REVIEW

Occupational Cancers with Chemical Exposure and their Prevention in Korea: A Literature Review

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Abstract

The usage and types of chemicals being developed, with diversified new exposure of workers, are of natural concern to occupational disease. In Korea, with industrialization, application of many chemicals has increased. A large proportion of mortality and disease is due to cancer, and the causal hazardous agents include chemical agents, like heavy metals and so on. Due to the long latency period with malignancies and the fact they are usually found after workers' retirement, it is suggested that management policies must be established to prevent occupational cancers occurring among workers in Korea. To give a general description about the efforts to prevent the occupational cancer with exposure to chemicals, articles on the trends of occupational cancers were reviewed and summarized with related research and efforts for prevention in Korea. It is important to improve the understanding of occupational cancer and help to maintain sustainable and appropriate measures to guarantee workers safety and health.

Keywords: Occupational cancer - chemicals - prevention - Korea

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Introduction

The usage and types of chemicals become developed, specialized, diversified, and newly exposed workers are concerning to occupational disease. In Korea, with the industrialization, the uses of many chemicals have increased since the 1970s. As a consequence, there have been increasing the occupational diseases caused by poisonous chemicals, such as heavy metal poisoning, solvent poisoning and occupational cancer from late 1980s. Many actions have been taken for prevention by the government, employers and employees or unions. In the 1990s most chemical related diseases and pneumoconiosis have rapidly decreased due to improving work environment. Occupational cancers are increasing because of their long latency, although the use of carcinogenic substances are reduced, limited, and even banned (Kang and Kim, 2010).

To analyze the characteristics of the occupational diseases, we compensated with the Industrial Accident Compensation Insurance that is operated by the Korea Labor Welfare Corporation (KLWC). About 1.0% of all diseases were cancer, and the causal hazardous agents were chemical agents, heavy metals and so on. It was suggested that a management policy must be established to prevent occupational cancers occurring among workers in Korea (Ahn et al., 2004).

The proportion of cancer as a cause of death in Korea has been continuously increasing. In 2000, about 24% of deaths were caused by cancer. Occupational exposure would have contributed to the development of some cancers. It would have accounted for more than 2,000 cancers in a year if 4% of all cancer or 10% of lung cancer was regarded as arising from the work environment. However, occupational cancer has not been reported as much as expected. Many cases of occupational cancers have been reported such as lung cancer due to exposure to asbestos, chromium, exhaust gases, coke oven emissions, and silica, as well as leukemia due to exposure to benzene or other solvent and bladder cancer arising from exposure to benzidine salts. Special attention is required to detect occupational cancer due to their long latency period and the fact they are usually found after retirement (Kang et al., 2001). Chromium, asbestos and cokes were the most frequent exposed agents. The commonest exposure agent in the ascertained cancer cases was asbestos and cokes. The occupational cancer surveillance system using data linkage analysis on the workers exposed to hazardous agents was the most feasible and efficient method in Korea (Lee et al., 1999).

Approximately 2% to 8% of all cancers are thought to be due to occupation. In addition, occupational and environmental cancers have their own characteristics, e.g., specific chemicals and cancers, multiple factors, multiple causation and interaction, or latency period. Concerning carcinogens, asbestos/silica/wood dust, soot/polycyclic aromatic hydrocarbons [benzo(a) pyearene], heavy metals (arsenic, chromium, nickel),

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aromatic amines (4-aminobiphenyl, benzidine), organic solvents (benzene or vinyl chloride), radiation/radon, or indoor pollutants (formaldehyde, tobacco smoking) are mentioned with their specific cancers, e.g., lung, skin, and bladder cancers, mesothelioma or leukemia, and exposure routes, rubber or pigment manufacturing, textile, painting, insulation, mining, and so on (Yang, 2011). A research was performed to evaluate the occupational relationship on 190 cases of cancer selected out of 622 cases of cancer. The cancer developing organ in the order of relative frequency was lung, followed by liver, urinary bladder and skin for male, liver, followed by lung, skin and urinary bladder for female. There were two cases of suspected occupational relationships in the lung cancer cases. Occupational cancer is likely to increase in the near future, so the efforts to detect occupational relationships with cancer should be continued (Bae et al., 1999). In Korea, heavy and chemical industries underwent rapid growth during the 1970s. The first occupational cancer was mesothelioma due to asbestos, reported in 1993 (Kim et al., 2010). The Occupational Safety and Health Research Institute (OSHRI) of the Korea Occupational Safety and Health Agency (KOSHA) has conducted epidemiologic investigations and research on occupational cancer since 1992. These investigations showed that various kinds of occupational cancers, such as mesothelioma, lung cancer, leukemia, non-Hodgkin's lymphoma, and bladder cancer.

The proportion of carcinogen-exposed workers was measured in a nationwide survey, first conducted in Korea in 1994, those who use the chemical in the workplace. Efforts have been made to obtain more information on the prevalence of carcinogen-exposed workers in Korea. According to the electronic database of claims for occupational cancer of Korea Workers' Compensation and Welfare Service (COMWEL) electronic database, among claims for occupational cancer, the most common was digestive cancer. On the other hand, the highest approval rate was for mesothelioma claims, followed by respiratory cancer, lymphoid or hematopoietic cancer. By industry, claims were most common in manufacturing, but the approval rate was highest in mining and quarrying (Lee et al., 2011). At the request of COMWEL, OSHRI has investigated workers and the workplaces that are involved in claims of occupational disease to evaluate work-relatedness since 1992. The most common causative agent of lung cancer was asbestos, followed by hexavalent chromium, polycyclic aromatic hydrocarbons (PAHs), and crystalline silica. Asbestos exposure was related to all cases of malignant mesothelioma. Other types of respiratory cancer that have been investigated include laryngeal cancer, nasal cancer, and nasopharyngeal cancer (Kang et al., 2001).

An occupational disease surveillance system have been established to monitor trends in occupational disease and to identify sentinel cases since 1999, supported by OSHRI. In Korea, two types of surveillance systems are used. The first is the regional occupational surveillance system for preventing occupational hazards at the local level. The second is a nation-wide occupational surveillance system for specific target diseases, such as occupational lung cancer, occupational asthma, and malignant mesothelioma. It is difficult to predict the trend for the future incidence of occupational cancer, but it could demonstrate that occupational respiratory cancer has increased during the last 10 to 20 year. Important programs and regulations are in place to prevent and control occupational cancer, such as banning all forms of asbestos, workplace exposure monitoring, and occupational disease surveillance systems. Indeed, more efforts to advance the systems for the prevention and management of occupational cancer are needed in response to changing technology and work environments.

In this review, we summarize the trends of occupational cancer in Korea, researches about it and our efforts to prevent. It is important to improve the understanding of the occupational cancer and help to keep a sustainable, appropriate measures for workers safe and health against it.

Methods

This review study was conducted through an extensive review of the literature. Literature review techniques were used to find relevant articles in South Korea with industrial hygiene, in vitro assay, in vivo study and epidemiologic literature.

Extensive internet searching was used as the primary tool for this review. Various websites including Google Scholar (http://scholar.google.com), ScienceDirect (www.sciencedirect.com), and PubMed (http://www.ncbi.nlm.nih.gov/pubmed/) were also searched. Also, we searched the following databases: Elsevier, SpringerLink, EMBASE, and Wiley Online Library, using the combinations of the following key words; the ending date of searched publications was December 2012.

Searches were conducted using keywords similar to the following: occupational cancer, chemicals AND worker OR environment OR occupation AND health. These searches yielded more than 100 references. The references were reviewed further for information regarding its prevention. As a result of this further examination, the 82 citations were deemed relevant to this study and are included as references in this report.

