

Occupation and Cancer

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ABSTRACT

Occupational cancer is malignant neoplasm caused by exposures to carcinogenic agents at workplace. It is estimated that one out of every three people will subsequently develop cancer during their lifetime in industrialized countries. Undeveloped countries are also at increasing risk due to transfer of hazardous industries. An occupational cancer does not differ either pathologically or clinically from their counterparts, and treated with the same approaches as similar cancers that are not related to occupational exposures. Whereas, the identification of occupational cancers in public health terms is very important, because all occupational cancers are preventable like other occupational diseases. Physicians generally underestimate the questioning of occupational history of their patients. However, a complete and detailed query of their occupations, and the determination of agents, which they exposed in workplace simply provide us earlier diagnosis, even prevention of occupational cancers. In occupational settings, the most successful measure for the prevention of occupational cancer is the complete removal of known or suspected carcinogenic agents from the workplace. Substitution, changing production process, industrial hygiene practices and education of employees may reduce exposure levels and prevent development of cancer. So that, occupational cancers can be successfully prevented without any harm to industry.

Keywords: Occupational cancer, Occupation, Prevention

ÖZET

Meslek ve Kanser

Mesleki kanser, işyerinde karsinojenik etkene maruziyet sonucu oluşan malign neoplazmdir. Endüstrileşmiş ülkelerde her üç kişiden birinde yaşamları boyunca kanser görülebileceği tahmin edilmektedir. Mesleki kanserlerin patolojileri ya da klinikleri mesleki maruziyete bağlı olmadan gelişen kanserlerden farklı değildir ve aynı şekilde tedavi edilirler. Ancak, mesleki kanserlerin tanısı halk sağlığı açısından çok önemlidir, çünkü bütün mesleki kanserler, diğer bütün mesleki hastalıklarda olduğu gibi, önlenebilir. Hekimler genellikle hastalarının mesleklerini sormayı ihmal ederler. Oysa, tam ve detaylı bir meslek anamnezi ve işyerinde maruz kalınan etkenlerin belirlenmesi, bize mesleki kanserin kolaylıkla erken tanısı hatta önlenmesi imkanını sağlar. Mesleki kanserlerin önlenmesinde en başarılı önlem, bilinen ya da şüphelenilen karsinojenin işyerinden tamamen uzaklaştırılmasıdır. İkame (Zararlı maddenin yerine daha az zararlı olanın kullanılması), üretim prosesinin değiştirilmesi, endüstriyel hijyen uygulamaları ve çalışanların eğitimi maruziyet düzeyini azaltabilir ve kanser gelişimini önleyebilir. Böylece, endüstriye zarar vermeden mesleki kanserler önlenebilir.

Anahtar Kelimeler: Mesleki kanser, Meslek, Önleme

INTRODUCTION

The cancer is a multifactorial disease resulting from genetic, environmental exposure, and lifestyle factors. Occupational cancer is malignant neoplasm caused by exposures to carcinogenic agents at the workplace.¹ Many workers are unaware of those potential hazards in their workplace, which makes them more vulnerable to cancer. Nearly 5-15% of cancers are attributed to occupational exposures, but for bladder cancer this value may reach as high as 20%.^{1,5} In industry, there are many potential exposures to carcinogens that can cause cancer. It is estimated that one out of every three people will subsequently develop cancer during their lifetime in industrialized countries.^{2,5,6} Although 885 chemicals are estimated to be possible carcinogenic agents, only 22 chemicals among them are group I (carcinogenic to humans) carcinogenic agents.⁵

The first occupational cancer was reported in 1775 by Percival Pott describing scrotal cancer in children climbing up narrow chimneys that were still hot and sweeping them.^{1,3,7} Pott clearly identified soot as the cause of scrotal cancer in London chimney-sweeps. But, an experimental model for soot carcinogenesis was established almost 150 years after the original epidemiological data of Pott.⁸ It was not until the 1940s that a PAH, benzo[a]pyrene, have ability to induce skin cancers in laboratory animals, and it is an ingredient of soot.^{3,9}

An occupational cancer does not differ either pathologically or clinically from their counterparts, and treated with the same approaches as similar cancers that are not related to occupational exposures.^{1,5} The identification of occupational cancers in public health terms is very important, because all occupational cancers are preventable like other occupational diseases with appropriate industrial hygiene practices and legislations.^{2,3,5,10}

