

## MALNUTRITION LEADING TO CANCER BY SOME ENVIRONMENTAL HAZARDS

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Received: 01-10-2010; Revised: 31-10-2010; Accepted: 11-11-2010

### ABSTRACT

Environmental hazards or contaminants may cause malnutrition or cancer, and malnutrition ultimately causes many diseases, including cancer both in human beings and animals. Malnutrition is directly responsible for 300,000 deaths per year worldwide in children younger than 5 years in developing countries. However, cancer is the second leading cause of human deaths in the world and claims over 6 millions. At least 35% of all cancers worldwide are caused by incorrect diet. In the case of colon cancer, malnutrition may account for 80% of the cancer cases. Hence, the food eaten must not only be nutritious but also it must be complete and clean without any contamination, otherwise the person eating the food would get ill even the food is nutritious. If the right food is not consumed in right amounts by a person, it results in malnutrition. The most important environmental or xenobiotic (foreign) chemicals causing malnutrition and cancer are polychlorinated biphenyl congeners, pesticides, food-related mycotoxin and its derivatives, ultraviolet screen, camphor, some metals, fungicides, algicides, oestrogens, retinoids, pyrethroid insecticides, pentachlorophenol,  $\beta$ -hexachlorocyclohexane, etc.

**KEYWORDS:** Cancer, diet or food, environmental hazards, malnutrition, xenobiotics.

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## INTRODUCTION

Cancer is an abnormal growth and proliferation of cells. It is a frightful disease because the patient suffers pain, disfigurement and loss of many physiological processes. Cancer may be uncontrollable and incurable, and may occur at any time at any age in any part of the body. It is caused by a complex, poorly understood interplay of genetic and environmental factors. Cancer continues to represent the largest cause of mortality in the world and claims over 6 millions<sup>1-4</sup>. In another report<sup>5</sup>, it has been disclosed that the incidence of cancer is increasing worldwide, and it is the second leading cause of death. It has been pointed out<sup>2,6-8</sup> that cancer can be caused in one of the three ways: incorrect diet, genetic predisposition and via the environment. At least 35% of all cancers worldwide are caused by incorrect diet, and in the case of colon cancer, diet may account for 80% of the cases. When one adds alcohol and cigarettes to the diet, the percentage may increase to 60%. The genetic predisposition gives rise to 20% cancer cases. Thus the majority of cancers are being associated with a host of environmental carcinogens.

Nutrition is closely associated with health. If a person eats right kind of foods in right amounts, that person will keep good health provided no other factors intervene. If the right food is not consumed in right amounts by a person it results in 'malnutrition' (mal-noo-trish-un). This malnutrition can result in either inadequate or excessive intake of food<sup>9</sup>, which can ultimately lead to many diseases<sup>2,10</sup>. Malnutrition is directly responsible for 300,000 deaths per year in children younger than 5 years in developing countries and contributes indirectly to over half the deaths in childhood worldwide. Globally, with 113.4 million children younger than 5 years affected as measured by low weight for age. The overwhelming majority of these children, 112.8 million, will live in developing countries with 70% of these children in Asia, particularly the south-central region, and 26% in Africa. An additional 165 million (29%) children will have stunted length / height secondary to poor nutrition<sup>2,11</sup>.

Several reports indicate that environmental and food hazards or contaminants, including xenobiotics (environmental or foreign chemicals) such as oestrogenic endocrine disruptors (xenoestrogens), certain therapeutic agents (e.g., antibiotics, antihypertensive drugs, etc.) may cause various types of cancer<sup>12</sup>. The 'endocrine disruptors' influence the normal functions of oestrogens, thereby cause the cancers of several organs. Chemicals, industrial wastes, pesticides, oral contraceptives (OCs) or oestrogens, detergents, food additives and plastics, all are sources of environmental toxins and endocrine disruptors. The potential endocrine disruptors such as antibiotics, hormones, plasticizers and non-ionic surfactants are becoming the priority pollutants. Most of these have been shown as carcinogenic<sup>12-13</sup> or they may contaminate the diet or food, thereby causing malnutrition<sup>2</sup>.

In view of the above facts, an attempt has been made through this review article to explore out the certain environmental and food contaminants or hazards, leading to the development of many cancers or malnutrition.

## MALNUTRITION AND CANCER

Malnutrition refers to both undernutrition and overnutrition. 'Undernutrition' means inadequate intake of right food, while 'overnutrition' means excessive intake of right food<sup>9</sup>. Deficiency of energy and protein may result in 'protein energy malnutrition' (PEM), which can be defined as a range of pathological conditions arising from a deficiency of protein and energy, and is commonly associated with infections<sup>2,14</sup>. This disorder has very serious consequences, leading to cancer and / or death. PEM is the major nutritional problem in India and is widely prevalent among children (0-6 years) but is also observed as starvation in adolescents and adults, mostly lactating women, especially during periods of famine or other emergencies<sup>2,15</sup>. If a person eats right kind of foods in right amounts, that person will keep good health provided no other factors intervene. The food eaten must not only be nutritious but also it must be complete and clean without any contamination, otherwise the person eating the food would get ill even the food is nutritious<sup>2,16</sup>.

