Review article
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Spreading of carcinogens and mutagens in the environment of Armenia and possible ways of cancer prevention

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The data concerning the spreading of carcinogens and mutagens in the environment of Armenia are presented. These data show that soil, air, water and therefore some food products are polluted and dangerous for human health including carcinogens. Because of poor living standard in Armenia, most people consume food and cigarettes of low quality, whereas fresh fruits and vegetables are not available in enough quantity even on a seasonal basis. In many regions of Armenia the content of heavy metals and pesticides in agriculture food products exceed several times the hygienic limits. At present, we cannot recognize any appropriate opportunity to prevent cancer in Armenia.

KEY WORDS: *Mutagens; Carcinogenesis; Environmental Pollution; Neoplasms; Armenia*

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INTRODUCTION

Species, individuals and tissues are not equally cancer prone. This is one of the reasons why a variable reaction to carcinogenic factors, environmental and endogenous, is observed in relevant investigations. Ontogeny, popularly known as aging, and different combinations of factors provide additional variations. The different relations of the organisms suffering from neoplasms, especially developing neoplasms and combinations of environmental factors complicate and diversify the comparative oncologic pictures of various neoplasms, including regressive development. The latter can be induced by therapy or occurs spontaneously.

Countries of the industrialized world vary in their cancer frequency and specificity from developing countries to which the Republic of Armenia belongs. The ethnic and racial varieties differ in both groups of countries, industrialized and developing, regarding the question of carcinogenesis. The single factors involved in cancer development act in a variable manner to environmental variability of the purity of agents in diet and other types of consumption. The preventive aspects come variably in appearance.

Cancer still remains one of the major causes of human death in the whole world. Various cancers have various causes and detection of these causes may give the chance to prevent cancer development (1). In the USA., tobacco related cancers account for 30-35% of the total causes, tobacco and alcohol related 3-4%, diet related 35- 42%, occupational and environmental exposure related cancers account for 5% (2).

In this paper we tried to present data concerning the spreading of carcinogens and mutagens in the environment of the Republic of Armenia and some of the potential ways to prevent cancer. As in the USA., cancer is the second leading cause of death after cardiovascular diseases and stroke in Armenia (16.5% of all deaths in 1998) (3, 4).

TABACCO AND DIETARY FACTORS

Among all identified carcinogenic products tobacco is the product responsible for the most cancer cases, particularly lung cancer, but also for the cancer of urinary tract, bladder, oral cavity, pharynx, larynx, and esophagus.

We studied the micronuclei in bone marrow erythrocytes induced by mainstream tobacco smoke obtained from cigarettes widely consumed in Armenia using a mice model (5). Tobacco smoke obtained from cigarettes produced in Armenia is 2-3 times more clastogenic than smoke obtained from those produced in the USA. A high positive correlation was observed between the clastogenic/mutagenic activity and carcinogenic potency of xenobiotics (1). Therefore, we conclude that local cigarettes are more dangerous for human health and may be more carcinogenic than cigarettes produced in the USA. Smoking is a very serious problem because 65% of Armenian males and 30-35% of females are

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smokers. These data suggest that tobacco related cancer contribution in Armenia is significantly higher than in the USA.. Now, one of two tobacco companies of Armenia uses modern Canadian technology for cigarettes production. In near future, our goal will be the study of mutagenic action of smoke obtained from these cigarettes.

It is clear that many dietary factors may have causative or protective roles in cancer etiology. In the western world, diets high in fat, which typically represent 40% of calories, are correlated with high risk of breast, ovary, endometrium, pancreas and large bowel cancer. Dietary fats also have an important role in promotion of diet-related carcinogenesis (1). Some investigations in Armenia showed that fat contained only 30% of calories in diet before the collapse of the USSR (6). Vegetable oils contribution was only 10% of fat calories. After the collapse of the USSR and independence of Armenia the living standard of most people significantly decreased. At present, fat contains only 25% of the total calories in the diet of the majority of Armenians. Vegetable oils contribution is now 85% of fat calories. We suggest that fat related carcinogenesis in population of Armenia is lower than in western countries.