MECHANISMS OF CARCINOGENESIS

Carcinogenesis is considered to have at least three stages: initiation, promotion and progression. Initiation is an irreversible mutation in the DNA caused by an interaction with a carcinogenic agent. This mutation is necessary, but not sufficient, for the development of cancer. Several occupational agents

are associated with p53 mutations such as ultraviolet light, vinyl chloride, and asbestos.^{1,3,11} Promotion (epigenetic mechanism) consist of particular processes facilitating cancer development. In this phase, mutated cells are stimulated for proliferation.³ Progression is the development of malignant neoplasms from benign tumors.^{1,11}

Occupational carcinogenic agents may increase the risk of cancer development at the stage of initiation by causing mutations in DNA or at the promotion phase by various "epigenetic" mechanisms, which do not involve DNA damage, including increased cell proliferation. Almost all occupational carcinogens are demonstrated to be mutagenic agents, and therefore occupational cancers appear to be started at the stage of initiation, and multiple mutations are required for the development of cancer. This explains the long "latency" period of occupational cancers. Besides, further required mutations may never occur after occupational exposures, and cancer may never develop. On the other hand, some occupational exposures such as benzene, arsenic, phenoxy herbicides are not mutagens, but seems to act as promoting agents. Therefore latency period may be shorter than the initiating occupational carcinogenic agents.^{1,2,5}

Occupational cancers have a long latency period that is not less than 10-15 years and may be much longer such as 40-50 years observed in the case of asbestos-related cancers. Therefore, the presentation of some occupational cancers may appear in the retirement period.^{1,5}

DIAGNOSIS OF OCCUPATIONAL CANCERS

The characteristics of occupational carcinogenic agent and the long latency period make the recognition of occupational carcinogens very difficult and lead to uncertainty over which occupational exposures cause cancer.^{2,3} A worker may be exposed to many different carcinogens in workplace, and he could not remember the causative agent, since exposure may be long past. Therefore it is difficult to find the responsible agent, and population-based epidemiological approaches may be required.⁵

There are some characteristics that may help us to differentiate occupational cancers related to work.

For instance, some occupational cancer for a group of workers may be observed by an obvious excess of cancers than normally expected in general population. Workers may talk about many cancer cases at work.¹ It is easier to detect association of occupational cancer with exposure in case of unusual cancers.⁵ Those types of uncommon cancers called 'Signal Tumors' are related with specific occupation such as a liver angiosarcoma may be an indicative of past exposure history to vinyl chloride monomer.¹ However, occupational cancers are frequently observed in more common histological types. Therefore, those type of more common cancers, such as squamous cell carcinoma of lung, are very difficult to identify since they may be due to asbestos, arsenic, nickel.⁵ A younger age at presentation with cancer may suggest an occupational cancer particularly for tumors commonly observed in later stages of life such as urothelial tract cancers under 50 years.¹

OCCUPATIONAL CARCINOGENIC AGENTS

Specific scientific methodologies are used for the detection of occupational causes of cancer: (1) epidemiological studies, (2) animal studies, and (3) laboratory studies performed on the biological features of the agents.⁵

The International Agency for Research on Cancer (IARC) is a scientific agency to identify and evaluate carcinogenic hazards of physical, chemical or biological agents to humans. In the monographs of IARC, some 885 agents have been evaluated.^{1,2,5} However, only 22 agents are found to be occupational carcinogenic agents. Table 1-2 shows occupational exposures known or strongly suspected to cause cancer in humans.

Some important agents have not been assessed by IARC such as ionizing radiation and electromagnetic fields. Our current knowledge of occupational exposures and cancer relationship is not complete, and no clear evidence exist on exposed workers for many experimental carcinogenic agents. On the other hand, we have extensive evidences of increased cancer risk in particular industries and occupations, although we have no specific etiological agents.²

OCCUPATIONAL CANCERS

LUNG CANCER

The major cause of lung cancer is cigarette smoking. Lung cancer due to occupational exposures ranges from 3-40%. However, it is very difficult to differentiate occupational causes from lung cancer associated with smoking and several types of lung cancer are the combination of occupational factors and smoking. Furthermore, the long latency period makes the determination of casual relationship even more difficult. Nevertheless, both non-occupational and occupational lung cancer is a preventable disease.¹¹ The exposure to asbestos, radon, chloromethyl ethers, PAHs, nickel chromium, and inorganic arsenic are all independent risk factors from smoking for the development of lung cancer. However, smoking synergistically enhanced the effects of those occupational carcinogens such as asbestos.^{3,5,12}

