

# Reproductive and Developmental Hazard Management

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The magnitude, characterization, and control of occupational and environmental reproductive and developmental health risks are areas of active scholarly investigation. Scientific, epidemiological, and toxicological data concerning reproductive and developmental health risks have been determined for some chemicals, but data on many chemicals, physical agents, and biological agents are limited and, in some instances, nonexistent. Consequently, there may be considerable uncertainty about what action should be taken to adequately manage potential workplace reproductive health hazards.

The American College of Occupational and Environmental Medicine (ACOEM) has developed this guidance document to assist physicians and occupational health professionals in managing reproductive and developmental risks and uncertainties. This guidance describes measures to assess the magnitude of potential reproductive and developmental risks in the workplace and presents options to manage the uncertainty associated with these risks.

## BACKGROUND

Industrial exposure limits promulgated for most chemical agents by the US Occupational Safety and Health Administration (OSHA), that is, permissible exposure limits (PELs), or those of the American Conference of Governmental Industrial Hygienists (ACGIH), that is, threshold limit values (TLVs), have in most cases been established without considering protection from adverse reproductive or developmental health effects. Therefore, compliance with OSHA exposure limits for many compounds may not ensure protection of reproductive health. Employees have the right to know about potential reproductive health hazards that are encountered in the workplace and the right to work in an environment that is free of significant reproductive health risks.

Reproductive toxicity is classically defined as the occurrence of adverse effects on the reproductive system of the male or female that may result from exposure to environmental agents. This toxicity may be expressed as alterations to female or male reproductive organs, related endocrine system, or abnormal pregnancy outcome.<sup>1</sup> However, some definitions for reproductive toxicity also include subsequent effects on the offspring.<sup>2</sup> Developmental toxicity can be defined as “the occurrence of adverse effects on the developing

organism that may result from exposure before conception (either parent), during prenatal development, or post-natal to the time of sexual maturation. Adverse developmental effects may be detected at any point in the life span of the organism.”<sup>2,3</sup>

In the US, all-encompassing “fetal protection policies,” which categorically exclude large classes of workers from specific tasks or types of employment, are illegal. The US Supreme Court ruled in the *Johnson Controls* decision that an employer could not exclude fertile women from lead-exposed jobs, holding that limitations on employment during pregnancy must relate to ability to perform the duties of the job, and that decisions on exposure of the fetus must be the right of the fully informed mother.<sup>4</sup> Therefore, decisions on reducing occupational exposure to potential reproductive or developmental hazards and on work restrictions should be based on an individualized risk assessment for each employee and workplace reproductive policies must avoid gender discrimination.

## MAGNITUDE OF WORKPLACE REPRODUCTIVE HEALTH PROBLEMS

Although the number of women in the workplace increased from 30 million in 1970 to more than 73 million in 2015,<sup>5</sup> it is important to remember that many toxicants affect both male and female reproductive function and thus managing reproductive hazards is not confined to concerns about women of reproductive age. There are no reliable estimates concerning the number of either male or female workers who are at a significant risk of exposure to reproductive toxicants.<sup>6</sup> However, reproductive health concerns among both workers and the general public are increasingly being raised in both the clinical setting and in the media.

## EPIDEMIOLOGICAL DATA

Some of the uncertainty about specific toxicants that may present reproductive or developmental risk and its magnitude can be explained by the methodologic challenges of epidemiological studies addressing these questions. For example, spontaneous abortions commonly occur among the general population and some studies suggest that up to 40% of conceptuses undergo spontaneous abortion before the first missed menstrual period.<sup>7</sup> Consequently, spontaneous abortion (miscarriage) can occur without a woman’s knowledge, making monitoring of this endpoint difficult. Other adverse outcomes might require very large study populations to have sufficient power to detect differences in exposure groups or to allow attribution of risk.<sup>8</sup>

As well, reproductive studies can be confounded by multiple factors such as maternal age, history of sexually transmitted infections, frequency of sexual activity, and nutritional status, which are challenging to adjust for in statistical analyses. Other factors that can affect fertility, such as smoking, alcohol, medication, and drug use, general health, and socioeconomic status, can be more readily adjusted for in analyses. Thus, epidemiology studies must be examined in a context of the body of literature available, mindful of their limitations such as study design and recall bias and ultimately as only part of the assessment of the potential hazard a certain toxicant or exposure scenario presents.

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## REPRODUCTIVE AND DEVELOPMENTAL TOXICITY

Human reproduction involves multiple precisely timed processes, with windows of susceptibility beginning before conception for both the male and female and continuing through the birth of the offspring. A detailed description is beyond the scope of this document, but can be found in comprehensive texts on human reproduction and obstetrics (Appendix A). Reproductive toxic effects can occur in either parent or the offspring. Characteristics that distinguish reproductive toxicity from other toxic effects include the following: (1) adverse effects in an exposed person that may only manifest in the fetus or offspring (eg, an exposure to a reproductive toxicant in a male may produce an effect in the conceptus); (2) an effect such as infertility that may not become evident until children are desired and may therefore go unnoticed for long periods; and (3) normal reproductive function is only expressed intermittently. Disturbances of the reproductive process from occupational reproductive hazards can produce a broad range of potential adverse effects.

