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# Chemical Exposures During Pregnancy: Dealing with Potential, but Unproven, Risks to Child Health

### Chemical Exposures During Pregnancy: Dealing with Potential, but Unproven, Risks to Child Health

#### 1. Introduction

The concept that maternal exposure to certain chemicals and drugs during pregnancy and lactation can have detrimental effects on the fetus/baby is not new. Adverse effects on fetal development and long term health due to cigarette smoking and alcohol consumption during pregnancy are particularly well documented. This has led to the provision of guidelines and advice to women who are pregnant on the consequences of these lifestyle choices for unborn babies. In contrast, there is no official antenatal advice or guidelines that inform women who are pregnant or breastfeeding of the potential risks that some chemical exposures could pose for their babies. Instead, they are faced with frequent 'chemical scare' stories in the media which are often inaccurate or exaggerated. Subsequently, these stories create understandable anxiety for women who are pregnant or breastfeeding. The purpose of this document is to raise awareness of the current issues surrounding chemical exposure during pregnancy and breastfeeding, so that women are armed with sufficient facts to enable them to make an informed decision as to whether or not they might wish to take some form of positive action in regards to chemical exposures throughout their pregnancy.

#### 2. Mother as 'gatekeeper' of her baby's future health

The mother is the guardian of her baby's development and future health; any external influences on the baby predominantly come from the mother. This important conceptual point may not be fully appreciated by many women that are pregnant. It is being increasingly recognised that predisposition to some adult health disorders is determined by the quality of the baby's development in the womb and soon after birth. Altered predisposition to adult diseases such as obesity, type II diabetes and cardiovascular disease provide strong examples of diseases affected by prenatal development.<sup>3</sup> It is possible that this may place a daunting responsibility on the mother, but it also provides an opportunity for positive action on her part if she is motivated to do so. Positive action to give the baby the best possible start in life with the least predisposition to subsequent disease can be executed via healthy lifestyle changes and choices during the planning and maintenance of pregnancy and breastfeeding. Examples of this are; refraining from smoking and drinking, and eating a balanced diet during pregnancy.

#### 3. Increasing concerns over chemical exposure

In recent years there has been increasing concern over the potential for exposure of environmental chemicals to the mother and baby to cause adverse health effects in the child.<sup>4</sup> Epidemiological research has linked exposure to some of these chemicals in pregnancy with adverse birth outcomes; pregnancy loss, preterm birth, low birth weight, congenital defects, childhood morbidity, obesity, cognitive dysfunction, impaired immune system development, asthma, early puberty, adult disease and mortality (cardiovascular effects and cancer).5 In addition, impairment of fertility and fecundity in women6 and impairment of testicular development and reproductive function in males, have been associated with fetal exposure to everyday chemicals in the environment. Although this list may raise concern, it is emphasised that these studies support associations and do not infer causality, raising uncertainty. Moreover, the effects are generally small and some of the cited studies show no association between disease and chemical exposure, which also raises uncertainty. One way in which this can be addressed is by researching the effects of chemical exposure to animals that are pregnant. These studies seek to show if experimental exposure to the chemical(s) in question during pregnancy can subsequently induce the relevant disorder(s) in offspring. Such an approach does not provide unequivocal evidence for harm in the human. Often the level of chemical exposure is much higher in animal studies so extrapolation to humans is inappropriate. Other difficulties with extrapolation of animal studies to humans are that women are exposed to hundreds of different environmental chemicals, not just one.8 This makes the assessment of risk extremely complex.

Another confounding factor is that virtually all women who are pregnant are exposed to certain chemicals because they are found in everyday products. The chemical bisphenol A is found in drinks and food cans and phthalate esters are found in plastics, carpets, fabrics, personal care products and glues. This makes it difficult to identify whether such exposures exert any effect at all because there is no unexposed 'control' group with which to compare the data. Media scare stories that are largely based on unproven claims add to the uncertainty. These stories also raise understandable anxieties in mothers about the potential effects of chemical exposures on their unborn child. It may be difficult for mothers to effectively deal with the uncertainty of chemical exposure risks, particularly when taking the scientific uncertainty into account. One option is not to do anything. But, this may cause anxiety levels to rise which could be deleterious for mother and baby. In this instance, the approach recommended is for such women to put 'safety first'. That is, to assume that risk is present even when it may be minimal or eventually proven to be unfounded. This is often referred to as the 'precautionary approach'.