MESOTHELIOMA

Mesotheliomas are classisical example of "signal tumors". Because almost all cases of malignant mesothelioma are related to asbestos or erionite exposure. Mesothelioma has a long latency, generally 20 to 60 years from the first asbestosis exposure.^{3,11,13,14}

NONMELANOMATOUS SKIN CANCERS

The primary causes of skin cancer in industry are ultraviolet radiation (solar), PAHs, arsenic, and ionizing radiation. Unna in 1890 reported changes in the skin of sailors, and shown increased skin cancers due to prolonged exposure to the sun.^{2,3,9,15-18} Percival Pott shown the increased incidence of scrotal cancer in chimney sweeps in 1775, and PAHs, which was demonstrated to be the real cause of scrotal cancer later in 1940s. Skin cancers may also related with arsenic ingestion, inhalation and from skin contact.^{3,9} Ionizing radiation ,currently, is not responsible for skin cancers due to strict industrial controls and occupational legislations.^{2,3,9,15}

BLADDER CANCER

It is estimated that one fifth of all bladder cancers may result from occupational exposures. Rehn

Table 1. Chemicals, groups of chemicals or mixtures for which exposures are mostly occupational (excluding pesticides and drugs)*: Group 1- Carcinogenic to humans.²

Exposure	Human target organ(s)	Main industry/use
4-aminobiphenyl	Bladder	Rubber manufacture
Arsenic and arsenic compounds**	Lung, skin	Glass, metals, pesticides
Asbestos	Lung, pleura, peritoneum	Insulation, filter material, textiles
Benzene	Leukemia	Solvent, fuel
Benzidine	Bladder	Dye/pigment manufacture, laboratory agent
Beryllium	Lung	Aerospace industry/metals
Bis(chloromethyl)ether	Lung	Chemical intermediate/ by-product
Chloromethyl methyl ether (technical grade)	Lung	Chemical intermediate/by-product
Cadmium and cadmium compounds	Lung	Dye/pigment manufacture
Chromium compounds	Nasal cavity, lung	Metal plating, dye/pigment manufacture
Coal-tar pitches	Skin, lung, bladder	Building material, electrodes
Coal-tars	Skin, lung	Fuel
Ethylene oxide	Leukemia	Chemical intermediate, sterilant
Mineral oils, untreated and mildly treated	Skin	Lubricant
Mustard gas (sulphur Mustard)	Pharynx, lung	War gas
2-naphthylamine	Bladder	Dye/pigmet manufacture
Nickel compounds	Nasal cavity, lung	Metallurgy, alloys, catalyst
Shale-oils	Skin	Lubricants, fuels
Soots	Skin, lung	Pigments
Talc containing asbestiform fibers	Lung	Paper, paints
Vinyl chloride	Liver, lung, blood vessels	Plastics, monomer
Wood dust	Nasal cavity	Wood industry

* Evaluated in the IARC Monographs, Volumes 1-6 (1972-1995) (excluding pesticides and drugs)

** This evaluation applies to the group of chemicals as a whole and not necessarily to all individual chemicals within the group.

described a high incidence of bladder cancers among aniline dye workers in 1895. The first occupational bladder cancers in the United States were reported among workers exposed to β -naphthylamine or benzidine and alpha-naphthylamine in 1934. The incidence of bladder cancer is the highest in industrialized countries, and the incidence in less developed countries is about 70% lower than in the United States.^{2,3,11,19,20}

A substantial evidence exist for an increased risk of bladder cancer among plumbing, tobacco, metal, heating and air conditioning workers.^{11,21-23} The

latency period between exposure and bladder cancer was estimated to be about 20 years.³

BRAIN CANCER

Occupationally-related brain cancer is not clearly reported. However, ionizing radiation is a strong risk factor for brain cancer. Some reports shown that brain cancer may increase among workers exposed to polyvinyl chloride (PVC), and electrical, electronics, and petrochemical workers.^{2,11,24-28}

Table 2. Chemicals, groups of chemicals or mixtures for which exposures are mostly occupational (excluding pesticides and drugs): Group 2A- Probably carcinogenic to humans.²

