



[Science Archives \(ISSN:2582-6697\)](http://www.sciencearchives.org)

Journal homepage: [www.sciencearchives.org](http://www.sciencearchives.org)



<https://doi.org/10.47587/SA.2022.3407>



Review Article

## Risk factors of cancer: a review

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Received: Oct 2, 2022/ Revised: Nov 28, 2022/ Accepted: Oct 29, 2022

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### Abstract

Cancer has been known since BC., with rare incidence. At that time, some scientists tried to treat cancer, and some tried to find out the reason(s) behind the occurrence of cancer, and they put up many hypotheses. Nowadays, with all progression in medical technology and diagnostic methods, the causes of cancer remain unclear. But the causes of cancer can be an interaction between a person's genetic factors and external carcinogens factors that can be divided into physical, chemical, and biological carcinogens. In this review, the risk factors of cancer were discussed.

**Keywords:** Cancer, Chemical Factors, Physical Factors, Biological Factors, Heredity.

### Introduction

The development of cell accumulation can migrate to other tissues and metastasize to distant sites, resulting in significant morbidity, eventually causing the death of a patient, this is known as cancer. Several alterations in the expression of genes which cause an unbalanced ratio of cellular proliferation and cell death are what lead to aberrant cell growth, or cancer, in humans (Ruddon, 2007). Additionally, it can be regarded as a set of illnesses affecting multicellular organisms that are characterized by excessive growth brought on by genetic changes that induce dysregulation of the body's regular program for cell division and differentiation (Valavanidis, 2018). Among characteristics of cancers possess the capacity to expand uncontrollably, insensitivity to anti-growth signals, no longer as dependent on growth factors, imbalanced function, induction, and sustainment of angiogenesis, invading surrounding tissues, and metastasizing (Hanahan and Weinberg, 2011).

Evidence of certain cancer types being related to specific exposure or lifestyle is ancient. In the 1700s, the observation of nasal cancer found an association with tobacco snuff. Also,

in the same era, they found a relationship between cancer in the scrotum in adolescent men who worked in their youth as chimney sweeps (Weinberg, 2014). Currently, experts estimate that over half of all cancer deaths, and more than 40% of cancer cases reported in 2014 were brought on by possibly preventable cancer risk factors (Islami et al., 2018; Emmons and Colditz, 2017).

Most cancers are thought to develop from a single clone of cells that are regarded to be precursors and may have had their genes harmed by exposure to carcinogens (Pelengaris and Khan, 2013). These carcinogens can come from endogenously produced substances like oxygen radicals or external factors like chemicals, radiation, or infections with viruses, bacteria, or parasites. Most of these carcinogens cause hits and the number of times a person's DNA has been struck. These hits are believed to be mutational, resulting in DNA base alterations or chromosomal damage. A malignant event may begin with one, six, or more hits, depending on the specific type of event.

However, several strikes are nearly always necessary for a malignancy to advance to a fully developed invasive

metastatic form. Exceptionally, childhood-related cancers like leukemias and sarcomas that strike children, the average age at diagnosis, are over 65, making it clear that cancer is an aging illness (Noone et al., 2018; Knudson, 1971). The current review is designed to learn more and focus on the risk factors that a person may be exposed to, which could make cancer more likely to occur.

In the following and a simplified manner, the most important risk factors of cancer will be discussed:

### Chemical Factors

Chemicals like Benzene, beryllium, vinyl chloride, arsenic, and asbestos are considered chemical carcinogens. Exposure to these chemicals can cause cancer in humans, but cancer development depends on the amount, time, and persistence of exposure (Valavanidis and Vlachogianni, 2009). These substances can cause chromosomal translocations, base substitution (point) mutations, gene amplification, activation of cellular oncogenes (proto-oncogenes), or inactivation of suppressor genes. One fairly typical example is the inactivation of the p53 gene, which is seen in half of the human malignancies, and the activation of the ras proto-oncogenes in both cultured animal models and mammalian cells (Harris, 1991).

Additionally, after cells are exposed to carcinogens such as the carcinogenic metals nickel, cadmium, or arsenic, carcinogen-induced epigenetic modifications, like those in methylation of DNA or acetylation of histone, these changes found to result in alteration in gene expression patterns. Both histone deacetylation and DNA hypermethylation, which can change the structure of chromatin and lead to tumor suppressor genes being epigenetically silenced, have been related to nickel's carcinogenic effects (Law et al., 2019). Also, individuals' exposure to tobacco and secondhand smoke possesses many harmful effects due to chemicals found in smoke that damage DNA or lower the DNA repair mechanisms, bringing about genetic and epigenetic changes that promote the growth of cancer (Barrow et al., 2017; Vaz et al., 2017).

