EXPOSURES OF ENVIRONMENT FOR RISK OF ORAL CANCER

Sharma Nishant *1,2, Srivastav B.R.1 and Shrivatav Archna2
1. Cancer Hospital and Research Institute, Gwalior (INDIA)
2. College of Life Sciences, Gwalior (INDIA)

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ABSTRACT
Exposure to a wide variety of natural and man-made substances in the environment plays a key role for risk of oral cancer. Stress, physical and mental abuse, nutrition and diet, exposure to toxins, pathogens, radiation and chemical as environmental factors and determinants of growth and body composition can contribute to the risk of some human cancers such as oral cancer. This article explains which factors of environmental plays a role on carcinogenesis, especially focusing on oral cancers. These factor reduces, repair of DNA damage and control of cell signaling and cell cycle in the effect of environment exposure. Tobacco, alcohol consumption is the most important identified cause of oral cancer followed by exposure to toxins, nutrition and diet, physical activity, infections due to viruses and radiation.

Key Words: Oral cancer, Environmental factors, DNA, Cell signalling, Nutrition

INTRODUCTION
Oral cancer is among the leading cancer type in South Central Asian men1. In India, oral cancer is the leading cancer type among men and third most common cancer among women.2 Oral cancer is a heterogeneous group of cancers arising from different parts of the oral cavity, with different predisposing factors, prevalence and treatment outcomes, oral cancer is the 6th most common cancer in men and 14th in women with more than 30,000 new cases occurring each year.3 Cancer can affect any part of the oral cavity, including the lips, tongue, mouth and throat. There are 2 kinds of oral cancer: Oral cavity cancer and oropharyngeal cancer. Oral Precancerous Lesions (PCL) such as leukoplakia and Sub Mucous Fibrosis (SMF) are early indicators of damage to the oral mucosa with a transformation rate of 2-12% to frank malignancies.4 Since, the 18th century it has been recognized that exposure to environmental factor plays a major role in the etiology of human cancers. Soot was found to be carcinogenic causing scrotal cancers in chimney sweepers.5-7 Since, then it has been established that environmental factors play a dominant role in a majority of sporadic cancers.8-10 Stress, physical and mental abuse, nutrition and diet, exposure to toxins, pathogens, radiation and natural and man-made substances as environmental factors and determinants of growth and body composition can contribute to the risk of some human cancers such as oral cancer.

However, all individuals exposed to the same type and dose of carcinogen do not develop cancer. It is now understood that cancer development is not only due to exogenous or endogenous carcinogens but their interactions with genes that are involved in the environmental factors, these carcinogens reduces, repair of DNA damage and control of cell signaling and cell cycle in the effect of environment exposure. Due to carcinogen exposure, development of sporadic cancers may be facilitated by accumulative effect of mutations or polymorphisms in these genes. Under this polygenic model, each allele confers small genotypic risk which combine additively or multiplicatively to confer a range of susceptibilities.11 Thus, cancer is the product of interaction of genetic factors and environmental
exposures like ionizing radiation, smoking, specific infectious agents, and dietary factors, which develops over along time and goes through many stages. This article explains which factors of environmental plays a key role on carcinogenesis, especially focusing on oral cancers.

DISCUSSION

Interaction of environmental factors and genes

Environmental factors such as viruses, radiation, natural and man-made substances interact with cells, throughout our lives. Mechanisms to repair damage to our genes and healthy lifestyle. However, over time, substances in the environment may cause gene alterations, which accumulate inside our cells. While many alterations have no effect on a person’s health, permanent changes in certain genes can lead to cancer.

Tobacco

Exposure to the carcinogens in tobacco products such as cigarette, cigar and pipe smoking, chewing tobacco, snuff, and exposure to Environmental Tobacco Smoke (ETS or secondhand smoke) are all linked to increased oral cancer risks. Smokeless tobacco has been linked to cancers of the mouth, and ETS has been implicated in lung cancer. Cigarette smoke contains more than 100 cancer-causing substances. The risk for cancers of the mouth, is further increased among smokers who also drink more than two drinks/day. India is the fourth-largest consumer of tobacco in the world. The third-largest producer of tobacco after China and Brazil. There are about 250 million tobacco users in India who account for about 19% of the world’s total 1.3 billion tobacco users. India’s tobacco problem is made more complex by the fact that tobacco is used in various forms in different parts of the country. The prevalence of all types of tobacco use among men is about 47% (11%–79% in different states) and among women, smokeless tobacco use varies between 0.2% in Punjab and 61% in Mizoram (Where the prevalence of women’s smoking reaches a high of 22%). Among school-going children in grades, through 10, current tobacco use varies from 2.7% in Himachal Pradesh to 63% in Nagaland. In India, at least 800,000 deaths every year are related to tobacco use (700,000 of them due to smoking). The carcinogenic mechanisms of tobacco smoking are not well understood. Smoking is a severe oxidative stress and smoke contains a wide variety of mutagens and carcinogens. The oxidants in cigarette smoke (mainly nitrogen oxides) deplete the body’s antioxidants. Thus, smokers must ingest two to three times more ascorbate than non-smokers to achieve the same level of ascorbate in blood, but they rarely do. Paternal smoking may increase the risk of birth defects and childhood cancer in offspring.