Exposure*	Human target organ(s)	Main industry/use
Acrylonitrile	Lung, prostate, lymphoma	Plastics, rubber, textiles, monomer
Benzidine-based dyes	–	Paper, leather, textile dyes
1,3-Butadiene	Leukemia, lymphoma	Plastics, rubber, monomer
<i>p</i> -Chloro- <i>o</i> -toluidine and its strong acid salts	Bladder	Dye/pigment manufacture, textiles
Creosotes	Skin	Wood preservation
Diethyl sulphate	–	Chemical intermediate
Dimethylcarbamoyl Chloride	–	Chemical intermediate
Dimethyl sulphate	–	Chemical intermediate
Epichlorohydrin	–	Plastics/resin monomer
Ethylene dibromide	–	Chemical intermediate, fumigant, fuels
Formaldehyde	Nasopharynx	Plastics, textiles, laboratory agent
4,4'-Methylene-bis- 2-chloroaniline (MOCA)	Bladder	Rubber manufacture
Polychlorinated biphenyls	Liver, bile ducts, Leukemia, lymphoma	Electrical components
Silica	Lung	Stone cutting, mining, glass, paper
Styrene oxide	–	Plastics, chemical intermediate
Tetrachloroethylene	Oesophagus, lymphoma	Solvent, dry cleaning
Trichloroethylene	Liver, lymphoma	Solvent, dry cleaning, metal
Tris(2,3-dibromopropyl) phosphate	–	Plastics, textiles, flame retardant
Vinyl bromide	–	Plastics, textiles, monomer
Vinyl fluoride	–	Chemical intermediate

* Evaluated in the IARC Monographs, Volumes 1-6 (1972-1995) (excluding pesticides and drugs)

THYROID CANCER

Ionizing radiation is a well-documented cause of thyroid cancer. Epidemiological studies of Atomic Bombing to Hiroshima and Nagasaki, Chernobyl nuclear reactor incident, and Marshall Islands following aboveground detonation of an atomic bomb in 1954 clearly showed that ionizing radiation increase the risk of thyroid cancer.¹¹

SINONASAL CARCINOMAS

Several occupational exposures are related to sinonasal carcinomas. Especially, some studies clearly showed that wood dust increase the risk of sinonasal cancer 15-45 fold.^{29,30} Sinonasal cancers

have been also shown in female workers exposed to radium used for painting dials of watches and in radon chemists.³ Furthermore, exposure to nickel compounds in refining processes, and hexavalent chromium in pigment manufacturing may also increase the risk of sinonasal cancer.¹¹

LARYNGEAL CANCER

Asbestos exposure in miners, shipyard workers, asbestos product manufacturers, and insulators has been shown to increase laryngeal cancer incidence.^{3,31-34} Occupational exposure to solvents was associated with an increased risk of hypopharyngeal/laryngeal cancer.³²⁻³⁴

ESOPHAGEAL CANCER

Some studies showed that the risk of esophageal cancer is high in workers exposed to tetrachloroethylene, mustard gas, silica dust, asbestos, combustion products, sulphuric acid, and ionizing radiation.^{2,11,35} Workers in metal-grinding operations, metal polishers and platers, and drycleaners have been reported to be at increased risk of esophageal cancer.¹¹

HEPATIC ANGIOSARCOMA

Liver angiosarcoma has a strong causal relationship with vinyl chloride and arsenic exposure such as arsenical pesticides, arsenic-contaminated wine.^{2,3,11,27,36-38}

KIDNEY CANCER

Several studies reported that kidney cancer is associated with exposure to chlorinated aliphatic hydrocarbons.^{2,11,39} Increased risk of renal cell cancer has been shown for dry-cleaning workers, painters, iron and steel industry workers, coke oven workers, firefighters, asbestos-exposed workers, textile workers, gasoline station attendants, nickel-smelting workers, lead-smelter workers, oil refinery workers, truck drivers, electric power utility workers, farmers, and printers.^{11,40}

PANCREATIC CANCER

Occupational exposures to nickel, chlorinated hydrocarbon solvents, chromium, polycyclic aromatic hydrocarbons (PAHs), organochlorine insecticides, silica dust, and aliphatic and aromatic hydrocarbons may cause pancreatic cancer.^{2,11,41,42} An elevated pancreatic cancer risk among dry cleaners and among workers exposed to cadmium was demonstrated in independent meta-analyses. Elevated pancreatic cancer mortality was also shown in cohort studies among workers processing vinyl resins and polyethylene, producing chlorohydrin with potential exposure to ethylene dichloride and bis-chloroethyl ether (BCEE), and manufacturing DDT, leather tannery workers.^{11,43}

COLORECTAL CANCER

Increased colon cancer has been reported among workers exposed to mineral oils used in printing,

cellulose acetate fiber and polypropylene and textiles are at increased risk of colorectal cancer.^{2,11,44} Some studies shown that higher incidence among the most sedentary compared to the most active occupations.^{2,45,46}

