

Reproductive effects caused by chemical and biological agents

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[Respirable Crystalline Silica](#)

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Introduction

Occupational exposure to chemical or biological agents may be harmful to workers' reproductive health, inflict damage on the genetic material of the cells of male and female workers, or evoke adverse effects on their sexual function and fertility. Some chemicals and infectious agents may also be harmful to the pregnancy and hazardous to the foetus. Such agents are often referred to generally as 'reprotoxic substances'. They include a variety of potentially harmful chemical agents e.g. some solvents, metals, pesticides and other chemicals. Prevention of the harmful effects of occupational exposures requires assessment and management of reproductive risks in the workplace. European legislation obliges employers to ensure that the work environment is safe for the reproductive health of the workers, pregnant workers, and offspring.

Reproductive effects and mechanisms of action

Effects of occupational exposure on the reproductive system of men and women may become manifest as alterations in sex hormone levels, diminished libido and potency, menstrual disorders, premature menopause, delayed menarche, ovarian dysfunction, impairment of semen quality, and reduced male and female fertility. Toxic exposures can cause direct cell damage in the developing sperm and eggs. Maternal exposure during pregnancy may disturb foetal development by either directly or indirectly interfering with maternal, placental, or foetal membrane functions. Toxic exposures can induce many wide-ranging effects, e.g. foetal death, intrauterine growth retardation, preterm birth, birth defect, postnatal death, disturbances in cognitive development, and changes in immunological sensitivity, or childhood cancer. The mother's exposure at work to chemicals may also cause contamination of her breast milk.^[1]

Some chemicals with hormonal activity, so-called endocrine disrupters, may alter the function of the endocrine system and consequently cause adverse reproductive effects, e.g. poor semen quality and damaged reproductive tissues in men and some gynaecological medical conditions in women (endometriosis, benign noncancerous tumors and infections of reproductive organs). Many chemicals, such as polychlorinated organic compounds, pesticides, phthalates, bisphenol A, brominated flame retardants and heavy metals have been identified as being possible [endocrine disrupters](#).

Difference in the timing, duration and dose of exposure may lead to different outcomes. Miscarriage or birth defects are the principal outcomes if exposure has occurred during the first trimester of pregnancy. Exposure later in pregnancy is more likely to shorten the duration of gestation, reduce birth weight and affect the development of the brain. A lower dose of a toxicant may cause birth defects, whereas a high dose may produce miscarriage or infertility.

Adverse effects on reproduction and development are often the result of exposure during the narrow, vulnerable periods of ovulation, formation of a mature sperm (spermatogenesis) and the formation of organs within the embryo (foetal organogenesis). Some effects may not become evident for years. For example, lead may gradually accumulate in maternal tissue only to be released during pregnancy or lactation. Some toxicants, such as antineoplastic agents (cancer chemotherapy drugs), may reduce the number of female germ cells, leading to a shortened reproductive life span.

Chemical exposure of both women and men may cause chromosomal abnormalities or gene mutations in the offspring. It may also disturb the development of the foetus through heritable changes (epigenetic mechanisms) in egg or semen cells, causing no change in the underlying DNA sequence of the organism; instead, non-genetic factors cause the organism's genes to behave (or "express themselves") differently. There is some evidence of epigenetic effects of paternal exposure that can impact on the pregnancy outcome, but human evidence is still not convincing ^[2]

Chemical agents

Exposure to a [reprotoxic substance](#) may be related to either one or to many reproductive outcomes, depending on both the substance, timing (before or during pregnancy), duration of the exposure and the dose of the agent absorbed. Adverse reproductive effects of some chemical agents that have been reported in human studies are

shown in Table 1.

