

## **Etiology and primary cancer prevention**

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*Cancer is a common name for a group of approximately 180 different diseases of more or less known etiology, and accordingly also of different possibilities of their prevention. Development of a particular type of cancer depends on a range of different factors from the environment, lifestyle, genetic makeup, and chance. Primary prevention involves changing lifestyle and environmental factors by health education and legislation. Several factors associated with an increased cancer risk as smoking, alcohol beverages, diet, reproductive and sexual behaviour, occupation, environmental pollution, certain drugs, ionising and nonionising radiation, biologic and psychological factors are discussed along with the possible preventive measures.*

**Key words:** cancer, neoplasms-etiology; primary prevention

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### **Introduction**

Cancer is a common name for a group of approximately 180 different diseases of more or less known etiology, and accordingly also of different possibilities of their prevention. Carcinogenesis is a complex multistage process characterized by an irreversible change of the cell; in its further course the process results in an uncontrolled tumor growth and, if untreated, it invariably ends with a lethal outcome. The natural course of the disease is long, the period from the initial cell change to the clinical evidence of disease – i.e. latent period being 10 to 15 years or even more for a majority of cancers. Development of a particular type of

cancer depends on a range or different factors from the environment, lifestyle, genetic makeup, and chance.<sup>1</sup>

Carcinogens associated with the environment and lifestyle, chemical, physical and biological agents, act as initiators, promoters or cocarcinogens. The initiators are genotoxic substances which cause irreversible cell change, mutation. Nevertheless, a tumor will develop only if after mutation the cell has been exposed also to the activity of promoters. In view of the primary prevention it is important to note that the effect of promoters is dose dependent and also reversible.<sup>2</sup> Cocarcinogens alone cannot initiate or promote malignant growth but they increase the metabolic activation of other carcinogens.

Neoplasms are ultimately the result of interplay between hereditary and environmental factors. The hereditary predisposition manifests itself in different ways. There can be mutation of individual genes present in rare hereditary syndromes, decreased ability for deoxyribonuc-

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leic acid repair and the associated predisposition for somatic mutations, variability in the metabolism of chemical carcinogens, and hereditary disorders in the immune response.<sup>3</sup>

Carcinogens are investigated in laboratory and epidemiologic studies. The former comprise short-time tests on cell cultures and bacteria, as well as long-term animal experiments. Analytical epidemiological studies, both cohort and case-control are used to give direct answers to the question on carcinogenicity for humans.<sup>4</sup>

From the historical point of view, the first carcinogens discovered were those associated with a particular occupation, e.g. scrotal cancer in chimney sweeps and cancer of the urinary

bladder in workers involved in aromatic amine production.<sup>5</sup> This fact is also responsible for the generally prevailing opinion that a majority of cancers can be attributed to the environmental pollution with chemicals. The results of various studies show, however, that pollution of both working and living environment play only a minor role in the total cancer burden.<sup>1</sup> Most of it is ascribed to carcinogens associated with lifestyle, smoking, excessive alcohol drinking, diet, excessive exposure to the sun.

In 1981 Doll and Peto estimated the proportion of cancer-related deaths in the United States that could be ascribed to the known risk factors (Table 1):<sup>1</sup>

**Table 1.** Proportion of cancer deaths attributed to various different factors.

Factor	Percent of all cancer deaths	
	best estimate %	range of acceptable estimates %
tobacco	30	25-40
alcohol	3	2-4
diet	35	10-70
food additives	<1	-5*-2
reproductive and sexual behaviour	7	1-13
occupation	4	2-8
pollution	4	<1-5
industrial products	<1	<1-2
medicines and medical procedures	1	0.5-3
geophysical factors	3	2-4
infection	10?	1-?
unknown	?	?

\* Some factors are protective, thus negative value.

Here it should be pointed out that these data refer to mortality. UV radiation, on the other hand, causes skin cancer which practically never appears among causes of death, and therefore the proportion of this cancer in incidence is greater.

