Botha, E. (2021) Chemicals and fertility. Teoksessa Tuomi, J. (toim.) Preconception health and care - Handbook for education. Tampereen ammattikorkeakoulun julkaisuja, sarja B, raportteja 135, s. 277-288.

URL: http://urn.fi/URN:ISBN:978-952-7266-60-1

Chemicals and fertility

Elina Botha, PhD, Senior Lecturer in Midwifery
Tampere University of Applied Sciences
Finland

Abstract

It has long been known that chemicals in the environment can act as endocrine disruptors and have a holistic effect on human health. Awareness of the effects of endocrine disruptors on sexual and reproductive health, and fertility in particular, has increased, as has the research available on it. Pollution, pesticides, phthalates, and bisphenol A impair the fertility of both males and females. In some occupational groups, there are additional risks in working conditions in terms of fertility. These groups include professionals working in the oil industry and beauty industries. This article will equip sexual and reproductive health professionals with reasoned information to help them develop their fertility protection skills when guiding youth and young adults. This guidance allows youth and young adults to choose more wisely to avoid any unnecessary chemical load to protect their health and fertility.

Keywords: environment, chemicals, endocrine disruptors, fertility

Tiivistelmä

On jo kauan tiedetty, että ympäristön kemikaalit voivat toimia hormonihäirikköinä ja vaikuttaa ihmisen terveyttä kokonaisvaltaisesti heikentäen. Tietoisuus hormonihäiriköiden vaikutuksista seksuaali- ja lisääntymisterveyteen, ja erityisesti hedelmällisyyteen, on lisääntynyt, samoin siitä saatavilla oleva tutkimustieto. Ilmansaasteet, kasvien tuholaismyrkyt, ftalaatit ja bisfenoli A heikentävät sekä miehen, että naisen hedelmällisyyttä. Joillakin ammattiryhmillä työolosuhteisiin liittyy hedelmällisyyden kannalta lisäriskejä. Näihin ryhmiin kuuluvat öljyteollisuudessa, sekä kauneusaloilla työskentelevät ammattilaiset. Tämän katsauksen avulla seksuaali- ja lisääntymisterveyden ammattilaisille saavat käyttöönsä perusteltua tietoa, jonka avulla he voivat ke-

hittää hedelmällisyyden suojeluun liittyvää osaamistaan ohjatessaan nuoria ja nuoria aikuisia. Tämän ohjauksen avulla nuoret ja nuoret aikuiset voivat valita viisaammin välttääkseen turhaa ja ylimääräistä kemikaalikuormaa suojellakseen terveyttään ja hedelmällisyyttään.

Avainsanat: Ympäristö, kemikaalit, hormonaaliset haitta-aineet, hedelmällisyys

Introduction

Our environment, and the chemicals in it, have a negative impact on health and fertility in many ways. An individual's chemical burden might be difficult to control in every situation, but it is good to be aware of all factors. It is also important for professionals and decision-makers to be aware of these factors in the environment that are affecting fertility. The first study, which found that chemicals in the environment act as endocrine disruptors and impair fertility, dates to 1970 by Ratcliffe. So, we cannot talk about a new phenomenon.

Endocrine glands secrete hormones that strongly affect the functioning of the human body. Endocrine disruptors are chemicals that behave like hormones in the body by interfering with this sensitive system (Bergman et al. 2012). An endocrine disruptor can work in two ways. It can block the hormone receptor, preventing the hormone from binding to the receptor, so that the desired reaction does not occur. The disruptor can also mimic the body's own hormone, which means that the reaction begins even when it should not. (Finnish Institute for Health and Welfare (THL) 2019a.)

A big amount of scientific data is currently being produced regarding different chemicals affecting the delicate endocrine system. The impact of chemicals on fertility, and especially on sperm, has been studied comprehensively over the past few years. This article is based on a systematic data retrieval of meta-analyses, and systematic literature reviews from the years 2013–

2018. Good scientific practice has been respected in the acquisition and analysis of the data. This article will focus on the findings.

Activity of endocrine disruptors

Endocrine disruptors have a negative effect on health and fertility in many ways. According to human and animal studies to date, they reduce semen quality, cause genital malformations (e.g. undescended testicles), pregnancy problems (prematurity and low birth weight), thyroid problems, cancers (breast, ovarian, testicle and prostate cancers) and obesity (Bergman et al. 2012).