Agent	Industry or occupational group	Reported effects of female exposure	Reported effects of male exposure
Organic solvents in general	Painting, degreasing, shoemaking, printing, dry cleaning, metal industry and several other fields of industry	Reduced fertility, menstrual disorders, foetal loss, birth defects, preterm birth, neurobehavioral effects, childhood leukaemia	Delayed conception, reduced semen quality, foetal loss, birth defects
Benzene	Petrochemical industry, laboratory personnel	Foetal loss, reduced fertility, low birth weight,	
Carbon disulfide	Viscose rayon industry	Menstrual disorders	Decreased libido and potency
Some ethylene glycol ethers and their acetates	Electronics industry, silk screen printing, photography and dyeing, shipyard painting, metal casting, chemical industry, other industries	Reduced fertility, foetal loss, birth defects, menstrual disorders	Reduced semen quality
Tetrachloroethylene	Dry cleaning, degreasing	Reduced fertility, foetal loss	
Toluene	Shoe industry, painting, laboratory work	Reduced fertility, foetal loss	
Metals			
Lead	Battery industry, lead smelting, foundries, pottery industry, ammunition industry and some other metal industries	Reduced fertility, foetal loss, preterm birth, low birth weight, birth defects, impaired cognitive development	Reduced semen quality, reduced fertility, foetal loss, birth defects
Inorganic mercury	Lamp industry, chloralkali industry, dental personnel	Reduced fertility, menstrual disorders, foetal loss	Foetal loss
Pesticides ^a	Agriculture, gardening, greenhouse work	Reduced fertility, foetal loss, birth defects, preterm birth, reduced foetal growth, neurodevelopmental effects, childhood leukaemia	Reduced sperm quality, reduced fertility, foetal loss, birth defects, childhood cancer
Pharmaceuticals			
Anaesthetic gases	Operating rooms, delivery wards, dental offices	Foetal loss, reduced birth weight, preterm birth, birth defects, reduced fertility	
Nitrous oxide	Operating rooms, delivery wards, dental offices	Foetal loss, reduced birth weight, reduced fertility	
Antineoplastic agents	Hospital workers, pharmaceutical industry	Menstrual dysfunction, reduced fertility, foetal loss, premature birth, low birth weight, birth defects	
Carbon monoxide	Iron and steel foundries, welding, food industry, car repair, service stations	Preterm birth, intrauterine death	

^a Examples of pesticides with adverse effects in men include dibromochloropropane (DBCP), 2,4-dichlorophenoxyacetic acid (2,4-D), ethylene dibromide, chlordecone, carbaryl, alachlor, atrazine and diazinon

Table 1: Some chemical agents associated with adverse effects on reproductive health in human studies

Source: Overview by the authors

Organic solvents

Maternal occupational exposure to high levels of solvents may increase the risks of miscarriage, birth defect and low birth weight [\[3\]](#), [\[4\]](#), [\[5\]](#), [\[6\]](#). An increased risk of miscarriage has been observed among workers in manufacturing, dry cleaning, painting, shoe-making, pharmaceutical, audio speaker, semiconductor and laboratory industries. In some studies, exposure to solvents has also been related to preterm birth, neurobehavioral effects and childhood leukaemia [\[7\]](#), [\[8\]](#), [\[9\]](#). The main routes of exposure are via inhalation and through the skin. Most solvents pass through the placenta and can be excreted from the mother in her breast milk.

Some studies suggest that solvent exposure is associated with delayed conception in women, but the evidence for males is less convincing [\[10\]](#), [\[11\]](#), [\[12\]](#). Menstrual disorders have also been observed in exposed women [\[13\]](#). In men, solvent exposure has been associated with reduced semen quality and altered hormone levels [\[14\]](#), [\[15\]](#). The limited evidence on the effects of paternal solvent exposure on pregnancy outcome is somewhat inconsistent. Some studies have indicated that solvent exposure in fathers may be associated with birth defects in their offspring [\[16\]](#), [\[17\]](#).

Particular solvents which have been associated with adverse effects in human studies include benzene, carbon disulphide, some glycol ethers and their acetates, tetrachloroethylene and toluene. Some other solvents, for example formamide and dimethylformamide, have induced adverse effects in animal experiments. Concomitant exposure to a mixture of solvents is common, making it difficult to determine the contribution of one solvent alone to the adverse reproductive effects.