#### 4. Understanding how and when exposure can occur

If mothers wish to reduce their exposure to environmental chemicals, an initial understanding of when such exposures occur is necessary. For some environmental chemicals, all humans are exposed and this may occur via numerous routes, some of which we cannot modify. For example, phthalates are used in many plastics, but also in many common domestic products such as glues, floor coverings and cars. Other chemicals are present in the air that we breathe, 10 such as combustion products known as polycyclic aromatic hydrocarbons (PAHs). These are difficult to avoid completely but exposure can still be reduced by avoiding direct and secondary cigarette smoke, barbecues and bonfires. The main focus of this paper will now focus on examples of chemical exposures that are modifiable.

#### 5. Chemicals in food

Food is an important source of exposure to environmental chemicals and can occur in several ways. Dichlorodiphenyltrichloroethane (DDT) and polychlorinated biphenyls (PCB) accumulate in adipose tissue/fat which is known as lipophilic. These accumulate in the food chain and are passed along it, although these are now banned. Studies have associated human fetal exposure to these chemicals with adverse birth outcomes listed previously. Fortunately, exposure to these compounds is declining progressively. However, additional precautionary steps can reduce this further. Such compounds tend to accumulate in oily fish, which are otherwise considered 'healthy'. Avoiding the over–consumption of such fish by limiting it to once per week is a sensible step. There is an additional incentive for this step as some fish, such as tuna, also accumulate heavy metals such as mercury and lead. It has been well established that mercury and lead are linked to problems in fetal and child development. It is because of this that current UK guidelines advise pregnant women to reduce or eliminate their consumption of oily fish during pregnancy.

Eating plenty of fruit and vegetables in pregnancy is strongly recommended despite the possibility that these may contain pesticide residues. It is widely perceived that such exposure to pesticides is an important health threat. Realistically, pesticides are so rigorously regulated that human exposure via food residues is usually minimal, even in non–organic products. Most people are unaware that food can also be contaminated by chemicals from handling equipment used in food processing. Chemicals can also leach into food packaging and containers, including food and beverage cans. Fresh food will generally contain fewer non–food chemicals and/or lower levels than processed oven–ready/microwave–type meals. This can be illustrated by reference to two ubiquitous chemicals used in various plastics (and other uses), namely phthalate esters and bisphenol A. When individuals were switched for 3 days from their normal food sources to the same foods freshly sourced and unpackaged, the levels of bisphenol A and a key phthalate in their urine decreased by 65% and 53% respectively. When they resumed their normal

eating practices, their exposures returned to the pre–intervention levels. Importantly, individual's internal tissue exposure to chemicals is also likely to be affected by variations in the gut microbiota, <sup>14</sup> which are probably dependent on an individual's diet and health.