Cells in the testicles are metabolically sensitive and hormone responsive, which makes male fertility very susceptible to hormones, especially endocrine disruptors (Alves et al. 2013). Male fertility relies heavily on a well-functioning hypothalamic–pituitary–testicular (HPT) axis which is, among other things, a system that regulates the production of male hormones (Comninos et al. 2014). Male reproduction, development and sexual characteristics are controlled by the HPT axis (Dhole & Kumar 2017). Androgens, i.e. male hormones, cause the development of gender characteristics typical of a man, in the same way that female hormones (estrogens) cause the development of female gender characteristics in women.

Women also need male hormones, but too high androgen levels can cause menstrual disorders, and for example hirsutism, which is excessive unwanted hair growth. Too high androgen levels in a woman can also cause infertility. (Tiitinen 2019.) In men, excessive production of estrogen can cause gynecomastia, i.e. breast growth (Mustajoki 2019). This is a transient and normal phenomenon in puberty, but later may indicate an excessive effect of endocrine disruptors, such as estrogens, in the environment. Endocrine disruptors can also affect women's delicate hypothalamus-

pituitary-ovarian (HPO) axis function. Endocrine disruptors can affect estrogen levels, follicle count, egg cell quality, embryo attachment and quality, and cause risks for normal healthy pregnancies (Karwacka et al. 2019).

Normal endocrine function can be disrupted in many ways, for example by harming normal metabolism. Environmental compounds and chemicals that promote human weight gain are called obesogens. Roughly described, obesogens contribute to the formation of adipocytes (also known as lipocytes or fat cells) by disrupting metabolism, thereby increasing the formation and growth of the fat tissue. The tissue of the reproductive system includes fat tissue, which makes them a particularly sensitive environment for chemicals (Reame et al. 2014). Subcutaneous fat tissue stores fat-soluble environmental chemicals and toxins. The more fat tissue in the body, the more toxins are stored there as a burden for the body (Hughes 2005). Obesogens also affect the physiology and metabolism of the testicles, which in turn can directly affect sperm formation (Cardos et al. 2017).

Effects of hundreds of chemicals on fertility

More than 800 chemicals have been identified or suspected in the world that can act as endocrine disruptors in the human body. Not only humans, but also animals suffer from these chemicals. According to a study in the United States, each pregnant woman was exposed to 43 different chemicals in her life (Woodruff et al. 2011). Scientific research into the health hazards of these chemicals is still ongoing, but there is a great need for more research.

Substances that are known environmental toxins and are suspected of acting as endocrine disruptors are Dioxins, PCB compounds, fire extinguishing agents, pesticides, fluorinated compounds (e.g. PFAS, PFOA, PFOS), Bisphenol A, Parabens,

Phthalates, organic tin compounds and Methylmercury (Finnish … 2019b). Not all of these disrupt the hormones needed for reproduction, but also impair health in other ways and therefore indirectly also affect fertility. Exposure to harmful chemicals may occur before pregnancy, during pregnancy, in childhood, adolescence, adulthood and old age (American College of Obstetricians and Gynecologists (ACOG) 2013). Harmful effects may be programmed into genes and cause for instance breast cancer later in adulthood (Doherty et al. 2010).

Air and traffic pollution that burden cities and their inhabitants has been studied to reduce fertility (Checa Vizcaíno et al. 2016; Lafuente et al. 2016). It is suspected that these environmental toxins are particularly detrimental to men's ability to reproduce (Bonde et al. 2016). Plant pesticides such as DDT and HCH have a particular impact on sperm count and mobility (Martenies et al. 2013).

Cosmetics for personal hygiene often contain parabens and phthalates, which are also suspected of being endocrine disruptors (Dodson et al. 2012). Women of childbearing age are generally high-level consumers of cosmetics. This has been shown in studies as high levels of phthalates and parabens in their urine (Silva et al. 2004; Calafat et al. 2010). Braun et al. (2014) found in their study that pregnant women who use body lotion, perfume, makeup, hair gel and nail polish had significantly more phthalates and parabens in their urine than women who did not use such a large amount of cosmetics. This can be particularly harmful to the fetus in early pregnancy, as it is then particularly sensitive to the effects of endocrine disruptors (Rice et al. 2000). In addition to cosmetics, phthalates are found in adhesives, electronics, packaging materials, toys, paints, medicines, some foods, and textiles (Finnish … 2019b). There is sufficient evidence that phthalates are toxic to reproductive health. However,

there are still gaps and contradictions in this information and research. Low phthalate exposure does not appear to pose a high risk to female fertility (Kay et al. 2013), but it appears to have a debilitating effect on sperm quality even at lower exposure (Kay et al. 2014). The effects of exposure to continuous and large amounts of phthalates and other chemicals on fertility remain partially unknown but still of concern (Kay et al. 2013). However, it is known that phthalates act as weak antiandrogens, i.e. counter effects of male hormones. Phthalates reduce sperm count, mobility and increase DNA destruction and deformities in sperm (Cai 2015; Bonde et al. 2016; Høyer et al. 2018).

