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Necessity for a National Carcinogen List in Korea, Based on International Harmonization

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Cancer has been the leading cause of death in Korea for the last 30 years. Cancer patients' 5-year survival rate between 2005 and 2009 was 62.0%, representing a highly advanced standard of care, as much as developed countries in the EU and the US. The Korean government formulated its first 10-year plan for cancer control in 1996 and has been carrying out a second 10-year plan for cancer control since 2006. But despite the Korean government's efforts, the cancer burden in Korea continues to increase. Many separate laws have gone into effect concerning the management of carcinogen exposure. However, there are no integrated regulatory laws or management systems against carcinogen exposure in Korea. Dead zones remain where carcinogen exposure cannot be controlled properly in Korea. In this paper, we suggest the need to establish a national carcinogen list based on international harmonization as a prerequisite for a paradigm shift in cancer control policy from treatment to primary prevention.

Keywords Cancer control, Collaborative risk management, National carcinogen list, Primary prevention

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Introduction

Cancer has been the leading cause of death in Korea since 1983 [1]. About 178,000 people develop cancer annually, with an age-standardized rate of 321.3 per 100 thousand in 2009. This cancer incidence rate is less than the 335.0 per 100 thousand rate in the US (2008), but higher than the 280.0 per 100 thousand in the UK (2008) and 247.3 per 100 thousand in Japan (2008). Cancer patients' 5-year survival rate between 2005 and 2009 was 62.0%, which showing how far the state of the art has advanced globally. The five leading primary cancer sites in 2009 were stomach, colon, lung, liver, and prostate among males, whereas the most common cancer sites among females were thyroid, breast, colon, stomach, and lung [2].

According to recent research findings, infection and smoking are the most important contributing factors in Korea. The smoking rate in Korea is still high, 46.9% in men and 7.1% in women in 2009 [3]. The fractions of all cancers attributable to infection were 25.1% and 16.8% for cancer incidence in men and women, and 25.8% and 22.7% of cancer mortality in men and women, respectively. Over 97% of infection-related cancers, such as stomach cancer and liver cancer, were attributable to infection with *H. pylori*, hepatitis B virus (HBV), hepatitis C virus and human papilloma virus [4]. Occupation is also an impor-

tant attributing factor at 7.8% [5-7], compared with France [8], which reported 2.4% as the attributable fraction (AF) of occupation to cancer. Drinking alcohol, reproductive factors, obesity, and physical inactivity are minor factors, as each is less than 2%. AFs of radiation and environmental pollution were not calculated because of insufficient data in Korea. But there are reliable data supporting the considerable environmental burden of diseases, including cancer. The World Health Organization (WHO) reported the surprising news that Korea ranked in 50th place in the world in the burden of disease for environmental risk in 2007. By another method, Yoon [9] suggested that Korea ranked in 25th place in the world in the burden of disease for environmental risk in 2007. The prevalence of people exposed to environmental tobacco smoke (ETS) in Korea is still high, at 44.9% in males and 34.2% in females in 2009 [10]. Smoking by husbands also affects the incidence of lung cancer in Korean women [11]. Many people have been exposed to asbestos in the vicinity of asbestos textile industries and mines in Korea [12], even though the Korean government completely prohibited the use of asbestos in 2009. Air pollution is the main cause of the environmental burden of diseases in Korea [9]. Especially near highways and high traffic areas, people are exposed to traffic-related air pollutants, including diesel exhaust particles (DEP). DEP was classified as a definite human carcinogen (group 1) by the International Agency for Research on Cancer (IARC) last year based on sufficient epidemiological evidence [13-15]. Taking environmental carcinogens, such as ETS, asbestos, and DEP, into consideration, AFs due to environmental exposure in Korea may be higher than 0.2%, which was the estimated AF% in France [16].

Recently in Korea, some issues related to carcinogen exposure have received much media attention, i.e., the first compensation case of breast cancer in a laborer exposed to shift work, radiation and organic solvents [17], the announcement of IARC's decision on the carcinogenicity of radiofrequency radiation exposure by mobile phone use [18] and DEP [19], as well as the Fukushima nuclear power plant accident in a neighboring country. These have made the Korean people much more concerned about exposure to carcinogens.

Cancer Management in Korea

With its rapidly aging population, reducing the cancer burden at the national level has become one of the major public health issues in Korea. The government formulated its first 10-year plan for cancer control in 1996. In 2000, the National Cancer Center was established and the Cancer Control Division was set up within the Ministry of Health and Welfare. The Cancer Control Act was legislated in 2003. Korea's major national cancer control programs included anti-smoking campaigns, HBV vaccination, cancer registration and networking, reinforcement of research and development activities for cancer control, education and training for cancer control and prevention, management of the national cancer information center, a mass screening program for five common cancers, caring for cancer patients at home, financial support for cancer patients and designation of regional cancer centers [1]. The second 10-year plan for cancer control was initiated in 2006 to make up for flaws in the first plan and establish an efficient 10-year national cancer plan for a cancer control management system. The goals for the second plan are as follows: intensifying cancer prevention by stricter management of cancer risk factors, early screening of all people for cancer, extension of support for cancer patients, reinforcing security for cancer patients, strengthening support for rehabilitation and palliative medicine for cancer patients, establishment of infrastructure for active national cancer management, development of diagnostic and therapeutic technology, enforcement of education and public relations to make it touching to people, and a systemic cancer registry and management. The second 10-year plan for cancer control provides a framework to prepare a great shift in cancer policy from primarily treatment oriented to precautionary health promotion.