Age-standardized incidence rates of gastric cancer in Armenia were significantly lower than mean rates in the USSR (1.5 times) (7,8) and at present they are considerably lower than in Russia (9). It has been suggested that the cause of it is an increased level of Mg ions in drinking water in most regions of Armenia because Mg can protect experimental gastric cancer (10).

Armenia practically has no control system for the quality of imported food. A danger arises in handling the inferior quality products in the domestic trade, originating overseas and locally. It was found that many imported and local food products contained compounds dangerous for human health, such as pesticides (3-20 times above the hygienic limits), and some of them had mutagenic and carcinogenic properties (11).

Most studies have found that a diet rich in green and yellow vegetables and fruits is associated with lower risk for development of the cancer of the digestive tract (esophagus, stomach, colorectum), of the respiratory tract (larynx and lung), of the upper aerodigestive tract (oral cavity and pharynx) (12-13). The consumption of expensive fresh fruit and vegetables among the majority of the population in Armenia is very low and is usually on seasonal basis and results in a very low intake of vitamins A, C, and E.

ENVIRONMENTAL POLLUTION

Another hazard for human health is the pollution caused by many dangerous agents including heavy metals in soil. Investigations conducted in 1996 indicated that the level of heavy metals (Pb, Cd, Hg, Ni, Cu, Zn, Mn, Fe) in fruit and vegetables grown in some areas of Armenia were remarkably higher than hygienic limits and thus became dangerous for human health (14-15).

The above presented data show that fruit and vegetables grown in some regions of Armenia are hazardous for human health. They are quite opposite to the findings of most studies that a diet rich in fruit and vegetables is associated with lower risk for development of cancers of the digestive and respiratory tracts. We assume that contribution of nutritional factors to overall causes of cancer in Armenia is much higher than in the USA (35-42%).

Up to 1988, Armenia was a developed, industrial part of the USSR and had many factories. Industrial processes in some of them were carcinogenic for humans (IARC Group 1) (aluminum production, boot and shoe manufactures, furniture making, rubber industry) (1). At present, these plants are only partly working. Yerevan has a big chemical plant, the fifth largest in the whole world, manufacturing synthetic chloroprene rubber. In 1999, carcinogenicity of chloroprene was reevaluated by the experts of the IARC from Group 3 to Group 2B (possibly carcinogenic to humans). The findings of retrospective studies of the cohort of chloroprene workers from Armenia showed an increased disease incidence and mortality due to liver cancer (16). Investigations carried out from 1974 to 1976 showed that level of chromosomal aberrations in lymphocytes of workers and concentration of chloroprene in the air at working place were significantly increased (17). Chloroprene rubber plant and "Polyvinylacetate" plant produced many chemical compounds clastogenic for laboratory animals (18-19). Unfortunately, the concentration of chemicals in the ambient air of chloroprene and some other chemical plants is now also two to five times higher than the hygienic limits. The chromosomal aberrations level in lymphocytes of workers was found to be significantly higher than in the controls (20). The concentration of chemicals dangerous for human health (benzo[a]pyrene, sulfur and nitrogen oxides, formaldehyde, Cd, Pb, Ni, Cu, Cr) in the air was evaluated in big cities of Armenia during 1978-1988. These investigations showed that this parameter in Yerevan, depending on the year of study, exceeded analogous parameter in Vladivostok (Russia) 8.5-22 times (due to chemical plants and transport) (6). Vladivostok was one of the cities of the USSR with the minimal level of chemicals dangerous for human health in the ambient air. The number of cars and buses in Armenia is now two times smaller than it used to be not long ago, (because of immigration and high prices of motor fuel) and aluminum production is stopped. BP concentration in ambient air of Yerevan is significantly decreased but instead of this carcinogenic agent increased levels of other carcinogens (formaldehyde and benzene because of poor quality of used fuel) are detected (3).