### Developmental Toxicology

Developmental insult to the offspring can occur through toxicant exposures to either parent before conception, via exposures to the mother during pregnancy, and by exposures after birth via lactation or direct exposure to the child. Toxicants that cause mutations, epigenetic changes, or other damage to germ cell DNA can cause developmental toxicity (if they do not result in death of the germ cell). Germ cell lines and organ systems have different critical windows of development. Therefore, exposure to the same dose of a toxicant will have very different effects depending on the developmental stage of the fetus and offspring when the exposure occurs. The axiom that “the dose makes the poison” holds true for developmental toxicology only if one also takes into account the developmental stage at which the dose was delivered. Detailed reviews of critical developmental windows for different organ systems and their relevance to developmental toxicology have been published.<sup>9</sup> The spectrum of possible adverse developmental effects from toxicant exposure includes death of the conceptus or offspring, malformation, altered function, decreased growth, and increased risk of diseases, such as cancer, heart disease, and diabetes, later in life.

### AVAILABILITY OF REPRODUCTIVE TOXICOLOGY DATA

Occupational exposure to reproductive toxicants may occur via inhalation, skin absorption, or ingestion. However, there may be limited or no toxicological information available for many industrial chemicals. A recent review summarizes the scientific evidence linking environmental exposures to chemicals and radiation with human adverse pregnancy outcomes.<sup>10</sup> Several agents such as dibromochloropropane (DBCP), ionizing radiation, lead, and 2-bromopropane have been known to affect human spermatogenesis.<sup>3,11,12</sup> Ionizing radiation and 2-bromopropane have also been recognized as destroying ovarian follicles.<sup>11,12</sup> Table 1 outlines some of the most commonly recognized reproductive hazards by occupation and industry, recognizing that both the relative potency of the hazards listed and the strength of the evidence for their reproductive effects may vary. Table 2 lists some of the infectious agents that may affect fertility and fetal development. A much broader range of agents are recognized as having an effect upon, or the potential to produce, reproductive or developmental toxicity based on animal toxicology studies. A more detailed review of the potential risks of specific workplace exposures can be undertaken using the data sources for reproductive hazards listed in Appendix A once a work history and job tasks are ascertained.

## FRAMEWORK FOR THE ASSESSMENT OF REPRODUCTIVE AND DEVELOPMENTAL HEALTH RISKS

The assessment of occupational reproductive and developmental risks, like any risk from an occupational hazard, involves several distinct steps, including hazard identification, dose-response assessment (when applicable), exposure assessment, and risk characterization. The process of risk assessment may require a multidisciplinary team of occupational health professionals from several disciplines, including occupational medical specialists, toxicologists, obstetrician/gynecologists, and exposure assessment specialists, such as industrial hygienists, and other health professionals.

Some workplaces have comprehensive occupational medicine and industrial hygiene resources and can assess workplace exposures and hazards throughout the worksite. In workplaces with appropriate engineering controls, existing industrial hygiene data may be able to confirm that all chemicals are well controlled, such that air concentrations are quite low or nondetectable and skin exposures are precluded by controls, work practices, or use of appropriate personal protective equipment (PPE). Review of the chemicals in use should be able to identify a subset of agents that might pose reproductive or developmental hazards at some dose (recognizing the limitations in the toxicology database). Regular review of new scientific study information from reproductive/developmental toxicity studies permits timely updates of risk characterizations.

A thorough medical and occupational and environmental history is essential. In addition to routine past medical and surgical history, family history, and prescription and over-the-counter medication and supplement history, a thorough gynecological and obstetric history should be obtained from the woman, and a reproductive history should be obtained for her partner. In addition, occupational tasks encountered in many jobs, such as heavy lifting or hard physical work, may affect pregnancy outcomes and these risk factors should be ascertained in an occupational history. A detailed exposure history of chemical, physical, and biological agents to which the employee is potentially exposed at work and in the home is critical. In addition, the work exposures of her partner should be identified. These would include active and inert ingredients. Safety data sheets (SDSs) can be obtained from employers to assist in identifying the components of various products used in the workplace. Pertinent nonoccupational factors in the social and personal history of both parents, such as alcohol, smoking, exercise, hobbies, or use of other drugs, personal care products, and cleaning agents that may also affect reproductive outcomes should be sought, in addition to medical conditions, and prior reproductive history.

A hazard evaluation of the agents to which the employee and her partner are exposed at work as well as at home then needs to be completed to identify which agents may pose reproductive or developmental risks. SDSs provide a source of information regarding the constituents in materials. Nevertheless, the manufacturer may not reveal the identity of all the ingredients in the product, as they are allowed to withhold that information for trade secret ingredients. In addition, SDSs vary in quality and detail, reflecting the resources and capabilities of the authors. Often, SDSs contain limited or no information regarding the potential reproductive and developmental toxicity of the ingredients; thus, one cannot rely solely upon the toxicology information they contain. However, new US and European Union regulations require manufacturers to incorporate a classification of ingredients according to the scheme provided by the United Nations Global Harmonized System, including their potential reproductive toxicity. After the phase-in period, these new SDSs should facilitate hazard identification by hazard type and include reproductive toxicity and carcinogenicity.<sup>13</sup> (See

