GreenFacts
Facts on Health and the Environment

Scientific Facts on
Endocrine Disruptors

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Level 2 - Details on Endocrine Disruptors

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This Digest is a faithful summary of the leading scientific consensus report produced in 2002 by the International Programme on Chemical Safety (IPCS): *"Global Assessment of the state-of-the-science of Endocrine Disruptors"*

The full Digest is available at: https://www.greenfacts.org/en/endocrine-disruptors/

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- Each question is answered in Level 1 with a short summary.
- These answers are developed in more detail in Level 2.
- Level 3 consists of the Source document, the internationally recognised scientific consensus report which is faithfully summarised in Level 2 and further in Level 1.

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1. What are Endocrine Disruptors (EDCs)?

1.1 What is the endocrine system?

The endocrine system is a complex system consisting of glands in the body that produce hormones. Examples are the thyroid gland in the throat, the pituitary gland in the brain, the adrenals, pancreas and ovaries in the abdomen, and the testicles, which lie outside the abdomen.

Hormones act as chemical messengers, controlling many basic functions, such as growth, development, reproduction, how food is utilised in the body, blood pressure, blood glucose levels and fluid balance. Examples of hormones are insulin from the pancreas, which controls blood glucose, and the sex hormones, oestrogen from the ovary and testosterone from the testicles, which affect reproductive function.

Hormones are carried in the blood stream to distant target organs or cells where they perform particular functions. Examples are the pituitary hormone from the brain which causes the ovary to release an egg, or the hormones from the adrenal gland which prepare the body to face stress. Other hormones are released within an organ or tissue – a collection of cells related by their functions – and act locally within the organ or tissue, such as preventing an egg maturing in the ovary.

The endocrine system also includes a third group of hormones called 'neurohormones' which are released by nerve cells either locally or into the blood stream where they act further away.

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1.2 What is the definition of endocrine disruptors?

Endocrine disruption is not, in itself, a measure of toxicity – the occurrence of adverse health effects. Rather, it is considered to be a change that may lead to harmful effects. For example, a potential endocrine disruptor (pED) is a foreign substance or mixture that possesses properties that might be expected to lead to endocrine changes in an individual life form, in its offspring, or in populations.

An endocrine disruptor (ED) is, therefore, defined as a foreign substance or mixture that alters function(s) of the endocrine system, consequently harming an individual life form, its offspring, or populations.

Please note that there is no widely accepted list of endocrine disruptors or potential endocrine disruptors and that the IPCS document summarised here does not provide such list. The European Commission is developing a candidate list of substances in order to set priorities for further evaluation of their role in endocrine disruption (COM(2001) 262 final) [see http://ec.europa.eu/environment/endocrine/documents/comm2001_en.htm]

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1.3 Why is there concern about endocrine disruptors?

Recent years have seen growing concern among scientists and the public at large about endocrine disrupting chemicals (EDCs) that may interfere with the endocrine system and cause harmful effects.

The presence of EDCs in our environment raises concerns because:

- harmful effects have been observed on reproduction, growth and development in some species of wildlife, both aquatic and terrestrial,
- there are increases in some human reproductive disorders and some cancers which could be related to disturbance of the endocrine system, and
- adverse effects from some environmental chemicals known to act on the endocrine system have been observed in laboratory animals.

This has provoked many national and international organizations, as well as scientific and public interest groups, to initiate research programmes, conferences, workshops and expert panels to address and evaluate EDC-related issues.

2. How do EDCs act?

2.1 What are the mechanisms involved in EDC action?

Research clearly shows that endocrine disrupting chemicals (EDCs) can act in a number of ways in different parts of the body. Most studies have focused on the influence of EDCs on hormone receptors, which are the parts of cells in target tissues that hormones lock on to, in order to trigger an effect. EDCs, by occupying the same receptor sites in the target cells as the natural hormone would do, can mimic the effect of a hormone or block its action.

Other ways in which EDCs can work – such as disrupting hormone production, transport or breakdown – have been shown to be equally important. However, for most studies showing a link between EDC exposure and harmful effects, the mechanisms of ED action are poorly understood.

This makes it difficult to distinguish between direct and indirect effects. So care must be taken when using the results of laboratory studies to predict effects in wildlife populations or in humans in the 'real' world. Knowledge of the similarities and differences in the endocrine systems of different animal species and humans is also important when trying to predict effects in one species from observations in another.

A combined body of evidence (epidemiological and laboratory data) will be necessary to understand the situations in which EDC exposure may affect endocrine systems.

2.2 What are the major life stages when EDCs could act?

Despite the lack of comprehensive information on how endocrine disrupting chemicals (EDCs) can act, there are particular stages in animal and human lifecycles that are known to be vulnerable to endocrine disruption.

What is known at present is that:

- exposure to EDCs during the early development of the endocrine system, such as in the womb, or during childhood, may permanently alter its function or its reactions to various signals in the body,
- exposure during adulthood may not show significant effects as the body is more able to adapt,
- the same exposure levels may produce different effects during different life stages or even seasons,
- interactions between different parts of the endocrine system may result in effects which cannot be predicted from existing knowledge, sometimes occurring in unexpected places in the body.

There is considerable knowledge about hormonal responses at the molecular level, but little is known about how these molecular changes might affect health. Until such information becomes available, it will remain difficult and controversial to attribute harmful effects to EDCs.