Some specific solvents

Some glycol ethers and their acetates have been able to trigger adverse reproductive and developmental effects in animal species exposed by different routes of administration. In manufacturing workers, exposure to ethylene glycol ethers has been related to an increased risk of miscarriage, birth defects, reduced fertility and prolonged menstrual cycles [\[10\]](#), [\[18\]](#), [\[19\]](#), [\[20\]](#). In particular, exposure to 2-methoxyethanol and 2-ethoxyethanol has been associated with reduced semen quality in shipyard painters, metal casters, chemical industry workers and workers in the semiconductor industries [\[14\]](#). In the EU some glycol ethers and their acetates are classified as substances that may damage or are suspected of damaging fertility and the unborn child.

Glycol ethers are used in paints, inks, varnishes, and cleaning agents. The use of the most toxic glycol ethers has declined from the mid-1990s these being gradually replaced with less toxic glycol ethers. In line with this development, past exposure to glycol ethers was found to be associated with low sperm quality, whereas the glycol ethers in use in 2000 – 2001 did not seem to have any impact on human semen characteristics [\[21\]](#). However, in another study, occupational glycol ether exposure during the later years was related to low motile sperm count [\[22\]](#).

Exposure to carbon disulphide which is used primarily in the production of viscose rayon, may produce adverse reproductive effects in males and females. Decreased libido and potency and altered sex hormone levels have been found in studies in male workers exposed to high levels of carbon disulphide [\[15\]](#). In women, menstrual disorders, including irregular cycles and unusual menstrual bleeding, have been reported [\[23\]](#). Dry-cleaning work with high level of exposure to tetrachloroethylene has been associated with an increased risk of miscarriage [\[24\]](#). There is limited evidence suggesting exposure can also reduce fertility.

An increased risk of miscarriage has been observed among shoe workers, audio speaker factory workers and laboratory workers exposed to toluene [\[25\]](#). Reduced fertility has been described for toluene exposure in women but not in men [\[11\]](#), [\[12\]](#). Toluene abuse during pregnancy can lead to serious adverse reproductive outcomes [\[26\]](#), but occupational exposure to toluene is clearly lower than the exposure situation in abusers. In some studies, benzene exposure has been found to increase the risk of miscarriage and decrease birth weight [\[27\]](#), [\[28\]](#), [\[29\]](#).

Lead, mercury and cadmium

There is historical data linking heavy maternal exposure to lead with reduced fertility and increased risk of miscarriage, and lead is still the most extensively studied metal exposure. In addition, animal and human studies of reproductive outcomes point to an adverse role for exposure to mercury and cadmium. Occupational

exposure to lead and lead compounds may occur in many industries (Table 1). Historically heavy maternal exposure to lead has been linked with increased risk of miscarriage but the evidence of the risks of current low occupational exposure levels is scarce. Exposure to lead at blood lead levels at or above 1.9 µmol/l, is detrimental to semen quality. In fact, many of the lead compounds have been classified as carcinogens or as suspected carcinogens.

Women's exposure to lead may cause menstrual disorders and, at low exposure levels, pregnancy induced hypertension and preterm birth, and reduce birth weight ^[30], ^[31], ^[32], ^[33]. First-trimester foetal exposure seems to impair neurodevelopment of the foetus and child's mental development ^[34], ^[35] whilst exposure at around 28 weeks' gestation is critical for the child's intellectual development.

Exposure of pregnant and breastfeeding women to lead and its derivatives is prohibited under the EU Directive 92/85/EEC ^[36] if the exposure might jeopardise safety or health. The recommended level of the blood lead (B–Pb) among pregnant and lactating women has been proposed to be the same as limit of the unexposed population, which in many countries is 0.2–0.3 µmol/l (~4–6 µg/dl).