**TABLE 1.** Potential Reproductive Toxicants by Occupations

Occupations	Potential Reproductive Toxicants
Artists	Cadmium, mercury, lead, toluene, organic solvents
Athletes	Performance-enhancing pharmaceuticals
Aviation	Hydrocarbons and solvents (n-hexane, tri-ortho-cresyl phosphate, aviation fuels) carbon monoxide
Carpenters, loggers	Formaldehyde, arsenic, creosote, toluene
Concrete workers, masons	Chromium
Divers, commercial	Nitrogen narcosis, decompression effects, oxygen toxicity, carbon dioxide asphyxia
Domestic/building maintenance workers	Cleansers, formaldehyde, hexachlorophene
Dry cleaning workers	Chlorinated solvents
Electricians	Lead, polychlorinated biphenyls (PCBs) and related compounds
Electroplaters	Cadmium
Exterminators	Pesticides-organophosphates, fertilizers, fungicides, nematocides
Farmers	Infectious agents, pesticides, fertilizers, diesel exhaust
Firefighters	Carbon monoxide, other products of combustion (acrolein, cyanide) hyperthermia
Floor and carpet layers	Solvents (adhesives and glues)
Florists and groundskeepers	Pesticides: organophosphates and organochlorines, fertilizers, fungicides, nematocides
Food preparers, caterers	Phthalates, infectious agents, alcohol-based food warmers
Hairdressers, cosmetologists, nail salon workers	Solvents, formaldehyde, phthalates, dyes (paraphenylenediamine), thioglycolate, cosmetics containing lead and/or nanoparticles
Health care workers	Waste anesthetic gases, ionizing radiation, ethylene oxide, antineoplastic agents, infectious agents
Jewelers	Solvent degreasers, soldering fluxes
Mechanics	Degreasers, trichloroethylene, lead, carbon monoxide, diesel exhaust, ethylene glycol
Military personnel	Lead, explosives-nitrates, solvents, degreasers
Morticians	Formaldehyde, infectious agents
Painters, furniture refinishers	Methylene chloride (carbon monoxide), lead, solvents (toluene, Stoddard solvent), isocyanates, glycol ethers
Plumbers	Lead, chlorofluorocarbons, glues and solvents (toluene, styrene) metal soldering flux
Police and security guards	Assault, lead, nitrates, selenium, solvents – clandestine drug lab chemicals
Printers	Toluene, solvents, glycol ethers
Roofers, road/transportation workers	Carbon monoxide, polycyclic aromatic hydrocarbons (coal tar, asphalt fumes)
Sanitation and sewer workers	Asphyxiants (Hydrogen sulfide, methane), infectious agents
Service workers (food service, personal care, retail)	Phthalates, infectious agents
Semiconductor and electronics industry workers	Glycol ethers, arsenic compounds
Ship and dockyard workers	Lead, styrene, glycol ethers
Shoemakers	Solvents (benzene, hexacarbons, vinyl chloride)
Smelters and metal re-claimers	Lead
Veterinarians and animal care workers	Anesthetic gases, ionizing radiation, pesticides, infectious agents

Appendix A for resources that may be useful in identifying reproductive/developmental hazards.)

Next, the extent of the employee's and her partner's exposures to the agents identified as reproductive or developmental hazards must be assessed (exposure assessment). Estimates of frequency of exposure, duration of exposure, and route(s) of exposure, and concentration or intensity should be obtained for each agent that may cause reproductive effects. It is also important to ascertain whether any exposure control measures, such as engineering controls or PPE, are used in the workplace or at home. If the employer has conducted personal exposure monitoring for the employee or her partner (eg, radiation dosimetry) or ambient exposure measurements in the workplace, the results should be obtained and reviewed. A worksite evaluation by an industrial hygienist may be very useful. For selected agents, such as lead or mercury, biological monitoring may aid in quantifying exposure.

Risk characterization considers all the gathered data on toxicity and exposure to determine whether the employee's and/or her partner's estimated levels of exposure to the agents that have been identified as potential reproductive and developmental hazards pose a risk. Their estimated exposure levels should be compared with levels that have been demonstrated or strongly suspected to cause adverse reproductive effects in epidemiological studies or animal studies. When attempting to determine safe or unsafe levels

of exposure to humans by extrapolating from the results of animal studies, a safety or uncertainty factor is typically applied to relevant dose levels observed in the animal studies, such as the NOAEL (no observed adverse effect level) or LOAEL (lowest observed adverse effect level).

In the classical risk assessment paradigm, if either the employee or her partner is exposed to an agent above or near levels associated with adverse effects, then there is considered to be a significant risk. However, in the real world, there often are incomplete data both on the hazard identification side and on the exposure side, and recommendations must be made based on the available information.

Risk communication is the next critical step in which the employee and her partner are provided with the information they need to make informed decisions about the reproductive health risks of their exposures. It is important to answer all questions fully and to provide the best available information, including a discussion of the limitations of that information.

Risk management is the final step in the evaluation. It requires that the physician, patient, her partner, and their employers work together to decrease or eliminate any potential workplace (or nonworkplace) reproductive risks that were identified. Exposure reduction or elimination is the most desirable approach to risk management. Options include eliminating the chemical(s) or

**TABLE 2.** Infectious Agents Affecting Fertility and Fetal Development

Organism	Occupational Risk	Sterility (M, F)	Perinatal Mortality	Prematurity	IUGR	Other Perinatal/ Neonatal Outcomes
<i>Herpes simplex II</i>	Health care	F > M	+	+	+	Meningitis, seizures
Hepatitis B	Health care, sex workers	–	–	–	?	Carrier state
Human immunodeficiency virus	Health care, sex workers	–	?	+	+	
Cytomegalovirus	Health care	–	+	+	+	Meningitis, seizures
Parvovirus B19	Institutional outbreaks (schools, day care centers, human services)	–	+	–	–	Fetal anemia, hydrops
Rubella	Health care, schools, day care	–	+	+	+	Meningitis, seizures, cardiac defects
<i>Leptospira interrogans</i>	Agriculture, sewerage workers	–	+	+	?	Spontaneous abortion, Jaundice, Hepatorenal failure
<i>Listeria monocytogenes</i>	Agriculture, animal care	–	+	+	+	Spontaneous abortion, neonatal sepsis, jaundice, meningitis
<i>Brucella</i> spp.	Agriculture, animal care	–	–	+	+	Spontaneous abortion, Epididymo-orchitis
<i>Toxoplasma gondii</i>	Animal care (cats)	–	+	+	+	Meningitis, seizures, sepsis, chorioretinitis, microcephaly
Zika virus	Outdoor workers	–	+	–	+	Microcephaly, intercranial calcifications