SOFT TISSUE SARCOMA

Liver angiosarcoma is considered as a “signal” cancer of occupational etiology. Vinyl chloride is a well-known cause of liver angiosarcoma. Ionizing radiation is an established cause of soft tissue sarcomas. Dioxin has been shown to be associated with occupational soft tissue sarcomas.^{2,11,47}

HEMATOLOGIC CANCERS

LEUKEMIA

Acute nonlymphocytic leukemia (ANLL) and chronic myelogenous leukemia (CML) have been linked to occupational exposure, and CML has been called an industrial disease. Radiation is the most conclusively known leukemogenic factor in human. Maximal risk occurs 4-7 years after exposure to ionizing radiation. Workers at risk secondary to exposure to ionizing radiation include radiologists, radiation therapists, nuclear medicine physicians and radiation technicians working with X-rays in the medical workplace, workers in nuclear power plants, military personnel working in nuclear tests, and uranium miners.^{3,48,49}

Epidemiologic studies have demonstrated significant increase in leukemia incidence in workers with past exposure to benzene.^{2,3,11,50} It has been shown that there is a 21-fold increased death risk from leukemia in workers exposed to benzene for 5 years or more. Ethylene oxide organic hydrocarbons exposure has been associated with an increased risk of leukemia. The increased risk of leukemia after exposure to electromagnetic fields is unclear.^{3,11,51,52}

LYMPHOMA

Several reports shown that chemical industry workers and farmers in Scandinavia, Europe, North America, Australia, and New Zealand are at risk for non-Hodgkin's lymphoma. Some studies reported that paper workers, chemists, rubber workers, and firefighters are at increased risks of lymphoma.

Some chemicals such as phenoxyacetic acid herbicides, dioxins, and benzene have been suggested as causative agents for lymphoma.^{2,11,53-55}

MULTIPL MYELOMA

An association between multiple myeloma and ionizing radiation exposure has been observed in the survivors of the atomic bombings of Hiroshima and Nagasaki. Some epidemiologic studies suggest an association of exposure to dioxin, benzene and multiple myeloma. Exposure to petroleum products, heavy metals, pesticides, diesel-engine exhaust and asbestos is concerned, but those studies are small, and not conclusive.^{2,3,56,57}

DISCUSSION

High labor costs and strict legislations in industrialized countries cause the transfer of hazardous industries to the developing countries due to insecure status of workers, the lack of legislative protection, low wages and unemployment in those regions.^{2,58,59} Therefore, the incidence of occupational cancer has not been reduced worldwide, since occupational exposures have been transferred to the developing world. The industrial activity is fragmented in the form of small industries in developing world, and these small production facilities have been using old machineries in unsafe buildings. Employers in those places cannot even provide safe environmental workplace conditions and precautions such as personal safety equipments due to their limited financial resources. Furthermore, workers have poor training and education in those facilities. These small enterprises are generally scattered, and health and safety enforcement agencies have difficulties to inspect those facilities.²

Primary prevention is to prevent the onset of a disease. It is the most important and easiest way to deal with any kind of disease including malignant disorders. In occupational settings, the most successful measure for the prevention of occupational cancer is the complete removal of known or suspected carcinogenic agents from the workplace.^{2,60} However, the determination of causative relationship between cancer and carcinogenic agent requires a long latency period. In several instances, industrialized countries missed their chance to pre-

vent occupational cancers. However, those experiences may be a great chance for developing countries to take earlier precautions for preventing occupational cancers.^{2,61}

Substitution, in many cases, is another major method for prevention, since complete removal of a carcinogenic agent is mostly not possible due to economical or political judgements.^{2,59} In this manner, changing production process as well as industrial hygiene practices may alternatively reduce exposure levels. Education of employers, employees and managers is also an essential steps for prevention. Risk based legislations and social policies support these training approaches.¹¹

Physicians generally underestimate the questioning of occupational history of their patients. However, a complete and detailed query of their occupations, and the determination of agents, which they exposed in workplace simply provide us earlier diagnosis, even prevention of occupational cancers. Furthermore, the awareness of occupational physicians about the industrial cancer risks at pre-employment or periodical examinations is also crucial in the prevention of occupational cancers.⁶²

In conclusion, the occupational cancer prevention measurements in industrialized world has shown us that occupational cancers can be successfully prevented without leading our industry to collapse, and several different approaches is highly possible by using the experiences of developed countries if satisfactory legislations and control of occupational carcinogenic agents are provided.

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