallocatechin-3-gallate* in green tea inactivates vascular endothelial growth factor (VEGF) receptors, leading to the apoptosis of sick cells in lymphocytic leukemia (17). As this growth factor is a *cytokine* necessary for tumor angiogenesis, it is believed that green tea can have an effect on other types of tumors. More examples of phytochemicals in other food can be given. It is argued that the *licopene* in tomato reduces digestive system, prostate, urinary bladder, skin and cervix cancer risks. The phytochemicals such as *glycosides*, *indol*, *isothiocyante* and *sulphoraphane* in vegetables like broccoli, cauliflower

and cabbage reduce the damage of cell DNA, the activity of sex hormones and/or metabolites, which pose risk in disease, and suppress the enzymes that trigger tumor growth. The *allylic sulphides* in onion and garlic have a preventive effect by strengthening the immune system, accelerating the elimination of carcinogens and stimulating the enzymes, which suppress the proliferation of tumor cells. The *flavonoids* in food such as fruits, vegetables, tea, cacao and wine function as antioxidant and they scavenge free radicals. They activate *glutathion-S-transferase* (GST), which in turn detoxifies foreign substances with mutagenic potential.

The human intestinal flora is both beneficial for health and also has pathogenic potential. The **Probiotics**, which are formed by the improvement of intestinal microbial balance, are live microorganisms beneficial for animal organisms. **Prebiotics**, which hold colon bacteria at a certain level and/or stimulate their growth and activity, are indigestible food ingredients beneficial for the host. **Symbiotics** are the combination of probiotics and prebiotics, and they are beneficial to the host as they implant and improve the live microbial diet supplement in the gastrointestinal region. All of these reduce the risk of cancers such as colon and rectum cancers by maintaining the intestinal balance of the host.

Nitrites, nitrates and nitrosamines: The sources of nitrite and nitrate intake are drinking water, vegetables, processed meat products, and ready and/or half-ready food such as pickles in the preparation of which sodium and potassium nitrate are used. The nitrates from food are reduced to nitrites, which are, in turn, transformed into nitrosamines through N-nitrosation reaction. It is shown that most nitrosamines have carcinogenic effect on animals. This effect can be reduced by diets rich in antioxidants such as vitamin C (18).

We make our food ready for consumption by applying various methods. Chemicals such as polycyclic aromatic hydrocarbons and heterocyclic amines, which are formed during these cooking methods, have mutagenic effects on the organism. These substances occur more in food that are cooked on coal grill or heated for many times. In order to prevent the formation of such substances, the cooking method should be chosen in accordance with the food, the use of high level of heat should be avoided, the food should not contact with fire directly and other food with antioxidant ingredients, especially with vitamins E and C, should be made available.

Suggestions for Prevention from Diseases and Measures to be Taken

1- Preserve healthy body weight, pay attention to keep the Body Mass Index (VKG) between 18.5 –25.0, balance the daily energy intake and energy expenditure, take the necessary measures at the Ministerial level regarding the increasing number of obese individuals in Turkey,

2- Keep the energy level achieved from daily fat consumption between 15–30%, include fatty meats and fried food in the diet carefully, avoid letting the daily energy intake from red meat to exceed 10%, reduce the amount and cost of trans fatty acids in fatty products,

3- Increase daily consumption of fresh vegetables and fruits to at least five portions or more, pay attention not to let the daily energy intake from these to fall below 7%, consume plenty of vegetables of mustard and sulphur content, keep flavors such as garlic, onion, mint, parsley and green salad and other green vegetables in your menu, ensure that they are grown in healthy conditions,

4- Consume dry legumes in our menu in balance with other food, increase the intake food of complex carbohydrate content, ensure that 45–60% of the daily energy intake comes from underprocessed or unprocessed foods with high level of polysaccharides and proteins of plant origin, keep the energy intake from refined sugar below 10%, prefer natural desserts such as honey and grape molasses instead of table or tea sugar and ensure to increase the production and consumption of the former,

5- Avoid alcohol, smoking, refined food with high additive content, prefer natural food to these. Keep away from smoking environments. Alcohol consumption is not suggested and it is suggested to those who consume alcohol habitually to stop this habit; if the use of alcohol is restricted, limit the daily energy intake from alcohol for males to 5% and for females to 2.5% of total daily energy intake; ensure the necessary measures to be taken to reduce air pollution,