IUGR, intrauterine growth restriction.

agent(s) or replacing it with a safer one, implementing or improving engineering controls, designing and enforcing safer work practices, and issuing or upgrading PPE. If none of these can achieve a safe environment, restrictions or a temporary transfer may be required. If the employer cannot or will not reduce exposure and no unexposed job locations for a temporary transfer are available, then the employee may face the difficult decision of removing herself from the workplace or continuing to work in a situation that poses potential reproductive risks. Temporary disability benefits may not be available for an individual attempting to avoid exposure to prevent a possible adverse reproductive outcome. Temporary disability benefits are more likely to cover a pregnant woman in situations deemed to be high risk or with current pregnancy complications. Permanent removal from a job is the least desirable action, and it is important to help the employee and her husband evaluate all other possible options and uncertainties that might still exist with other workplace assignments.

The following case studies are intended to illustrate the application of these principles to evaluation of individual workers.

### Case #1: Pre-Conception—A Male or Female Employee Indicates Intention to Conceive

A 29-year-old emergency department (ED) nurse is referred because she and her husband would like to try to conceive, but she is concerned about possible effects of her work exposures during early pregnancy. Her spouse is employed as a plant operator in the sunscreen industry.

This is in many ways the ideal scenario because the employee is seeking advice *before* she becomes pregnant. This scenario provides the opportunity to optimize health and work and home environments before conception. However, insufficient data on some chemicals' or agents' reproductive health effects, legal issues, and confounding factors may make this task more difficult. It is also important to remember that as approximately 49% of all pregnancies in the US are unintended, employees may not seek advice about possible exposures before pregnancy.<sup>14</sup>

Performed as outlined in the framework above, a hazard evaluation and risk characterization of nursing work in the ED may disclose a broad range of potential hazards, including exposures to infectious diseases, radiation, manual patient lifting,<sup>15</sup> and traumatic injury. However, in many cases, these hazards can be controlled or obviated to reduce risks to conception and to early pregnancy while the employee continues in productive work. Review and updating of the employee's immunization status can prevent the transmission of many vaccine-preventable diseases, including rubella and hepatitis B, which have adverse consequences for the fetus. Workplace hazard controls, such as the use of universal precautions for the prevention of infection transmission, x-ray protection procedures, and policies to reduce workplace violence and trauma, should be reviewed and examined and compliance measures reinforced if needed. Personal monitoring data, such as x-ray film badges, can be reviewed and an estimate of exposure and the effectiveness of control measures can be judged. These actions have the additional beneficial effect of protecting the employee's coworkers, many of whom may also be considering conceiving or have other health concerns over work. Close attention to mitigating the overall risks of the workplace is also valuable in helping to assure that inadvertent exposure to an unintended or unforeseen pregnancy has been reduced as much as possible. Given assurance that known or suspected hazards are properly controlled, the provider can be reassuring about continuation of work during conception and early pregnancy. Finally, careful attention should also be paid to specific circumstances of the work that may change over time, and recommendations adjusted as needed. For example, if a high risk of exposure to infections, such as H1N1 influenza or rubella, which are associated with congenital anomalies and other adverse obstetric outcomes, becomes apparent during an outbreak or pandemic, the provider should consider the possibility of job transfer or other means to reduce risk at conception or early pregnancy.

### CASE #2: Pregnancy—An Employee Indicates She Is Pregnant

A 32-year-old aircraft maintenance technician, whose duties include engine testing, refueling, and repair of airplanes and

helicopters, is referred to the occupational physician after a positive pregnancy test. Her supervisor requests your recommendations regarding her fitness for duty. On the day of her clinic visit, it has been 8 weeks since her last menstrual period.

This is a much more common scenario than Case #1. It is too late to prevent exposures during the pre-conceptional period and embryonic period, when many of the major organ systems are forming. A hazard evaluation and exposure assessment similar to Case #1 of employee's occupational and home environments needs to be performed in order to characterize the risks of the exposures that have already occurred and those that can be changed or stopped to prevent further possible damage. Examples of possible hazards she may have been exposed to include jet fuel, degreasing agents, and other solvents. Exposure to organic solvents during pregnancy has been associated with an increased risk of spontaneous abortion and may also be associated with an increased risk of birth defects.<sup>16,17</sup> However, organic solvents represent a diverse group of chemicals with differing toxicological properties, and the epidemiological database is insufficient to draw conclusions about the reproductive and developmental toxicity of most individual organic solvents. An airplane technician may be exposed to high noise levels that may reach up to 120 dB during engine testing, and there is some suggestion that high noise exposures may affect the fetus (although this is controversial).<sup>18</sup> In this example, the pregnant technician can readily protect her cochlear hair cells with well-fitted ear-muffs and plugs, but this can leave the fetus relatively unprotected because the abdominal wall, myometrium, and amniotic sac tissues can only attenuate high-frequency (> 500 Hz) sounds by 20 to 35 dB, and allow low-frequency (< 500 Hz) sounds to pass without attenuation.<sup>19</sup>

If the risk assessment indicates that significant exposures to developmental toxicants may have occurred, the development of the major organ systems can be evaluated with fetal ultrasound examination. If significant exposure to mutagens may have occurred, then referral to a genetic counselor or maternal fetal medicine specialist may be indicated. Termination of pregnancy is rarely indicated unless there is frank maternal poisoning or documented fetal effect. If exposure is negligible or low, then reassurance is generally indicated. In the intermediate situation in which no maternal poisoning or documented fetal effects have occurred, but the risk characterization leads to the conclusion that significant developmental risks exist in the workplace or home, then prevention of continued exposure to these risks must be the priority. In all these situations, it is important to fully communicate the risk characterization to the patient, including an assessment of the uncertainties and limitations in the conclusions that have been reached.