Bisphenol A (BPA) has been used to make polycarbonate plastics and epoxy resins. BPA is used in plastic cutlery, cups, beverage bottles and canned coatings. BPA is also found in the thermal paper of cash receipts. BPA used in baby bottles, pacifiers, and food packaging for children under three years of age is prohibited in the EU. Most of the exposure to BPA is through food. BPA is released to food from plastic coatings, plastic products containing food and plastic bottles. BPA can also be obtained from room dust, plastic toys, or cosmetics. BPA is toxic to fertility because it interferes with female and male hormones in the body. (Finnish … 2019c.) The effects may be estrogenic, anti-estrogenic, androgenic or antiandrogenic. Experimental animal studies by Ziv-Gal & Flaws (2016) found that BPA has a very detrimental effect on the structure of the ovaries, fallopian tubes, and uterus, as well as on the functioning of the hypothalamic-pituitary-ovarian axis. BPA was also seen to interfere with the menstrual cycle and prevent the embryo from attaching in the uterus. BPS and BPF have come to replace the notorious BPA, but their effects have proved to be as harmful as BPA's. These substitute chemicals are as hormonally active as BPA and impair fertility. (Rochester & Bolden 2015.)

Different occupational groups have different chemical exposures and, as a result, risks of fertility decline. Chemicals used in the oil industry clearly reduce the quality of sperm. They also have a disruptive effect on reproductive hormone receptors (Balise et al. 2016). In addition, chemical exposures of beauticians and hairdressers significantly impair their fertility if compared to their chemical exposure to the rest of the population (Kim et al. 2016).

Phthalates, BPA, plant pesticides and tobacco are the most harmful of all chemicals to the functioning of the ovaries. These chemicals are harmful to women of all ages, from the fetus to the grandmother and are highlighted if there has been repeated exposure in several stages of life. These chemicals destroy antral follicles in the ovaries, i.e. small resting follicles which contains an immature egg, and can cause premature menopause in women. (Vabre et al. 2017.)

Conclusion

Can the results of animal testing be fully, or even partially, applied to humans? Animals, such as mice or rats, may have different reactions to a chemical in the environment than humans. It is not possible to research all the chemical effects on humans, for ethical reasons alone, but also for safety reasons. In these studies, animals may be given a dose containing a strong chemical, which in the results indicates possible human effects. However, people are not exposed to the doses or amounts used in these experiments in their daily lives. Many chemicals play a small part in everyday life and therefore do not need to be concerned about (Finnish … 2019b). However, it would be important to try to somehow control better how much and which chemicals are used by better lifestyle choices.

Laboratory conditions can vary from country to country, for this reason studies cannot always be fully compared. When reading the results, it should be remembered that there are always a lot of confounding factors when studying people. A person can never be completely isolated from their environment or, for example, from their diet, so that it can be said for certain that it is a particular substance or product that affect gametes. Fertility is the sum of many factors; it may be impossible to say that only one factor is decisive in decline in fertility. Fertility and the factors affecting it accumulate together in the couple and together affect the likelihood of having healthy children.

How can these endocrine disruptors be avoided? Here are good guidelines from Finnish Institute for Health and Welfare (THL) (2019a):

- When cooking, use only containers that are made for cooking, storage and heating food.
- Drinking bottles intended for single use should only be used once, not continuously.
- Products containing plastics purchased outside the EU can be a risk to health.
- It is advisable to follow the instructions for use and warnings that come with detergents.
- Cosmetics and excessive use of chemicals should be avoided or used as little as possible during pregnancy.
- In addition to these, organic food should be favoured, if possible. They often contain fewer chemicals than ordinary products.

With these measures, everyone can reduce their own exposure to chemicals and endocrine disruptors.

In its statement, ACOG (2013) proposes that sexual and reproductive health actors must be involved in developing interventions and measures to better understand the effects of chemicals in the environment and to protect fertility from these harms, by all possible means. These chemicals in the environment affect a person at all stages of the life course, however, visibly wounding fertility, regardless of the time of exposure.

Fortunately, the individual is not alone at the mercy of chemicals in our societies. The use of chemicals that have proved harmful is limited or prohibited by international agreements and laws (Finnish … 2019b) in the EU. This eases anxiety about the huge chemical load but leaves room for the individual's own ability to choose more wisely and, where possible, protect their own fertility and health.