In spite of the national cancer control plans, the cancer burden has increased continuously in Korea. The increasing number of cancer patients in Korea poses devastating social and economic consequences for households, communities, and countries as well. Cancer may be a major impediment to socioeconomic development in Korea. Therefore at this point, we need to steer the main direction of cancer control policy toward carcinogen management and primary prevention of cancer. It is urgently needed to define the carcinogenicity of suspect substances and monitor their exposures.

Laws Related to Carcinogen Control in Korea

The Korean Toxic Chemicals Control Act (TCCA) was implemented in 1991 by the Ministry of Environment (MOE) for the general management and control of industrial chemicals in Korea. The latest version (Act No. 895) took effect on March 21, 2008. The purpose of this Act is to prevent any risk caused by chemicals to human health. The National Institute of Environmental Research is responsible for new chemical notifications under the Act. The Korea Chemicals Management Association of MOE is responsible for accepting declarations on details of other chemicals and applications for confirmation certifi-

cates. But there are many exemptions. For example, radioactive substances prescribed by the Atomic Safety Act; medicines, non-pharmaceutical drugs, and cosmetics by the Pharmaceutical Affairs Act; technical ingredients and agrochemicals by the Agrochemicals Control Act; fertilizers by the Fertilizer Control Act; foods and food additives by the Food Sanitation Act; explosives by the Control of Firearms, Swords, Explosives, etc. Act; and toxic gases by the High-Pressure Gas Safety Control Act. Carcinogens are prescribed by many authorities, such as the Ministry of Health and Welfare, MOE, Ministry of Labor, Ministry of Science and Technology and Ministry of Agriculture, according to their properties and legislation in Korea (Table1). The TCCA covers new chemicals, toxic chemicals, observational chemicals and restricted or banned chemicals. But some carcinogenic chemicals are not regulated by the TCCA.

Internationally, the WHO Resolution on Cancer Control (WHA58.22) [20] provides a strong impetus for countries to develop programs aimed at reducing cancer incidence and mortality. The IARC was established in May, 1965 through a resolution of the XVIIIth World Health Assembly as an extension of the WHO. The IARC releases authoritative data and publications about carcinogenicity [21-23]. Europe and the US have carried out the task of defining carcinogens and classifying them with criteria. Hazard information including usages and amount in circulations have been received from companies for all chemicals with more than 1 ton in circulation in the Registration, Evaluation, Authorization and Restriction of Chemicals (REACH), EU. Based on lists of dangerous substances, assessments of carcinogens and rankings are being done in the EU [24-26]. The US National Toxicology Program (NTP) determines carcinogens based on authoritative data from the IARC combined with its own animal experimentation data. The NTP prepares the report on carcinogens (RoG) on behalf of the Secretary, Health and Human Services. The 12th RoC, the latest edition, was published on June 10, 2011. The 13th RoC is under development. The RoC is a congressionally mandated, science-based, public health report that identifies agents, substances, mixtures, or exposures (collectively called "substances") in our environment that may potentially put people in the US at increased risk for cancer. But there are some critics of the NTP. The NTP's report is limited because it evaluates few agents and does not distinguish between probable and possible human carcinogens on its B-list [27-29].

Many countries are making international collaborative networks with the IARC and WHO to share their carcinogen lists (Table 2) [30-33]. The Korean government is also trying to classify carcinogens by introducing a Globally Harmonized System of Classification and Labeling of Chemicals (GHS). The MOE and Labor has provided information about GHS Material Safety Data Sheets (MSDS) on 43,000 chemicals since 2009. The MOE is trying to build a chemical registration and assessment system based on GHS and the IARC's carcinogen list. However, there are no integrated regulatory laws and management systems guarding against carcinogen exposure in Korea. Many separate laws have been put into effect to manage carcinogen exposure (Table 1). Yet some carcinogens are still not regulated by the Toxic Chemicals Control Law in Korea (Table 3)

Table 1. Overview of laws related to carcinogen management in Korea

Disease or carcinogen	Legislation (Law)	Authorities
Cancer	Cancer Control Act National Health Promotion	Ministry of Health and Welfare
Pesticides	Agricultural Chemicals Control	Ministry of Agriculture
Industrial chemicals	Toxic Chemicals Control	Ministry of Environment
	Industrial Safety and Health	Ministry of Employment and Labor
Pharmaceutical products	Pharmaceutical Affairs	Ministry of Health and Welfare
Cosmetics	Cosmetic	Ministry of Health and Welfare
Food additives	Food Sanitation	Ministry of Health and Welfare
Radioactive substances	Atomic Energy	Ministry of Science and Technology