Finally, steps must be taken to reduce or eliminate the identified risks. The tiered risk management strategy outlined for Case #1 also applies here, but in this case of a pregnant employee, temporary disability leave is a possible option if the preferred alternatives of exposure reduction/elimination or temporary job transfer are not available and if one has concluded that the aircraft maintenance technician is subject to high-risk workplace exposure(s). Some pregnant employees may not wish to reveal their pregnancy to their employers. They may feel that it is intrusive to disclose their pregnancy or fear that they will be laid off if they disclose their pregnancy. Although it is illegal for an employer to terminate a worker because of pregnancy, such fears may not be groundless for some workers. In such situations, it is important for the physician to help the pregnant worker to fully understand and weigh the potential medical consequences of her decision.

As previously noted, about 49% of all pregnancies are unplanned.<sup>14</sup> Pregnancy may not be recognized early enough for reassignment to protect a fetus during critical periods of development. These realities may reduce the effectiveness of a recommendation for self-reporting pregnancy. In addition, a requirement

for employee notification of pregnancy, intended pregnancy, or infertility status to the employer may be viewed as intrusive and some employees may feel that this requires them to disclose intimate personal details. Such disclosure may include health information that would otherwise be protected under federal law. Employees may, for whatever reason, choose not to identify themselves as being at risk, making passive and universal preventive measures, as well as no-fault exposure reporting programs, all the more important.

### CASE #3: Infertility

A 53-year-old firefighter and his wife, a 44-year-old hairdresser, have been trying to conceive without success for 2 years. They are concerned that occupational exposures have caused their troubles. Several issues are raised by this case. Fertility declines with age in both men and women. Twenty percent of married women aged 40 to 44 years are infertile.<sup>20</sup> The chances for conception in less than 12 months in partners of men older than 40 years are half those of men younger than 25 years of age.<sup>21</sup> On the contrary, both husband and wife in this scenario are employed in occupations that involve exposures to chemicals and, in the case of the husband, physical agents such as heat. Exposure to heat, resulting in increased scrotal temperature, has been associated with decreased semen quality.<sup>22,23</sup> Hairdressers have been reported to have slightly lower fecundability (per cycle probability of conception) than controls,<sup>24</sup> and hairdressing involves potential exposure to numerous chemicals (Table 1, hairdressers), some of which have been shown to cause reproductive toxicity in animal studies.<sup>25</sup>

A fertility specialist should evaluate both partners, as such an evaluation may yield the cause of infertility in many couples. It is estimated that 30% to 40% of infertility is due to male infertility issues such as sperm abnormalities; 45% to 55% is due to female infertility issues such as ovulatory problems; and 30% to 40% is due to tubal or peritoneal dysfunction.<sup>26</sup> Decreased libido, impotence, intercourse timing, and intercourse frequency also affect fertility. Hazard evaluation, exposure assessments, and risk characterization should be done for both partners as outlined for Case #1. If there is significant workplace or home exposure to an agent known to cause infertility, then the couple needs to be informed of the available data and involved in decision making. The same, tiered risk management strategy outlined for Case #1, with the same caveat that temporary disability leave is not likely to be an option, applies in this case.

### Case #4: Lifting

A healthy 28-year-old woman who works in the stockroom and shipping area of a manufacturing plant consults you to ask about the need for restrictions on lifting in her job; her last period was 10 weeks ago. This is her second pregnancy; the first pregnancy and birth were without complications. She frequently lifts and stacks boxes that weigh 15 to 20 pounds across her 8-hour shift; infrequently (four to five times per day), she will have to lift stacks of materials that weigh 40 pounds.

Questions are often directed to the contribution of physically demanding work and adverse pregnancy outcomes. Epidemiologic investigations have yielded mixed results. A meta-analysis of numerous studies demonstrated small but significant associations of high physical exertion, including heavy lifting, with preterm and small-for-gestational age birth, with odds ratios for these outcomes of 1.22 and 1.37, respectively.<sup>27</sup> Prolonged standing and high cumulative work fatigue were also associated with preterm birth, although some later studies have failed to confirm these findings.<sup>28</sup> On the contrary, leisure-time physical exertion, such as aerobic exercise, has not been found to be detrimental in pregnancy. More recently, guidelines for lifting in pregnancy were developed using the National Institute for Occupational Safety and Health's

(NIOSH's) lifting equation and applying its load reduction factors to changes in body habitus during mid and late pregnancy; these indicate that repetitive lifting at knee-to-shoulder height be limited to approximately 10 to 20 pounds, depending on frequency and duration of lifting.<sup>29</sup> The limitations suggested by this guidance are well within the bounds that have not been associated with adverse effects on pregnancy. Given the uncertainty in findings related to work physical demands and adverse outcomes, a reasonable course in the case above would be to attempt to limit heavy exertion and 40-pound lifting immediately; reduce frequent lifting to no more than 20 to 25 pounds beginning at approximately the 20th week of pregnancy, and to further reduce this limit to about 15 pounds by the third trimester. Many individuals will also begin to self-limit lifting tasks, as body mechanics change with increasing gestational age. It is also important to remember that pregnancy-related joint laxity may limit some physically demanding tasks. Restrictions may be more stringent if there is a history of a condition that may be affected by lifting, such as cervical insufficiency or preterm birth.