And we discussed the future prospect of occupational cancer in Korea, the significance with preventive efforts for workers health

Types of Occupational Cancers with Industrial Chemicals

The Korean Occupational Exposure Limits (KOEL) data included number of industry and workers exposed, type of carcinogen and their exceeded ratio, type and size of industry in each year. The most common carcinogen exceeding KOEL were found to be formaldehyde, benzene, ethylene oxide and chromium (VI). The carcinogens with the highest level of over-exposure were in the order of formaldehyde, benzene, ethylene oxide and asbestos. Benzene, ethylene oxide and chromium (VI) were the most frequently over-exposed carcinogen with the highest level (Phee, 2011). The main carcinogens were asbestos, crystalline silica, radon, polyaromatic hydrocarbons

(PAHs), diesel exhaust particles, chromium, and nickel (Leem et al., 2010).

Benzene is the most important cause of occupational leukemia in Korea. Considering the estimated PAF in this study, the annual number of occupational LHP cancer (51 cases during 10 year period), might be underreported within the compensation system (Kim et al., 2010). Benzene has been used in various industries as glues or solvents in Korea. Claims for compensation of hematopoietic diseases related to benzene have been rising even though the work environment has been improved. It was reviewed the claimed cases investigated by KOSHA between 1992 and 2000. Korean workers were not highly exposed to benzene and the level of exposure was mostly less than 1 ppm. However, there might be an excessive risk of hematopoietic disorders due to relatively high past exposure. The OEL value of benzene was amended to 1 ppm from 10 ppm in 2002 and was effective since July 2003 (Kang et al., 2005).

Asbestos causes several asbestos related diseases (ARDs). Not only occupational asbestos exposure but also environmental asbestos exposure can cause ARDs. In Korea compensation for workers with ARDs has been provided by workers' compensation. The first wave of asbestos problems arose from occupational exposure directly involving asbestos production, the second wave arose from usage of asbestos products, and the third wave would be related to asbestos ubiquitous in the environment (Kang et al., 2012). The asbestos textile industry is characterized by the highest asbestos ambient air concentration of those workers who have suffered from high incidence of lung cancer, malignant mesothelioma, and other ARDs. High lung cancer and malignant mesothelioma mortality rates among asbestos textile workers were established. A large number of environmentally exposed residents as well as severity of health problems among asbestos textile workers would cause huge social problems (Kang et al., 2009). Asbestos has been widely used in Korea since the 1970s, therefore, a large number of Korean workers, especially who engaged in the industries of asbestos textiles, shipbuilding, or construction, have been exposed to asbestos occupationally. It has also been revealed that about 60% of malignant mesothelioma patients have experiences to be exposed to asbestos in the past. However, mesothelioma has increased greatly in recent years in Korea, and it is expected to increase continuously considering asbestos consumption, as it happened in other countries which used large amounts of asbestos (Kim et al., 2009). To report a case of lung cancer caused by long-term asbestos exposure in a shipyard, the biopsy samples and bulk sample using a transmission electron microscope (TEM) equipped with an energy dispersive X-ray analyzer (EDX). The concentration asbestos fibers in the workplace exceeded the occupational exposure limits of asbestos. These findings strongly suggest that this patient's lung cancer was related to the long-term asbestos exposure (Yoon et al., 2004). Compensation for asbestos-related cancers occurring in occupationally-exposed workers is a global issue; this is also an issue in Korea. 60 cases of asbestos-related occupational lung cancer and mesothelioma that were compensated during 15 year; from 1993 (the year the first case was compensated) to 2007. The meaningful duration of asbestos exposure for lung cancer and mesothelioma cases was 19.2 and 16.0 year, respectively. The meaningful latency period for lung cancer and mesothelioma cases was 22.1 and 22.6 year, respectively. The major industries associated with mesothelioma cases were shipbuilding and maintenance and manufacture of asbestos textiles. The major industries associated with lung cancer cases were shipbuilding and maintenance, construction, and manufacture of basic metals. Considering the current Korean use of asbestos, the number of compensated cases in Korea is expected to increase in the future but not as much as developed countires (Ahn et al., 2009). The magnitude of asbestos-related health problems in Korea has been underestimated due to under-diagnosis, incomplete reports, and shorter duration of exposure. A nationwide surveillance system for asbestos exposure and malignant mesothelioma should therefore be implemented (Lee et al., 2009). Although asbestos mining and manufacturing has started in Korea since the 1920s, it was not until the 1980s that the broader social democratic movement heightened public awareness of the health problems associated with exposure to asbestos.

It was reported the limited evidence of carcinogenic effect of welding fumes to human and in vitro tests, but not known the biochemical mechanism (Rim et al., 2007). The soluble hexavalent chromium Cr (VI) used in industrial welding is an environmental contaminant widely recognized to act as a carcinogen, mutagen and teratogen towards humans and animals. The carcinogenic potential of metals is a major issue in defining human health risk from exposure (Sellappa et al., 2010). According to the toxicological and epidemiological studies, hexavalent chromium is associated with increase of lung cancer risk. Genotoxic effects, such as chromosomal aberrations, and cellular oxidative DNA damage by reactive oxygen species (ROS) produced by hexavalent Cr exposure may play an important role in its carcinogenesis (Maeng et al., 2003). In conclusion, the lung case could be associated with his task including welding, gousing, and this association could be attributed to carcinogenic potential of the nickel and chromium in the fume (Yi et al., 2000).

Direct Black 38, a kind of benzidine-based azo dye, is widely used as a dye for fabric, leather, cotton, cellulosic material, paper, wool, silk, and so on. Benzidine-based azo dyes are proven as a mutagen and linked to bladder cancer (Won et al., 1996).

Inorganic arsenic (As) is considered a human carcinogen because it is associated with cancers of skin, lung, liver and bladder in exposed populations. Arsenic (As) is a known human carcinogen; however, very little is known about the health consequences of occupational exposure to As (Vuyyuri et al., 2006).

The contents of Table 1 are showing the industrial carcinogens classified with occupational safety and health act in Korea.

Lung cancer is the leading cause of cancer death, and the incidence of malignant mesothelioma is expected to increase sharply in the near future. Although information about lung carcinogen exposure is limited, it is estimated

Table 1. Industrial Carcinogen Classified with Occupational Safety and Health Act in Korea*