It should no longer be thought that the aim is solely to have a healthy child as a result of healthy parents and pregnancy. Considering current research, the goal is for the future children to be healthy throughout their lives, as a result of healthy parents and pregnancy. The goal is long-term, as healthy children are wanted to be able to have healthy children themselves. The goal of health is over-generational. (Boekelheide et al. 2012; Sutton et al. 2012.) Due to their fertility and reproductive intentions, youth and young adults represent the most important stage of human development and life that affects overall health. During adolescence, a window opens to the possibility of over-generational health. If a young person avoids endocrine disrupting chemicals as much as possible at this stage of life, they will be offered the best possible view of their own health and of their offspring (Gustafson 2018). Professionals promoting sexual and reproductive health play a key role in this, guiding youth and young adults to identify and know the environmental effects on fertility when they are at this very critical stage of their lives, to choose wisely – whenever possible.

References

Alves, MG., Rat, L., Carvalho, RA., Moreira, PI., Socorro, S. & Oliveira, PF. 2013. Hormonal control of Sertoli cell metabolism regulates spermatogenesis. Cellular and Molecular Life Sciences, 70, 777–793.

American College of Obstetricians and Gynecologists (ACOG). 2013. Exposure to toxic environmental agents. Committee Opinion No. 575. Obstetrics and Gynecology, 122, 931–935.

Balise, VD., Meng, C., Cornelius-Green, J., Kassotis, CD., Kennedy, R. & Nagel, S. C. 2016. Systematic review of the association between oil and natural gas extraction processes and human reproduction. Fertility and Sterility 106 (4), 795–819.

Bergman, Å., Heindel, JJ., Jobling, S., Kidd, KA. & Zoeller RT. 2012. Endocrine disrupting chemicals, summary for decision-makers. IOMC. United Nations Environment Programme (UNEP) and WHO. Available https://apps.who.int/iris/bitstream/handle/10665/78102/WHO_HSE_PHE_IHE_2013.1_eng.pdf;jsessionid=E2276EFD8021B987D7AC63BD7B077F6B?sequence=1 Read 10.1.2021.

Boekelheide, K., Blumberg, B., Chapin, RE., Cote, I., Graziano, JH., Janesick, A., Lane, R., Lillycrop, K., Myatt, L., States, JC., Thayer, KA., Waalkes, MP. & Rogers, JM. Predicting later-life outcomes of early-life exposures. Environmental health perspectives, 120(10), 1353–1361.

Bonde, JP., Flachs, EM., Rimborg. S., Glazer, CH., Giwercman, A., Ramlau-Hansen C, & Bräuner, EV. 2016. The epidemiologic evidence linking prenatal and postnatal exposure to endocrine disrupting chemicals with male reproductive disorders: A systematic review and meta-analysis. Human Reproduction Update 23, (1), 104–125.

Cai, H., Zheng, W., Zheng, P., Wang, S, Tan, H., He, G. & Qu, W. 2015. Human urinary/seminal phthalates or their metabolite levels and semen quality: A meta-analysis. Environmental Research, 142, 486–494.

Calafat, AM., Ye, X., Wong, LY., Bishop, AM. & Needham, L. L. 2010. Urinary concentrations of four parabens in the U.S. population: NHANES 2005-2006. Environmental Health Perspectives, 118, 679-685.

Cardos, A., Alves, M., Mathur, P., Oliveira, P., Cavaco, J. & Rato, L. 2017. Obesogens and male fertility. Obesity Reviews, 18(1), 109–125.

Checa Vizcaíno, MA., González-Comadran, M. & Jacquemin, B. 2016. Outdoor air pollution and human infertility: A systematic review. Fertility & Sterility 106(4), 904.e1.

Doherty, LF., Bromer, JG., Zhou, Y., Aldad, TS. & Taylor, HS. 2010. In utero exposure to diethylstilbestrol (DES) or bisphenol-A (BPA) increases EZH2 expression in the mammary gland: an epigenetic mechanism linking endocrine disruptors to breast cancer. Hormones and Cancer, 1, 146–155.

Finnish Institute for Health and Welfare (THL). 2019a. Chemicals should be evaluated as mixtures and not individually – traditional risk assessment can underestimate health hazards. Available https://thl.fi/fi/-/kemikaaleja-tulisi-arvioida-seoksina-eika-yksittain-perinteinen-riskinarviointi-voi-aliarvioida-terveyshaittoja Read 13.12.2020.