### Case #5: Lead

A 32-year-old lead battery worker inquires about the possibility of becoming pregnant and wants to know whether her child may be adversely affected by her past lead exposure. She has worked at her current job for 10 years and has had annual blood lead levels recorded as part of a medical surveillance program. None has been greater than 18 micrograms per deciliter ( $\mu\text{g}/\text{dL}$ ) of blood. Her current blood lead level is 14  $\mu\text{g}/\text{dL}$ . A zinc protoporphyrin level is 65  $\mu\text{g}/\text{dL}$  blood (upper limit of normal by laboratory 70). She has not had symptoms referable to lead exposure.

Recognition of the adverse neurocognitive and developmental effects of lead on the fetus and child has greatly increased over the past two decades. Recommendations have been made that maternal blood lead levels be no greater than 10  $\mu\text{g}/\text{dL}$  at conception and during pregnancy to reduce the risk of neurological effects including cognitive delays.<sup>30,31</sup> Infants' and children's lead levels should be kept at 5  $\mu\text{g}/\text{dL}$  or lower.<sup>31</sup> In addition, there is evidence that suggests an increased risk of spontaneous abortion at maternal lead levels above 10. Recommendations are therefore targeted at the delaying of conception until maternal levels are consistently below 10 and ideally below 5  $\mu\text{g}/\text{dL}$ . This may entail providing a transfer to a job away from lead exposure and frequent monitoring of blood lead levels for women wishing to conceive. However, additional risks may become apparent for women who have had long-term occupational exposure to lead; as lead is deposited in bone with chronic exposure, the maternal body burden is increased beyond that which may be reflected by a blood lead level. Maternal osteoclastic activity increases in the second and third trimesters as a means of mobilization of calcium for the developing fetal skeleton. This phenomenon may lead to increased release of lead from bony storage depots and an unanticipated rise in maternal blood lead. Consultation with an experienced toxicologist may be helpful in estimating body lead burden. As calcium supplementation may inhibit maternal bone remodeling during pregnancy and reduce lead release into the maternal and placental circulation from bony stores,<sup>32</sup> it should be considered in pregnant women with a past history of significant occupational lead exposure.

Lead provides an example of a toxin for which medical surveillance should be considered for populations at risk of exposure to a significant reproductive hazard. Data obtained from surveillance programs may be useful to the provider in evaluating current and past exposures to lead as part of a risk characterization. In addition, surveillance data can be used to help determine the efficacy of workplace controls. However, surveillance standards should be viewed in the light of the best information currently available. For example, the current OSHA lead standards, 1910.1025 for general industry (promulgated in 1978), and

1926.62 for the construction industry (promulgated in 1993), recommend removal from work if a pregnant woman's lead level is 30  $\mu\text{g}/\text{dL}$  or higher. This standard is inadequately protective and should be revised downward in light of two decades of data on the adverse effects of perinatal lead exposure.

### TEMPORARY REASSIGNMENT

In all of the scenarios presented, temporary reassignment should be recommended if the risk assessment determines that there is exposure to a reproductive or developmental toxicant that cannot be adequately controlled through engineering or work practice controls alone. When PPE may be required to control exposure, temporary reassignment should be considered if there is a significant exposure to a known reproductive hazard because PPE may not offer perfect protection and because there are limited data on respirator use during pregnancy.<sup>33</sup> The need for temporary reassignment will also be affected by an individual's medical history or risk factors.

### LEGAL CONSIDERATIONS

The main source of antidiscrimination protection afforded the pregnant employee is the 1978 Pregnancy Discrimination Act (PDA) Amendment to Title VII of the Civil Rights Act of 1964. Federal law protects against discrimination due to pregnancy, childbirth, or related medical conditions, and applies to employers, as well as state and local governments and labor organizations. PDA states that "Women who are pregnant or affected by related conditions must be treated in the same manner as other applicants or employees with similar abilities or limitations."<sup>34</sup> Thus, the employer should treat a pregnant employee unable to perform her job the same as other temporarily disabled employees. "For example, if the employer allows temporarily disabled employees to [perform modified tasks], perform alternative assignments or take disability leave or leave without pay, the employer also must allow an employee who is temporarily disabled due to pregnancy to do the same."<sup>34</sup> PDA also asserts that pregnant employees who are able to perform their jobs should be allowed to continue working, which includes situations in which women may have been absent for a pregnancy-related condition and have now recovered and can return to work. PDA does not determine or mandate the length of time an employee can take off during pregnancy or after delivery, only that pregnant workers should be treated the same as other temporarily disabled employees for the purposes of job modification or leave time, as well as for related benefits such as vacation calculation, pay increases, and accrual of seniority. If a pregnant woman does take time off, the job should be held for her as it would be for others on sick or disability leave, and any continuance or accrual of benefits that would occur during other types of disabilities should also relate to pregnancy-related conditions. In determining accommodations or leave for pregnancy-related conditions, the employer is permitted to require the pregnant employee to submit information from her physician regarding her inability to work or need for job reassignment before granting any leave or reassignment.<sup>35</sup>