Class	Chemicals	CAS No.	Class	Chemicals	CAS No.	Class	Chemicals	CAS No.	Chemicals	CAS No.
1A	Nickel	7440-02-0	1B	Gasoline	8006-61-9[g]	2	Hydrogen peroxide	7722-84-1	Ethyleneglycol monobutyl etheracetate	112-07-2
	(Soluble compounds, as Ni, Insoluble Inorganic compounds, as Ni)			Refractory ceramic fibers (Respirable fibers)	-[h]		Mineral wool fiber	-[k]	Ethyl benzene	100-41-4
	Nickel carbonyl, as Ni	13463-39-3		4-Nitrodiphenyl	92-93-3		Naphthalene	91-20-3	Ethyl acrylate	140-88-5
	4,4'-Methylenebis (2-chloroaniline)	101-14-4		Nitrotoluene (o, m, p-isomers)	88-72-2		Lead (Inorganic dust & fumes, as Pb)	7439-92-1	Chlorinated camphene	8001-35-2
	Wood dust (Western red cedar, Inhalable fraction)	-		2-Nitropropane	79-46-9		n-Butyl glycidyl ether (BGE)	8/7/30	Allyl chloride	107-05-1
	Wood dust (All other species, Inhalable fraction)	-		Dinitrotoluene	25321-14-6		N-Vinyl-2-pyearrolidone (NVP)	88-12-0	Ethyl chloride	75-00-3
	Beryllium & Compounds	7440-41-7		Dimethylnitrosoamine	62-75-9		n-Phenyl-β-naphthyl amine	135-88-6	Vanadium pentoxide	1314-62-1
	β-Naphthylamine	91-59-8		Dimethyl carbamoylchloride	79-44-7		Nickel (Metal)	7440-02-0	(Respirable fraction or fume)	
	Benzene	71-43-2		Dimethylformamide	68-12-2		Nitromethane	75-52-5	Methyl iodide	74-88-4
	Benzo(a) pyearene	50-32-8		1,1-Dimethylhydrazine	57-14-7		Nitrobenzene	98-95-3	Welding fumes and dust	-
	Benzidine	92-87-5		1,2-Dibromoethane	106-93-4		Dimethy1aniline (N,N-Dimethylaniline)	121-69-7	Titanium dioxide	13463-67-7
	1,3-Butadiene	106-99-0		Dianisidine	119-90-4		Dimethy1aminobenzene	1300-73-8	Isophorone	78-59-1
	Butane	106-97-8		Diazomethane	334-88-3		Diethanolamine	111-42-2	Carbaryl	63-25-2
	Arsenic & Soluble compounds, as As	7440-38-2		3,3-Dichlorobenzidine	91-94-1		Di(2-ethylhexyl)phthalate	117-81-7	Carbon black	1333-86-4
	bis-(Chloromethyl)ether	542-88-1		1,2-Dichloroethane	107-06-2		Dieldrin	60-57-1	Catechol	120-80-9
	Silica (Crystalline quartz) (Respirable fraction)	14808-60-7		Rubber solvent (Naphtha)	8030-30-6[i]		Dioxane (Diethyl dioxide)	123-91-1	Captan	133-06-2
	Silica (Crystalline cristobalite) (Respirable fraction)	14464-46-1		4,4'-Methylenedianiline	101-77-9		Diuron	330-54-1	Kerosene	8008-20-6
	Silica (Crystalline tridymite) (Respirable fraction)	15468-32-3		β-Propiolactone	57-57-8		Dichlorodiphenyltrichloroethane (D.D.T)	50-29-3	Cobalt (Metal dust & fume)	7440-48-4
	Silica (Crystalline tridymite) (Respirable fraction)	1317-95-9		Benzoyl chloride	98-88-4		Dichloromethane	75-09-2	Cumene	98082-8
	Ethylene oxide	75-21-8		Benzotrichloride	98-07-7		Dichloro acetic acid	79-43-6	Crotonaldehyde	4170-30-3
	Cadmium oxide (Production)	1306-19-0		Vinyl bromide	593-60-2		Dichloroacetylene	7572-29-4	Chlorodiphenyl (54% Chlorine)	11097-69-1
	Arsenic trioxide (Production)	1327-53-3		VM & P Naphtha	8032-32-4[i]		1,1-Dichloroethylene	75-35-4	Chlorobenzene	108-90-7
	Arsine	7784-42-1		Carbon tetrachloride	56-23-5		Dichloroethylether	111-44-4	Chloroacetaldehyde	107-20-0
	Asbestos (All forms)	-[a]		Antimony trioxide (Production)	1309-64-4		Dichloropropene	542-75-6	Chloroform	67-66-3
	Strontium chromate	6/3/93		Stoddard solvent	8052-41-3[i]		Diphenylmethanediisocyanate	101-68-8	Chlordane	57-74-9
	4-Aminodiphenyl	92-67-1		Silicon carbide	409-21-2[j]		Dihydroxybenzene	123-31-9	Tetranitromethane	509-14-8
	Lead arsenate, as Pb(AsO4)2	7784-40-9		Acrylonitrile	107-13-1		Lindane	58-89-9	Tetramethyl lead, as Pb	75-74-1
	Nickel subsulfide	12035-72-2		Acrylamide	79-06-1		Methyl tert-butyl ether (MTBE)	1634-04-4	Tetraethyl lead, as Pb	78-00-2
	L.P.G (Liquified petroleum gas)	68476-85-7[b]		Ethylene glycol methyl ether acetate	110-49-6		Methyl chloride	74-87-3	1,1,2,2-Tetrachloroethane	79-34-5
	Ethanol	64-17-5[c]		Ethylenimine	151-56-4		Methyl hydrazine	60-34-4	Tetrahydrofuran	109-99-9
	o-Toluidine	95-53-4		1,2-Epoxypropane	75-56-9		Molybdeunum (Soluble compounds)	7439-98-7	Toluene-2,4-diisocyanate (TDI)	584-84-9
	Uranium (Soluble & insoluble compounds, as U)	7440-61-1		2,3-Epoxy-1-propanol	556-52-5		Benomyl	17804-35-2	Toluene-2,6-diisocyanate (TDI)	91-08-7
	Cadmium and compounds, as Cd	7440-43-9		Benzyl chloride	100-44-7		2-Butoxyethanol	111-76-2	Tributyl phosphate	126-73-8
	Chromyl chloride	14977-61-8		o-Tolidine	119-93-7		Bromacil	314-40-9	Trichloroacetic acid	76-03-9
	Chromite ore processing (Chromate), as Cr	7440-47-3		Captafol	6/2/29		Bromoform	75-25-2	1,1,2-Trichloroethane	79-00-5
	Chromium (VI)compounds	18540-29-9		Chrysene	218-01-9		Ethyl bromide	74-96-4	p-Nitrochlorobenzene	100-00-5
	(Water insoluble inorganic compounds, and Water soluble)			2-Chloro-1,3-butadiene	126-99-8		Vinyl cyclohexenedioxide	106-87-6	p-Dichlorobenzene	106-46-7
	Lead chromate, as Cr	7758-97-6		1-Chloro-2,3-epoxy propane	106-89-8		Vinyl acetate	108-05-4	p-Toluidine	106-49-0
	Lead chromate, as Pb	7758-97-6		Trichloroethylene	79-01-6		Antimony trioxide (Handling & use, as Sb)	1309-64-4	Phenyl ethylene	100-42-5
	Zinc chromate, as Cr	13530-65-9		1,2,3-Trichloropropane	96-18-4		Cyclohexanone	108-94-1	Pentachlorophenol	87-86-5
	Chloromethyl methylether	107-30-2		Perchloroethylene	127-18-4		Aniline & homologues	62-53-3	Furfural	98-01-1
	Chloroethylene	75-01-4		Phenyl glycidyl ether (PGE)	122-60-1		3-Amino-1,2,4-triazole (or Amitrole)	61-82-5	Furfuryl alcohol	98-00-0
	Particulate polycyclicaromatic hydrocarbons (as benzene solubles)	-[d]		Phenyl hydrazine	100-63-0		Acetaldehyde	75-07-0	Propoxur	114-26-1
	Formaldehyde	500-00-0		Propane sultone	1120-71-4		Asphalt Petroleum) fumes	8052-42-4	Pyearidine	110-86-1
	Sulfuric acid	7664-93-9[e]		Propylene imine	75-55-8		(as benzene soluble aerosol, Inhalable fraction)		Aldrin	309-00-2
	Nickel sulfide roasting (Fume & dust, as Ni)	16812-54-7		Hydrazine	302-01-2		Allyl glycidyl ether (AGE)	106-92-3	Hexachlorobutadiene	87-68-3
	Coal tar pitch volatiles (Benzene solubles)	65996-93-2		Hexamethyl phosphoramide	680-31-9		α-Naphthyl amine	134-32-7	Hexachloroethane	67-72-1
	Particulates not otherwise regulated	-[f]		Dimethy1 sulfate	77-78-1		α-Naphthylthiourea (ANTU)	86-88-4	Hexone	108-10-1
	(no more than 1% crystalline silica)						α-Methyl styearene	98-83-9	Heptachlor	76-44-8