The measures of primary prevention aimed to completely eliminate or diminish as far as possible the exposure to carcinogens are on one

hand considered a task of general public interest; legislation and surveillance should be implemented to ensure suitable living and working conditions. On the other hand, health education should be directed into increasing the awareness of the fact that cancer prevention can be most effectively realised by changes of lifestyle. This does not mean, however, that despite a large proportion of environment-related cancers, pri-

mary prevention could result in a cancer incidence decrease to the same extent. Namely, we still do not know all risk factors associated with the most frequent cancers (e.g. colorectal and prostate cancer in males and breast cancer in females), and on the other hand, fixed life habits such as smoking and diet are difficult to change. A decrease of lung cancer incidence in male population of the U.S.A., where smoking is on the decline, indicates, however, a certain success of primary prevention.<sup>4</sup>

### **What can we do to reduce cancer incidence at this time?**

#### *Smoking*

Though the causative association between smoking and lung cancer was established as late as in the 50's of this century,<sup>6,7</sup> today we can already conclude that approximately 85 % of all lung cancers in males and 75 % in females are attributable to smoking. Thus, smokers consuming two or more packs of cigarettes daily are 15–25-times more likely to die of lung cancer than nonsmokers.<sup>8,9</sup> Tobacco smoke represents a combination of initiators and promoters. It contains at least 3600 ingredients. The main carcinogens are found in its solid part, i.e. tar. Particularly its polycyclic aromatic hydrocarbons act as contact carcinogens e.g. in the lung, larynx and pharynx, whereas remote organs are affected by substances such as *nitrosamines* and *aromatic amines* that are absorbed and activated. Cigarette smoking is associated also with cancers of other sites such as oral cavity, esophagus, urinary bladder, renal pelvis, pancreas, uterine cervix, and possibly also the liver.<sup>10,11,12</sup> The magnitude of cancer risk depends on age at start of smoking, duration of smoking, tar content in the tobacco smoke and intensity of inhalation (depth and rate of inhalation and duration of smoke detention in the lung). Nonsmokers exposed to environmental tobacco smoke are also at higher risk of cancer.<sup>13</sup> Pipe smoking increases the risk of cancer of the lip; pipe and cigar smoking are associated with an increased risk of cancer of the oral

cavity, pharynx, esophagus and lung whereas the associated risk of bladder cancer is lower than in cigarette smoking. Chewing and snuffing of tobacco is associated with cancer of the oral cavity.<sup>4</sup>

The fact that lung cancer is difficult to detect in an early stage when it is still curable renders the prevention of this disease all the more important. In as many as two thirds of the patients the disease is detected only when advanced well beyond the possibility of cure. Therefore, the most effective measure for diminishing the incidence of tobacco-related cancers is never to smoke at all, or to give up smoking. It has been shown that the risk of cancer for ex-smokers decreases with length of time since stopping smoking, almost reaching the non-smokers' level 10–15 years after the cessation of smoking.<sup>14</sup> Though the decrease of lung cancer incidence, observed in the male population of some West-European countries and North America, could be ascribed not only to an actual decrease in the rate of smokers, but partially also to the use of cigarettes with low tar content and filters, it is still true that a safe cigarette does not exist, and there will probably never be one.<sup>4</sup> Therefore, a proper health education encompassing the youngest population group, supported by corresponding legislation should be most effective.