Reduced sperm count, other types of impaired semen quality and modest changes in hormone levels have been reported when blood lead levels are at or above 1.9 µmol/l ^[37]. Regardless of the well documented toxicity to sperm cells, exposure to lead seems to have no or only marginal impact on men's ability to father children at current occupational exposure levels. Studies of couple fertility, miscarriage and birth defects, have shown conflicting results. ^[38]

There are many different mechanisms and sites of action that can play a role in the reproductive toxicity of lead. Lead is transferred across the placenta, and at birth the blood-lead concentration in the umbilical cord is close to that of the mother. Lead is only a weak mutagen but exposure of both women and men may disturb the development of the foetus through an epigenetic mechanism. In men, lead may interfere with sperm DNA chromatin stability that is essential in maintaining the sensitive fertilisation process ^[39].

Inorganic mercury is transferred to the foetus although it also accumulates in the placenta. Female occupational exposure to mercury may cause menstrual disorders, delayed conception, and increase the risk of miscarriage ^[40], ^[41]. Animal experiments have provided some evidence of adverse effects on female and male fertility, and exposure to mercury vapor may cause fetotoxicity or other adverse reproductive outcomes ^[42], ^[43]. Evidence on reproductive effects in men is limited but exposure to mercury has been reported to decrease sperm count and quality ^[43], and has also been linked with an increased risk of miscarriage ^[44].

Cadmium may act as an endocrine disruptor (endocrine disruptors may alter the function of the endocrine system and consequently cause adverse reproductive effects, e.g. poor semen quality and damaged reproductive tissues in men and some gynaecological medical conditions in women). Cadmium is known to accumulate in the placenta, which may decrease the transport of micronutrients, e.g. zinc, to the foetus ^[45]. Cadmium has also been reported to affect semen quality ^[43]. In animals, cadmium has shown embryotoxicity, teratogenicity, and adverse postnatal effects ^[42].

Welding

Welding fumes typically include many agents with potential reproductive toxicity, e.g. hexavalent chromium, nickel, cadmium, manganese, and carbon monoxide. Research data on the effects on reproduction is mainly of men. Earlier studies have reported an increased risk of infertility and reduced semen quality among male welders. Studies from the late 1980's suggested that mild steel welding, rather than stainless steel welding, could be hazardous. However, studies of delayed conception and of impaired semen quality from the mid-1990s, did not indicate impaired reproductive capacity among welders. The decline in exposure levels in Western countries may explain the positive development ^[46]. However, the findings of one well-designed study indicated that spouses of stainless steel welders were at increased risk of suffering a miscarriage ^[47]. Overall, the evidence on reproductive toxicity of welding is mixed and inconclusive.

Pesticides

Human studies indicate that exposure to pesticides may be harmful for reproductive health. Both men and women can be exposed in agriculture and greenhouses. Pesticides enter the body mainly through the skin, but also via inhaled air or through ingestion. The name pesticides refers to herbicides, insecticides, fungicides and fumigants. The most common chemical groups are organophosphates, carbamates, and phenoxyherbicides. Some pesticides (e.g., carbaryl, benomyl, ethylenthiourea, maneb, zineb, thiram) have demonstrated reproductive and/or developmental toxicity in experimental animals.

Female exposure

There is some evidence that exposure to pesticides can reduce female fertility but the results are inconsistent. Exposure to pesticides may also increase the risk of birth defects, miscarriage, or foetal death^[48]. In most studies, the risk could not be attributed to any individual pesticide. However, exposure to biologically persistent chlorinated hydrocarbons has been linked to miscarriage^[49]. In particular, two studies using biological exposure measures found an increased risk of early pregnancy loss in women with a high serum level of preconception DDE, a metabolite of DDT^[50], ^[51].

Maternal occupational exposure to pesticides seems to increase the risk of childhood leukaemia. Pesticide exposure has also been linked with other cancer types, e.g. lymphomas, cancer of the brain and nervous system, Wilm's tumor^[note 1], and Ewing's sarcoma^[note 2], but the increased risk may also be related to childhood exposure^[52], ^[53]. The findings for paternal exposure are inconsistent.

