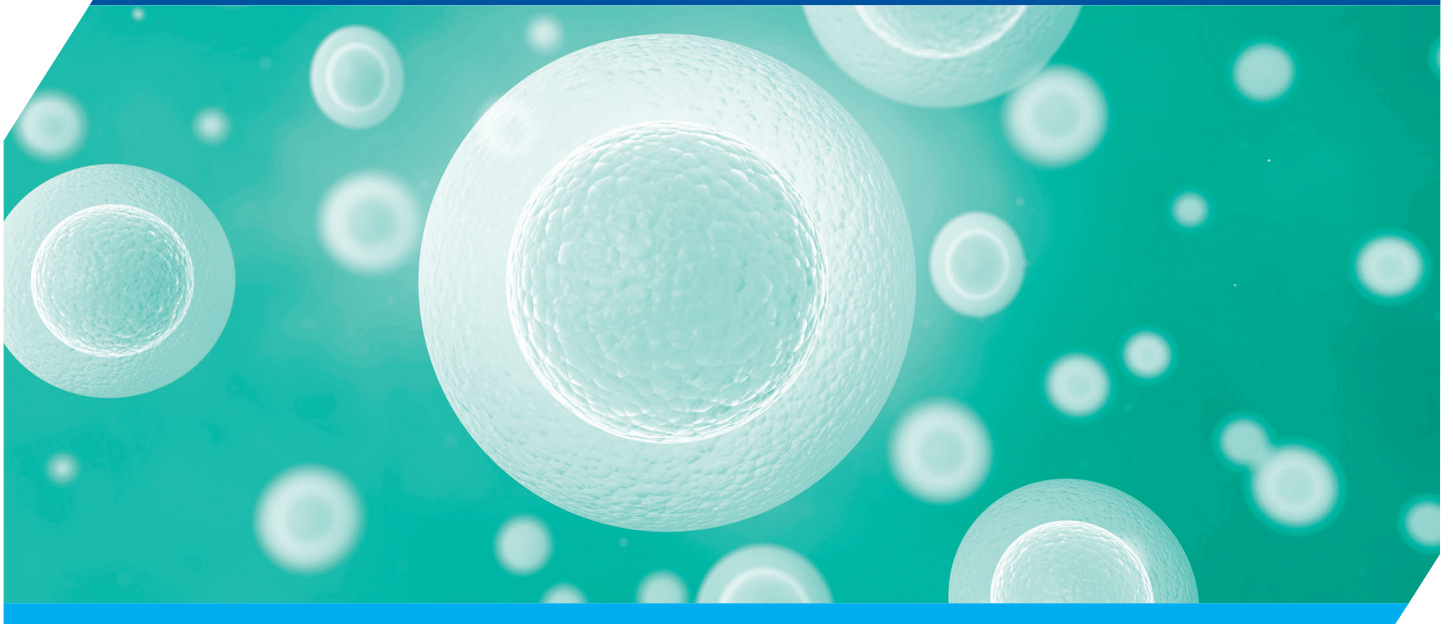




The
Fertility Society
of Australia

Pre-Conception Health Special Interest Group



The effects of environmental chemicals on fertility and fecundity

There is increasing evidence demonstrating the negative effects of environmental chemicals, especially endocrine disrupting chemicals (EDCs), on reproduction and development [1, 2], including several studies that have found elevated levels for several chemicals among those seeking assisted reproductive technologies. This is a summary of the available human data for the effects of environmental chemicals on adult male and female fertility and fecundity. There are also potential associations of environmental chemicals with recognised reproductive disorders (e.g. cryptorchidism or endometriosis), however these are outside the scope of this summary.



The effects of environmental chemicals on fertility and fecundity

Many environmental factors can affect male and female fertility and fecundity. Of particular concern is the potential impact of environmental chemicals on reproduction. These chemicals include naturally occurring compounds, but the greatest fears are around the increasing number and quantities of man-made compounds. These encompass more than 800 endocrine disrupting chemicals (EDCs) found in everyday items, including the plastics of food containers, personal care items, food products, as well as in manufacturing and industrial and agricultural processes [1]. Due to their many and varied uses, multiple routes of exposure are possible. Once released into the environment, exposure occurs via inhalation, absorbance, but mainly by ingestion from contaminated food and water. Most EDCs act via, interfere with, or mimic, steroid hormones - predominantly oestrogen and androgen pathways, or thyroid hormones [1, 2].