Other laws aimed at protecting the pregnant employee are the Equal Employment Opportunity Act, the Americans with Disabilities Act (ADA), the related ADA Amendments Act (ADAAA) of 2008, and the Family and Medical Leave Act (FMLA). ADA and its 2008 amendments require reasonable accommodation by the employer on behalf of a worker with a qualified disability, unless the disabled worker presents a direct threat to her own or others' health and safety, or the accommodation imposes an undue hardship on business operations. Until recently, pregnancy and related conditions had not been considered a qualifying disability under ADA, as the condition was considered temporary and of finite duration, as well as, in most cases, representing a normal physiological human state. In response to a rising number of complaints of pregnancy-

related discrimination, as well as a broadening of the definition of qualifying disability under ADA, the US Equal Employment Opportunity Commission (EEOC) has recently provided guidance for compliance and enforcement of nondiscriminatory employment practices for the pregnant worker. This guidance is based on the premise that, although pregnancy itself may not be disabling, other conditions that co-occur with pregnancy may prevent effective performance of one's job during and after pregnancy. Job functions such as lifting capacity, ability to wear a respirator, or exposure to some chemical, physical, or biological hazards may be affected; pregnant workers may develop back pain, carpal tunnel syndrome, multiple gestations, history of preterm labor, or gestational diabetes that may be disabling through delivery and the puerperium.

EEOC's 2014 compliance guidance indicates that employers will be held to the same standard in accommodating pregnant workers as it does for other temporarily disabled employees based on PDA and ADA. If, for example, injured workers are provided with temporary modified duty, such as light-lifting jobs, until recovery, these must be made available on the same basis to accommodate pregnant workers who are similar in their ability or inability to work.

The broader application of these laws and the new EEOC guidance to workplace pregnancy discrimination is being currently tested. The US Supreme Court issued a ruling in a relevant case (*Young v UPS*) in March 2015 that indicates employers will likely have to meet a high legal burden to justify accommodating other disabled employees but not pregnant women. Although the legal implications of this decision and other cases are not yet settled, employers should be aware that relevant disability statutes are being applied to pregnancy by EEOC, and that policies and plans should be developed to provide equal access to work and accommodations in a pregnancy-blind manner.

FMLA may be another legal recourse for employees who must leave or adjust work because of pregnancy or its complications. FMLA covers private sector employers with at least 50 employees within a 75-mile radius. Employees must have worked for the employer for at least 12 months or 1250 hours. Covered employers are required to provide up to 12 weeks of unpaid medical leave (job protected) during a 12-month period to eligible employees for childbirth and newborn care, adoption or foster care placement, care for immediate family members with a serious health condition, or to handle a serious personal health condition including maternity-related medical conditions. A health care provider must attest to the presence of a health condition in order for an employee to obtain medically related leave under the FMLA, and physicians should be clear and thorough about the medical and ancillary requirements of their patients when completing required forms for leave under FMLA.

If accommodation or modified work cannot be provided for a pregnant worker, physicians should be aware that "disability" is usually narrowly defined by insurance carriers and may not cover situations wherein employees are removed from work to prevent potential harm from occupational exposures. Even when disability leave is granted, compensation may be inadequate to assure economic security, especially for an already low-paid worker.<sup>36</sup> Loss of corollary benefits, such as health insurance, may compound the worker's problem. As noted, certain individuals may not qualify for FMLA, including those who work for small companies who have not met the time requirements of the job, or who may come under the purview of other federal agencies. Providers should be aware of these situations, and assist both patient and employer in navigating the difficult requirements of both safe work and economic security.

As with any US worker, the pregnant employee is afforded some measure of protection under other federal laws governing the responsibilities of employers to provide safe workplaces.<sup>37,38</sup> The

OSH Act creates an affirmative duty for employers to assure a baseline level of workplace safety for their employees. The employer must provide workers with protection against personal injury and illness resulting from hazardous working conditions. The General Duty Clause of the OSH Act states that the employer should provide "a place of employment . . . free from recognized hazards that are causing or are likely to cause death or serious physical harm . . . [and should] assure so far as possible . . . safe and healthful working conditions."<sup>37</sup> Thus, although the OSH Act does not include a specific pregnancy standard, the General Duty Clause could reasonably be applied to known exposure and workplace hazards to pregnancy. This approach has been adopted in the past by OSHA in other areas.

The above discussion presents examples of a few federal anti-discrimination protections afforded pregnant women in the workplace. There are other federal protections, and perhaps more importantly, nearly every state jurisdiction in the US also has state-specific protections that provide additional or more stringent protections. The employer is invariably held to both (federal and state) sets of protections, and, in those instances wherein there is a conflict between federal and state law, the employer is generally held to the higher or more stringent of the two standards. The practitioner should be aware that these other protections exist.

Currently there are few, if any general protections or rights of monetary recovery under US federal law that apply to women who are planning to become pregnant or to individuals who believe that their infertility, pregnancy loss, or adverse birth outcomes are due to workplace exposures. Although the *Johnson Controls* decision and other judicial decisions have upheld the right of the mother to make informed choices on occupational exposure during pregnancy, a duty remains on the part of the employer to reduce workplace exposure to toxic substances.<sup>4</sup> The civil tort system in every state jurisdiction would typically provide the venue to pursue any damages through civil litigation.

## INDIVIDUAL VERSUS POPULATION-BASED INTERVENTIONS

Whereas temporary reassignment is an action taken at the level of the individual worker, consideration should be given to developing population-based programs to reduce the potential effects of reproductive hazards in the workplace. Primary prevention of adverse reproductive health effects includes worker education to reduce individual-level risk factors, and programs can be developed for employees in areas such as smoking cessation, reducing alcohol and drug abuse, avoiding behaviors that increase the risk of sexually transmitted diseases, improving nutrition, and exercise promotion. In addition, workers should receive all relevant information regarding the presence of potential reproductive toxicants in the workplace, as well as education and training in appropriate measures to reduce exposure to these hazards, including engineering controls, administrative controls, and provision of PPE. The advantage of these approaches is that they identify and proactively control exposures before conception and can help assure that the workplace is promoting healthy work for all employees. Workers should also be counseled on the potential presence of significant reproductive hazardous exposures in their home or during other activities. These may include lead- or solvent-based craft or hobby materials and traditional ethnic medicines and remedies. All workers (male and female) with potentially significant exposure to reproductive hazards should be encouraged to present to an occupational health provider or their primary physician for pre-conception counseling and to inform the occupational health service when pregnancy is confirmed. Sometimes the management of individual workers will be informed by the use of biological monitoring studies for the individual toxins.