6- Consume the food groups in the national food pyramid peculiar to Turkey at the suggested amounts and by preparing them in a healthy way,

7- Avoid coal grilled, fried and smoked food, avoid salty food such as pickles and salted food, cook your food at low heat, ensure that the daily salt intake of adults to remain below 6 grams, assist the activities to increase the awareness of the population on these issues and to change the eating habits of the people,

8- Keep away the food from conditions, in which mold and fungi can develop, pay attention to keep rapidly deteriorating food in cold or in the freezer,

9- Pay attention to the determination of the level of chemical contaminants, pesticides, wastes and additives in food to be within the safe limits and monitoring this at the national level, increase effectiveness by cooperating with institutions relevant to the subject,

10- Always do regular exercise, ensure and enhance this habit by organizing collective exercise in various institutions,

11- Inform the public on the disease and the prevention methods regularly, and in order to illustrate the relationship between the disease

and nutrition, prepare a map of cancer types peculiar to Turkey by conducting a countrywide research on food consumption, detecting the quantity and frequency of consumption of certain food in the regions and establishing a relationship between these and the disease.

References:

1. Preventing chronic diseases: A vital investment, Genova, WHO, 2005.
2. T.C. Sağlık Bakanlığı (The Republic of Turkey, Ministry of Health)
3. World Health Statistics 2006, WHO, Geneva, 2006.
4. Okasha M, McCarron P, McEwen J, Smith GD, Body mass index in young adulthood and cancer mortality; a retrospective cohort study, *J.Epil. Comm. Health* 2002; 56:780–84
5. Ha Jee S, Ohrr H, Sull JW, Yun JE, Ji M, Samet, JM, Fasting serum glucose level and cancer risk in Korean men and women, *JAMA*, 2005; 293:194–202.
6. Michaud DS, Fuchs CS, Liu S, Willet WC., and et.al., Dietary glycemic load carbohydrate sugar and colorectal cancer risk in men and women. *Cancer. Epil. Biomar. Prev*, 2005; 14: 138–47.
7. Byers T, Nestle M, Mc Tierman A and et al., 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 Cancer J. Clin.*, 2002; 52:92-119.
8. Alberts DS, Martinez ME, Roe DJ and et al., Lack of effect of the high fiber cereal supplement on the recurrence of colorectal cancers; a systemic review and meta-analysis, *Lancet*, 2004; 92:181-88.
9. Aksoy M, Beslenme ve Kanser (Nutrition and Cancer), *Çağ Mat. Ankara*, 1984.
10. Simopoulos AP, Robinson, J, *The Omega Diet*, Harper Perennial pub., 1999.
11. Aksoy M, Nutritional genomics veya nutrigenomiks, Uluslar arası Katılımlı Ulusal Kanser Haftası Toplantı Kitapçığı (Nutritional genomics or nutrigenomics. The Meeting Booklet of the National Cancer Week with International Participation), Ankara, 2005.
12. Michoud DS, Augustsson K, Rimm EB, Stamfer MJ, and et.al., A prospective study on intake of animal products and risk of prostate cancer. *Cancer Causes Control* 2001; 12: 557–67.
13. Bjelakovic G, Nikolova D, Simonretti RG, and et.al., Antioxidant supplements for prevention of gastrointestinal cancers: a systematic review and meta-analysis . *Lancet*, 2004; 364: 1219–28.
14. Correa P, Fontham ET, Bravo JC and et.al., Chemoprevention of gastric dysplasia; randomized trial of antioxidant supplements and antihelicobacter pylori therapy. *J.Natl.Cancer Inst.* 2000; 92; 181–88.
15. Lucock M, Is folic acid the ultimate functional food component for disease prevention. *Brith. Med.J.*, 2004;328:211-15.
16. Benamouzing R, Chaussade S, Calcium supplementation for preventing colorectal cancer; where do we stand? *Lancet*, 204; 364:1197-99.
17. Beliveau R, Gingras D., Green tea prevention and treatment of cancer by nutraceuticals, *Lancet* 2004; 364: 1021-22.
18. Eyre H, Kahn R, Robinson M, and the ACS/ADA/AHA Collaborative Writing Committee; Prevention cancer, cardiovascular disease and diabetes: A common agenda for the American Cancer Society, the American Diabetes Association and the American Heart Association. *CA Cancer J Clin.* 2004; 54:190–207.