Evidence review

Chemical and where it is found	Effects on male fertility/fecundity	Effects on female fertility/fecundity
<p>Phytoestrogens</p> <p>Includes isoflavonoids, flavonoids, coumestans, stilbenes, and lignans.</p> <p>Phytoestrogens are naturally occurring plant-derived compounds found in a variety of foods with oestrogenic and anti-oestrogenic properties [3].</p>	<p>Few studies with conflicting findings.</p> <p>In fertile men, one study found no effect while another found an association between higher urinary levels of isoflavones and reduced normal sperm morphology.</p> <p>Urinary phytoestrogen concentrations have not been associated with increased time to pregnancy (TTP) in fertile couples or with clinical outcomes in couples undergoing ART.</p>	<p>Few studies with conflicting findings.</p> <p>In premenopausal women, higher phytoestrogen intake was associated with reduced LH and FSH concentrations and longer menstrual cycles [4].</p> <p>Among women undergoing ART, isoflavone intake was positively associated with having a live birth.</p>
<p>Bisphenols (BPA/BPS/BPF)</p> <p>Widely used in plastic products, lining of tin cans and thermal sales receipts. Leaches from many products.</p> <p>Present in the urine of 95% of people tested.</p>	<p>Few studies of BPA with conflicting findings [5].</p> <p>No studies on the analogues BPS or BPF which are used as replacement in 'BPA free' products.</p> <p>Urinary BPA is associated with altered oestrogens, androgens, gonadotrophins and sex hormone binding globulin (SHBG) concentrations. In occupationally exposed men, higher BPA levels were associated with worse sperm parameters.</p> <p>In general populations, one study found detectable urinary BPA increased risk of low sperm parameters. Another study found no association.</p> <p>Among people trying to conceive, no associations has been found between BPA concentration and TTP, fertilisation and live birth rates [5].</p> <p>May exert secondary negative effects on fertility, due to their association with obesity and type 2 diabetes.</p>	<p>Higher serum BPA concentrations have been reported in infertile women, compared with those of fertile women.</p> <p>Among healthy women, BPA exposure has not been associated with increased TTP or reduced fecundity [6].</p> <p>Among women undergoing ART, several studies and meta-analyses have identified that BPA exposure and urinary concentrations are associated with lower circulating oestrogen levels; oocyte yield and quality; blastocyst formation; as well as higher implantation failure and miscarriage rates.</p> <p>May exert secondary negative effects on fertility, due to their association with obesity and type 2 diabetes.</p>

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Chemical and where it is found	Effects on male fertility/fecundity	Effects on female fertility/fecundity
<p>Phthalates</p> <p>Includes di-esters and mono-esters.</p> <p>Added to plastics to increase flexibility and durability and found in toys, footwear, food packaging, medical devices, and personal care products.</p> <p>Detected in >95% of people tested.</p>	<p>Epidemiological studies provide evidence for negative associations between mono-ester phthalate exposure and reproductive hormones; sperm concentration, count, and morphology; and TTP [7]. Stronger evidence exists for detrimental effects on sperm motility and quality.</p>	<p>No firm conclusions can be made regarding possible effects of phthalates on female fertility and fecundity, despite the growing body of evidence of negative effects from animal studies [8].</p> <p>Conflicting evidence exists for their effects on TTP and early pregnancy loss.</p>
<p>Parabens</p> <p>Structurally similar to BPA. Sub-classes include methyl, propyl and butyl parabens.</p> <p>Used as preservative and anti-microbial agents, and found in food, cosmetics and personal care products.</p> <p>Detected in >90% of people tested and levels are > five-fold higher in women than in men.</p>	<p>Urinary paraben concentrations have not been associated with changes in plasma steroid hormone concentrations or semen parameters in idiopathic infertility but butyl parabens have been linked to sperm DNA damage [9].</p> <p>In couples undergoing ART, paternal urinary paraben concentrations were not associated with fertilisation rates, embryo quality or implantation rates [10].</p>	<p>Insufficient evidence exists to determine effects of parabens on female fertility and fecundity.</p>
<p>Persistent organic pollutants (POPs)</p> <p>Compounds in the environment that often accumulate in adipose tissues.</p> <p>Includes ‘superfamilies’ that have different characteristics and biological effects:</p> <p>a) Polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs) and diphenyl ethers (PBDEs). Used in electrical devices, industrial lubricants, paints until 1979 (PCBs). Found in flame retardants of furniture (PBB and PBDEs).</p> <p>b) Polychlorinated dibenzo-p-dioxins (PCDDs or dioxins). By-products of industrial processes – metal and paper production, wood incineration, or heating plastics.</p>	<p>a) Evidence for a negative effect of PCBs on sperm motility is robust. There is weak evidence for effects of PBBs, PCBs and PBDEs on hormone concentrations (including testosterone), stronger evidence for negative effects on sperm parameters (particularly for PCBs on motility and DNA integrity) and fecundity [11].</p> <p>b) Occupational exposure was associated with increased gonadotrophins and decreased testosterone in the serum among chemical production workers.</p> <p>As data are limited, no statement can be made about the possible effects of dioxin concentrations in non-occupational environments.</p>	<p>a) High PCB exposure was associated with longer menstrual cycles [12] and early onset menopause.</p> <p>In ART, PCBs and PBDEs were associated with decreased fertilisation rates, lower rates of high-quality embryos and increased implantation failure [13].</p> <p>Exposure to certain PCBs is linked to longer TTP.</p> <p>b) No clear evidence exists to allow conclusions of effects of dioxin on female fertility and fecundity.</p>



