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Review Article

Reproductive Toxic Chemicals at Work and Efforts to Protect Workers' Health: A Literature Review

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ABSTRACT

A huge number of chemicals are produced and used in the world, and some of them can have negative effects on the reproductive health of workers. To date, most chemicals and work environments have not been studied for their potential to have damaging effects on the workers' reproductive system. Because of the lack of information, many workers may not be aware that such problems can be related to occupational exposures. Newly industrialized countries such as Republic of Korea have rapidly amassed chemicals and other toxicants that pose health hazards, especially to the reproductive systems of workers. This literature review provides an overview of peer-reviewed literature regarding the teratogenic impact and need for safe handling of chemicals. Literature searches were performed using PubMed, Google Scholar, and ScienceDirect. Search strategies were narrowed based on author expertise and 100 articles were chosen for detailed analysis. A total of 47 articles met prespecified inclusion criteria. The majority of papers contained studies that were descriptive in nature with respect to the Medical Subject Headings (MeSH) terms and keywords: "reproductive and health or hazard and/or workplace or workers or occupations." In the absence of complete information about the safe occupational handling of chemicals in Republic of Korea (other than a material safety data sheet), this review serves as a valuable reference for identifying and remedying potential gaps in relevant regulations. The review also proposes other public health actions including hazard surveillance and primary prevention activities such as reduction, substitution, ventilation, as well as protective equipment.

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1. Introduction

Chemicals are ubiquitous substances with both positive and negative effects found in workplaces across the globe. Together with other agents (e.g., radiation and bacteria), chemicals may also negatively affect the reproductive systems of male and female workers (Table 1). Several environmental chemicals are suspected to be responsible for adverse health effects on the reproductive system in various organisms [1]. Exposure to toxicants before and after conception can affect parents, fetuses, and newborns. Pregnant women tend to be concerned about three of the most common occupational health hazards (i.e., tobacco smoke, video-display terminals, and the quality of indoor air). In addition, biological stressors such as shift work may also negatively impact workers' reproductive systems. Despite the controversies and uncertainties

about these factors and the lack of data regarding other potential occupational health hazards, the consequences of toxic exposure are necessary issues that have to be delicately broached by occupational health and safety counselors in their discussions with pregnant workers [2]. It is worth noting that, with the exception of reproductive toxicants listed in the Korean Occupational Safety and Health Act (Table 2), the potentially damaging effects of chemicals to workers' reproductive systems have not been extensively reviewed in the literature.

Despite the lack of information about possible reproductive health effects, many potentially toxic substances are still used in a variety of workplaces, and many workers are exposed to such hazards every day at work. Given certain toxicant-workplace scenarios, some workers may develop sexual or reproductive problems. Because a material safety data sheet is composed of many

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Table 1
Examples of reproductive hazards to humans*

Hazard	Outcome
Proven reproductive hazards (based on human studies)	
Anesthetic gases	Miscarriage, death of newborn
Diethylstilbestrol	Cancer
Hepatitis B	Newborn hepatitis, liver cancer
Organic mercury	Cerebral palsy, brain malformation
Lead	Miscarriage, premature birth
Polychlorinated biphenyls	Low birth weight
Radiation	Miscarriage, brain defects, skeletal defects
Suspected reproductive hazards (based on human studies)	
Carbon monoxide	Slowed growth
Cytotoxic drugs	Miscarriage
Ethylene oxide	Miscarriage
Hexachlorophene	Birth defects
Organic solvents	Cleft palate, miscarriage, newborn infection, childhood cancer
Physical stress (including heat)	Prematurity
2,4,5-Trichlorophenol	Miscarriage
Vinyl chloride	Brain defects
Suspected reproductive hazards (based on animal studies)	
Acrylonitrile	
Arsenic	
Cadmium	
Dioxin	
Glycol ethers	
Inorganic mercury	
Organochlorine pesticides	
Polybrominated biphenyls	

* Note. Sourced and modified from "Clinical occupational medicine," by L. Rosenstock, M.R. Cullen, 1986. W. B. Saunders Company, London. Adapted with permission.

different sections, the toxicological and health information may only have one or two lines about the reproductive toxic impact of any chemical on diverse workers found in any workplace. However, the need for regulations regarding personal protective equipment for workers handling chemicals is recognized, albeit not implemented uniformly for couples who are pregnant or planning to have a child. Thus, collecting more information about the reproductive toxic impacts of chemicals in terms of occupational health and safety continues to be a thriving area of research, although data tend to be confined to individual laboratory studies published in specialty journals. In addition, there is a paucity of review articles on this topic. This review summarizes important current and pending developments in the field of known/potential reproductive toxic chemicals used in the workplace and addresses some of the potential health implications.

