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# Environmental Carcinogens and the Kinds of Cancers They Cause

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## ABSTRACT

*Environmental carcinogens are ubiquitous but often avoidable if aware of the inherent dangers. These environmental carcinogens often involve synthetic derivatives of industrial byproducts in addition to solvents, heavy metals, pesticides, radioisotopes, and even carcinogenic microbes. The likelihood of being exposed to carcinogens in one's lifetime is highly probable, especially with regard to sun exposure or even radon. Although there are far too many carcinogens to either list or explain in one review, this document contains a wide variety of well-known and lesser known carcinogens found in the environment.*

## INTRODUCTION

Chemical carcinogens in particular have been studied for over a century even though much of the earlier studies did not pinpoint the chemicals responsible for oncogenesis or the cellular targets. Early epidemiological studies and animal experimentation shed light on potential carcinogens that in turn was used to limit exposure of these chemicals to the public. Patterns began to emerge with regard to exposure to environmental carcinogens and the forms of cancer they caused. Exposure to these agents typically caused cancer in regions where there is plenty of surface area like skin, lung, and gastrointestinal tracts.

Eventually the research began to focus on genetic changes associated with cancer. Genomic changes were documented and proposed mechanisms for oncogenesis began to emerge. Carcinogens were classified in groups associated to their similar molecular structure and mechanisms associated with carcinogenesis. Heavy metal carcinogenesis, with regard to its ability to create free radicals and reactive oxygenated species (ROS), became better understood. Intercalating agents were found to disrupt cell activity associated to DNA replication, transcription, DNA editing, and chromosome stability.

Epigenetic modifications were documented from exposure to environmental carcinogens. The

term epigenetics differentiates itself from genetic changes since changes do not involve alterations in the primary DNA sequence. Instead, the heritable changes in gene expression that do not involve changes in the primary DNA sequence are constituted in the definition of epigenetics. Environmental carcinogens have the potential to cause aberrant methylation by way of oxidative stress.

Environmental carcinogens can also include pathogenic microorganisms. Although significantly more research has gone into viral causes of cancer, there is potential for bacterial, trematode, and fungal causes of carcinogenesis. These microorganisms often create chromosomal instability by either inserting DNA in oncogenes or tumor suppressor genes like with viruses or by mechanisms associated with inflammation, or toxin release.

Although exposure to many of environmental carcinogens is avoidable, there are others that are more ubiquitous. Many environmental carcinogens originate from the production of chemical which not only can be occupational hazards but detrimental pollutants. Unfortunately the discovery of many environmental carcinogens were discovered long after their production; most notably would be asbestos. Exposure to heavy metals and radioisotopes can become problematic to miners who may unwittingly expose themselves to various mineral deposits. Smoking and secondhand smoke contains various chemical carcinogens in addition to heavy metals and is significantly more avoidable than it was a few decades ago.

## TOBACCO

Tobacco use is known to contribute to the development of many forms of cancers including lung, bladder, gastric, and oral cancers. There are various carcinogens found in smoking, chewing, and snuffing tobacco that include polycyclic aromatic hydrocarbons (PAH), N-nitrosamines and aromatic amines [1]. Cigarette smoke alone has over 5,000 known chemical constituents [2]. However, carcinogenesis is much more closely linked to the 73 known carcinogens in smoking tobacco [2, 3] and the 28 known carcinogens in chewing tobacco and snuff. Of the 73 known

carcinogens in tobacco smoke, 20 are known lung carcinogens. These lung carcinogens include PAH, nicotine-derived nitrosamine ketone (NNK), cadmium, radioactive isotope 210P, and volatile chemicals like 1,3-butadiene [4, 5]. Of these compounds and elements, PAH and NNK have the most robust evidence of their tumorgenic potential in particularly laboratory animals [6-8].

