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# ENVIRONMENTAL CARCINOGENESIS AND ITS GLOBAL IMPACT: A REAL THREAT, OFTEN NEGLECTED

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**ABSTRACT**

The health impact of environment carcinogens is real. These occupational and environmental carcinogens have a significant impact in the overall general health of the population. These agents range from solar radiation, tobacco smoke, asbestos, arsenic or other occupational chemical hazards. There has been greater incidence of cancer development among general populations with the increased levels of environmental carcinogens globally in recent times. It is necessary to define the role of these agents in cancer causation and strive for future endeavors which can be achieved through the improvement of the work based environment and formulation of a strategic plan for the overall assessment and preventive measures.



## INTRODUCTION

There is a growing incidence of global cancer burden in the last few decades. There are more than 30 known carcinogens to human including environmental and occupational agents (1). The cancer burden of occupational exposure is substantial with 68,808 new cases per year, accounting for approximately 4.5% of all cancers (2). Factors contributing to carcinogenesis are not only attributed to aging, hereditary factors or lifestyle choices but also to the growing concentrations of environmental carcinogens. The majority of carcinogenic agents induce cancer by interrupting the genetic makeup of a cell and tumor promotion. This phenomenon can be induced by a plethora of agents including chemical, physical and biological agents (3). Occupational and environmental carcinogens are the growing concern due to their role in functional disability. They typically affect areas of the body like skin, nasal passage, lung or GI tract, where there is likelihood of easy exposure (4).

World health organization (WHO) has confirmed that approximately 24% of disease burden worldwide are directly linked with modifiable environmental factors (5). Environmentally linkage is a common association in the developed counties due to the larger per capita disease burden. The complexities of the problem can be weighed due to the fact that occupational carcinogens are associated with 8-24% of global lung cancer cases, though this value is usually underreported (6). Underreporting can be explained by the limited knowledge of occupational exposure and lack of interest while collecting occupational history by physicians, as well as stigma associated with smoking and the long latency of exposure pattern leading to cancer.

### *Environmental carcinogen*

Environmental carcinogenic agents have an enduring impact on public health. It is not easy to apprehend the causative potential of many environmental carcinogens to cancers due to their varied form. Among the commonly known carcinogens: tobacco smoke, solar radiation and asbestos may have engendered the largest number of people (7). Exposure from combustible indoor pollution such as tobacco smoke is one of most potential carcinogen for lung cancer development. Along with tobacco smoke, asbestos and arsenic have been strongly linked with lung and skin cancer. But solar radiation dictates as the commonest cause of skin cancer among all other environmental agents, responsible for basal cell carcinoma, squamous cell carcinoma and malignant melanoma (8).

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***Smoking***

Smoking, including the second hand smoke, is a major carcinogen. There are approximately 1.3 billion smokers in the world, and 26% of all the cancers are due to tobacco cigarettes (9). Among 1.56 million deaths from lung cancer, 90% are attributed to chronic cigarette use (10). **Smoke** contains heavy metals and other chemical carcinogens, particularly polycyclic aromatic. They are the major causes of lung cancer as well as oral, gastric, esophageal, laryngeal, liver, renal, ureter, bladder and cervical cancer.

Tobacco has over 8000 chemical constituents with 73 known carcinogenic agents like: polycyclic aromatic hydrocarbons (PAH), benzene, N- nitrosamines and aromatic amines. PAH is a product of incomplete combustion while N-nitrosamine, a derivative of nicotine. They have been found to alter methylation patterns. They directly interfere with apoptosis and specifically relate to induction of oral cavity cancer. The mechanism of tumor induction from tobacco is by formation of covalent bonds between the carcinogenic compound and DNA leading to adducts that establish as permanent mutations. These mutations occur through miscoding during the replication process interaction with oncogenes KRAS and tumor suppressor gene TP53 causing chromosomal damage. (11)