The effects of environmental chemicals on fertility and fecundity

Chemical and where it is found	Effects on male fertility/fecundity	Effects on female fertility/fecundity
<p>Pesticides, herbicides and insecticides</p> <p>The many chemicals classified under these categories (e.g. organochlorines and organophosphates) can act via several hormonal pathways. Because people often are simultaneously exposed to multiple chemicals and concentrations, it is difficult to assess their effects on fertility and fecundity.</p>	<p>Two of the most well-studied are DDT and DDE. Studies of numerous chemicals have identified adverse effects on sperm characteristics (quality and function), including decreased motility, increased DNA damage, and mitochondrial dysfunction [1].</p> <p>Occupational exposure is associated with lower <i>in vitro</i> fertilisation rates, increased TTP [14], and higher miscarriage rates.</p>	<p>In several studies, occupational exposure to combinations of pesticides or individual pesticides appears to alter menstrual cycle lengths, reduce fertility and can result in an increased TTP and risk of miscarriage [14].</p>
<p>Heavy metals</p> <p>Includes aluminium, arsenic, cadmium, chromium, lead, mercury, molybdenum and nickel.</p> <p>Exposure occurs through smoking, air pollution, dental fillings, consumption of contaminated food and drink, and contact with petrol, industrial and household products.</p> <p>Bioaccumulation of heavy metals in tissues is common over a lifetime.</p>	<p>The strongest evidence exists for the negative effects of lead, and to a lesser extent cadmium and mercury, on sperm parameters and hormone concentrations [15]. Lead seminal plasma concentrations are negatively associated with sperm parameters [15] and IVF success rates, and positively associated with a premature acrosome reaction. Occupational exposure to high [8] lead levels is associated with a longer TTP.</p> <p>Increased urinary cadmium is positively associated with serum LH and testosterone in occupationally exposed workers [16]. In the general population cadmium is found to negatively affect sperm parameters, especially sperm counts that are reduced in some but not in other studies [15]. In ART, couples semen concentrations are not linked to a longer TTP.</p> <p>Only limited evidence exists about the possible association between concentrations of mercury, aluminium, arsenic, chromium, molybdenum and nickel and steroid hormone concentrations or semen characteristics; existing evidence is conflicting [15,16].</p>	<p>Relatively few studies in women compared with those in men have investigated associations between heavy metals and fertility.</p> <p>Among women receiving fertility treatment, blood lead concentrations are negatively associated with fertilisation rates.</p> <p>Higher blood cadmium levels in women, independent of their partners, are associated with longer TTP [17], although other studies report equivocal effects of cadmium on fertility.</p> <p>Menstrual cycle abnormalities are identified in women occupationally exposed to mercury. Dental assistants with high mercury vapour exposure have a longer TTP than unexposed women.</p> <p>In the general population, however, no associations have been found between blood mercury concentrations and fertility [17]. Equally, in women receiving fertility treatment, no association between mercury and IVF outcomes have been identified.</p>



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Chemical and where it is found	Effects on male fertility/fecundity	Effects on female fertility/fecundity
<p>Fossil fuels and air pollutants</p> <p>Air pollution encompasses numerous compounds (particulate matter between 2.5 to 10 µm in diameter), nitrogen dioxide, sulphur dioxide, and ozone released by the combustion of fossil fuels [25].</p>	<p>A systematic review of the effects of occupational and residential exposure to oil and gas extraction activities identified strong evidence for effects on steroid hormone receptors and some evidence for detrimental effect on sperm motility, with inconsistent findings with respect to other sperm parameters [18].</p> <p>No robust studies have been undertaken on air pollution and male fecundity.</p>	<p>Exposure to oil and gas extraction activities identified increased miscarriage rates in women with occupational exposure, with conflicting findings for women with residential exposure [18].</p> <p>Studies of the effects of air pollutants, report equivocal results [19], however fertility rates are decreased in the general population with higher traffic-related pollution.</p>
<p>Ionising and electromagnetic radiation</p> <p>Ionising radiation exposure can be medical-related or caused by atomic disaster.</p> <p>Electromagnetic field (EMF) radiation exposure occurs daily through emission from mobile phones, microwave ovens, high voltage power lines and other electrical appliances.</p>	<p>Occupational and low-level ionising radiation exposures are associated with reduced sperm counts, perturbed sperm motility and increased morphological abnormalities, DNA fragmentation and global hypermethylation [20, 21]. However, it is not associated with change in TTP among occupationally-exposed men [22], residents near nuclear power plants [23], or after gonadal X-ray examinations [24].</p> <p>Both occupational and general population exposure studies report equivocal effects of EMF, although sperm motility and DNA fragmentation and blood hormone levels are commonly affected negatively [15, 25]. Mobile phone usage is negatively associated with several sperm parameters. The effects of EMF are mainly believed to occur from disruption of testicular heat regulation. EMF effects related to fecundity are currently unclear.</p>	<p>Little robust evidence exists on adverse effects of low-dose radiation exposure on fertility. Peri-conceptual exposure to low-dose radiation is not associated with a change in TTP in female nuclear plant workers [22] or those couples living near nuclear waste processing plants [23]. However, diagnostic radiography in adolescent girls is associated with an increased TTP and miscarriage rate in adulthood [26].</p> <p>EMF effects on female fertility have rarely been studied in the general population, with no clear evidence to substantiate possible effects. Occupational shortwave EMF exposure has been associated with an increased TTP, but not in all studies [27]. Evidence exists for exposure-dependent increases in miscarriage risk [28].</p>