India is facing a great problem of malnutrition. The malnutrition is the single largest cause to the high rate of infant and child mortality and morbidity in India. The diet surveys showed that about 30% of the families surveyed consumed inadequate amounts of food to provide the necessary nutritional requirements. It was also known that an adequate diet contributed to high mortality and morbidity in the general population particularly in infants and pregnant women. The single major factor responsible for a wide prevalence of malnutrition in India is the poverty. About 50% of our people live below poverty line

and even after spending 80% of their income on food, they cannot have a balanced diet<sup>17</sup>. There is an increased risk of malnutrition associated with chronic diseases such as cancer, and diseases of intestinal tract, kidney and liver. Patients with these chronic diseases, especially cancer may lose weight rapidly and become susceptible to undernourishment because they can not absorb valuable vitamins, calories and iron<sup>2</sup>.

Malnutrition predisposes a person to infection. On the other hand, infections lead to malnutrition. This inter-relationship and synergistic effect of malnutrition and infections often lead to a high incidence of cancer and / or deaths. The people who take contaminated or malnutritious diet are at greater risk of cancer. In relation to cancer, malnutritional factors act as primary effectors in four situations: carcinogens in food articles, affected bioavailability of nutrients, non-nutritive dietary items and harmful contaminants. The malnutrition acts as carcinogen in many ways to produce cancer in human beings and animals. Nutritional carcinogenesis may occur due to ingestion of toxins, nutritional deficiency or malnutrition, non-bioavailability of the micronutrients and inactivation of the metabolic enzymes (i.e., mixed- function oxidases) present in the liver. Thus the aetiological role of malnutrition preceding clinical cancer has been firmly established<sup>18</sup>. People who are malnourished may be skinny or bloated. Their skin is pale, thick, dry, and bruises easily. Rashes and changes in pigmentation are common. Hair is thin and pulls out easily. Other symptoms of malnutrition include: anaemia, diarrhoea, loss of reflexes and lack of coordination, etc.<sup>19</sup>. All these signs and symptoms are correlated with those of many cancers<sup>2</sup>.

### **ENVIRONMENTAL HAZARDS AS CARCINOGENS**

Several reports indicate that environmental contaminants or hazards can cause either malnutrition or cancer. It has been reported<sup>20</sup> that many factors have a major effect on increasing the rates of oral, colon, lung and breast cancers. Some of these factors include increased infections, more use of pesticides, low consumption of fruits and vegetables, increased consumption of alcohol and red meat, more smoking, high industrial pollution, more exposure to sun, decreased physical activity and high occupational exposures. The major portion of chemicals to which humans are exposed is naturally occurring, that are carcinogenic at large doses. Almost every fruit and vegetable contains natural carcinogenic pesticides. Many natural chemicals are ingested as carcinogens from cooking food like roasted coffee. They include caffeic acid, catechol, dichlorodiphenyltrichloroethane (DDT), furfural and benzo(a)pyrene, etc. Food additives (e.g., allyl isothiocyanate, alcohol, butylated hydroxyanisole and saccharin), mycotoxins (e.g., aflatoxin and hepatitis B virus) and synthetic contaminants (e.g., polychlorinated biphenyls and tetrachlorodibenzo-p-dioxin) are also mutagenic and carcinogenic. Further, aryl hydrocarbons such as dioxins, polychlorinated biphenyls (PCBs) and polycyclic aromatic hydrocarbons (PAHs) have been reported<sup>21</sup> to bind at the cellular aryl hydrocarbon receptor (AhR), leading to the toxicity and carcinogenicity.

Humans are exposed to dioxins (belong to a group of halogenated aromatic hydrocarbons) mainly through contaminated foods. A dioxin compound, 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD) is the most toxic congener. The TCDD, benzo(a)pyrene and PCBs can activate AhR, which subsequently induce expression of cytochrome P4501A1 (CYP1A1) and P4501B1 (CYP1B1) enzymes. The oxidative stress caused by induction of cytochrome P450s is one of the toxic effects of dioxin. Pesticides such as insecticides (viz., carbaryl, carbosulfan, DDT, methoxychlor, dieldrin, endosulphan, sumithrin, organophosphorus compounds like malathion and parathion, etc.) and herbicides (viz., alachlor, metolachlor, quarternary ammonium, atrazine, pentachlorophenol, etc.) have become a part of environmental contaminants due to their widespread use in agriculture and disease control. Many pesticides are immunotoxic and found to suppress the cell-mediated immunity<sup>12</sup>. Pesticides such as DDT and alachlor can behave like endogenous oestrogen and function to suppress apoptosis in estrogen receptor (ER)-positive human breast cancer<sup>22</sup>. Wesseling *et al.*<sup>23</sup> reported that some pesticides and related chemicals may act as carcinogens. These xenobiotics adversely affected the lymphocyte function<sup>24</sup>, and increased the oxidative stress and lipid peroxidation in various tissues<sup>25</sup>.