#### *Alcohol*

Alcoholic beverages increase the risk of cancer of the oral cavity, larynx, pharynx and esophagus. There is a multiplicative interaction between alcohol and tobacco in inducing cancers of all these sites.<sup>4</sup> Different studies have shown that health hazard is associated with all types of alcoholic beverages and not only with strong spirits.<sup>15</sup> In studies in many countries, associations have been observed between the cancer of the rectum and beer consumption.<sup>4</sup> Though alcohol itself is not a carcinogen but rather a modulator of carcinogenesis which is induced by a chemical procarcinogen, it also can function as a tumor promoter and/or cocarcinogen. But *acetaldehyde*, a metabolite of ethanol, is

carcinogenic, and most probably increases the risk of esophageal cancer in non-smoking alcoholics.<sup>16</sup> Primary liver cancer is frequent in alcoholics who also suffer from liver cirrhosis. The role of alcohol in the etiology of breast cancer is not clear yet. A substantial number of case-control studies and cohort studies pointed out an association between alcohol intake and breast cancer. When such an association has been observed, the relative risks have generally been between 1.5 and 2 for intakes of alcohol that varied, by study, from 1 g/day to over 40 g/day.<sup>17</sup> The modest elevation in relative risk is potentially important because of the high incidence of breast cancer in many countries, and so attributable risk may be substantial.

As a possible prevention measure, reducing of daily intake of alcoholic beverages is by far the most important. It is recommended not to drink more than the equivalent of two small drinks per day.<sup>18</sup>

### Nutrition

Through nutrition people are exposed to the greatest variety of different agents. The risk of cancer can be influenced either by foods and nutrients in their natural form, or by substances generated during the course of their storing, processing or digestion. Subject to investigation are also various additives used in order to preserve the food or change its color and taste, as well as unintentionally added substances such as pesticides, artificial fertilizers and industrial pollutants. On the other side, there are some dietary factors, which are known to play a protective role in the etiology of cancer. Further, cancer risk is also indirectly associated with hypernutrition, as well as with malnutrition, devoid of biologically valuable ingredients.<sup>1</sup>

Among the dietary factors implicated in the etiology of certain cancer sites are *heterocyclic aromatic amines* which are produced during frying and broiling of meat and fish, *salt* and salted foods, smoked food, *nitroamines* produced from nitrates and nitrites and excessive fat consumption. Food storing gives rise to carcino-

gens such as *mycotoxins* (e.g. aflatoxins) which are associated with liver cancer. Fruit and vegetables are protective for most epithelial cancers, owing to their content of fibres, vitamins and minerals.<sup>4</sup>

During the last 50 years, the incidence of stomach cancer has been generally decreasing. The risk of this cancer is increased by excessive salt intake, smoked food and nitroamines. Gastric cancer is presumably preceded by chronic atrophic gastritis caused among other things also by excessive salt intake and previous *Helicobacter pylori* infection.<sup>19</sup> Fruit and vegetables are protective for stomach cancer because of the vitamins A, C and E.

While the results of descriptive epidemiologic studies and animal experiments support an association between increased dietary fat intake and increased risk of breast cancer, evidence from analytic epidemiological studies is less consistent. Although few are significant, several of the retrospective studies of dietary fat indicate a small increase in risk, but prospective studies to date provide no support to the dietary fat hypothesis in breast cancer.<sup>20, 21, 22</sup> For colon cancer, accruing data from case-control and cohort studies tend to support an etiologic association.<sup>23, 24, 25</sup> Information on associations of fat intake with incidence of rectal, prostate and endometrial cancer is still limited.<sup>25</sup>

High consumption of fruit and vegetables is associated with decreased risk of cancer of most sites. The association is most marked for epithelial cancers of the respiratory and alimentary tracts and less convincing for hormone-dependent cancers. The consumption of vegetables and fruit in the raw form appears especially beneficial.<sup>26</sup> A large number of potentially anticarcinogenic agents are found in these food sources, including carotenoids, vitamins C and E, selenium, dietary fibre, dithiols, glucosinolates, indoles etc. They induce detoxification enzymes, inhibit nitrosamine formation, provide a substrate for formation of antineoplastic agents, dilute and bind carcinogens in the digestive tract, alter hormone metabolism, have an antioxidant effect and inhibit carcinogenesis by quenching free radicals or singlet oxygen.<sup>27</sup>

It is presumed that calcium contained in dairy products, vegetables and fish also exerts a protective effect on colonic cancer.<sup>28</sup>