Gene interactions and tobacco exposure

The three xenobiotic metabolizing enzymes CYP1A1, GSTM1 and GSTT1 significantly alter oral cancer risk singly and in combination. The long-term SLT (loose-leaf chewing tobacco) use is prominent for risk of oral cancer some products and much of this risk has been attributed to the presence of TSNAs (tobacco-specific n-nitrosamines) or nitrous oxides, which are combustion by-products of fire-curing.

Diet/weight/physical activity

Though diet is thought to account for about one-third of cancer risk. Calorie-restricted diet feeding markedly decreases tumor incidence and increases lifespan. A wide array of compounds in fruits and vegetables in addition to antioxidants may contribute to the reduction of cancer. Folate deficiency, one of the most common vitamin deficiencies, causes extensive chromosome breaks in human genes. An understanding of mechanisms for the marked effect of dietary restriction on aging and cancer is becoming clearer, and may in good part be due to reduced oxidative damage and reduced cell division rates. Consumption of adequate fruits and vegetables is associated with a lowered risk of degenerative diseases such as oral cancer. Consumption of six food items (i.e., milk, meat, cheese, carrots, green vegetables and fruits) were inversely and significantly correlated with development of oral cancer. The strongest protection was apparently attributed to the frequent consumption of fruits.
(antioxidants and fiber), which appears to be a particularly important protective factor against development of oral cancer.\textsuperscript{36} Optimal levels of daily allowance of micronutrients like vitamin C, E, antioxidants, zinc, \( \beta \)-carotene and folate are effective in prevention of oral cancer. Antioxidants can inhibit or decrease the production of components, which can induce cancer caused from frying or broiling protein and foods that generate heterocyclic amines.\textsuperscript{37}

Being overweight or obese appears to be one of the most important modifiable causes of cancer, Height was unrelated to oral cancer risk. Body mass index (weight in kilograms/height in metres squared) was inversely associated with risk (P for trend<0.001).\textsuperscript{38}

Stress is known to activate the body's endocrine or hormonal system which in turn causes changes in the immune system. There is no specific evidence that changes in the immune system caused by stress directly cause cancer. There is strong evidence that stress, physical and mental abuse, increases the risk for oral cancer.

**Alcoholic drinks**

Heavy drinkers (more than two drinks/day) have an increased risk of cancer, particularly among those who also smoke.\textsuperscript{39} Epidemiological studies carried out in India and abroad have shown that increased alcohol consumption is causally associated with cancers at various sites, mainly oral cavity.\textsuperscript{39,40} Alcohol is a major risk factor for oral cancer and a study published in December 2011 estimated that, in 2010, around 37\% of oral and pharyngeal cancers in men and 17\% in women in the UK were linked to alcohol.\textsuperscript{41}

**Radiation exposure**

Only high frequency radiation such as ultraviolet (UV) radiation and Ionizing Radiation (IR) has been proven to cause cancer in humans. Ultraviolet (UV) radiation from the sun, sunlamps, or tanning beds causes premature aging of the lip skin and DNA damage that can lead to melanoma and other forms of lip cancer. The International Agency for Research on Cancer states there is limited evidence for an association between solar radiation and lip cancer.\textsuperscript{42} According to a World Health organization report, the evidence is mainly indirect, such as the fact that most occur on the lower lip, which receives more sun exposure than the upper lip.\textsuperscript{43}

**Microorganism**

Infectious agents such as viruses and bacteria clearly contribute to the development of several types of cancer. According to American cancer society human papilloma virus may contribute to the development of about 25\% of oral cancer cases. There is evidence that infection with high-risk Human Papilloma Viruses (HPV) increases risk of oral cancer, particularly HPV-16.\textsuperscript{44-48} According to a World Health Organization report, the evidence is mainly indirect, such as the fact that most occur on the lower lip, which receives more sun exposure than the upper lip.\textsuperscript{49}

**Natural and manmade chemicals**

Exposure to certain chemicals, pesticides and metals can increase an individual's risk for cancer. Carcinogens in this category include nickel, cadmium, vinyl chloride and benzene. These carcinogens may act alone or in combination with another carcinogen, such as cigarette smoke, to increase risk for cancer. A study of pesticides sales different parts of Brazil and cancer mortality rates a decade later finds pesticide sales show statistically significant correlation with the mortality rates for several cancers, including cancer of the lip.\textsuperscript{50} A Swedish study based on a cancer registry of agricultural workers finds an increased risk of cancer of the lip by a factor of greater than 2.\textsuperscript{51} These chemicals damage to DNA in cells can lead to cancer. However, cells can often repair DNA damage. If the damage is extreme, the cells may die. Unrepaired DNA damage can lead to mutations or changes, in genes and mutations in certain genes can cause cancer.

**CONCLUSION**

The complex process of carcinogenesis is mainly due to gene alteration with environmental factors. The risk increases individuals are exposed to environmental toxicants such as chemicals in cigarette smoke, alcohol and physical and mental status. To advocate a healthy diet this can also
help prevent oral cancer. This baseline can be applied to a larger population study, both to verify the observation and to conduct mechanistic investigations.

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This fight against drilling in the Arctic Refuge is a fight about our principles. It’s about standing up for our environment, our families and our future, and I won’t give up this fight.

Senator John Kerry