*According to the Governmental Notification No. 2012-31. Exposure limits of chemicals and physical agents. Mnistry of Employment and Labor, Republic of Korea. Class 1A means the chemicals which have sufficient evidence of carcinogenicity to humans. Class 1B means the chemicals which have limited evidence of carcinogenicity in both animals and humans or sufficient evidence of carcinogenicity in experimental animals. Class 2 means the chemicals which have limited evidence from a person or an animal, but do not have enough evidence for classification as class 1. Etc.: [a]TWA 0.1 count/cm^3, [b]Limited to 0.1% or more butadiene, [c]Limited to alcohol drinking, [d]1A~2 (Differences in carcinogenicity class, depending on the type of chemicals), [e]Limited to strong acid mist, [f]Limited to less than 0.1% of silicon oxide crystals, [g]Only occupational exposure of gasoline vapor, [h]Limited to weight ratio is more than 18% of oxides of alkali and alkaline earth metal oxides, unspecified form of artificial silica fiber, [i]Limited to 0.1% or more benzene, [j]Limited to the fibrous material (including the whisker-form crystal), [k]Limited to weight ratio is more than 18% of oxides of alkali and alkaline earth metal oxides, unspecified form of artificial silica fiber that the number of workers exposed to carcinogens has declined. Main causative agents of occupational lung cancer included asbestos, hexavalent chromium, and crystalline silica. Compensated malignant mesotheliomas were associated with asbestos exposure. Occupational respiratory cancer has increased during the last 10 to 20 year though carcinogen-exposed population has declined in the same period. More efforts to advance the systems for the investigation, prevention and management of occupational respiratory cancer are needed (Lee and Kim, 2010).

The proportion of lung cancer cases to which occupational exposure contributes is reported to be in the range of 9-15% (Kim et al., 1995). In Korea, that was estimated at 7% (Lim et al., 2010). Another example is asbestos-related diseases. Asbestos-exposed workers who have primary lung cancer or malignant mesothelioma could be compensated if they have asbestosis, signs of asbestos exposure such as pleural plaque, or a history of asbestos exposure for more than 10 year (Lee et al., 2009). However, most cases claimed for occupational diseases are evaluated on a case-by-case basis by the COMWEL, and some of them are investigated in depth by the OSHRI in KOSHA to determine whether they are work-related. The types of exposure included the manufacture of asbestos-containing products, use of asbestos-containing products in the manufacturing process, and handling of asbestos-containing products in the course of work. The most common industries related to occupational malignant mesothelioma were shipbuilding and repair and the manufacturing of asbestos textiles (Ahn et al., 2012). An elevated risk of lung cancer was found among cohorts of male workers exposed to carcinogenic heavy metals including arsenic, beryllium, cadmium, chromium, and nickel, but the association was not significant. An analysis of a cohort of carcinogen-exposed workers indicated an excess of lung cancer in asbestos-exposed workers (Jeong et al., 2011).

Although not targeting respiratory cancer, several occupational cohort studies have been conducted to examine the risk of cancer. Park et al. (2005) reported no significant association between the iron and steel industry employment and lung cancer. A case of lung cancer (small cell carcinoma) was reported occurring in a worker exposed to coke oven emissions. The lung cancer occurring in this patient was seen as an occupational disease due to exposure to coke oven emissions (Lim et al., 2002).

Malignant mesothelioma and lung cancer are representative examples of occupational cancer. Lung cancer is the leading cause of cancer death, and the incidence of malignant mesothelioma is expected to increase sharply in the near future. Although information about lung carcinogen exposure is limited, the compensation for occupational respiratory cancer has increased after 1992. The majority of compensated lung cancer was due to underlying pneumoconiosis. Other main causative agents of occupational lung cancer included asbestos, hexavalent chromium, and crystalline silica. Related jobs included welders, foundry workers, platers, plumbers, and vehicle maintenance workers. Compensated malignant mesotheliomas were associated with asbestos exposure. Epidemiologic studies conducted in Korea have indicated an elevated risk of lung cancer in pneumoconiosis patients, foundry workers, and asbestos textile workers. More efforts to advance the systems for the investigation, prevention and management of occupational respiratory cancer are needed (Lee and Kim, 2010). The lung cancer mortality in Korea has increased remarkably during the last 20 years. The main carcinogens were asbestos, crystalline silica, radon, polyaromatic hydrocarbons (PAHs), diesel exhaust particles, chromium, and nickel. It was estimated that about 11.7% of the incident lung cancer was preventable. This reveals the potential to considerably reduce lung cancer by intervention in occupational fields (Leem et al., 2010).

Pancreatic cancer, although an uncommon tumor, is one of the most lethal tumors. The occupational and genetic conditions may play important role in the etiology of pancreatic cancer (Lee, 2004).

The first report on an occupational bladder cancer in Korea was the 41 years old man who worked as a dyer for 17 years at two dyeing factories, which handled nylon and polyester fabrics in Daegu. He was exposed to many kinds of dyes during weighing, mixing, dissolving and dyeing processes. Among many kinds of acid, disperse and direct dyes that he has been exposed to, several dyes have confirmed to contain benzidine-based dyes, one was o-tolidine-based dye, and one was o-dianisidine-based dye. He was exposed to the definite occupational carcinogen even though the level was relatively lower than that of dye manufacturers. These evidences support that the dyer's bladder cancer could be related to the occupational exposure to benzidine-based dyes (Kim et al., 1999). It was founded the significant correlation between the bladder cancer in the age of 40s and the industrial exposure indicator. Future analytic studies should be fruitful in identifying more occupational risk factors for bladder cancer. Investigation of cancer incidence including geographic variations and difference by age may identify patterns suggesting occupational exposures (Paek et al., 1995). Reproductive dysfunction as a result of 2-bromopropane poisoning was first reported in Korean workers. 2-bromopropane poisoning caused severe reproductive effects in Korean workers. A few cases of occupational bladder cancer have been reported in Korea, whereas other cancers of the urinary tract have not been reported after occupational exposure (Park et al., 2010).

Occupational Cancers with Industries or Jobs

There are specific jobs with chemical environment from welding, road pavement, construction industry, semiconductor, foundry, cement, mining, shipbuilding, steel, even to agriculture, bus driver, health care worker and firefighters. Job types associated with occupational lung cancer cases were: 30.2% with maintenance, 24.5% with welding; 11.3% with grinding; 7.5% with foundry; 5.7% with driving, casting, and painting and 26.4% with 'other'. These results indicate that past exposure to occupational carcinogens remains an important determinant of occupational lung cancer occurrence (Lim et al., 2010).