The protective effect of fibres for colon cancer has not been fully explained yet; thus it is not clear whether it should be ascribed to fibres *per se* or rather to other ingredients of fruit and vegetables. Likewise, also the protective role of fibres contained in cereals remains to be clarified.<sup>29</sup> Their protective action against breast cancer, which has been revealed by some epidemiological studies, is attributable to an increased estrogen secretion in feces, but plant antiestrogens may be involved also.<sup>27</sup>

In comparison with other risk factors, the impact of various additives in food (e.g. colors, preservatives, substances aimed to change color, consistency or taste of the food) is believed to be of minor importance.<sup>1</sup> It should be stressed, however, that the use of these chemicals should be controlled by legislation.

Based on the present knowledge, a balanced diet is recommended, whereas with respect to cancer prevention, the following guidelines should be followed:<sup>18</sup>

1. Reduce fat intake to less than 30% of total calories with no more than 10% of total calories from saturated fats, 6–8% as polyunsaturated fats, and the remainder as monounsaturated fats. Appropriate dietary changes involve choosing leaner meats, fish, eating poultry without skin, choosing low-fat dairy products and avoiding the use of added fat such as butter. Increased fish consumption is recommended in substitution for meats containing high levels of saturated fatty acids. With the reduction of dietary fat the calories missing should be substituted by whole grain and cereal products rather than by sugars.

2. Consume a variety of vegetables and fruits.

According to the World Health Organisation, 400 g/day of fruits and vegetables is recommended.<sup>30</sup> A major part of the ingested fibres should be derived from foods, particularly vegetable, rather than foods artificially enriched with fibre during manufacture.

3. Adjust exercise and food intake to maintain healthy body weight.

The key to this recommendation is balance of energy intake to match energy expenditure. The balance of exercise and food intake is particularly important in controlling obesity, and hence should be recommended to lower the risk of obesity associated cancers.

4. Avoid use of dietary supplements.

With a balanced diet according to these recommendations, there will be adequate consumption of all vitamins, other essential micro-nutrients and minerals, so there is no need for dietary supplementation. There is a belief widely held by the public that if something is good, more is better. The fallacy of this belief is found in the risk of toxic effects from megadoses of some substances, such as vitamin A and selenium. Taking a supplement but failing to reduce fat or consume adequate fruits and vegetables may place an individual at an unnecessarily increased risk of disease, overwhelming any possible benefits that the supplement may have brought.

5. Limit the use of salt and the consumption of salty, saltpreserved food and nitrates.

A suitable target is in the order of 6 g/day. It is an action especially to be stressed in the countries, where the incidence of stomach cancer is still high, such as in Slovenia.

These recommendations are directed to children from the age of 2, as well as adults of all ages. The applicability to children is important as for some cancers, particularly stomach and breast cancer, the effect of dietary risk factors may commence at an early age, i.e. in childhood and adolescence. Parents should therefore ensure that a correct dietary pattern is established early in life.

### *Reproductive and sexual behaviour*

Reproductive and sexual behaviour is associated with cancers of the genital organs. Thus, breast cancer is more frequent in females with an early menarche, late menopause, who have never given birth or had their first child after the age of 35 years.<sup>31</sup> This is indicative of an

influence of sexual hormones though the exact mechanism of this action has not been explained yet.<sup>32</sup> An advanced age at first birth also increases the risk of endometrial and ovarian cancers.<sup>4</sup> It has also been found that cancer of the uterine cervix is more common in women with a history of early sexual life and who had multiple sexual partners.<sup>33</sup> Viral transmission has been suggested as the most probable reason for that; among the suspected viruses, those belonging to papilloma group have been studied most extensively.<sup>34</sup>

As to breast cancer prevention, apart from the recommendations for greater physical activity balanced nutrition, maintenance of normal body weight and earlier age at first birth, no other preventive measure have been suggested so far. Since recently, several trials are carried out on preventive use of tamoxifen in women at high risk. The opinions on these investigations are controversial, as it has not been clarified yet whether the benefit of such a treatment outweighs its potential hazard for healthy women.<sup>35, 36</sup> Beginning of sexual life at a later age and not changing sexual partners are suggested as preventive measures against cervical cancer; probably, condom and diaphragm can also be regarded as a useful protection.