Male exposure

Today the pesticide dibromochloropropane (DBCP) is banned but previously it was used as a soil fumigant and nematocide, and it is now recognized as a major testicular toxin. Long-lasting severe exposure has caused irreversible sterility (azoospermia, no sperm) or oligospermia (too few sperm)^[54]. Another fumigant with adverse effects on male reproduction, ethylene dibromide (EDP), has also been banned. Moreover, adverse effects on semen quality have been found for exposure to some herbicides e.g. 2,4-dichlorophenoxyacetic acid (2,4-D), alachlor and atrazine, and three insecticides, chlordecone (Kepone™), carbaryl, and diazinon^[46], ^[54].

There is some evidence that exposure to the pesticides currently used in farming or greenhouses can be hazardous for male reproduction. Conflicting findings on the effects of male exposure on couple fertility and adverse pregnancy outcome may be related to the level and type of exposure which may vary considerably according to the type of work and also between geographical areas. For example, a prolonged time to become pregnant was observed among Dutch fruit growers^[55], the findings among Finnish greenhouse workers provided limited evidence of reduced fertility^[56], but in Denmark no difference in fertility was seen between exposed conventional farmers and unexposed organic farmers^[57]. In addition, some but not all studies have reported increased risk of miscarriage or birth defects in spouses of exposed men.

Pharmaceuticals

Anaesthetic gases

Several studies have shown an increased risk of miscarriage among women occupationally exposed to anaesthetic gases in operating theatres, delivery wards, dental offices and veterinary surgeries^[58]. In some of the studies, the exposure has also been related to birth defects and low birth weight^[59], ^[60]. Adverse reproductive outcomes have especially been found in situations when anaesthetic gases were delivered without a gas scavenging system^[note 3] which is the technique to remove exhaled and waste anaesthetic gases^[61], ^[62]. Efficient scavenging equipment, good ventilation and equipment for the administration of anaesthetics help to minimize the exposure levels at the workplaces.

With respect to the specific anaesthetic gases, halothane and nitrous oxide have been shown to both be fetotoxic and teratogenic in animals. Exposure to nitrous oxide, the only anaesthetic gas to have been studied separately in humans, has been associated with an increased risk of miscarriage, reduced birth weight and a longer time to become pregnant in dental nurses or midwives^[59], ^[40]. Concerning isoflurane and enflurane, an experts' committee concluded that the lack of human data precludes a reliable assessment of their effects, but there was sufficient animal data and it indicated that they should not be classified as reproductive toxicants^[63].

Antineoplastic agents

Nurses and other hospital workers may be exposed to antineoplastic (cancer chemotherapy) drugs during the preparation, administration, nursing and cleaning activities. Exposure can also occur in laundries, pharmaceutical companies, veterinary clinics, home care and nursing homes^[64]. Handling of antineoplastic agents in hospitals has been associated with menstrual dysfunction, reduced fertility, miscarriage, premature birth, low birth weight, and birth defects of the offspring^[65], ^[66], ^[67]. It has to be remembered that many of these drugs are also carcinogens. However, no increase in the risk for miscarriage or birth defects was found in a study conducted in settings where safety measures had been adopted to protect the healthcare personnel against exposure to antineoplastic drugs^[68]. Exposure can be minimized by wearing protective garments and using protective equipment (for example closed infusion systems), adopting good work practices and increasing awareness of workers of the potential hazards. The risk of exposure is probably highest in the preparation of drug solutions, which requires specific prevention measures. Therefore, some countries have

adopted a policy of transferring pregnant workers who would be required to prepare antineoplastic drug solutions to other jobs. Information on preventing exposure to antineoplastic and other hazardous drugs in health care settings is available^[63].

Other pharmaceuticals

Some drugs have known adverse effects on the development of the foetus. Pharmaceutical factory workers and nurses may be exposed to drugs and vitamins. Unfortunately there is limited data on the effects of occupational exposure. It is known that excess vitamin A is teratogenic in many species, and diethylstilbestrol (DES) is a known human reproductive hazard. Some sex hormones have induced masculinization of female foetuses and feminization of male foetuses in animal experiments. Azathioprine, cyclosporin A, and some antiviral agents, such as acyclovir, ganciclovir, ribavirin, and zidovudine have also induced adverse reproductive effects in animal experiments^[70].