***Arsenicosis***

Arsenic is a serious global public health concern with greater than 200 million individuals at exposure risk. Arsenic exposure is one of the most common causes of skin cancer. It also has a strong links to lung, bladder, liver and kidney cancer. In the United States, there are approximately 5297 cases of annual arsenic related lung cancer. (12) Arsenic is also known to exacerbate risk of lung cancer in tobacco smokers. Arsenic exposure results from contaminated water, food or occupational hazards (13). Chronic arsenic has been a major carcinogen, due to its metabolites interrupting many processes and leading to cardiovascular, renal and nervous system diseases. Unfortunately, there are no effective treatment modalities for Arsenicosis due to its complicated metabolism (14).

The carcinogenic mechanism of arsenic is due to its induction of series of reaction including reduction, oxidation and methylation. The metabolites of these processes are in fact having more potent carcinogenic properties than the non metabolized arsenic form. These metabolites interfere with phosphorylation, thereby inhibiting biochemical pathways as well as generation of free radicals that causes DNA damage. The potential carcinogenic effects of arsenic are the resultant of oxidative DNA damage, formation of alkali-labile sites, DNA-protein cross-linking, large deletion mutations, interference with spindle fibers and chromosomal aberrations. (15, 16)

***Asbestosis***

Asbestos is linked with malignant mesothelioma, a rare form of lung cancer, with approximately 10,000 deaths each year (12). It was used in many industrial applications including mining, thermal insulation, pipes, roofing, flooring, and plastics in the past (17). Though the use of asbestos has been banned, its remains can be found in old construction sites, soil and water. Substantial degree of exposure must occur in the environment over a prolonged amount of time to develop the cancer. Asbestos exposure has been linked with increased lung cancer incidence. Asbestos carcinogenesis occurs through various genotoxic effects. Asbestos fibers have been found to induce gene mutations, chromosomal aberrations and aneuploidy as well as mitotic instability (18). There is a synergistic association between asbestos and tobacco smoke. Lung cancer due to asbestos exposure has been linked with over expression and transformation of c-fos and c-jun genes and p53 mutations. Asbestos fibers also produce large amounts of iron derived free radicals that are damaging to DNA. It is hitched to a mitochondrial oxidative DNA repair enzyme Ogg1 that prevents oxidant induced apoptosis. (19)

***Radiation***

Radiation is known to cause 10% of all cancers (20). There are different forms of radiation, such as solar or ultra-violet (UV) or ionizing radiation. UV radiation is due to the sun's UV light reaching the earth's surface. It is linked to the induction of the melanoma, a malignant form of skin cancer. The carcinogenic property of UV radiation is through absorption of the wavelength by DNA causing direct damage forming cyclobutane dimers and photoproducts, leading to uncontrolled mutations. UV radiation can also generate reactive oxygen species causing oxidative cell damage.

Radon is another form of ionizing radiation and attributes to 50-54% of natural radiation exposure that is experienced in a lifetime (21). It causes 10% of lung cancer, with greater than 20 000 deaths annually (12). Radiation from radon affects many sites of the body leading to skin, nasopharynx, larynx, lung, liver and hematopoietic and lymphatic malignancies. Radon is a radioactive gas and when inhaled, it causes penetration of decay particles into the pulmonary epithelium inducing DNA mutations. Radon is found in deposits in rocks and can reach toxic levels in groundwater collection in tunnels, mines and caves.

***Screening and preventive measures***

With a burgeoning of environmental carcinogenesis, there needs to be an efficient method of exposure assessment. A useful method for assessing exposure is by determining the levels of harmful chemical species that have been excreted into body secretions like saliva. Environmental chemicals in human tissues, body fluids and expired air are used to obtain exposure measurements, called internal dose. These internal doses of polycyclic aromatic hydrocarbons, heterocyclic amines, organochlorines, hormones and organic chemicals are a reliable indicator of exposure. (14) Effective and efficient screening is therefore essential as preventative efforts. A comprehensive screening approach can facilitate discovery of further biomarkers to aid in exposure detection and address new techniques for individualized prevention and assessment for environmental carcinogenesis.