### *Occupation*

Occupational cancer represents a minor part of the total cancer burden (approximately 4% of all cancers), though these are the cancers in which primary prevention is most effective. The group 1 of agents classified as carcinogenic to humans by International Agency for Research on Cancer<sup>37</sup> includes among others asbestos, some aromatic amines, arsenic, chromium (VI) compounds, vinyl chloride, solar radiation, mixtures as soots, coal-tars, coal-tar pitches, mineral oils as well as some complex exposures such as boot and shoe manufacture, furniture and cabinet making etc. The most common cancers due to occupation are those of the lung, paranasal sinuses, skin, urinary bladder and leukemias.

In studying all types of cancer, thus also

occupational ones, it should be kept in mind that the latent period, i.e. a period from the beginning of exposure to carcinogen to clinical onset of the disease, is generally 10–30 years long. Thus, it is possible that the causative agent is a substance which is no longer in use. On the other hand, the possibility exists that some substances, having come into use recently, may exert their carcinogenic effect some time in the future. Considering the latent period, and the recent increase in the production and use of numerous chemicals, it can be expected that the present incidence of occupational cancers does not yet reflect the effect of these substances.

Preventive measures are effective only when supported by corresponding legislation; in this way, the production and use of certain substances can be effectively banned, or adequate measures can be enforced to prevent or diminish the possibility that workers get in direct contact with the carcinogenic substance, depending on the risk involved and on the possibility to have the agent replaced by a less dangerous one.<sup>38</sup> The use of protective equipment always comes last in the row of available measures. Equal attention should be paid to proper health education of industrial technologists, managers and workers.

### *Environmental pollution*

American scientists believe that environmental pollution is not as important in etiology of cancer as it is often believed.<sup>1</sup> The association between air pollution and lung cancer is being studied, but apart from that, there are no other similar investigations carried out on possible relations with cancers of other sites. Polluted air contains several organic (e.g. polycyclic hydrocarbons, soots etc.) and inorganic (e.g. asbestos) agents considered to be carcinogenic for humans or certain animal species. As the risk of lung cancer is significantly influenced by other carcinogens such as active and passive smoking, occupational carcinogens and radon, it is very difficult to assess quantitatively the impact of air pollution on the risk of lung

cancer. It is presumed that 1% of all lung cancers in the U.S.A. can be attributed to the polluted air in more dense urbane areas.<sup>1</sup>

Drinking water was also found to contain a large variety of known and suspected carcinogens, e.g. heavy metals, halogenated hydrocarbons and asbestos. It is difficult to evaluate to what extent this pollution contributes to cancer incidence.<sup>4</sup>

In view of the primary prevention, we should aim to reduce as far as possible the air and water pollution, and to monitor the quality of these natural resources with respect to accepted standards.

### *Drugs*

Some drugs, particularly antineoplastic agents and combinations of agents (e.g. cyclophosphamide, MOPP), are also implicated in the etiology of cancer.<sup>37</sup> Considering their relevance for cancer treatment, the use of at least some of these drugs cannot be completely avoided. Therefore, combinations of more effective though less dangerous drugs are searched for.