The most common occupation among confirmed malignant mesothelioma was construction worker, and others included asbestos textile industry workers, welders at shipbuilding, soldiers, and manufacturing workers. Some patients had histories of environmental exposure, such as residence near a mine or repair the asbestos slate roof of their own house (Jeong et al., 2011). Lung cancer related jobs included welders, foundry workers, platers, plumbers and vehicle maintenance workers. Epidemiologic studies conducted in Korea have indicated an elevated risk of lung cancer in pneumoconiosis patients, foundry workers, and asbestos textile workers (Lee and Kim, 2010). A lung cancer with pleural asbestosis in a worker exposed to asbestos in manufacturing insulation and malignant pleural mesothelioma in a boilermaker and a plumber (Kim et al., 2009) were reported in the 1990s. Since 2000, reports have identified lung cancer associated with exposure to coke oven emissions (Lim et al., 2002), lung cancer in an asbestos-exposed shipyard repairman (Jeong et al., 2011), and lung cancer with silicosis in a plasterer exposed to cement dust contained silica (Lim et al., 1997). Significant association was observed for farmer, briquette stove users, agricultural chemicals users, and welding/fume exposures. Although there were elevated risks associated with production, home industry, transportation/storage/communication, lodgement/food worker and construction, none were statistically significant. As results, although smoking is important risk of lung cancer, occupation and resident environment are showing association of lung cancer. So further evaluation is necessary for occupation risk and take preventive measures (Kim et al., 1995). A case-study was reported of a silicosis sufferer with lung cancer, who was exposed to cement dust through plastering and waterproof work in the construction industry. It was concluded that the patient's silicosis with lung cancer was an occupational-caused disease due to exposure to cement dust (Kim et al., 2008). Road pavement workers are exposed to many known carcinogens in their complex occupational environment (Sellappa et al., 2011). Construction industry workers are exposed to many known carcinogens in their complex occupational environment (Sellappa et al., 2010). Professional bus drivers are exposed to environments containing air pollution and ROS that can induce cellular oxidative stress and DNA damage (Han et al., 2010).

During the fabrication of silicon wafers, many toxic chemicals, a strong electric field and hazardous equipment are used. The process allows the integration of a three-dimensional array of electric circuits onto a silicon wafer substrate. Wafers are sliced from single crystal silicon and subject to a series of steps during the fabrication process, which alternatively adds and then selectively removes materials in layers from the surface of the wafer to create different parts of the completed integrated circuit (Park et al., 2011). There was no significant increase of leukemia in the Korean semiconductor industry. However, the incidence of non-Hodgkin's lymphoma (NHL) in females and thyroid cancer in males were significantly increased even though there was no definite association between work and those diseases in subgroup analysis according to work duration. This result should be interpreted cautiously, because the majority of the cohort was young and the number of cases was small (Lee et al., 2011).

Although the information was obtained from health insurance data, which has limitations such as accuracy and completeness, the number of foundry workers diagnosed with lung cancer was significantly higher than that of non-foundry workers. Therefore, a well-designed cohort study should be followed to confirm the higher lung cancer rates in foundry workers (Ahn et al., 2000). Foundry workers are potentially exposed to a number of carcinogens. It was conducted to describe the cancer incidence associated with employment in small-sized Korean iron foundries and to compare those findings to the Korean population. Overall cancer morbidity in foundry workers was significantly higher than that of Korean general population. Lung cancer and lymphohematopoietcic cancer in production workers were significantly high compared to Korean general population. Stomach cancer in fettling and lung cancer in molding and in fettling were there significant elevations compared to office workers. In this study, statistically significant excess lung cancer was observed in production workers comparing to Korean general population and office workers. Also, cancer morbidity of overall cancer, lung cancer and stomach cancer was significantly increased with duration of employment at ten and more years comparing to Korean general population. These findings suggest in causal association between exposure to carcinogens during foundry work and cancer morbidity (Ahn et al., 2010).

Several studies have been conducted evaluating the carcinogenic effects of cement, but the results have been inconclusive, even though some cancers, such as lung and gastrointestinal cancers, have a suspected association with cement dust exposure (Koh et al., 2012). Cement contains hexavalent chromium, which is a human carcinogen. However, its effect on cancer seems inconclusive in epidemiologic studies. The cohorts consisted of male workers in 6 Portland cement factories in Korea. Cancer mortality and incidence in workers were observed from 1992 to 2007 and 1997-2005, respectively. There was an increased standardized incidence ratio for stomach cancer of 1.56 in production workers. The standardized mortality ratio for lung cancer increased in production workers. However, was not statistically significant. Our result suggests a potential association between cement exposure and stomach cancer. Hexavalent chromium contained in cement might be a causative carcinogen (Koh et al., 2011). Hence, this study investigated the potential relationship between exposure in the cement industry and the development of various cancers. There are also a potential association between exposure in the cement industry and an increased risk of stomach and rectal cancers (Koh et al., 2012).

It was to assess mining workers' exposures to potentially carcinogenic air contaminants with major non-carcinogenic contaminants in various types of mines in Korea. But the carcinogenic metals were detected at relatively high levels in air samples from coal iron and limestone mines. It was found that the miniers of all the mines were exposed at lower levels to mixture of potential carcinogens and that particularly the coal miners would have the higher risks of cancer with pneumoconiosis (Shin et al., 2002).

Cancer is a major concern in shipbuilding. Since the 1970s, shipbuilding and repair has been a strategic industry in Korea, which made Korea the world's largest shipbuilding country. The study is to investigate the cancer incidence in shipyard workers in Korea. The observed increase in stomach, liver, and lung cancers among production workers suggests that some occupational factors in the shipyard might have contributed to the increased cancer risk (Jeong et al., 2011). The retrospective cohort study was to investigate the relationship between exposure of Korean workers to petrochemicals in the refinery/petrochemical industry and lymphohematopoietic cancers. The cohort consisted of 8,866 male workers who had worked from the 1960s to 2007 at one refinery and six petrochemical companies located in a refinery/petrochemical complex in Korea that produce benzene or use benzene as a raw material. The results showed a potential relationship between leukemia and lymphohematopoietic cancers and exposure to benzene in refinery/petrochemical complex workers. This study yielded limited results due to a short observational period; therefore, a follow-up study must be performed to elucidate the relationship between petrochemical exposure and cancer rates (Koh et al., 2011). A petrochemical worker with aplastic anemia was referred to. He worked in a petroleum resin-producing factory and had been exposed to low-level benzene. Most risk predictions for benzene exposures have been based on rubber workers who were exposed to high concentrations. In this paper, it was reported the case of aplastic anemia induced by low-level benzene exposure (Baak et al., 1999). In the iron and steel industry, workers are potentially exposed to a number of carcinogens and are involved in a number of processes of a hazardous nature. Cancer morbidity at two Korean iron and steel complexes was analyzed using Poisson regression methods. Work histories were merged with the national cancer registry for 44,974 workers who were followed from 1988-2001. Lung cancer morbidity was significantly elevated at the affiliated plants against the parent plants, and all-cancer morbidity was significantly elevated for maintenance workers compared to office and production workers. Lymphohematopoietic cancer incidence was higher in the coke plants and stomach cancer incidence was higher in the maintenance departments. This recent steelworker cohort exhibits possible excess cancer morbidity in some processing areas. Further follow-up of this cohort and alternate study designs such as case-control study will be needed to elucidate the relationship of exposure and health risks of iron and steel workers (Ahn et al., 2006).

Agriculture in every industrialized country is one of the most hazardous occupations. Respiratory illnesses are common problems among the agricultural work force. The most frequent cause of respiratory illness is organic dust from livestock production and handling grain or hay that may produce bronchitis, asthma-like condition, irritation of the mucosa of the upper airways and eyes, and organic dust toxic syndrome. Overall cancer seems to be lower. However, there are several cancers for which the farming population may be at increased risk, including NHL, leukemia, multiple myeloma, brain, prostate, and skin (Lee, 2010). The relationship between agricultural pesticides and colorectal cancer incidence was investigated in the Agricultural Health Study. Chlorpyrifos use showed significant exposure response trend for rectal cancer, rising to a 2.7-fold increased risk in the highest exposure category. Aldicarb was associated with a significantly increased risk of colon cancer, based on a small number of exposed cases, with the highest exposure category resulting in a 4.1-fold increased risk. In contrast, dichlorophenoxyacetic acid showed a significant inverse association with colon cancer but the association was not monotonic (Lee et al., 2007).