Nicotine is found in all three forms of tobacco use. Although nicotine does not have mutagenic properties, it does have the capacity to inhibit apoptosis which is an important part of tumorgenesis in addition to acting as a tumor promoting agent by increasing protein kinase activity. Cytochrome P450 can activate nicotine derived nitrosamine ketone as a carcinogen via CYP2A6 [9]. Carcinogen substrates are made more hydrophilic when metabolized by cytochrome P450, glutathione S-transferases, and UDP-glucuronosyl transferase and essentially become a more reactive species that can interact with nucleophilic sites of DNA which can form DNA adducts. These DNA adducts, if not repaired, can lead to aberrant changes during polymerization leading to permanent SNP which may contribute to oncogenesis. Thousands of mutations in smokers have been detected in the lungs of smokers and involved mutations in regulatory genes including KRAS and TP53 [10-13]. There is a multitude of other cancers associated tobacco use listed in Table 1.

**Table 1:** Tobacco use is known to cause many forms of cancers. A breakdown of the kinds of cancers that tobacco causes is listed in the figure below.

| Carcinogen | Cancers |
|---|---|
| **Tobacco** | Mouth, Nose, and Throat, Larynx, Trachea, Esophagus, Lungs, Stomach, Pancreas, Liver, Kidneys and ureters, Bladder, Colorectal, Cervix, and Leukemia |

## ORGANOCHLORINES

Polychlorinated biphenyls (PCBs) are known carcinogens that can be found in the environment of both marine and terrestrial organisms. It is unclear whether background exposure represents a threat with regard to oncogenesis. Dioxin like PCBs (DL-PCBs) are known for their toxicity in addition to their carcinogenic qualities (table 2). The health risks have largely been assessed by

various exposures associated with 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) or its toxic equivalents (TEQs) with regard to toxic equivalency factors (TEF). TCDD is a class I human carcinogen [14, 15] and is known to cause lymphoma, and fibrosarcomas [16]. The carcinogenic effects of TCDD involves oxidative damage of the chromosome in addition to altering signal transduction pathways and the replication cycle [17].

Mixtures of PCB were tested on various cell lines to test their mutagenic potential. Aroclor 1254 (a commercial mixture of PCBs) was shown to induce chromosomal damage in human lymphocytes [18, 19]. PCBs are known to covalently link macromolecules including DNA to proteins in rat liver microsomes [20-22]. Most studies using PCB mixtures had negative results with regard to carcinogenic potential since carcinogenicity is dose dependent.

## POLYCYCLIC AROMATIC HYDROCARBONS

Polycyclic aromatic hydrocarbons (PAHs) are known carcinogens with varying levels of carcinogenicity and toxicity (table 2). PAHs are found in complex mixtures in the environment, cigarette smoke, vehicular exhaust, occupational settings, and even pharmaceuticals. The major mechanisms of PAH-induced carcinogenesis involves the binding of PAHs to DNA. This process may first involve the PAH to become activated after it is metabolized by CYP1A1, 1A2 and 1B1 [23-25]. Many of PAHs' tumorigenic and mutagenic capacity is associated with covalently binding to DNA or by depurinating DNA leaving abasic sites [26-28]. Most PAH DNA adducts are associated with the PAH either having a bay or fjord region where PAH with fjord regions have a greater mutagenic and tumorgenic potential [29-32]. Mutagenic potential can either activate oncogenes or inactivate tumor suppressor genes. PAHs have the capacity to inactivate P53 tumor suppressor gene as documented in lung and breast cancer [33-34]. In addition to P53 deactivation, the proto-oncogene RAS can be activated by mutations associated with PAHs as observed in vivo [35-36].

## VOLATILE ORGANIC COMPOUNDS

Volitile organic compounds (VOC) can either be indoor or outdoor pollutants that have various impacts on health, especially if there is long term exposure (table 2) [37]. These compounds include toluene, formaldehyde, benzene, styrene, and chlorinated hydrocarbons. Chloronated hydrocarbons include trichloroethylene, tetrachloroethylene, chlorophorm, and carbon tetrachloride. Although exposure to many of these VOCs can be acute, there are long term risks associated with continuous exposure to these chemicals.

Formaldehyde is a group 1 carcinogen [38] and is used in various industrial environments in addition to house hold items. Squamous cell carcinoma of the nasal cavity is a consequence of chronic exposure to rats that have either ingested the formaldehyde by contaminated drinking water or after continuous exposure through inhalation (table 2). In humans, nasopharyngeal cancers, lymphohemaopoietic cancers, and sinonasal cancers were more common among those that were exposed to formaldehyde than the control [39-41]. Glutathione-dependent enzymes metabolize formaldehyde and create formic acid or carbon dioxide before it is eliminated by the body. However, not all formaldehyde is metabolized and the remaining formaldehyde creates DNA-DNA crosslinks, protein-DNA crosslinks [42], breaks in DNA strands [43-45], in addition to fostering an environment that causes chromosomal aberrations and sister chromatid exchange [46-48].