Abbreviations:

- ART** Assisted reproductive technology
- DDE** Dichlorodiphenyldichloroethylene
- DDT** Dichlorodiphenyltrichloroethane
- FSH** Follicle stimulating hormone
- IVF** In-vitro fertilisation
- LH** Luteinizing hormone
- TTP** Time to pregnancy



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Summary

For most environmental chemicals, including EDCs, no or few large reproductive human studies exist. Evidence from these suggest that several have a direct negative effect on male and female fertility and fecundity [1, 2]. In men there is strong evidence to support negative effects on sperm motility and DNA integrity of phthalates (monoesters MEHP and MBP), PCBs, PBDEs, pesticides including DDE, lead, ionising and EMF radiation, and on sperm count and morphology of lead and ionising radiation. For male fecundity (TTP), moderate evidence supports a negative association with monoester phthalates, PCBs and pesticides including DDE.

Fewer studies have been undertaken in women, with only moderate evidence of negative effects on oocyte quality, implantation and miscarriage rates of BPA or PCBs. Stronger evidence exists of a negative association with fecundity (TTP) for PCBs and pesticides including DDE.

To date, fewer fertility effects are identified in women than men, though this likely reflects the difficulty in accessing oocytes relative to sperm for study, rather than the lack of actual effects. It should also be noted that commonly a statement cannot be made regarding many environmental chemicals, most likely due to a lack of study, not because an association does not exist. Determining the effect of an individual EDC is also confounded by the presence and action of multiple EDCs in the environment. This may explain why low levels of a single EDC are often not associated with fertility issues, as these may result instead from added effects of many EDCs working at low concentrations. Far more research is thus required to categorically establish the effects of individual EDCs on fertility and fecundity of both males and females.

Clinical recommendations

Men and women should limit their exposure to environmental chemicals, especially EDCs, where possible. Clinical advice as to the management strategies that may help lower exposures to improve fertility and fecundity includes:

- drink water/soft drinks from glass or hard plastic bottles, rather than soft plastic bottles. BPA, phthalates and other plasticisers are used to make plastics in bottles flexible

- avoid heating food in soft plastic takeaway containers or those covered in cling wrap or foil. Instead, place food in china or glass bowls and cover with paper towel or a china plate before heating
- consume fewer processed/pre-canned/pre-packaged foods as this will reduce the intake of BPA, phthalates and plasticisers that coat the inside of cans and plastic wrappings
- wash fresh produce prior to consumption to reduce the intake of pesticides, fungicides, herbicides and chemicals that may have been sprayed on them
- limit the amount of oily fish and fatty meats to reduce the intake of POPs, pesticides, heavy metals and fat-soluble chemicals that can accumulate in animals
- reduce the use of personal care products with high concentrations of chemicals (make-up, shampoos, hair colourings etc.) and choose paraben free products
- avoid handling sales receipts and exposure to strong solvent based chemicals (paints, cleaning products, glues etc), industrial processing chemicals, heavy metals, smoke, ionising radiation
- limit mobile phone usage and contact to reduce exposure to electromagnetic radiation
- be aware that replacement analogues, such as for BPA (e.g. BPS and BPF), are not necessarily 'safer' options.

For individuals or couples receiving fertility treatment, in particular those diagnosed with idiopathic infertility, it is recommended to obtain detailed information on their lifestyle, and possible occupational and general exposure to environmental chemicals. It may also prove informative to analyse urine, reproductive fluids and tissues, as well as non-reproductive tissues (hair and adipose) for current and cumulative environmental chemical concentrations.

For more information about pre-conception health visit

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