Other chemical agents

Exposure to carbon monoxide may occur in welding work, iron and steel foundries, the alimentary industry, and in smoking procedures, as well as in car repair and service stations where there may be car exhaust gases. Carbon monoxide is transported through the placenta and levels in the foetus can become higher than those in the mother's blood. With connection with maternal carbon monoxide intoxications, there have been reports of premature birth, intrauterine deaths and brain injuries in the infant^[71].

Some phthalates have been shown to adversely affect reproduction in laboratory animals, but human data on their effects is scarce. Exposure has been linked to hypospadias^[note 4] (a birth defect of the genitalia among male infants) and anti-androgenic effects^[note 5] in newborns^[72], ^[73]. Examples of tasks with potential exposure to phthalates include polyvinyl chloride (PVC) film manufacturing, PVC compounding, phthalate (raw material) manufacturing and work in rubber industries and nail-care salons^[74]. Other exposures that may have adverse effects on the reproductive health include bisphenol A, benzo(a)pyrene, brominated flame retardants, environmental tobacco smoke, ethylene oxide and polychlorinated biphenyls.

Biological agents

Infectious agents, like toxoplasmosis, listeriosis, rubella, herpes, varicella, hepatitis B and C, cytomegalovirus, human parvovirus B19 and human immunodeficiency virus, can cause foetal loss, foetal growth retardation, congenital anomalies, mental retardation or systemic disease^[75]. Most observations of reproductive risk are based on general population studies rather than on any [particular occupational groups](#).

Hepatitis B and C, rubella virus, varicella zoster virus, and toxoplasma

Hepatitis B and C, and rubella virus constitute a risk to reproductive health, particularly among health care workers while especially veterinary staff may be exposed to toxoplasma. Non-immune pregnant personnel should not have to care for patients with measles, rubella, varicella or herpes zoster^[76], as these viruses may harm the foetus. However, most of the workers already have immunity against the common viral diseases (e.g. varicella) or have been vaccinated against these viruses (e.g. rubella and measles). Hepatitis B virus (HBV) vaccination is recommended for all hospital staff at risk of contamination of blood or other secretions of HBV-positive patients. A vaccine is also available against varicella. The ways to prevent infectious diseases include safe work practices and providing alternative jobs or maternity leave for non-immune pregnant workers. According to the European Union directive (92/85/ETY), pregnant workers should not perform duties for which an assessment has revealed a risk of exposure to toxoplasma or rubella virus, unless they have been demonstrated to be adequately protected against such agents by immunization^[36].

Cytomegalovirus and human parvovirus B19

Studies on cytomegalovirus and human parvovirus B19 have consistently revealed a higher risk of these infections among women with occupational contacts with children than in other women. About 30–60% of women of reproductive age are seronegative and susceptible to suffer infection. Viruses are transmitted from mother to foetus with a transmission rate of 25–50%. Unfortunately, no vaccinations are available against these viruses. Risk of both infections can be diminished by good basic hygiene, including hand washing.

Cytomegalovirus is the most common cause of congenital infection. Most infected children are asymptomatic. However, a minority of affected children can suffer long-term complications including neurologic diseases, learning disability, deafness and blindness.

B19 infection has been particularly elevated among nursery school teachers and women working with groups of children participating in after-school activities but also among elementary school teachers as compared with other pregnant women^[77]. B19 infection can cause foetal anemia that may lead to foetal accumulation of fluid, edema, underneath the skin of the foetus, especially in the neck and in body cavities (hydrops), miscarriage and intrauterine foetal death^{[78], [79]}.

Risk assessment

EU directive 92/85/EEC requires employers to assess the health and safety risks to pregnant and breastfeeding workers, and if needed, to change working conditions or offer suitable alternative work^[36]. If this is not feasible, the worker should be granted leave in accordance with the national legislation. The EU has also developed guidelines for the assessment of hazardous agents and processes as well as on what preventive measures can protect pregnant and breast feeding workers from the adverse effects of occupational exposure^[80].