Molecular cancer epidemiology can provide biomarkers leading to a more polished assessment of environmental carcinogenic exposure. It also allows for detection of low exposure levels that can be applied to a wider population-based study of cancer etiology. Genetic markers also play a significant role in early detection and screening procedures. With the peak in genomic medicine, there should be an interest in environmental cancer occurrence with epigenetic. The future of tackling environmental carcinogenic agents can be found in epigenetics and biomarkers. Epigenetics is the heritable changes in gene expression that is caused by mechanisms aside from DNA sequence alteration. These

markers of DNA damage constitute DNA and protein adducts, chromosomal aberrations, micronuclei and sister chromatin exchanges, which have been known to be induced by variety of exposures. It was seen that methylation of CpG promoter sequences and histone modification are common findings in cancer. (16) The value of epigenetic studies and environmental carcinogenesis can offer novel insight into how environment influences biological pathways.

There are various protocols that can be implemented to reduce the environmental burden on public health highlighting the importance of exposure and promoters. Reducing sun exposure during the peak UV hours as well as increasing sunscreen protection leads to a lower risk of cancer development. Integrating preventative measures and advocating public education as well as frequent home and building testing will help with detection of radon in indoor settings. Arsenic ingestion may result from food and water contamination and having strict control over these aspects supports in preventative measures of arsenic exposure (22). Government and industry agencies should lower the maximum tolerable levels of arsenic in food and water products. Public awareness and screening methods to reduce the risk of potential exposure will strengthen the public health policies against these environmental and occupational hazards.

## DISCUSSION

Cancer burden of occupational exposure is substantial accounting for the increasing incidence of lung cancer among others. Understanding the health risk is an important initial step in preventing disease and injuries. A particular disease or injury is often caused by more than one associated factors, which means that multiple interventions are available to target each of these risks. In turn, most risk factors are associated with more than one disease, and targeting those factors can reduce multiple causes of disease. Most people at risk overlook the significance of job-related exposure. The intense fear surrounding the poor prognosis adds to the under reporting of exposure related cancer. Health centers' in many countries have been trying to incorporate systemic screening of occupational exposure through the self-administered questionnaire and specialized consultation to improve early detection and reporting of work based exposure and hazards. A barrier to the self-administered questionnaire is reading comprehension. This emphasizes the importance of accompanying the patient and ensuring they understand every step of the consultation process during a scheduled visit. Different measures can be undertaken including provision of work based hygiene, advanced safety practices and safer management of toxic substances in occupational settings (5).

Environmental carcinogens are vast and are of different varieties. The prevalence of exposure will differ in various regions of the world with each specific carcinogen relevant to cancers at a particular site. By quantifying the impact of risk factors on diseases, evidence-based choices can be made about the most effective interventions to improve global health. Although it is not easy to distinguished cancers from environmental agents and other causes, it can however be helpful to compare the geographical and time related incidence of cancer necessary to promulgate a future plan. In order to understand the risk of cancer from environmental carcinogens, studying epidemiological incidents globally will give better insight into patterns of exposure to prevent and protect population at risk. It is necessary that these exposure and related diseases burden be addresses early with the formulation of specific work based safety measures. A more strict legal regulation and an increase in public awareness on environmental and occupational hazards seems a most feasible plan for the time being.

## CONCLUSION

There is a plethora of environmental and occupational agents that have been shown to be carcinogenic. Exposures to these carcinogens occur mostly in the workplace. It is crucial to screen patients effectively and ask detailed information regarding occupation exposure due to added risk of occupational and environmental carcinogens. Further understanding on the mechanism of these carcinogens and use of exposure biomarkers will provide a better insight into environmental and occupational hazards and preventive measures.

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