Several mutagenic substances can be found in tobacco smoke's particle or vapor phases and carcinogenic substances, such as benzo (a)-pyrene, nickel, radioactive polonium-210Po, dibenzo (a) anthracene, nitrogen oxides, cadmium, hydrazine, urethan, nitrosodiethylamine, and formaldehyde (Alberg et al., 2014). Additionally, because nicotine and flavorings are delivered to users as an aerosol, smoking e-cigarettes exposes people to toxicants that up the chance of DNA damage (Stratton et al., 2018; Rubinstein et al., 2018).

### Physical factors

#### Diet and Exercise

It is a challenge to find a certain relationship between food or diet and cancer because food has both mutagenic and

carcinogenic agents. Also, it has healthy materials, like phytochemicals, that prevent cancer. The enzymes involved in the biotransformation process metabolize these molecules, or at least the majority of them, and according to Patel and collages (2018), any alteration that happens in the genetic polymorphisms or in the way these enzymes work can alter the likelihood of acquiring cancer. Numerous epidemiological research and experimental investigations show that high-fat (animal fat) diets raise the risk of breast, colon, prostate, and pancreatic cancer (Prentice and Sheppard, 1990). Based on these animal studies and epidemiological research, it has been suggested that increasing dietary fat consumption acts by excreting bile acids, which can be transformed into carcinogens or promoters of cancer (Carroll, 1991).

Additionally, carcinogenic compounds, produced by high temperatures during the cooking of meat, these were heterocyclic amines and polycyclic aromatic hydrocarbons, found to linked with increased cancer risk (Goederham et al., 1997; Kazerouni et al., 2001). Additionally, the colon may transform nitrites and similar molecules found in smoked, salted, and some processed meat items into cancer-causing N-nitroso compounds (Bingham et al., 1996). Additionally, high colonic iron levels may facilitate the production of mutagenic free radicals (Lund et al., 1999). Aflatoxin B1, a common food contaminant, can induce liver cancer. Some specific foods are associated with certain malignancies, such as a high-salt diet, which has been associated with stomach cancer (Park et al., 2008). Exercise and cancer are related, as inactivity is thought to increase the risk of developing the disease by affecting the weight of the human body and by bad effects on the immunity and endocrine systems (Kushi et al., 2012).

### Radiation

Radiation exposure from radioactive and UV sources increases the risk of developing cancer. The UV spectrum of sunlight has the most significant impact on photoaging and skin cancer development. UVR is classified into ultraviolet A (UVA) and ultraviolet B (UVB). Only 1-10% of the solar UVR energy that reaches the earth's surface is UVB, whereas 90-99% of it is UVA (WHO, 1994). UV radiation, primarily from sunlight, is to blame for a lot of non-melanoma skin cancers (Meeran et al., 2008). While UVB directly damages DNA and causes structural damage, UVA damages DNA indirectly by forming reactive oxygen species (ROS), which induce DNA breaks. These occurrences cause long-term mutations, which subsequently cause skin cancer (Brenner and Hearing, 2008).

A tiny but growing cause of radiation-induced malignancies is the medical use of ionizing radiation, particularly X-rays. Other cancers may be treated with ionizing radiation, but in certain situations, it may also result in the development of a different type of cancer (Brenner and Hall, 2007). The production of free radicals primarily brings on large-scale cellular damage from ionizing radiation. Over 1000 DNA bases are damaged in an average cell by 1 Gy (joule of energy absorbed per kilogram of mass), which also results in about

1000 SSBs (single-strand breaks) and around 40 DSBs (double-strand breaks). Cell survival probability is correlated with the presence of DSBs, that considered the most dangerous types of molecular damage (Pelengaris and Khan, 2013).

**Biological factors**

**Infections**

Although viruses are considered the most common infectious microorganisms that can cause cancer, parasites and bacteria can contribute to the development of some cancers, too (Cupić et al., 2005). The bacterial role in cancer initiation and development was previously discussed in previous work by our team (Shamran et al., 2022). Furthermore, oncoviruses, the viruses that cause cancer either directly or indirectly, and the types of cancer that cause it are mentioned in Table 1.

**Table 1. Viruses and Their Related Cancer Types**

Oncoviruses	Related Cancer
Human Papillomavirus	Cervical Cancer
Epstein-Barr Virus	B-Cell Lympho-Proliferative Nasopharyngeal Carcinoma
Kaposi's Sarcoma Herpesvirus	Kaposi's Sarcoma, Primary Effusion Lymphomas
Hepatitis B And Hepatitis C Viruses	Hepatocellular Carcinoma
Human T-Cell Leukemia Virus-1	T-Cell Leukemias

Viruses can encourage malignant cell changes, which are thought to be the first stage in the intricate process of oncogenesis. The viral genome's v-oncogene plays a role in altering the host cell's ability to proliferate, which results in the creation of new proteins that are responsible for the transformational properties (Judson et al., 1994). Oncogenic viruses have created a variety of complex techniques to disrupt vital biological processes in infected host cells. These pathogenic viruses can block cells from self-destructing by replicating their genetic material concurrently with the division of the host cell during cell division with minimum immune system exposure and apoptosis inhibition (Ewald, 2010).