Other legislation applicable to exposure to reprotoxic substances includes EU directive 2004/37/EC on the protection of workers from the risks related to exposure to carcinogens or mutagens at work, EU directive 94/33/EC on the protection of young people at work and EU directive 98/24/EC on the protection of the health and safety of workers from the risks related to chemical agents at work^{[81], [82], [83]}.

Before one can conduct a proper [risk assessment](#), agents that are potentially harmful to reproductive health and the offspring need to be identified at the workplace. Useful health and safety information on chemicals can be found on [Safety Data Sheets](#) (SDS), and some other sources, e.g. technical documentation or material from manufacturers. Safety Data Sheets usually provide information on the properties of the substance, the dangers to health, and guidance for the protection of workers. Essential health and safety information on chemicals can also be found on some on-line international databases, e.g. the International Chemical Safety Cards. It is recommended to seek [expert advice on](#) potential harmful agents and how to avoid the risks. Instructions are also available on assessing exposure to hazardous drugs at work, their safe handling, and developing workplace procedures for using equipment that functions to reduce exposure^[69].

Some agents have been classified in the EU as known or suspected human reproductive toxicants. This is indicated by hazard statements (H, new EU classification) or risk phrases (R, old EU classification) which may be found in Safety Data Sheets. Hazard statements for reproductive toxicity are as follows:

- H360: May damage fertility or the unborn child (R60, R61)
- H361: Suspected of damaging fertility or the unborn child (R62, R63)
- H362: May cause harm to breast-fed children (R64)

For example, some glycol ethers and their acetates, carbon disulphide, carbon monoxide, toluene, some phthalates, bisphenol A, lead, mercury, benomyl, and maneb have been classified as substances that may or are suspected of damaging fertility and the unborn child. According to the EU directive 92/85/ETY risk assessment and management should also be done, if pregnant and breast feeding workers could be exposed to genotoxic or carcinogenic agents. Carcinogenic agents that may cause changes in the genetic material of the cell are considered harmful for the reproductive health because they may also induce changes in the cells of the developing foetus. For example, benzene has been classified as a substance that may cause cancer or genetic defects.

It is important to assess the magnitude, frequency and duration of exposure. Occupational hygienic measurements or [biological monitoring](#) can be used for assessing the level of exposure to chemical agents. The measuring results can be compared to Occupational Exposure Limits (OEL) that have been set to prevent occupational diseases or other adverse effects in workers exposed to hazardous chemicals. The OELs may not take reproductive effects into account and thus expert assistance will be needed in the risk assessment.

Preventing biologic risks is mandatory according to Directive 2000/54/EC^{[84], [85]}. Risk assessment for biological agents should consider the nature of the agent, how infection is spread, how likely contact is, and what control measures there are^[86].

Both the employer and workers should be informed about risk assessment results. It is also important to inform women and men beforehand, for example during the pre-employment medical examination, of any potentially harmful occupational exposures and protective measures to prevent any adverse reproductive effects. Women should be advised to contact health services immediately after becoming pregnant or when planning to become pregnant. Research and prevention have mainly focused on the effects of maternal exposure and there is a lack of knowledge about the adverse effects on male reproductive system. However, there is an increasing volume of information highlighting the vulnerability of the male reproductive system. Thus, prevention should be directed to all workers.

Prevention

The employer's duty is to protect the reproductive health of both male and female workers. Employers should take the necessary measures to prevent or reduce exposure to the level where no risk exists, if the [risk assessment reveals a risk](#) to a worker's pregnancy or her breastfeeding of the infant ^[36]. In the case of male workers, special attention should be paid to those chemicals that are known to impair male fertility. Prevention or reduction of exposure of workers can be done in several ways in accordance with the widely recognised [hierarchy of control](#), e.g.

- Eliminating or substituting hazardous chemicals for safe alternatives,
- Improving the work environment by collective protection measures, such as the enclosure of the emitting process, local exhaust ventilation, general ventilation, changing work tasks and habits into safe procedures
- Use of personal protective equipment
- Moving the pregnant worker to another job
- Granting leave to the pregnant worker in accordance with national legislation, if none of the above measures is feasible.