2. Methods

We collected information from peer-reviewed literature on the occupational health hazards posed by toxicants that may impact the reproductive systems of workers, with a view to the prevention of work-related diseases. Topics discussed included when and how reproductive damage occurred, what kinds of reproductive health problems could occur, how workers could tell if a chemical or work situation posed hazards to their reproductive health, how workers were protected, and the role of the health and safety representative. Literature searches were performed using the following sites: PubMed (<http://www.ncbi.nlm.nih.gov/pubmed>), Google Scholar (<http://scholar.google.com>), and ScienceDirect (<http://www.sciencedirect.com>). The search strategy used a combination of the following Medical Subject Headings (MeSH; National Center for Biotechnology Information, Bethesda, MD, USA) terms and keywords:

"reproductive and health or hazard and/or workplace or workers or occupations and/or prevention or protection." The search results were further narrowed by reviewing titles and abstracts. Additional missing case reports were identified by reviewing the references of the review articles and bibliographies found on scholar.google.com. Disagreements in information from the articles and conference abstracts were resolved by further discussion. Based on the literature data, about 100 potential articles were found. A total of 47 articles that met the inclusion criteria were chosen for detailed analysis.

3. Results

Reproductive toxicology is focused on the risks, mechanisms, outcomes, and prevention of harmful exposure to reproductive toxic chemicals in the workplace. Preconception and postconception exposures of fertile men and women to reproductive toxic chemicals at work may detrimentally affect the parents and their children. Adverse effects on the structural and functional components of male and female reproductive systems may lead to impaired fertility or infertility of exposed workers. According to the World Health Organization (2013) [3], infertility is defined as "a disease of the reproductive system defined by the failure to achieve a clinical pregnancy after 12 months or more of regular unprotected sexual intercourse. An inability to become pregnant with a live birth, within five years of exposure based upon a consistent union status, lack of contraceptive use, non-lactating and maintaining a desire for a child. Infertility may be caused by an infection in the man or woman, but often there is no obvious underlying cause." Reduced fertility may be expressed as a reduction in the number of live births, reduced odds of conception, or increased time to pregnancy [4]. Reproductive hazards in the workplace have been investigated over several decades using workplace experience and epidemiology studies, as well as studies in laboratory animals. Each of the reproductive and developmental stages can potentially be disrupted by exposure of humans or laboratory animals to specific toxicants. Various endocrine-disrupting chemicals may adversely affect the sex and reproductive organs of men and women. Furthermore, the reproductive well-being of women exposed to toxicants may be affected to the extent that negative health consequences are visible during each trimester of any potential pregnancy [5].

Data interpretation of exposure to hazardous chemicals in the workplace may be confounded by some factors, including age and ethnicity, and lifestyle factors such as smoking, diet, alcohol and recreational drug use, stress, noise, and work shifts [6]. The nature and magnitude of reproductive toxicities are often dependent on exposure levels, but these factors are difficult to assess in an occupational setting. Age is another confounder in assessing the health hazard posed by chemicals to the reproductive systems of females. Using ionizing radiation as an example, older women may have a higher cumulative exposure than younger women. The same analogy may hold true for chemicals [7]. Paternal exposure could also contribute to developmental toxicity, but it may be difficult to assess the impact of separate maternal and paternal exposures. If only limited information exists on the potential human reproductive effects of chemicals, it may then be necessary to rely on data from laboratory animals. Many examples exist in the scientific literature of chemicals that induce reproductive and developmental toxicities, and the predictive value of these animals has proven to be useful in the safety assessment of chemicals [8]. It is important to have an understanding of these differences and recognize potential limitations in species extrapolation such as sperm count and concentration, motility, and chromosome morphology [8,9]. Developmental studies of toxicity in laboratory animals showed the importance of the following considerations: (1) divergent differentiation of structure, function, and physiology across species; (2)

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