#### 6. Personal care products and household chemicals

Another important source of chemical exposures for women is cosmetics/personal care products, 15 especially those applied to the skin over a large surface area to facilitate their absorption; moisturisers, sunscreens, cosmetics, fragrances, shower gels and hairsprays.<sup>16-17</sup> The amount of these products routinely used by women has increased dramatically in recent decades. Current legislation means that manufacturers are not required to name all potentially harmful chemicals in the ingredients list if they are not considered as an active ingredient. The use of the terms 'natural', 'non-toxic' and 'green' on packaging is unregulated. Examination of 43 'alternative' products bearing labels that indicated they were free of chemicals, reported the presence of 5 different phthalates despite no mention of phthalates in their ingredients. 18 A product favoured and rated by a popular environmental health website that was marketed for babies, children and adults with sensitive skin was also examined. In this product, phthalates were also the most common type of chemical to be found in the inactive ingredients. An increased use of baby care products such as lotions, powders and shampoo is associated with higher exposure to phthalates in babies.<sup>19</sup> These examples highlight the limitations of product labelling and demonstrate how women may be led to assume a product is 'safe' to use during pregnancy when not all ingredients have been taken into account. It is impossible to compile a list of such hidden ingredients because these are known only to the manufacturer of a specific product. Even suppliers of major use chemicals do not know all of the endpoint uses for the chemicals that they supply. Women are also exposed to chemicals from various household products. This includes; cleaning products, air fresheners, furniture, carpets/fabrics and DIY agents such as paint and glue. Polybrominated diphenyl ethers (PBDEs) is one chemical in household products that is used to make flame retardants in furniture, electronics and cars. Another is perfluorinated compounds (PFCs) that are used to make materials that are resistant to stain, oil and water.<sup>20</sup>

#### 7. Over the counter medicines and herbal remedies

Some analgesics, such as paracetamol, are recommended to be safe to use in early pregnancy. However, recent studies have shown that protracted paracetamol use in early pregnancy can increase the risk of incomplete testis descent (cryptorchidism)<sup>21</sup> and offspring asthma.<sup>22</sup> Two points are important in this regard. Firstly, most babies born to women who took paracetamol in pregnancy were unaffected; occasional use of paracetamol is unlikely to do harm and the benefits of pain relief will outweigh concerns about harm. Secondly, paracetamol is today viewed by some as a lifestyle 'feel–better' factor rather than a simple painkiller and these individuals are more likely to overuse paracetamol. The marketing of paracetamol with caffeine, known as 'paracetamol plus', may have helped to promote this practice.

A variety of drug prescriptions and dietary supplements contain phthalates in the tablet coating which brands them as inactive ingredients/excipients.<sup>23</sup> Due to this, phthalates are not required to be listed on product labels. This is another route by which over the counter medicines are everyday sources of unintentional chemical exposure.

It may be more concerning to note that 'herbal' or alternative 'natural' remedies are marketed as 'safe' for pregnant women. Alarmingly, these have not gone under any testing for safety of use. Thus, it is important for women that are planning or are pregnant to be aware that 'natural' products do not indicate they are safe for use during pregnancy. This is evident in the case of vitamin A/retinoids; they are essential for human health but can be potent inducers of fetal malformations if consumed in excessive amounts. This is why it is advisable for women who are pregnant to restrict their consumption of liver as this is where vitamin A is stored.

#### 8. Chemicals with endocrine-disrupting potential

The reason for the growing concern over everyday chemical exposure effects is because many of these chemicals have the potential to interfere with one or more hormone systems in the body, which play key roles in normal fetal development. These so–called 'endocrine disruptors', of which BPA plastics, PBDEs and phthalates are examples, have the potential to mimic/block endogenous endocrine hormone action and therefore disrupt normal fetal development. A relevant example of this is 'anti–androgenic' chemicals such as certain phthalates which can interfere with masculinisation of male fetuses, a developmental process which relies on normal production by the fetal testis of androgenic hormones early in pregnancy. Current risk assessments for endocrine disruptors suggest that the levels of human exposure to these chemicals are too low to pose a real risk. However, these risk assessments are performed for individual chemicals. Exposing rats that are pregnant to mixtures of 4–10 endocrine disruptors can have adverse affects, yet each chemical is ineffective at an individual level. The ways in which this data will be factored into safety assessment remains unclear at present, contributing to the aforementioned uncertainty surrounding the relationship between chemical exposure and fetal risks. Realistically, women that are pregnant are exposed to a complex mixture of hundreds of chemicals at low levels. But, methods for assessing the risk of exposure to complex chemical mixtures is not developed at present.