Table 2. International classification of carcinogenicity

Criteria of classification	Classification of carcinogenicity				
	IARC[a]	ACGIH[b]	EU[c]	NTP[d]	US EPA
Definite human carcinogen	Group 1 (109)	A1 (28)	Carc. 1A (92)	K (54)	Carcinogenic to humans
Probable carcinogen	Group 2A (65)	A2 (32)	Carc. 1B (813)	R (186)	Likely to be carcinogenic to humans
Suspicious carcinogen	Group 2B (275)	A3 (117)	Carc. 2 (165)		Suggestive evidence of carcinogenic potential
Unclassified carcinogen	Group 3 (503)	A4 (226)			Inadequate information to assess carcinogenic potential
Non carcinogen	Group 4 (1)	A5 (2)			Not likely to be carcinogenic to humans

IARC, International Agency for Research on Cancer: ACGIH, American Conference of Governmental Industrial Hygienists; EU, European Union; NTP, US National Toxicology Program; EPA, Environmental Protection Agency; Carc, carcinogen.

[a]From International Agency for Research on Cancer. Agents classified by the IARC monographs, volumes 1-107; 2012 [Internet] [30]; [b]From American Conference of Governmental Industrial Hygienists. 2010 TLVs and BEIs: based on the documentation of the threshold limit values for chemical substances and physical agents & biological exposure indices [31]; [c]From Institute for Health and Consumer Protection. Table 3.1 and Table 3.2 of Annex VI to the CLP regulation, as updated with the 1st ATP; 2012 [Internet] [32]; [d]National Toxicology Program. 12th report on carcinogens; 2011 [Internet] [33].

Table 3. Some carcinogens not regulated by the Toxic Chemicals Control Law in Korea

Material	Current management		Amount in circulation[a]
	Laws	Major contents	
1,3 butadiene	Explosive Safety Control	Explosive gas - Registration for import, manufacturing permission, stablishment of standards on storage and facilities	1.82 million ton
	Industrial Safety and Health	Hazardous substance for which occupational exposure limits are established - Exposure limits (TWA): 2 ppm	
Benzo[a]pyrene	Ambient Air Environment Conservation	Specified hazardous air pollutants Establishment of management standards on emission facilities (2011-)	Incomplete combustion
Phenacetin	Pharmaceutical Affairs	Medicines - Registration for import permission and manufacturing business	1 ton
8 methoxypsoralen	Pharmaceutical Affairs	Medicines	-
Azathioprine	Pharmaceutical Affairs	Medicines	-
Beryllium and its compounds	Industrial Safety and Health	Hazardous substance for which occupational limits are established - Exposure limits (TWA): 0.002 mg/m^3	0.4 ton
Silica, crystalline	Industrial Safety and Health Act	Hazardous substance for which occupational exposure limits are established - Exposure limits (TWA): 0.05-10 mg/m^3	2.85 million ton

TWA, time weighted average.
[a]From Kim PJ. Carcinogen assessment: management in Toxic Chemical Control Act and future perspective [34].

[34]. In these circumstances, it is inevitable there is a chance of exposure to some definite and probable human carcinogens in certain workers and citizens. There remain several dead zones where carcinogen exposures cannot be controlled properly in Korea. For example, crystalline silica, controlled by the Industrial Safety and Health Act, is a hazardous substance for which occupational exposure limits are established. Yet even though crystalline silica is a definite human carcinogen, there is no regulation by the TCCA. Besides crystalline silica, certain other definite human carcinogens, including 1,3-butadiene and beryllium, are not regulated by the TCCA in Korea (Table 3). The TCCA should be strengthened to regulate all chemical carcinogenic substances in circulation. Korean governmental bodies need to establish a national action plan on management of carcinogenic risk in Korea.

Conclusion

The importance of primary prevention has been recognized, but it has not been actively carried out because of limited budgets and difficulties in proving its effects in a short period of time. Current cancer control programs are focused on management of existing cancers. Under this system, all natural cycles, including etiologies, exposures, diseases, and aftereffects were not taken into comprehensive consideration. Effective cancer prevention strategies were not established in the current system.

A national carcinogen list in Korea should be established soon and should be based on the GHS.

To deal with some carcinogens in our environment that may potentially increase risk for cancer, we can start our own NTP, an interagency program to evaluate agents of public health concern by developing and applying tools of modern toxicology and molecular biology. This list may include three categories of substances and processes regarded as carcinogenic, primarily by IARC, and to a lesser extent, the Government's Annual Report on Carcinogens from an NTP-like program. If we can have national carcinogen lists, the Korean government could reach the first milestone on the way toward its final goal of primary prevention of cancer.

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Conflict of Interest

The authors have no conflicts of interest with the material presented in this paper.

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