Benzene is used in industry as a solvent and can be found in both air and groundwater in addition to cigarette smoke, automobile emissions, and gasoline (table 2). Benzene is metabolized in the body by either CYP2E1 or CYP2B1 depending on the concentrations [49]. Leukemia and most often non-lymphocytic leukemia are associated with exposure to benzene [50, 51]. There is some evidence that benzene exposure increases the likelihood of multiple myeloma, chronic lymphocytic leukemia, acute lyphocytic leukemia [52], and breast cancer in women [53].

## PESTICIDES

There are several varieties of pesticides including organochlorines, organophosphates, pyrethroids, and carbamates. Organochlorines, including DDT and chlordane, are typically in the

form of carbon rings composed of 5 or 6 members. Organophosphates have a common chemical structure which involves the phosphoric acid ester structure. Derivatives of pyrethin, which originate from flowers, comprise the pyrethroids. Carbamic acid derivatives form the class known as carbamates.

There are several organochlorine pesticide carcinogens with various mechanisms associated with oncogenesis. Chlorotriazine terbuthylazine can induce DNA damage human lymphocytes in addition to effecting the integrity of TP53 and c-myc genes [54]. B-hexachlorocyclohexane (β-HCH) is a pesticide that increases the mRNA expression of MMP-13 as well as increase the expression of proto-oncogenes cyclin D1, p27, and c-Neu and

can also accelerate the growth of mammary tumors in mouse models [55]. Activation of proto-oncogenes c-myc, c-jun, and c-fos and induction of PKC activity by hexachlorobenzine can cause tumors in the liver in addition to its toxicity [56]. Dichlorobenzene had similar findings where c-myc and Ha-ras expression changed in rats [57]. Organophosphates pesticides also have carcinogenic potential. Malthione can increase the protein expression of p53 and c-Ha-ras [58]. Both malthione and parathione have a history of inducing oncogenesis in epithelial breast cell in vitro [58]. The carbamate pesticide carbofuran damages the integrity of c-myc and TP53 genes in lymphocytes cultured in vitro [59].

**Table 2:** A variety of organic carcinogens have the potential to cause cancer. The environments where these carcinogens can be found as well as acute symptoms of exposure are listed. The mechanisms and these organic carcinogens varies from species to species however the acute symptoms are for the most part similar with the exception of asbestos.

| Carcinogens | Cancers | Source | Acute Exposure |
|---|---|---|---|
| **Organochlorines** | Breast, Colorectal, Pancreatic, Prostrate, Lung, Oral/Nasaopharyngeal, Thyroid, Adrenal, Lymphoma, and Gallbladder | Pesticides and Solvents | Nausea, Vomiting, Tremors, Coma, Seizures, Cough, Shortness of Breath, Seizures Agitation, Lethargy, and Unconsciousness |
| **Polycyclic Aromatic Hydrocarbons** | Breast, skin, lung, bladder, and Gasterintestinal | Cigarette Smoke, Vehicular Exhaust, Roofing Tar, Occupational Settings, and Pharmaceuticals | Nausea, Headache, Dermal Irritation, and Repertory Irritation |
| **Volatile Organic Compounds** | Lung, Leukemia, and nasopharyngeal, lymphohemaopoietic, and sinonasal | Air, Groundwater Solvents, Cigarette Smoke, Automobile Emissions, and gasoline | Nausea, Dizziness Headache, Drowsiness, Eye Irritation, and Respiratory Irritation |
| **Pesticides** | Breast, Colorectal, Pancreatic, Prostrate, and Gallbladder | Air, Ground Water, and Vegitation | Nausea, Vomiting, Tremors, Coma, Seizures, Cough, Shortness of Breath, Seizures Agitation, Lethargy, and Unconsciousness |