#### 9. Dealing with current uncertainty about the risks posed by environmental chemicals

Under normal lifestyle and dietary conditions, the level of exposure of most women to individual environmental chemicals will probably pose minimal risk to the developing fetus/baby. However, women who are pregnant are exposed to hundreds of chemicals at a low level. Potentially, this exposure could operate additively or interactively and raises the possibility of 'mixtures' effects. On present evidence, it is impossible to assess the risk, if any, of such exposures. Obtaining more definitive guidance is likely to take many years; there is considerable uncertainty about the risks of chemical exposure. The following steps would however reduce overall chemical exposure:

- use fresh food rather than processed foods whenever possible
- reduce use of foods/beverages in cans/plastic containers, including their use for food storage
- minimise the use of personal care products such as moisturisers, cosmetics, shower gels and fragrances
- minimise the purchase of newly produced household furniture, fabrics, non-stick frying pans and cars whilst pregnant/nursing
- avoid the use of garden/household/pet pesticides or fungicides (such as fly sprays or strips, rose sprays, flea powders)
- avoid paint fumes
- only take over-the-counter analgesics or painkillers when necessary
- do not assume safety of products based on the absence of 'harmful' chemicals in their ingredients list, or the tag 'natural' (herbal or otherwise).

It is unlikely that any of these exposures are truly harmful for most babies, but in view of current uncertainty about risks, especially those relating to 'mixtures', these steps will reduce environmental chemical exposures.

#### 10. Opinion

Despite uncertainty surrounding the effects of common environmental chemicals, mothers should be made aware of the sources and routes of exposure, the potential risks to the fetus/baby and the important role that the mother can play in minimising her baby's chemical exposure. Such information should be conveyed routinely at infertility, antenatal and well woman clinics as well as via the media. In this way, women will be made aware of the uncertainties which will enable them to make informed choices regarding lifestyle changes which can be made to minimise environmental chemical exposure to their unborn child.

