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Endocrine disruptors

## Endocrine-disrupting chemicals, a multifaceted danger



## Foreword

According to WHO, “Endocrine-Disrupting Chemicals” (EDC) are exogenous compounds or mixtures that alter the function(s) of the endocrine system and consequently cause adverse effects in an intact organism, or its progeny, or (sub)populations.

EDC have been described initially following the discovery of the dramatic effects of the insecticide DDT on workers in cotton fields. Rachel Carson wrote her memorable best seller “Silent Spring” in 1962, in which she describes a world where there is no more bird singing, because they have been eradicated by the environmental toxics. A second scientist, Theodora Colburn, organized the meetings that founded the domain of EDC (Wingspread conferences in Racine Wisconsin). At the same time, toxicants present in the Great Lake area were found responsible for malformation in alligators and fish.

It is however in the medical field that their mechanism of action was discovered, in women who received DES while they were pregnant in order to avoid pregnancy interruption, although this beneficial effect had never been demonstrated. Their children presented genital malformations, infertility, and in their daughters clear cell adenocarcinomas of the vagina had been observed. Further, the second generation presented also abnormalities with, in particular, a high rate of hypospadias in boys.

EDC are not hormones, but are called as such since some of the environmental chemicals use part of their pathways: hormone receptors, and/or modulation of enzymes activated or inhibited by natural hormones. As such they can mimic, block, or interfere with hormones involved in key functions. However, their action goes beyond classical hormonal pathways and uses multiple mechanisms, and some of these are clearly different from classical hormonal pathways. Further, some of these products that mimic the effect of natural hormones are, in fact, beneficial.

Although there are a wide variety of mechanisms of action, their effects are associated with a wide range of diseases, ranging from infertility, abnormalities of cognition, type-2 diabetes, obesity, and cancers.

More recently, the effects of the environment on male fertility have been reported, together with the description of a decrease in sperm counts as well as a rise in hypospadias and testicular cancers.

Their cost is supposed to be enormous, reaching € 163 billions every year in the European Union and even more in the USA.

This is the consequence of lifelong exposure, to multiple compounds, at various ages, including critical periods such as pregnancy or childhood. The discovery of the delayed effect of the toxicity occurring in foetal life has been remarkably hypothesized by David Barker, in the early nineties, with the concept of Developmental Origin of Health and Diseases (DOHAD).

Last but not least, a cumulative effect of these products that are efficient through different routes of contamination – air pollution, transdermal use, and oral administration – is possible. . . Finally, transgenerational toxicity through epigenetic modifications has also been demonstrated.

Experimental studies subsequently demonstrated the “non-classical” mechanisms of action of EDC, which do not act through the classical dose response curve of toxicology, and may involve multiple toxics in a cocktail effect. In addition, repeated low doses can produce toxicity.

The wide range of the risks related to EDC exposure is remarkable, and recent assessments suggest a very high cost to the society. It is therefore of utmost importance to continue research and screening of all these products, since their number increases every year. Political organizations, such as EU, are very much aware of this situation and of its extreme cost in terms of health consequences, and in terms of cost of the necessary research. Politicians are also trying to fight against the consequences of EDC and protect the population, e.g., with the recognition and the prevention of the use of new insecticides (cf. the debate on nicotinoids). However, the complexity of the mechanisms of EDC and the difficulty in implementing systematic screening make the task very difficult, and the term EDC remains imprecise, and certainly does not comprise all the mechanisms involved.

Endocrine disruption remains a field that deserves more research, in particular epidemiologic studies, and major political involvement. The complexity of the recognition of their toxicity makes screening difficult, and cannot be simplified, and as a consequence, criteria are lacking to allow adequate regulations that would set new standards beyond the existing risk assessment procedures to protect against EDC. Finally, human data remain challenging because of inherent limitations of epidemiologic and clinical studies. However, although the evidence is often incomplete, it is time to minimize the deleterious effects of EDC.

The French National Academies of Sciences, Medicine, Pharmacy, and Agriculture have therefore decided to organize a meeting involving multiple organisations as well as leading experts involved in this endeavour.

### Further reading

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