## NOTIFICATION OF PREGNANCY

The purpose of employer notification by an employee of her pregnancy is to provide an opportunity for counseling the employee during pregnancy when potential reproductive risk is most relevant and to facilitate reduction of exposures, when appropriate. The employer may request that the employee's personal physician confirm the pregnancy (or pregnancy concern) and/or comment on her ability to continue performing tasks associated with her job. However, the personal physician is often relatively unfamiliar with the workplace exposures and associated risks and job demands, so the communication between the occupational health professional and personal care provider is of vital importance. Notification is not an adequate substitute for aggressive risk assessment (to reduce or eliminate exposures to agents of potential concern) and communication, as in many cases notification of pregnancy may not be received until after the pregnancy is recognized and after the critical period of embryonic development. Employee notification of intended pregnancy, which is seemingly more intrusive, could offer the advantage of earlier intervention, but may conflict with employees' right to privacy at work. The Nuclear Regulatory Commission (NRC) has established a mechanism for a pregnant worker potentially exposed to radiation to declare a pregnancy to her employer and thereby obtain additional training, more stringent monitoring to assure that exposures fall within recommended maximum limits for pregnancy, and, if needed, to be work reassigned. Although such notification is not legally required, NRC encourages such reporting in order that pregnant women can be effectively protected by exposure reduction during the pregnancy,<sup>39</sup> and to notify such individuals that legal protection exists that would allow the worker to avail herself of these measures. Even if notification is encouraged, some employees may choose not to identify themselves as pregnant or as planning a pregnancy. Therefore, employers must be proactive in identifying and controlling potential workplace reproductive and developmental hazards.

## BREAST FEEDING POLICY

Health care providers who see nursing mothers who work in environments where they are exposed to substances that could be excreted in breast milk such as selected organic solvents, metals, pesticides, and pharmaceutical agents should assess whether exposure would be sufficient to produce significant concentrations in the breast milk of lactating employees. Human breast milk has been determined to contain a broad range of potentially toxic environmentally derived contaminants, typically at quite low concentrations.<sup>40,41</sup> Although the benefits of breastfeeding to the infant are thought to outweigh the risks of exposure to environmental chemicals in breast milk,<sup>42,43</sup> this may not apply to the occupational setting in which exposures of potential concern may be higher than those encountered environmentally by the general public.

Perhaps the best characterized example of such an exposure scenario for the infant is in breastfeeding from a lead-exposed mother. The Centers for Disease Control and Prevention (CDC) recommends allowing breastfeeding when the US mother's blood lead level (BLL) is 40 µg/dL or below.<sup>31</sup> Extensive studies correlating maternal BLL with the lead concentration in her breast milk can permit such precise advice.

Unfortunately, such detailed data are not available for the vast majority of chemicals or other toxicants found in human milk, some of which may be more concentrated in fat and in breast milk. Thus, the clinician must make recommendations on breastfeeding on a case-by-case basis. Important considerations include the chemical properties of the potential toxicants and the potential for exposure to the mother. Organic solvents, particularly halogenated hydrocarbons, which are generally fat soluble and poorly metabolized, can persist in body fat and accumulate in milk. For example, in mothers with significant occupational exposures to certain chemicals, their

breast milk might have concentrations of chemical contaminants that considerably exceed the levels that are permitted by the Food and Drug Administration in cow's milk.<sup>6</sup> Health hazards (eg, potential neurotoxicity or carcinogenicity) posed to the infant by the milk contaminant, as evaluated by a risk assessment process similar to that discussed above, should be considered. As part of hazard communication training, employees should be apprised of any health hazards that might result from the potential accumulation of chemical contaminants in breast milk. In these situations, the need for alternative duty or job reassignment should be considered when breast feeding is planned. In cases wherein significant uncertainty exists, job reassignment permits the infant to have the benefits of breastfeeding and provides peace of mind for both the employee and employer. In workplaces with good controls in place to prevent exposure, situations in which hazards may result to an infant through breastfeeding do not frequently arise.

## PARA-OCCUPATIONAL EXPOSURES

Physicians should also consider that the worker may bring work contaminants into the home environment that could affect the development of offspring, for example, with "take home" lead exposures.<sup>44</sup> A number of approaches may be used to reduce or avoid contamination of the home environment and thereby protect a developing fetus or developing infant and child. These include improved housekeeping in the workplace, employer laundering of work clothes and protective garments, the construction and use of "clean" and "dirty" change rooms, and mandatory use of showers at the end of the workday.

## REPRODUCTIVE HEALTH HAZARD MANAGEMENT OPTIONS

Several options should be considered in managing reproductive risks, performing risk assessments, and dealing with potential uncertainties. The decision to implement specific options at a specific workplace should be based upon an assessment of potential risks and upon the characteristics of the population at risk. Before implementing reproductive health hazard management measures in a company, legal review may be considered to ensure compliance with all federal, state, and other regulations pertaining to discrimination and protection of employees' rights and disabilities.

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## APPENDIX A – Additional Resources for Information about Reproductive Hazards

### Internet Resources

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