Health care is a labor intensive industry and, in most countries, health care workers (HCWs) are fast growing sector of the workforce. Variety of occupational hazard, such as biological, ergonomical, chemical, physical and psychological factors, have been reported in HCWs. Important carcinogenic chemicals in HCWs are formaldehyde, ethylene oxide and anticancer drugs, which have been reported to be cause of occupational lymphohematopoietic cancer. In addition to organizational factors, the shift work and night work causes serious health problem of HCWs. These risk factors can affect to chronic underlying disorder (Kim, 2010). Health care workers should pay attention to health disorders caused by physical factors to protect themselves against many hazards in hospitals (Lim, 2010). Healthcare workers are exposed to a variety of chemical agents used in many different areas and purposes. The chemicals could cause health problems to healthcare workers using them. Such as glutaraldehyde, formaldehyde, ethylene oxide gas, anesthetics. Some of the anti-neoplastic drugs such as busulfan, chlorambucil, cyclophosphamide, melphalan are group 1 carcinogens. Other miscellaneous chemical agents are heavy metals such as elementary mercury or lead and organic solvents such as toluene, xylene and acetone. Air levels of most above chemicals in Korean hospitals were relatively low. However, we have to make every effort to reduce the exposure level of these chemicals (Won, 2010).

Firefighters are facing occupational hazards such as exposures to a variety of carcinogens and toxic agents, heat, physical stress and psychological stress. This occupation involves an increased risk of particular health concerns including cardiovascular diseases and cancers. There are various carcinogens in the fire smoke. Many studies address that some types of cancers are related to firefighting. These cancers include brain tumors, cancers of hematopoietic and lymphatic systems, cancers of genitourinary tract, and skin cancers. To reduce the risk, it should be encouraged to use protective equipments efficiently and manage physically exerted firefighters appropriately at the fire scene (Han and Linton, 2008). Many professional emergency responders (ERs) who belong to the Korean National Emergency Management Agency (NEMA) have been cross-trained and serve multiple roles. As such, firefighters and other ERs in Korea are exposed to similar occupational hazards. Korean firefighters showed excess morbidity in several cancer types, including colorectal and urologic cancers, and NHL, demonstrating similar trends to previous studies for firefighters conducted in other countries. Increased incidence in these cancer types suggests occupational exposure to carcinogens and shift work (Ahn et al., 2012).

The contents of table 2 are shown the industrial carcinogens and their related jobs in Korea with IARC classifications.

Occupational Cancers with Molecular Epidemiology

It is possible in many situations to identify humans exposed to potentially toxic materials in the workplace and in the environment. There are biomarkers of exposure, effect/response and susceptibility may be influenced by the genotype existing in a population. The relationship between biomarkers and the various factors which affect them is complex. Sometimes the variables are not completely independent of each other (Anderson, 2001). Interest in occupational cancer is growing in Korea. Especially, lung cancer and malignant mesothelioma are well known occupational cancers. Also, a nationwide investigation of the hazardous agent-exposed population was quite limited, so more efforts are needed to estimate the lung carcinogen-exposed population. Few epidemiological studies have examined occupational respiratory cancer, and long-term cohort studies are thus far very limited. Nonetheless, it is expected that more research will be conducted in response to the increasing interest in occupational cancer. There is a report about biomarkers for early diagnosis and prevention of occupational diseases with many kinds of chemicals or compounds exposures in workplaces. But the limits of these biomarkers with regarded to monitoring of workers or animals are reported through a lot of tests (Jelmert et al., 1994). Cellular mutations related to chemical carcinogenesis usually caused by oxidative DNA damage, and a major product of this damage is 8-hydroxyguanine (oh8Gua) (Cheng et al., 1992).

To characterize changes in the expression of plasma proteins caused by exposure to 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD), plasma samples from workers at municipal incinerators was analyzed using two-dimensional gel electrophoresis (2-DE). TCDD treatment resulted in an increase in the mRNA and protein expression levels of AFP, but reduced albumin expression. According to our results, exposure to TCDD may induce liver disease or cancer, and the proteins identified in this study could help reveal the mechanisms underlying TCDD toxicity (Kang et al., 2005).

8-Oxo-7,8-dihydroguanine (8-oxoG), arguably the most abundant base lesion induced in mammalian genomes by ROS, is repaired via the base excision repair pathway that is initiated with the excision of 8-oxoG by OGG1 (Boldogh et al., 2012). 8-Oxo-7,8-dihydroguanine is one the most abundant base lesions in pro- and eukaryotic DNA. In mammalian cells, it is excised by the 8-oxoguanine DNA glycosylase (OGG1) during DNA base-excision repair, and the generated free 8-oxoG base is one of the DNA-derived biomarkers of oxidative stress in biological samples (Hajas et al., 2012). The urinary excretion of 8-oxoGua is a biomarker of exposure, reflecting the rate of damage in the steady state (Loft et al., 2012). Genotoxic effects, such as chromosomal aberrations, and cellular oxidative DNA damage by reactive oxygen species produced by hexavalent Cr exposure may play an important role in its carcinogenesis. There was a research on the levels of 8-hydroxydeoxyguanine (8-OH-dG) and its base excision repair activities in the lung tissues of rats that repeatedly inhaled a sodium chromate solution mist for 1, 2, and 3 weeks. The results suggest that the DNA damage caused by hexavalent Cr inhalation is induced by the generation of ROS and by inhibition of base excision repair activity during the earlier phase of exposure. However, the 8-OH-dG levels and its repair activities recovered to the level of the controls in the latter inhalation exposure period (Maeng et al., 2003). Single cell gel electrophoresis assay (comet assay) is a method to detect DNA damage from DNA chain excision and alkali labile sites, not chromosomal aberration, so it is possible to detect DNA damage from undivisible tissues. Alkaline comet assay as measured by single cell gel electrophoresis, on the other hand, accurately measures DNA fragmentation on a single cell level and allows analysis of subpopulation of cells. The assay was originally developed for measuring DNA damage of cells exposed to any genotoxic agent. In alkali condition, it can detect base modification, alkali-labile abasic site (AP site) formed when the damage site was inactively excised with DNA repair enzymes. And reported that it can measured the DNA damage in specific sites with FLARE (Fragment Length Analysis with Repair Enzyme) assay, the improved method of comet assay by treatment of endonuclease III or formamidopyrimidine DNA glycosylase (Fpg) (Rim et al., 2007). 8-Oxoguanine DNA glycosylase 1 (EC 3.2.2.23) is encoded by OGG1 gene and plays a key role in removing 8-oxo-7,8-dihydroguanine (8-oxoG) base in DNA lesion by ROS (Kim et al., 2012).