Finnish Institute for Health and Welfare (THL). 2019b. Environmental toxins. Available https://thl.fi/fi/web/ymparistoterveys/ymparistomyrkyt Read 13.12.2020.

Finnish Institute for Health and Welfare (THL). 2019c. Bisfenol A. Available https://thl.fi/fi/web/ymparistoterveys/ymparistomyrkyt/bisfenoli-a Read 13.12.2020.

Gustafson, C. 2018. Pete Myers, MD: Epigenetics and Endocrine Disruption. Integrative Medicine: A Clinician's Journal 17(6), 26–29.

Hughes, W. 2005. Essentials of environmental toxicology. Taylor & Francis e-library, 2nd ed., Philadelphia, USA.

Høyer, BB., Lenters, V., Giwercman, A., Jönsson, BAG., Toft, G., Hougaard, KS. & Specht, IO. 2018. Impact of di-2-ethylhexyl phthalate metabolites on male reproductive function: A systematic review of human evidence. Current Environmental Health Reports, 5(1), 20–33.

Karwacka, A., Zamkowska, D., Radwan, M. & Jurewicz, J. 2019. Exposure to modern, widespread environmental endocrine disrupting chemicals and their effect on the reproductive potential of women: an overview of current epidemiological evidence. Human Fertility, 22(1), 2–25.

Kay, VR., Bloom, MS. & Foster, WG. 2014. Reproductive and developmental effects of phthalate diesters in males. Critical Reviews in Toxicology, 44(6), 467–498.

Kay, VR., Chambers, C. & Foster, WG. 2013. Reproductive and developmental effects of phthalate diesters in females. Critical Reviews in Toxicology, 43(3), 200–219.

Kim, D., Kang, M., Choi, S., Park, J., Lee, H. & Kim, E. 2016. Reproductive disorders among cosmetologists and hairdressers: A meta-analysis. International Archives of Occupational and Environmental Health, 89(5), 739–753.

Lafuente, R., García-Blàquez, N., Jacquemin, B. & Checa, MA. 2016. Outdoor air pollution and sperm quality. Fertility and Sterility, 106 (4), 880–896.

Martenies, SE. & Perry, MJ. 2013. Environmental and occupational pesticide exposure and human sperm parameters: A systematic review. Toxicology, 307, 66–73.

Mustajoki, P. 2019. Breast growth in men (gynekomastia). Duodecim. Terveysportti. Available www.terveyskirjasto.fi Read 11.11.2020.

Ratcliffe, D. 1970. Changes attributable to pesticides in egg breakage frequency and eggshell thickness in some British birds. Journal of Applied Ecology, 7, 67–115.

Rice, D. & Barone, Jr. S. 2000. Critical periods of vulnerability for the developing nervous system: evidence from humans and animal models. Environmental Health Perspectives, 108 (Suppl 3), 511–533.

Rochester, JR. & Bolden, AL. 2015. Bisphenol S and F: A systematic review and comparison of the hormonal activity of bisphenol A substitutes. Environmental Health Perspectives, 123(7), 643–650.

Silva, MJ., Barr, DB., Reidy, JA., Malek, NA., Hodge, CC., Caudill SP., Brock, JV. Needham, LL. & Calafat AM. 2004. Urinary levels of seven phthalate metabolites in the U.S. population from the National Health and Nutrition Examination Survey (NHANES) 1999–2000. Environmental Health Perspectives, 112, 331–338.

Sutton, P., Woodruff, TJ., Perron, J., Stotland, N., Conry, JA., Miller, MD. & Giudice, LC. 2012. Toxic environmental chemicals: the role of reproductive health professionals in preventing harmful exposures. American Journal of Obstetrics & Gynecology, 207, 164–173.

Tiitinen, A. 2019. Liikakarvoitus. Duodecim. Terveysportti. Available www.terveyskirjasto.fi Read 13.12.2020.

Vabre, P., Gatimel, N., Moreau, J., Gayrard, V., Picard-Hagen, N., Parinaud, J. & Leandri, RD. 2017. Environmental pollutants, a possible etiology for premature ovarian insufficiency: A narrative review of animal and human data. Environmental Health: A Global Access Science Source, 16, 1–18.

Woodruff, TJ., Zota, AR. & Schwartz, JM. 2011. Environmental chemicals in pregnant women in the United States: NHANES 2003–2004. Environmental Health Perspectives, 119, 878–885.

Ziv-Gal, A. & Flaws, JA. 2016. Evidence for bisphenol A-induced female infertility: A review (2007–2016). Fertility and Sterility, 106(4), 827–856