## ASBESTOS

Asbestos is involved in several diseases including pleural plaque and effusion, fibrosis, as well as mesothelioma and lung cancer (table 3) [60-64]. Asbestos comes in two fibrous forms including the thin and strait fibers of amphibole and curved fibers in serpentine. Asbestos is composed of a silicate containing calcium, iron

and magnesium where silicon and oxygen are at the core [65, 66]. The immune system reacts to asbestos by having macrophages consume the asbestos which in turn kills the macrophages and releases cytokines and attracting more macrophages and fibroblasitic cells to create fibrous tissue and eventually forms a fibrous mass [67, 68]. Crocidolite and amosite, a form of asbesestos, contains iron which is thought to

create reactive oxygenated species (ROS) and reactive nitrogen species (RNS) that cause damage to DNA in addition to damaging nearby cells which is associated in the development of cancer [69-71]. Asbestos, like other environmental carcinogens, is thought to also induce chronic inflammation which is associated in the development of carcinogenesis [72-74]. DNA damage by ROS and RNS is formed because iron present in asbestos fibers, DNA damage associated with chromosome tangling, and absorption of other various carcinogens associated with asbestos fibers encompasses the carcinogenic activity of asbestos [75-77].

## RADIATION

There is speculation that radiation is the root cause for 10% of all cancers. Much of the initial dose related studies, with regard to ionizing radiation, were based on studies of medical radiation or exposure to radiation following nuclear detonation of atomic bombs at Hiroshima and Nagasaki. Radiation is known to induce leukemia and lymphoma, skin cancer, thyroid cancer, various sarcomas, lung cancer, and breast cancer [78]. Those that are most likely to be exposed to radiation include radiologists and miners. 10% of lung cancers can be associated with radon exposure from living in an area or working in an area associated with high levels of radon [79, 80]. Radon exposure is the leading cause of cancer from ionizing radiation [81]. Cancer caused by non-ionizing radiation is largely caused by exposure to ultraviolet (UV) radiation (IARC, 1992). UV exposure is dose dependent and a risk factor for skin cancers including basal cell and squamous cell carcinoma as well as melanoma (table 3) [82-85]. Exposure to UV radiation is largely based on lifestyle of the individual by either spending prolonged periods in the sun or by artificial means like tanning beds.

## METAL IONS

Arsenic (As), cadmium (Cd), chromium (Cr), and nickel (Ni) are metal ions that have been classified as carcinogens by the International Agency for Cancer Research (IARC) (table 3) [86-89]. Metals have the capacity to lead to aberrant cell growth by promoting changes in normal cellular function [90]. Common mechanisms for metals to promote cancer include formation of

free radicals, inducing aberrant methylation, as well as interact in a number of redox reactions [90, 91, 92, 93]. Additionally, metal ions can influence gene regulation in effected cells [94, 95, 96]. Although most metals have a weak mutagenic effect, many metals have the capacity to act as a co-carcinogen when other cancer causing agents are involved [90, 91, 97]. Initiation of cancer by metals involves the damage of DNA through the production of free radicals [90, 91, 98, 99]. Arsenic, cadmium, chromium, and nickel can also form reactive oxygenated, sulfur, or nitrogen species that can influence oncogenesis [90, 94, 95, 96, 100, 101-104].

Arsenic exposure is most common among miners, metal smelting industries, glass manufacturing, and even coal burning at industrial power plants (table 3) [105]. Arsenic contaminated drinking water in places like Bangladesh, India, and China occurred after alternative water sources were used in order to protect against contamination from pathogenic microogransism [106, 107]. Unlike other metal carcinogens, arsenic is quickly excreted from the body where up to 50% or arsenic is removed within 2 days for acute poisoning [105]. The toxicity of arsenic is significantly lower when the arsenic is methylated As(III) in comparison to methyl As(V) or As(III) species [108, 109]. Arsenic is known to change the redox potential of mammalian cells in vitro [110]. Methylated metabolites of Arsenic are respectively exclusively formed in the liver [111, 112] are more likely to produce $H_2O_2$, singlet oxygen, superoxide, and hydroxyl radicals. Although increased liver cancers were reported, the main target for carcinogenicity includes skin, lungs, and bladder in humans as well as animal models [107, 113-114].