As far as exogenous sex hormones are concerned, the estrogen replacement therapy, given to relieve symptoms of the climacteric, is associated with endometrial cancer.<sup>4</sup> Present evidence indicates no increased risk of breast cancer associated with prior use of oral contraceptives in women over 45 years of age.<sup>39</sup> There is a weak association between long term use of oral contraceptives and breast cancer diagnosed before the age of 36, and perhaps up to the age of 45,<sup>39</sup> especially if they were used before 25th year of age, or before first pregnancy.<sup>40</sup> On the other hand, oral contraceptives protect against cancers of the ovary and endometrium.<sup>36</sup>

### *Ionizing radiation*

Among the physical factors, ionizing radiation is certainly one of the most thoroughly studied carcinogens; besides, the standards and regulations referring to radiation protection are most complete. The consequences of medium dose

radiation were studied on survivors of the atomic bombs in Hiroshima and Nagasaki, on patients irradiated for medical reasons, as in persons occupationally exposed to ionizing radiation.<sup>4</sup> This radiation can cause all types of cancer, with the exception of chronic lymphatic leukemia and possibly Hodgkin's disease.<sup>41</sup> The influence of ionizing radiation depends on the type of rays (X or gamma, electrons, alpha particles and neutrons), the susceptibility of individual organs to radiation, the age at onset of exposure, and on sex. Also, the latent period differs with respect to different organs. Less is known about the consequences of low dose radiation.

In the last years, the presence of radon in dwelling places is a subject of great public concern. It has been known for a long time that the inhalation of radon from the uranium-radium decay chain, and particularly of its daughters bound to dust particles, causes lung cancer in uranium miners who have been for many years occupationally exposed to high concentrations of this gas.<sup>41</sup> The lung is affected by alpha particles that are emitted by the polonium daughters and damage only a thin layer of the exposed tissue. Radon in the environment originates from the earth surface, soil and minerals which contain a lot of radium. Radon emission from the surface of the continents represents four fifths of the total radon content (in the world). Underground and geothermal waters contain another 20% of dissolved radon, whereas all the oceans together contribute 1%. A very small proportion of radon in the environment can be ascribed to man's activity: 0.1% is due to uranium mines and deposits, and phosphate mining for artificial fertilizer production, whereas 0.002% result from fossil fuels, coal and earth gas burning. High concentrations of radon are not likely to occur in the outside environment since the air rich with radon mixes with the air from higher layers, whereas concentrations inside some buildings can be much higher owing to insufficient ventilation. Permeation through floor surfaces represents the most substantial source of radon in buildings, depending on the geological structure

of the ground. The highest concentrations can be found in the houses with wooden floors which are usually placed directly on the bare ground, whereas a thick concrete floor represents a considerable protection from radon permeation. A less important source is construction material, though it depends on the source of this material. In comparison with standard materials, the walls made of granite minerals, bricks from electrofilter ashes and walls of phosphate plaster contain higher quantities of radium and therefore represent a substantial source of radon in buildings.<sup>42</sup> It has been estimated that in the U.S.A. 10% of all lung cancers can be ascribed to radon in conjunction with smoking, whereas in Great Britain this proportion is 6%.<sup>43</sup> Namely, smoking and radon are supposed to act synergistically, but the two agents interact less than multiplicatively.<sup>43, 44, 45</sup> Excessive concentrations of radon in the homes can be avoided by respecting the accepted regulations for house-building and by regular ventilation.

The impact of too frequent, but above all unnecessary diagnostic radiographies should not be ignored either.<sup>46</sup> It has been pointed out that in up-to-date mammographies after the age of 50 the possible risk due to low dose radiation is outweighed by the benefit of early breast cancer detection.<sup>47</sup>

#### *Nonionising radiation*

*Ultraviolet radiation* is associated with the appearance of cancers of the skin and lip. Excessive sunbathing is also believed to increase the incidence of malignant melanoma.<sup>48</sup> Therefore, people are explicitly warned not to sunbathe between 11 a.m. and 3 p.m., and advised to use adequate protection equipment and creams.