These viruses frequently boost telomerase activity to promote immortality in infected cells (Knight et al., 2001; Terrin et al., 2008). Furthermore, virus-infected cells can invade different portions of the body, boosting the proliferation and transmission of viral particles by changing the adhesion characteristics between cells (Akula et al., 2002).

**Hormones**

Some hormones influence the growth of cancer in a variety of ways. According to numerous research, hyperinsulinemia is a significant cancer risk factor (Pisani, 2008). Studies conducted on animals (in vivo) and in tissue culture (in vitro)

demonstrated the mitogenic activity of insulin on both healthy mammary tissue and breast cancer cells (Gupta and Tikoo, 2013), and enhanced metastases in a breast cancer mouse model associated with hyperinsulinemia (Rostoker et al., 2013). Since cancer cells typically overexpress the receptor of insulin and the receptor of insulin-like growth factor1, high amounts of circulating insulin may accelerate the evolution of tumors by activating these receptors (Belfiore and Malaguarnera, 2011).

In addition, hormones have a significant role in sex-related malignancies. For instance, daughters of breast cancer survivors had more estrogen and progesterone higher amount than daughters of free-cancer women. Regardless of lacking a breast cancer gene, they still have the risk probability to developing breast cancer by the high levels of hormones. Similar to this, men of African heritage have much greater testosterone levels compared to guys of European descent. As a result, their risk of developing prostate cancer is also higher (Henderson et al., 2000).

**Heredity**

Inherited genetic mutations (Changes to the genome's structure and function are what define the condition) that are referred to as germline mutations increase the susceptibility of cancer in association with environmental factors (Ruddon, 2007). Researchers have linked more than 50 hereditary cancer syndromes with mutations in particular genes. If a member of a family exhibits symptoms of hereditary cancer syndrome, genetic testing can determine whether they carry one of these mutations. Certain signs may point to inherited cancers, according to the American Cancer Society (American Cancer Society, 2019), such are multiple instances of the same form of cancer (it is an unusual or rare disease), cancers that manifest at younger ages (like colon cancer, which manifests at 20 years of age), and the presence of multiple cancer types in a single individual (resembles a female with breast and ovarian cancer).

Additionally, siblings who have experienced more than one childhood cancer as well as malignancies that affect two of the same organs (such as both breasts, both kidneys, or both eyes) (like sarcoma in both a brother and a sister). Or cancer that affects a gender that isn't often afflicted (like breast cancer in males), or cancer that runs in families (like in a grandfather, father, and son). All of these symptoms could be a warning indication of hereditary malignancies. Almost all malignancies are not inherited (sporadic). An inherited genetic flaw is the main cause of hereditary malignancies. For instance, certain hereditary abnormalities in the BRCA2 and BRCA1 genes are correlated with 75 % of ovarian cancer and breast cancer risk factors (Roukos, 2009; NCCN, 2018) and Lynch syndrome, which affects roughly 3% of persons with colorectal cancer, that revealed HNPCC (hereditary nonpolyposis colorectal cancer) (Juhari et al., 2020).

## Conclusion

From this information, it can be concluded that cancer can be prevented by reducing the chances of exposure to certain risk factors, as some of these factors can be avoided, including tobacco use, physical inactivity, alcohol intake, poor diet, and obesity or simply by adopting a healthy lifestyle in terms of nutrition and movement. The possibility of getting these tumors can also be decreased by receiving an HPV vaccine, limiting exposure to the sun's UV rays, and avoiding indoor tanning beds. As for heredity, by observing family history and appropriate examinations, we can intervene medically at an early stage in the occurrence of cancer and thus increase the chances of recovery. Finally, further studies will be established for studying each of these risk factors in cancer initiation and development.

## Acknowledgments

The authors would wish to thank the Agriculture College, Al Muthanna University, Studies and Planning Department, University of Technology, and Environment Research Center, University of Technology, for their great support and scientific assistance.

## Ethical statement

The study was done under the supervision of the Agriculture College, Al Muthanna University, and Environment Research Center, University of Technology, Iraq.

## Conflicts of interest

The authors state that there is no conflict of interest.

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#### How to cite this article

Emaduldeen, H. A., Shamran, D. J., Mahdi, D. J., Mohammed, M. T. A. (2022). Risk factors of cancer: a review. *Science Archives*, Vol. 3(4), 284-288 <https://doi.org/10.47587/SA.2022.3407>

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