Cadmium is different than most metals as it is found in one valence state, CD(II). Cadmium can be found in paints, particularly yellow paint [115], as well as some batteries [93], and can be used as a stabilizing agent in plastics (table 3). Much of the exposure to cadmium comes from the metal refining process since much cadmium is often removed from copper as it is released into the atmosphere during heating [116]. Most people are exposed to cadmium in cigarette smoke [93]. Cadmium is considered a weak mutagen but it also regarded as a strong co-mutagen [89, 117, 118]. Although lung cancer predominates [89], the

prostate, pancreas, and kidneys are also sites for cadmium induced malignant transformation.

Chromium is found in a variety of manufactured products including chrome plating, welding, leather tanning, dietary supplements, and ferrochrome metals (table 3) [87, 119]. Environmental exposure from chromium includes engine emissions and cigarette smoke. There are various valence states of chromium with Cr(VI) being the most carcinogenic. Cr(III) is not carcinogenic and is involved in proper insulin binding and found in dietary supplements. Cr(VI) is more dangerous in its insoluble form and can line the epithelial tissue of the lungs and can accumulate to a level that increases carcinogenesis [120]. The mechanism involving Cr(VI) and oncogenesis is unclear but there is a likely connection between Cr(VI) and intracellular redox cycles associated with the creation of various reactive species in addition to DNA-protein crosslinks.

Nickel is commonly used in electroplating, found in circuitry, electroforming, in addition to batteries. Stainless steel is a nickel alloy found in various items including knives, building tools and jewellery (table 3) [121]. Although nickel by itself is non carcinogenic, various compounds including nickel oxides, silicates, and sulfides as well as soluble nickel salts are carcinogenic [122]. Nickel can be found in contaminated drinking water in addition to soil and rock. However, crystalline nickel is more dangerous especially if it is inhaled into the lungs and become lodged in where it is phagocytized by macrophages and epithelial cells [76]. For these reasons carcinogenesis associated with nickel is limited to the lungs since the phagocytosis of nickel brings the nickel ions toward the DNA of the epithelial cells [102, 122].

**Table 3:** The following inorganic carcinogens can be found in various locations. Although the metal ions listed have a significantly lower capacity to induce oncogenesis, they still have an opportunity to induce oncogenesis and are readily uptaken through various (often specific) channels.

| Carcinogens | Cancer | Source | Acute exposure |
|---|---|---|---|
| **UV Radiation** | Basal Cell and Squamous Cell Carcinoma and Melanoma | Sun and Tanning Beds | Sun Burn |
| **Radon** | Leukemia, Lymphoma, Skin, Thyroid, Various Sarcomas, Lung, and Breast | Soil | Emphysema, Pulmonary Fibrosis, Chronic Interstitial Pneumonia, Silicosis, and Respiratory Lesion |
| **Asbestos** | Lung, Mesothelioma, Gasterointestinal, Colorectal, Throat, and Kidney, Esophagus Gallbladder | Building Insulation | Coughing, Shortness of Breath, Pleural Plaques, and Pleural Effusions |
| **Cadmium** | Lung, Prostate, Pancreas, and Renal | Paints, Batteries, and Stabilizing Agent in Plastics | Nausea, Vomiting, Bronchitis, Pneumonitis, Pulmonary Edema, and Intra-Alveolar Hemorrhage, |
| **Chromium** | Lung | Chrome Plating, Welding, leather Tanning, and Ferrochrome Metals | Gastrointestinal Bleeding, Hemolysis, Coagulopathy, Seizures, and Pulmonary Dysfunction |
| **Nickel** | Lung | Electroplating, Circuitry, Electroforming, and Batteries | Nausea, Vomiting, Lassitude, Headache, Cough, Shortness of Breath, Abdominal Discomfort, Diarrhea, and Giddiness |

# MICROORGANISMS

Various kinds of microorganisms are known carcinogens to cause cancer. These microorganisms include viruses, bacteria, trematodes, and fungi. The mechanisms and the cancers they cause can be found in various journal articles. Bacteria, trematodes, and fungi will have a brief description of the mechanism associated with the various cancers they cause.