A case control study was conducted to evaluate the role of known risk factors (smoking and high-risk occupational history) and the genetic polymorphism of GSTM1 and GSTT1 in blader carcinogenesis in Korean men. Neither smoking nor high-risk occupational history was statistically significant risk factor of the bladder cancer. However, the GSTM1 null-type showed borderline significance and both GSTM1 and GSTT1 null-type was statistically significant risk factor of bladder cancer when compared with both normal genotype after age and smoking history were adjusted. The concurrent null-type of GSTM1 and GSTT1 increases the risk of bladder cancer in Korean men (Lee et al., 1999). Activity of enzymes involved in the metabolism of various carcinogenic xenobiotics is one of the most important host factors for cancer occurrence. It was performed to investigate whether the polymorphisms of N-acetyltransferase type 2 (NAT2) and GSTM1 are risk factors of bladder tumor and to evaluate the effects of their interaction on bladder tumor development. It was suggested that GSTM1 deletion may be a significant risk factor of bladder tumor (Kim et al., 1999). The study was performed to investigate whether the polymorphisms of NAT2, GSTM1 and GSTT1 are

Table 2. Industrial Carcinogens and Jobs using them with IARC Classification

Factor (chemicals etc.)	Industries or jobs	Target organ
Physical element, ionizing radiation	Medical doctor of radiology, radiologist, nucleolar worker, radium dial painter, underground miner, crewman	Bone, leuk(a)emia, lung, liver, thyearoid gland, etc.
Sunlight	Outdoor worker	Melanoma, skin
Dust, fiber, asbestos	Mining, milling, insulation, shipbuilding, sheet metal worker, cement	Lung, mesothelioma (larynx, gastrointestinal tract)
Erionite	Waste treatment, sewage, waste from agricultural industry, environmental pollution control system, cement condensate, building materials	Mesothelioma
Silica, crystalline	Granite, stonecutter, ceramic, glass, casting and metal worker	Lung
Talc containing asbestiform fibres	Production of chinaware, paper, paint and varnish, cosmetic	Lung, mesothelioma
Wood dust	Felling, lumbering, pulp, paper, paper board, furniture, cabinet, carpenter, construction	Nasal cavity, paranasal sinus
Metal and metallic compound, Arsenic and arsenic compounds	Refining of nonferrous metals, arsenic compound, agrichemicals, arsenic mining	Skin, lung (liver hemangiosarcoma)
Beryllium	Extraction and processing of beryllium, aerospace, electronic and nuclear industry, jewelry	Lung
Cadmium (compound)	Cadmium refining, production of dry cell, cadmium-cupper alloy, dye or pigment, plating	Lung
Chromium (VI) (compound)	Manufacturing of chromic acid, dye or pigment, plating, chromium alloy, stainless steel welding, preservation of wood, leather manufacturing, waste water treatment, ink, perfume, etc.	Lung
Nickel (compound), nickel oxide, nickel sulfide	Refining of nickel, welding	Lung, nasal cavity, paranasal sinus
Wood, fossil fuel and its by-product, benzene	Solvent for shoe manufacturing, chemicals, pharmaceuticals, rubber industry, printing, gas additive	Leuk(a)emia
Wood, fossil fuel and its by-product, coal tar and pitch	Manufacturing of purified chemicals, coal tar products, coke, aluminum, casting, pavement of a road and construction(roof, slater)	Skin (lung, bladder)
Mineral	Metalwork, machining, printing, production of cosmetic, medicine	Skin (bladder, lung, nasal cavity)
Vinyl chloride monomer	Manufacturing of polyvinyl chloride, refrigerant(before 1974), extraction of solvent, (vaporizing)high-pressure gas	Liver hemangiosarcoma (hepatocyte cancer)
BCME, CME	Media for manufacturing of plastic or rubber products, alkylating chemicals, ion exchange resin	Lung
Dyes of aromatic amine, 4-aminobiphenyl, benzidine, 2-naphthylamine	Manufacturing of dyes and pigment	Bladder
Agrichemicals, ethylene oxide	Chemical industry, sterilization, disinfection	Leuk(a)emia
2,3,7,8-TCDD	Herbicide of chlorophenol or chlorophenoxy, incinerator, PCB manufacturing, bleachinf of pulp or paper	Lung, sarcoma (most of the body)
Aflatoxin	Feed production, cargo shipping, processing of rice or corn	Liver
Mustard gas	Laboratory, soldier	Larynx (lung, pharynx)
Strong-inorganic-acid mists containing sulfuric acid	Processing of preserved thing, steel making, petrochemical industry, phosphatic fertilizer	Larynx (lung)
Formaldehyde	Pathologist, technician of medical lab, plastic or textile industry	Leuk(a)emia, nasal cavity, pharynx
Aluminium production	Volatile pitch, aromatic amine	Lung, bladder
Auramine production	2-naphthyl amine, auramine, other chemicals, pigment	Bladder
Boot and shoe manufacture and repair	Leather dust, benzene or other solvent	Leuk(a)emia, nose, paranasal sinus, bladder
Coal gasification	Coal tar, coal tar fume, PAHs	Skin, bladder, lung
Coke production	Coal tar fume	Skin, lung (bladder, kidney)
Furniture and cabinet Making	Wood dust	Lung
Haematite mining (underground) with exposure to radon	Radon, Silica	Lung
Steel founding and casting	PAHs, silica, metal fume, formaldehyde	Lung
Magenta production	Magenta, o-toluidine, 4,4'-methylenebis(2-methylaniline), o-nitrotoluene	Bladder
Isopropyl alcohol manufacture (strong-acid process)	Diisopropyl sulfate, isopropyl oil, sulfuric acid	Paranasal sinus, larynx, (lung)
Painter (occupational exposure as a)		Lung (bladder, stomach)
Rubber industry	Aromatic amine, solvent	Bladder, (stomach, larynx, leuk(a) emia, lung)

*Sourced by IARC monographs on the evaluation of carcinogenic risks to humans. From http://monographs.iarc.fr/ENG/Classification/crthgr01.php.

risk factors of bladder cancer and to evaluate the effects of their interaction on bladder cancer development. It was suggested that GSTM1 deletion may be a significant risk factor of bladder cancer. Since there have been much debates on causal relationship between slow acetylation and GSTT1 deletion, and bladder cancer, further studies are needed (Kim et al., 1998). The association between urinary 1-hydroxypyrene glucuronide (1-OHPG) levels, as an internal measure of polycyclic aromatic hydrocarbon (PAH) exposure, and glycophorin A (GPA) mutation frequency, as an early biologic effect indicator, was determined to establish whether genetic polymorphisms of glutathione S-transferase (GST) isoforms GSTM1 and GSTT1 play a role. Eighty-one workers including 38 employees directly involved in incinerating industry wastes were recruited from a company located in South Korea. It was suggested that the association between urinary 1-OHPG and GPA mutation might be modulated by the GSTM1 genotype (Lee et al., 2002). It was investigated that influenced the excretion of urinary 8-OH-dG in 78 firefighters. 53 Out of 78 firefighters were exposed to fire within 5 days of the study and 25 were not. 8-OH-dG was measured by ELISA and the distribution of the genotypes of CYP1A1, CYP2E1, GSTM1, and GSTT1 was measured by polymerase chain reaction (PCR). Smoking and CYP2E1 gene polymorphism may be important factors in carcinogenesis and the GSTT1 positive genotype may be a genetic susceptibility factor in firefighters who are exposed regularly to various chemical carcinogens (Hong et al., 2000).

Occupational exposures to certain metals, hydrocarbons and ionizing radiation are associated with increased lung cancer in workers; because these exposures continue, lung cancer remains an important problem in industrialized nations. The gravity of the lung cancer, specifically the low cure rate associated with the disease, has forced researchers to focus efforts at developing biological indicators (biomarkers) of carcinogen exposure and early, reversible effects. Biomarkers of several different stages of the carcinogenic process have been proposed. Industrial hygiene and occupational health emphasize exposure and disease prevention. For this reason, biomarkers useful in industrial hygiene practice are those which measure events prior to the initiation phase of carcinogenesis; markers of later events which have a greater positive predictive value may measure irreversible effects and are more appropriate for disease screening and epidemiology (Talaska et al., 1996). Carcinogen-DNA adduct analysis has potential for biomonitoring the earliest effects of exposure to many chemical carcinogens. So many researchers begin to use them as biomarker for monitoring the earliest exposure of carcinogens and develop the effective analytical techniques about them. A major project for biomonitoring workers with carcinogen-DNA adducts is to develop non-invasive samples instead of tissues of target organs such as bladder and lung. It could significantly measure the DNA adduct in exfoliated urothelial cells by using the above ^{32}P-postlabelling procedures, and use them to be biomonitoring workers who exposed carcinogens (Lee et al., 2000).