Recently, possible harmful effects of *low-frequency electromagnetic (EM) fields* have been frequently mentioned among physical factors. These appear in the vicinity of electric installations, transformations and electric appliances. It is still not clear to what extent an increased risk of leukemias in electro-industry workers can be ascribed to the effect of electromagnetic

fields and what proportion of these conditions is due to other carcinogens. It has also not been explained yet to what extent the EM fields influence the incidence of childhood leukemias.<sup>49, 50, 51</sup> The relevant radiation emitted by computer and TV screens decreases by distance so rapidly that a prolonged sitting in front of these sources in comparison with the risk of cancer is a much greater danger for eye or backbone damage.

In view of primary prevention, however, exposure to all types of radiation should be avoided whenever possible.

#### *Biological factors*

As to biological factors, hepatitis B virus is associated with liver cancer, whereas Epstein-Barr virus plays a role in the etiology of Burkitt's lymphoma, Hodgkin's disease, B-lymphomas and nasopharyngeal carcinoma. Human T-lymphotrophic virus-type 1 is a suspected cause of certain leukemias (particularly in Japan and Africa). Patients with AIDS are prone to developing Kaposi's sarcoma and non-Hodgkin lymphoma; these patients were also found to be more frequently affected by some other cancers such as Hodgkin's disease, cancers of the oral cavity, colon, testis and pancreas.<sup>4</sup> An increased risk of certain cancers in persons with HIV infection is attributed to immunosuppression, though the HIV seropositive individuals are at a greater risk of developing non-Hodgkin lymphomas or Kaposi's sarcoma even without measurable immune deficiency.

Among parasitic diseases, schistosomiasis is associated with cancer of the urinary bladder, whereas infection with liver flukes contributes to the etiology of cholangiocarcinoma.<sup>4</sup> On the whole, however, these etiological factors are of minor importance, at least in Europe.

Vaccination against hepatitis is suggested as a preventive measure to decrease the risk of liver cancer.<sup>52</sup>

#### *Psychological factors*

Psychological factors arouse great public interest though their role in the etiology of cancer



is far from clear. Though the theory that certain personality types are more prone to cancer dates back in the 18th century, scientific research on the influence of personality characteristics is scarce.<sup>4</sup> This is partly attributable to the unexplained biologic mechanisms responsible for possible influence of these factors; investigations are centred on the influence on hormonal and immune systems. On the other hand, such studies are associated with several methodological problems.

The results of studies aimed to explain a correlation between different personality types and cancer incidence are controversial. Some investigators have established an increased risk of cancer in depressive persons,<sup>53</sup> whereas others claim just the opposite: in their opinion, less depressive people are more prone to cancer.<sup>54</sup> Another group of investigators is trying to establish possible correlation between a previous exposure to stressful events and cancer. According to some of these reports, such events (e.g. loss of a relative, marital partner or friend) before the onset of disease were not associated with breast cancer, whereas such a correlation was confirmed for some other sites such as lung, stomach and childhood cancers.<sup>55</sup> Should psychological factors become a more relevant subject of future epidemiologic investigations, adequate and standardized methods for their evaluation would have to be searched for, and all other possible risk factors considered. It is not known yet to what extent it is possible to change personality characteristics, but certainly, the adverse effects of stressful life events can be successfully diminished by adequate education and support. The question whether, and to what extent, this contributes to cancer prevention, remains to be answered.

### Conclusion

In its program "Health for all by the year 2000", the World Health Organization has set the aim to reduce cancer mortality for 15% in the population under 65 years of age by the year 2000. This goal has been adopted also by

the European Community in its program »Europe against Cancer«. For the purposes of health education, European Code with 10 commandments for primary and secondary cancer prevention has been prepared. In view of primary prevention, measures such as smoking cessation and moderation of alcohol consumption, diet rich with fruit and vegetables, maintenance of ideal body weight, avoidance of excessive exposure to the sun and following health and safety instructions at work have been suggested.<sup>56</sup> With our program "Slovenia 2000 and Cancer" under way since 1990 we are following the one from European Community.<sup>57</sup> Besides health education, legislation and surveillance are equally important in primary cancer prevention.<sup>58</sup>

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