The mechanisms for viral causes of cancer typically involve the insertion of genetic material in chromosomes in either oncogenic or tumor

suppressor genes. Other viruses have oncolytic proteins and some cause inflammation which is associated with oncogenesis. These viruses include Epstein Barr Virus (EBV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Human Herpes Virus 6 (HHV-6), Human Herpes Virus 8 (HHV-8), Human Papillomavirus (HPV), Human T-cell Leukemia Virus Type 1 (HTLV-1), and Merkel Cell Polyomavirus (MCPyV) (table 4). EBV is typically asymptomatic but it has the potential to cause Hodgkin Lymphoma, Burkitt Lymphoma, diffuse large B cell lymphoma (DLBCL), pyrothorax lymphoma, Nasopharyngeal carcinoma, gastric carcinoma, and Leiomyosarcoma of the immunocompromised [123]. HBV and HCV are known to cause hepatocellular carcinoma (HCC) [124-126]. HHV-6 can cause oral aquamous cell carcinoma, Hodgkin's disease, non-hodgkin's lymphoma, and cervical carcinoma. HHV-8 is associated with elevated risk of Karposi's sarcoma and primary effusion lymphoma [127-130]. HPV is most associated with cervical cancer [131, 132]. HTLV-1 is known to cause adult T-cell leukemia and lymphoma [133-136] while MCPyV can cause Merkel cell carcinoma and small cell carcinoma [137-138].

**Table 4:** A list of viruses and the type of cancers that it causes shows an arrangement of different kinds of cancers specific to each virus with the exception of HBV and HCV. The mechanism of oncogenesis also varies significantly from virus to virus.

| Virus | Cancer |
|---|---|
| EBV | Hodgkin Lymphoma, Burkitt Lymphoma, Diffuse Large B Cell Lymphoma, Pyrothorax Lymphoma, Nasopharyngeal Carcinoma, Gastric Carcinoma, and Leiomyosarcoma |
| HBV/HCV | Hepatocellular Carcinoma |
| HHV-6 | Oral Squamous Cell Carcinoma, Hodgkin's Disease, non-Hodgkin's lymphoma, and cervical carcinoma |
| HHV-8 | Karposi's Sarcoma and Primary Effusion Lymphoma |
| HPV | Cervical Cancer |
| HTLV-1 | Adult T-Cell Leukemia/Lymphoma |
| MCPyV | Merkel Cell Carcinomas |

Bacterial infections that cause cancer are not as well researched as viral causes of cancer. Many of the mechanisms are either unknown or involve inflammation in particular regions that creates stress associated with the formation of oncogenesis. Bacteria that are known carcinogens include Borrelia burgdorferi, Chlamydia pneumoniae, Helicobacter pylori, Mycoplasma,

Samonella typhi-1, and Streptococcus bovis (table 5). Borrelia burgdorferi is known to cause primary cutaneous B-cell lymphoma [139-141] while Chlamydia pneumoniae can cause lung cancer [142]. The mechanism for both bacteria is primarily unknown but most likely involves inflammation. Helicobacter pylori is associated with gastric carcinoma and its mechanism of oncogenesis is likely caused by inflammation [143, 144]. Mycoplasma can also cause gastric carcinoma in addition to colon carcinoma. Its mechanism involves p53 suppression, NF-κB activation, and genetic instability [145-150]. Salmonella typhi-1 has the potential to induce oncogenesis in humans in the form of chlangiocarcinoma [151]. The mechanism involves the deconjugation of toxins that bind to DNA cause mutagenesis in addition to inflammation [152-154]. Streptococcus bovis has the ability to induce colorectal cancer by way of carcinogenic byproducts as well as inflammation [155-163].