Examples on how to phase out harmful chemicals and replace them with safer alternatives or techniques to reduce adverse health effects can be found in the Substitution Support Portal (SUBSPORT)^[87]. The portal includes case story database presenting practical real-case examples. For example, one of the case stories describes how printing inks based on organic solvents and used for the printing of plastic shopping bags were replaced by water-based inks in a company that manufactured plastic bags. This measure eliminated the need for toluene and 1-butanol in the printing process.

In most cases, infection risks can be avoided or minimised by adoption of simple control measures. These include using good basic hygiene practices (especially hand washing), preventing puncture wounds and cuts, avoiding exposure to sharp objects and protecting the skin^[88]. Suitable information, instructions and training should also be provided to the workers. The administration of available vaccines is recommended in risk occupations. However, pregnant women should not be immunized with live attenuated virus vaccines (e.g. mumps or measles). Many workers already have immunity against common contagious diseases. In the case of a major risk of exposure to a highly infectious agent, a non-immune pregnant worker should avoid exposure altogether. According to EU guidelines, the employer must ensure immunity testing (chickenpox, toxoplasmosis, parvovirus) for risk occupations, and job transfer or temporary leave during epidemics, if the pregnant worker has no immunity.

Some countries have specific legislation that intends to protect workers from reproductive health hazards in the workplace^[89]. For example in Finland, there is legislation that ensures special maternity leave for pregnant women. The Statute of Health Insurance Act includes a list of agents considered to be potentially harmful for pregnant women and guidelines have been issued on the levels of exposure that should not be exceeded during pregnancy. If safe work cannot be offered, the woman is entitled to special maternity leave and maternity allowance is paid by the Social Insurance Institution.

Research supports the importance of job adjustments in pregnancy and use of personal protective equipment. For example, pregnant women who experienced a change in work conditions following the use of a preventive measure (withdrawal from work or job reassignment) had lower risk of preterm birth than those who did not^[90]. Job adjustment in pregnancy was also associated with a reduced absence from work^[91]. Some studies also suggest that the risk of adverse outcome has been lower among pesticide exposed workers when protective equipment, such as gloves or a respirator, has been worn^[92], ^[93].

Outlook

The participation of women in the labour force is increasing but there is also evidence accumulating of the health effects from occupational exposure to reprotoxins. Therefore the European Commission has commissioned an analysis on the impacts of a possible amendment of the Carcinogens and Mutagens Directive 2004/37/EC to include category 1A and 1B reprotoxic substances^[94]. These substances are known human reproductive toxicants, based largely on human evidence (1A) or presumed human reproductive toxicants, based largely on evidence from experimental animals (1B).

As new evidence has been obtained that associates endocrine disruption and potential health problems the European Commission has established a legislative-based Community Strategy for Endocrine Disrupters^[95]. The strategy focusses on gathering scientific data on "candidate substances" with a view to prioritising testing, guide research and monitoring efforts, and identify specific cases of consumer use and ecosystem exposure. The long-term actions focus on review and possible adaptation of EU policy and European Community legislation.

Notes

1. [Jump up](#) Wilms' tumor or nephroblastoma is a cancer of the kidneys that typically occurs in children, rarely in adults.
2. [Jump up](#) Ewing's sarcoma is a malignant small, round, blue cell tumour. It is a rare disease in which cancer cells are found in the bone or in soft tissue. The most common areas in which it occurs are the pelvis, the femur, the humerus, the ribs and clavicle. Ewing's sarcoma occurs most frequently in teenagers and young adults.
3. [Jump up](#) System for the transport of exhaled and waste anaesthetic gases from the exhaust valve of an anaesthetic ventilator or anaesthetic breathing system into the atmosphere at a safe location away from the operating theatre.
4. [Jump up](#) Hypospadias is a birth defect of the urethra in the male that involves an abnormally placed urinary meatus (the opening, or male external urethral orifice)
5. [Jump up](#) Exposure to anti-androgens can disrupt the action of androgens in foetal life. Steroidal androgens regulate male sexual differentiation and any suppression of their effects in foetal life may have irreversible de-masculinizing effects later in life.

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