Epidemiological studies indicate a close association between the process of westernization and an increase in breast cancer incidence. Western countries showed a higher breast cancer risk due to environmental influence. The lifestyles, including oral or dietary habits are responsible for the incidence of many cancers. Diet having several compounds, either as dietary components or contaminants or

formed during food processing, has influence on the development of cancer. Mukherjee *et al.*<sup>12</sup> reported that zearalenone (a nonsteroidal compound produced by many *Fusarium* fungi species) can contaminate dairy products and cereals (e.g., barley, corn, maize, rice and wheat). Zearalenone may be a potential promoter of breast tumorigenesis. After consumption, food mutagens undergo metabolic activation or detoxification by different endogenous enzymes. Most mutagens begin their adverse effects at the DNA level by forming DNA adducts with carcinogenic metabolites. The N-nitro compounds, viz. N-nitrosamines and nitrosamides (e.g., N-nitrosoureas) are a large group of chemicals that are linked with the cancer pathogenesis. Humans are exposed to N-nitrosamines from a variety of foods and tobacco smoke. Some pesticides like atrazine can be converted into genotoxic N-nitrosamines (N-nitrosoatrazine) in the environment or digestive system. PAHs are environmental hazards formed during incomplete combustion of coal, oil, gas, garbage and other organic substances such as tobacco and different food items. Leafy vegetables can be a significant source of PAHs in the human diet. In general, PAHs occur in lower amount in cigarette smoke; human exposure is predominantly from dietary sources. Metabolic activation of PAHs results in DNA binding products. Thus, the westernized dietary habits, including smoking may increase the breast cancer risk. Many lipophilic carcinogens of tobacco smoke, e.g., PAHs like benzo(a)pyrene and N-nitrosamines can be stored in breast tissues. Some PAHs such as 7,12-dimethylbenz(a)anthracene (DMBA) and dibenzo(a,l)pyrene are potent mammary carcinogens.

Sen<sup>26</sup> cited that tobacco has unfortunately become a routine part of the personal environment in the world. In India, 40% of total cancer cases are tobacco related. Almost one fourth of the India's population (more than 250 million people) consumes tobacco. More than 10 million children below 15 years are addicted to tobacco. According to WHO, head, neck, lung, throat, urinary bladder, kidney, uterus and colon cancers are mostly caused by tobacco. Bidi is said to be more harmful than cigarette. Smoke tobacco contains more than 4,000 chemical compounds and at least 400 toxins, many of them are known carcinogens and irritants. Some airborne contaminants are PAHs, carbon monoxide and nitrogen dioxide, etc. Tobacco related chewing materials include pan (betel), pan masala, gutka, zarda, snuff, tobacco powder, areca nut and naswar, etc. These substances may increase the risk of oral cancer. Pan masala is unfortunately charged with polyaromatic hydrocarbons, organochlorine pesticides (DDT and BHC), narcotics, metals and minerals. About 15% of oral and pharyngeal cancers may be attributed to dietary deficiencies or malnutrition. Similarly, fungi (*Candida albicans*), viruses (human papilloma virus, hepatitis B virus, human T cell lymphotropic virus and human immunodeficiency virus), ultraviolet (UV) radiation, immunosuppression, certain occupations (farming and industries) and poor socio-economic status aids in the development of precancerous lesions or carcinoma.

The endocrine disruptors are xenobiotic (environmental / foreign) chemicals that adversely interfere with the natural functions of hormones<sup>12-13</sup>. Oestrogenic endocrine disruptors or xenoestrogens are widely distributed in environment. Several chemicals such as PCB congeners, pesticides (e.g., dieldrin and endosulphan), food-related mycotoxin zearalenone and its derivatives, UV screen and even some metals like cadmium can influence hormonal responses by binding to ER. The xenoestrogens interact with the binding pocket of the ER because they have chemical similarities to oestrogen (usually a phenolic A-ring). Many xenobiotic chemicals can interact with the enzyme systems that metabolize oestrogens; and by this process they may modulate the endogenous metabolism. The AhR or dioxin receptor has involvement with ER-mediated response pathways. Insecticides (e.g., sumithrin) and pentachlorophenol alter steroid signaling pathways. Other man-made chemicals acting as endocrine disruptors (related with oestrogens) are atrazine, DDT, oestrogens (e.g., oestradiol and ethinyl oestradiol), hexachlorophene and toxaphene, etc. All these can influence the physiological functions of oestrogen and modulate the non-genomic pathways<sup>12</sup>, which may cause various cancers.

#### ACKNOWLEDGEMENT

The author is grateful to Scientist Dr. Madhuri Sharma, Assistant Professor of Zoology & Biotechnology, NES Science College, Jabalpur, MP for valuable help and support.

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