**Table 5:** The bacteria listed above shows the various bacteria that are also carcinogens. Although the mechanisms for oncogenesis are respectively unknown, many of these bacteria cause inflammation which is associated with oncogenesis. Typically the infections must be chronic in order for these bacteria to promote the kind of inflammation necessary for oncogenesis.

| Bacteria | Cancer |
|---|---|
| Borrelia burgdorferi | Primary Cutaneous B-Cell Lymphoma |
| Chlamydia pneumoniae | Lung Cancer |
| Helicobacter pylori | Gastric Carcinoma |
| Mycoplasma | Gastric and Colon Carcinoma |
| Salmonella typhi-1 | Cholangiocarcinoma |
| Streptococcus bovis | Colorectal Cancer |

Carcinogenic trematodes are most common in southeast Asia and sub Saharan Africa. They are typically ingested by undercooked fresh water fish like with Opisthorchis viverrini and clonorchis sinensis or by contaminated drinking water like with Schistosoma haematobium. Clonorchis sinensis causes cholangiocarcinoma through a mechanism associated with inflammation [164] while Opisthorchis viverrini also causes cholangiocarcinoma through a mechanism involving the secretion of toxins in addition to an inflammatory response (table 6) [165]. Schistosoma haematobium mechanism for causing bladder carcinoma is predominately unknown but is thought to involve inflammation.

**Table 6:** A breakdown of trematode and their

corresponding cancers are listed below. Clonorchis sinensis and Opisthorchis viverrini are both common in the same region and an infection is likely from undercooked fish. Cholangiocarcinoma is also common among those infected by Clonorchis sinensis and Opisthorchis viverrini which puts an emphasis on proper diagnostics.

| Trematodes | Cancer |
|---|---|
| Clonorchis sinensis | Cholangiocarcinoma |
| Opisthorchis viverrini | Cholangiocarcinoma |
| Schistosoma haematobium | Bladder carcinoma |

Aspergillus flavus and Aspergillus parasiticus are carcinogenic fungi (table 7) that are better known for their production carcinogenic aflotoxin B1 [166, 167]. Although these fungi can contaminate food supplies with aflotoxin B1, the fungi itself is carcinogenic. These fungi are known to cause hepatocellular carcinoma from mechanisms involving the secretion of aflotoxin B1, 249ser mutations, and potentially causing mutations in p53 [168-174].

**Table 7:** Aspergillus flavus and Aspergillus parasiticus are very similar since they both secrete aflotoxins and are treated with the same kinds of drugs.

| Fungi | Cancer |
|---|---|
| Asperigillus flavus and Asperigillus parasiticus | Hepatocellular Carcinoma |

## CONCLUDING REMARKS

It is clear that the environment can influence the body and that the body interacts with the environment. It is also clear that environmental factors impact the body at a cellular and molecular level. These interactions with the environment can either be a part of healthy cellular growth and metabolism or can be detrimental to healthy cellular progression. There are many carcinogens in the environment and there are likely many more carcinogens that have yet to be discovered.

The carcinogens listed in this review have varying levels of carcinogenic potential. Many of which we are exposed to regularly at a low level and will never actually cause cancer. Although some occupations expose workers to a higher level of environmental carcinogens, there is potential for anyone to develop cancer from significant exposure to these carcinogens. Doctors that better understand the environmental risk factors associated with an occupation where there is a significant chance of being exposed to environmental risk factors may be able to screen for cancer and potentially diagnose cancer earlier. One environmental risk factor that is currently and often flagged is if the patient currently smokes or is around someone that smokes often. One can hypothesize that if doctors could screen patients for environmental causes of cancer early, they may be able to inform the patient of the risks and essentially reduce the opportunity for the cancer to develop.

It is also important for the doctor to recognize if the patient suffering from cancer is still exposed to the same carcinogens that caused the cancer in order to prevent any further damage to the body and allowing the patient an opportunity to detox. In addition to the genomic risk factors associated with cancer from one patient to the next, the doctor should also obtain information regarding the metabolism of the carcinogen as a risk factor. Although that information is not readily available to the public, understanding regarding to elimination of these carcinogens from the body might give light to the individual susceptibility to the carcinogens. This is particularly important for acute exposure of these carcinogens.

Detection and recognition of microbes and trematode infections that cause cancer may also be an early warning for doctors to treat the disease and be mindful that there is an elevated risk of oncogenesis. Awareness of the risk factors associated with cancer causation by understanding the environmental risk factors is important for the doctor but is also important for the people who might be exposed to these carcinogens. Epidemiologist and current government watchdogs and their respected regulation of carcinogens can detect facilities that have an elevated exposure to cancer and warn the general public.

## CONFLICT OF INTERESTS

Author states there are no conflicts of interest.

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