Tradescantia clone 02 was used to investigate mutagenic activity of ambient air in Yerevan. The obtained results showed that mutagenic effect exceeded the control level 5-9 times in the regions of Yerevan with intensive traffic and in those located close to the chemical plant when compared to the parts of Yerevan located far from industrial plants and with minimum car traffic (21-22). The high lung cancer incidence in big cities of Armenia observed now can be explained by the pollution of ambient air in past years because the latency period of human cancer is more than ten years. In villages the incidence of lung cancer is significantly lower and this supports our hypothesis.

Water probes from two rivers in Armenia were mutagenic in the Ames test due to many chemical agents at one time (heavy metals, pesticides). It is a very serious problem because several regions of Armenia use these waters as drinking water. Increased levels of herbicides, pesticides and heavy metals can be accumulated in fish (23). But according to Ames test drinking water in Yerevan is not mutagenic (23).

It is estimated that ionizing radiation causes 4% of all cancers, mostly as a result of natural radiation to which everyone is exposed (radon in the air, cosmic rays from outer space, external radiation from radionuclides in rocks, soil, and building materials, and internal radiation from the naturally radioactive traces of potassium, lead, and polonium in food) (24). Mean radioactivity from building materials in Armenia (mostly natural stones of volcanic origin) are 1.4 times higher than hygienic limits in the USSR (24). Three kinds of natural stones that are mostly used as building material are highly radioactive (251.6, 214.6 and 303.4 Bq/kg) [25]. During the last five years natural radiation level has remarkably increased up to 1.64 times in Yerevan (26); but the reason of this increase is still unknown.

Taking into account that water, soil, air and therefore fruits and vegetables and building materials contain many hazardous agents, we suggest that the contribution of environmental pollution to development of cancer is much higher than in developed countries.

During the period from 1970 to 1990 the most frequent cancer sites were lung, stomach, lymphatic/hemopoietic system, skin including melanomas and colon-rectum in males, and breast, stomach, lymphatic/hemopoietic system, cervix uteri, colon-rectum and skin including melanomas in females. During the '90s the most frequent cancer sites were lung, stomach, lymphatic/hemopoietic system, colon-rectum, urinary bladder and prostate in males, and breast, cervix uteri, colon-rectum, stomach, lymphatic/hemopoietic system and lung in females. Calculation of cancer incidence risk showed that it was 0.11% in 1970 and increased every five years up to 0.01% till 1990 when it reached 0.15%; in 1995 it was the same (0.15%) and in 1998 it was 0.17%. Therefore, cancer incidence risk was 1.5 times higher in 1998 than in 1970. We can conclude that cancer incidence in Armenia increases every year and the most frequent cancer sites, according to IARC data, are similar to those found for other developing countries (4).

CONCLUSION

We suggest that tobacco, nutrition and environmental pollution cause cancer rates in Armenia that are higher than in developed western countries. Effective primary prevention resulting in a reduction of cancer risk can be obtained by: (i) a reduction in the number of carcinogens to which humans are exposed, or (ii) a reduction of the exposure levels to carcinogens (27). In our opinion, cancer prevention in Armenia can be theoretically successful in case of tobacco related cancer. It is known that cessation of smoking leads to a progressively lowered risk of lung cancer (1). But unfortunately, newspapers, magazines, television and radio in Armenia advertise the cigarettes mostly produced in the USA. Therefore, the action against smoking is very difficult if not impossible. As for the cancer caused by nutrition, this problem is associated with a very low living standard in Armenia where 40% of the population live below the line of poverty. Consequently, we cannot recognize the method for the prevention of environmental cancers in the Republic of Armenia at present. In future, the prevention of neoplastic diseases in Armenia can only be performed by disintegration of cancer causing environmental factors. Therapeutic side effects and cancer complications are of secondary importance at present.

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