#### References

- 1. Rogers JM. Tobacco and pregnancy. Reprod Toxicol 2009;28:152–60.
- 2. Jacobs ED, Copperman ST, Joffe A, Kulig J, McDonald CA, Rogers PD. American Academy of pediatrics. Committee on Substance Abuse and Committee on Children with Disabilities. Fetal Alcohol Syndrome and alcohol related neurodevelopmental disorders. *Pediatrics* 2000;106:358–61.
- 3. Barker DJ. Developmental origins of adult health and disease. *J Epidemiol Community Health* 2004; 58:114–5.
- 4. World Health Organisation. *Endocrine disrupters and child health*. Possible developmental early effects of endocrine disrupters on child health. Geneva; WHO:2012.
- 5. Wigle DT, Arbuckle TE, Turner MC, Bérubé A, Yang Q, Liu S, et al. Epidemiologic evidence of relationships between reproductive and child health outcomes and environmental chemical contaminants. *J Toxicol Environ Health B Crit Rev* 2008;11:373–517.
- 6. Caserta D, Mantovani A, Marci R, Fazi A, Ciardo F, La Rocca C, et al. Environment and women's reproductive health. *Hum Reprod Update* 2011;17:418–33.
- 7. Skakkebaek NE, Rajpert–De Meyts E, Main KM. Testicular dysgenesis syndrome: an increasingly common developmental disorder with environmental aspects: Opinion. *Hum Reprod* 2001;16:972–8.
- 8. Egeghy PP, Judson R, Gangwal S, Mosher S, Smith D, Vail J, et al. The exposure data landscape for manufactured chemicals. *Sci Total Environ* 2012;414:159–66.
- 9. Woodruff TJ, Zota AR, Schwartz JM. Environmental chemicals in pregnant women in the United States: NHANES 2003–2004. *Environ Health Perspect* 2011;119:878–85.
- 10. Choi H, Perera F, Pac A, Wang L, Flak E, Mroz E, et al. Estimating individual–level exposure to airborne polycyclic aromatic hydrocarbons throughout the gestational period based on personal, indoor, and outdoor monitoring. *Environ Health Perspect* 2008;116:1509–18.
- 11. Muller AK, Bosgra S, Boon PE, van der Voet H, Nielsen E, Ladefoged, O. Probabilistic cumulative risk assessment of anti–androgenic pesticides in food. *Food Chem Toxicol* 2009;47:2951–62.
- 12. Muncke J. Exposure to endocrine disrupting compounds via the food chain: Is packaging a relevant source? *Sci Total Environ* 2009;407:4549–59.
- 13. Rudel RA, Gray JM, Engel CL, Rawsthorne TW, Dodson RE, Ackerman JM, et al. Food Packaging and Bisphenol A and Bis (2–Ethyhexyl) Phthalate Exposure: Findings from a Dietary Intervention. *Environ Health Perspect* 2011;119:914–20.
- 14. Snedeker SM, Hay AG. Do interactions between gut ecology and environmental chemicals contribute to obesity and diabetes? *Environ Health Perspect* 2012;120:332–9.
- 15. Duty SM, Ackerman RM, Calafat AM, Hauser R. Personal care product use predicts urinary concentrations of some phthalate monoesters. *Environ Health Perspect* 2005;113:1530–5.
- 16. Janjua NR, Frederiksen H, Skakkebaek NE, Wulf HC, Andersson AM. Urinary excretion of phthalates and paraben after repeated whole–body topical application in humans. *Int J Androl* 2008;31:118–30.
- 17. Witorsch RJ, Thomas JA. Personal care products and endocrine disruption: A critical review of the literature. *Crit Rev Toxicol* 2010;40 (Suppl 3):1–30.
- 18. Dodson RE, Nishioka M, Standley LJ, Perovich LJ, Brody JG, Rudel RA. Endocrine Disruptors and Asthma–Associated Chemicals in Consumer Products. *Environ Health Perspect* 2012;120:935–43.
- 19. Sathyanarayana S, Karr CJ, Lozano P, Brown E, Calafat AM, Liu F, et al. Baby care products: possible sources of infant phthalate exposure. *Pediatrics* 2008;121:260–8.
- 20. Wang M, Park JS, Petreas M. Temporal changes in the levels of perfluorinated compounds in California women's serum over the past 50 years. *Environ Sci Technol* 2011;45:7510–6.
- 21. Snijder CA, Kortenkamp A, Steegers EA, Jaddoe VW, Hofman A, Hass U, et al. Intrauterine exposure to mild analgesics during pregnancy and the occurrence of cryptorchidism and hypospadia in the offspring: the Generation R Study. *Human Reprod* 2012;27:1191–201.

- 22. Andersen AB, Farkas DK, Mehnert F, Ehrenstein V, Erichsen R. Use of prescription paracetamol during pregnancy and risk of asthma in children: a population–based Danish cohort study. *Clin Epidemiol* 2012;4:33–40.
- 23. Kelley KE, Hernández–Díaz S, Chaplin EL, Hauser R, Mitchell AA. Identification of phthalates in medications and dietary supplement formulations in the United States and Canada. *Environ Health Perspect* 2012;120:379–84.
- 24. Kortenkamp A. Low dose mixture effects of endocrine disrupters: implications for risk assessment and epidemiology. *Int J Androl* 2008;31:233–40.

This Scientific Impact Paper was produced on behalf of the Royal College of Obstetricians and Gynaecologists by:

Dr M Bellingham PhD, Glasgow and Professor RM Sharpe, PhD FRSE, Edinburgh

and peer-reviewed by:

Mr DI Fraser FRCOG, Norwich; Professor IA Hughes FRCP, Department of Paediatrics, School of Clinical Medicine, University of Cambridge, Cambridge;

Professor KM Main MD PhD, Copenhagen, Denmark; RCOG Women's Network; Royal College of Nursing (RCN) and Professor J Toppari MD PhD, Turku, Finland.

The Scientific Advisory Committee lead reviewer was: Professor SM Nelson MRCOG, Glasgow.

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