In probing the possible non-genotoxic molecular targets of cadmium-induced nasal toxicity, it was performed an mRNA differential display analysis for cadmium-treated human nasal septum carcinoma RPMI-2650 cells. It was suggested that cadmium-induced ROS cause up-regulation of AKR1C3 expression, at least partially via the activation of PI3K-related intracellular signaling pathways, and Nrf2 activation, thereby contributing to an adaptive intracellular response to cadmium toxicity (Lee et al., 2011). Diesel exhaust particles (DEP) are known to cause cardiopulmonary diseases due to their proinflammatory and cytotoxic effects. The phenomenon of apoptosis is a key event that successfully clears damaged cells, and its failure leads to the development of more serious diseases, such as lung cancer. The findings of this study suggest that DEP trigger apoptosis in J774A.1 macrophage cells via the activation of p53, followed by Bax (Yun et al., 2009).

At the cellular level, cadmium influences gene regulation, generation of ROS and inhibition of DNA repair activities. It increases expression of proto-oncogenes including c-fos, c-jun and c-myc, which could induce carcinogenesis. It also induces expression of metallothionein encoding gene. The binding of metallothionein proteins and cadmium ion might helps to occur cancer. Again, cadmium generates free radical involving hydroxyl radicals, superoxide anions, nitric oxide hydrogen peroxides. These free radicals damage DNA and decrease DNA repair protein activity. One of the factors which protects cell is antioxidants including superoxide dismutase (SOD), catalase, glutathione peroxide. Several studies have been reported that cadmium can change expression level of antioxidants in dose dependents manners. Hence, cadmium exposure might break the balance between antioxidants and ROS in high dose which may lead to cell death (Lee and Seo, 2009

Prospect for Occupational Cancer Prevention in Korea

Considering the current Korean use of chemicals, even newly registered, the number of compensated cases in Korea is expected to increase in the future. Cancer is one of the main causes of death worldwide. Many factors are responsible for the recent increase in cancer. Other known causes of cancer, such as occupational, genetic, and reproductive factors, play a lesser role in the global burden of cancer. Researches into the causes of cancer have revealed how many of the most common cancers can be prevented. Detection of many forms of the disease at an early stage can greatly improve the prospects for effective treatment, reducing deaths and enhancing quality of life (Yoo and Shin, 2003).

Primary prevention, which was successful in controlling occupational cancers, aims at minimizing exposures to carcinogens in healthy subjects and at favoring the intake of chemopreventive agents with dietary and pharmacological agents. Besides chemical carcinogens, often in the form of complex mixtures, the workplace may involve exposures to physical agents, such as sunlight and artificial illumination systems delivering UV radiation, or to biological agents, such as chronic viral infections (HBV, HCV, and HIV) associated with cancers. A controversial issue is the occurrence of threshold doses for carcinogens in the workplace and the environment (De Flora et al., 2011). Now, professional agency provide 927 kinds of IARC, 237 kinds of NTP, 351 kinds of ACGIH and 1,006 kinds of EU ECHA information on carcinogenic agents. Korea Ministry of Employment and Labor (KMoEL) provides carcinogenicity-related information of 190 chemical agents in accordance with the category of carcinogens guided by ACGIH (Table 1). KOSHA offers 13,232 kinds of GHS MSDS information including 2,484 carcinogenic substances. Therefore, carcinogenicity-related information of chemical substances, which are not available on the existing GHS MSDS DB, should be updated for the future reference (Lee et al., 2011).

The psychosocial factor increased the risk of chronic disease (hypertension, coronary heart disease, and musculoskeletal disease) and psychological diseases (alcoholism, depression, anxiety), shift work, specifically, was associated with an increased risk of cancer. It is required that worksite prevention programs be established in occupational as well as individual levels (Koh, 2010). Current OSH situations and issues in Korean electronics industry raise the need of changes in OSH culture. General adaptation of precautionary principle, internalization of costs, and extended responsibility of producers are needed urgently. The OSH professionals both in public and private sectors should support these agendas under their social obligation to protect workers' health (Kong, 2012).

Lots of chemicals including metal compounds such as arsenic, cadmium, chromium, cobalt, lead, mercury, and nickel are classified as carcinogens affecting human health through occupational and environmental exposure. However, the underlying mechanisms involved in tumor formation are not well clarified. Attention is paid to metal-induced generation of free radicals, the phenomenon of oxidative stress, damage to DNA, lipid, and proteins, responsive signal transduction pathways with major roles in cell growth and development, and roles of antioxidant enzymatic and DNA repair systems. Interaction of non-enzymatic antioxidants (carotenoids, flavonoids, glutathione, selenium, vitamin C, vitamin E, ginsenosides etc.) with cellular oxidative stress markers (catalase, glutathione peroxidase, and superoxide dismutase) as well as certain regulatory factors, including AP-1, NF-κB, Ref-1, and p53 is also reviewed. Dysregulation of protective pathways, including cellular antioxidant network against free radicals as well as DNA repair deficiency is related to oncogenic stimulation. These observations provide evidence that emerging oxidative stress-responsive regulatory factors and DNA repair proteins are putative predictive factors for tumor initiation and progression (Koedrith and Seo, 2011).

To prevent occupational cancer in coke oven plant workers, we must remodel the engineering procedure, begin comprehensive medical surveillance, educate workers on risks and the benefits of smoking cessation, and increase awareness of safety regulations in the workplace (Lim et al., 2002). Particularly, occupational exposure to high PAHs has been suspected to induce cancer. In addition, consumption of the Korean pears showed inverse association with level of urinary 1-hydroxypyrene (1-OHP), which is an exposure biomarker and metabolite of PAHs. Therefore, we investigated the effects of the Korean pears on level of urinary 1-OHP among male taxi drivers at Seoul, in a pilot study. It was suggested that the Korean pears may have chemopreventive effects on PAHs-induced cancer, particularly PAHs-high exposed people, via rapid excretion of bioactive intermediates (Lee and Yang, 2009).

Chemoprevention to protect the normal cells from the conversion to cancer cells using safe chemicals is becoming popular as an effective strategy to conquest the cancer. It has been reported that many ingredients in food were confirmed they have suppressive qualities in regard to carcinogenesis in each specific stage such as initiation, promotion and progression. This review focuses on many industrial carcinogens which workers are exposed to, the industries or jobs related, and the efforts to prevent the occupational cancer effectively by our Korean researchers (Rim and Kim, 2010).

In addition, nanoparticles, electromagnetic waves, and climate changes are suspected as future carcinogenic sources. As their carcinogenicity or involvement in carcinogenesis is not clearly unknown, proper consideration for them should be taken into account. For these purposes, new technologies with a balance of environment and gene are required. Currently, various approaches with advanced technologies--genomics, exposomics, etc.--have accelerated development of new biomarkers for biological monitoring of occupational and environmental carcinogens (Yang, 2011). These advanced approaches are promising to improve quality of life and to prevent occupational and environmental cancers.

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