2.3 What are the relationships between the EDC dose and effect?

The question of how much exposure to an endocrine disrupting chemical (EDCs) is necessary to produce an effect is perhaps the most controversial issue in endocrine disruption. One of the reasons for this is because EDCs often act by mimicking or counteracting the actions of hormones produced naturally by the body. These natural hormones are often more powerful than any foreign EDCs and are present in the body at levels already influencing biological function.

Since any EDC presence is an addition to these natural hormones, it can be argued that exposure to low doses of EDCs could have measurable additional effects on biological functions. In other words, EDCs could have no threshold for their activity – that is, any exposure, no matter how small, might trigger some effect.

Reports of EDC effects in laboratory animals at low doses are highly controversial and the subject of intense research. Scientists from different laboratories have not always been able to obtain the same results at low doses. Another issue is whether traditional testing methods are robust enough to pick up low-dose effects.

Similarly, there is controversy over the issue of synergy – that is, whether simultaneous exposure to EDCs with similar actions might produce a greater effect than the sum of their individual activities. Again, scientists from different laboratories have not been able to obtain the same results using combinations of EDCs.

The timing of exposure is also an important factor in how the body responds to different doses - both for humans and wildlife, with respect to effects on development, reproduction, cancer, the immune system and the nervous system.

At present no firm conclusions can be drawn about low-dose effects. Researchers are continuing to look at this possibility.

3. Do EDCs affect wildlife?

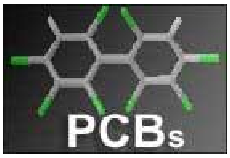
Several studies performed in the wild or with wildlife in the laboratory have shown that exposure to certain endocrine disrupting chemicals (EDCs) has adverse effects in some populations. These vary from subtle changes in body function and sexual behaviour to permanent effects on sex organ development. Most of the information comes from Europe and North America.

Some EDCs disappear quickly from the environment, while others persist. Aquatic animals – especially predators – have been most affected, but effects have also been found in animals living on land. Some of the damage observed in certain animals is likely to be due to endocrine disruption. In most cases, however, the link between exposure to EDCs and endocrine disruption is unclear.

3.1 What are the most illustrative examples of effects on wildlife?

3.1.1 **Mammals:** exposure to organochlorines (PCBs, DDE) has adversely affected Baltic seals' reproductive and immune systems, causing large population declines. These seals show signs of damaged endocrine systems, but exactly how these chemicals are causing these effects is not known.

3.1.2 **Birds**: Eggshell thinning and altered sex organ development have been observed in birds of prey exposed to the pesticide DDT, resulting in severe population declines. Birth defects have been found in fish-eating birds, which are directly related to exposure to another chemical, PCB, but the precise linkage to the possible underlying endocrine disturbance is uncertain.



See also GreenFacts' Digest on Polychlorinated biphenyls [see https://www.greenfacts.org/en/pcbs/index.htm]

3.1.3 **Reptiles**: A presumed pesticide spill in Lake Apopka (Florida, USA) provides a well-publicised example of potential endocrine disrupting chemical (EDC) effects on the decrease in alligator numbers. The alligators had a variety of sex organ and other developmental abnormalities attributed to exposure to high levels of various organochlorine contaminants that can affect the endocrine balance. Even though several explanations have been proposed, the precise cause of the changes in the alligators remains unknown.

3.1.4 **Amphibians**: Population declines in amphibians, such as frogs, have been seen in both unpolluted and polluted habitats worldwide. Currently, there is not enough information to know whether EDCs are the cause.

3.1.5 **Fish**: There is extensive evidence that chemicals found in the waste outflows from pulp and paper mills and sewage treatment plants can affect reproduction and development in fish. A variety of endocrine changes are involved, but it is not yet fully clear which chemicals are responsible for the changes or how they work.

3.1.6 **Invertebrates (animals without backbones)**: Exposure to tributyltin (TBT), a chemical used in antifouling paints, provides the clearest example in invertebrates of an endocrine effect caused by an environmental contaminant. The females of certain marine organisms, such as snails, slugs, whelks and periwinkles, develop male sex organs when exposed to TBT. This has resulted in worldwide declines in their populations. This ' masculinisation effect' is probably due to increases in the levels of male hormones in the females caused by TBT.

3.2 How reliable is the evidence in wildlife?

It has been suggested that wildlife studies provide early warnings about possible harmful effects on humans of exposure to endocrine disrupting chemicals (EDCs). But because there is such a variety of species and only a few have been studied, it is important not to jump to conclusions about EDCs. In addition, studies on the potential effects of EDCs on wildlife have mainly concentrated on individuals, rather than whole populations or communities of animals.

The way in which disturbances in sexual and reproductive functions, and impaired offspring survival, affect whole populations is difficult to quantify. Overall, the current scientific knowledge provides evidence that some abnormalities seen in wildlife are caused by chemicals that function as EDCs. However, in most cases, the evidence of a causal link between the abnormalities and exposure to particular chemicals is weak, and most effects have been observed in areas where chemical contamination is high.

4. Do EDCs affect human health?

At the moment there is no firm evidence that environmental endocrine disrupting chemicals (EDCs) cause health problems at low levels of exposure. However, the fact that high levels of chemicals can impair human health through interferences with the endocrine system, raises concerns about the possible harmful effects of EDCs. Increases in the occurrence of certain diseases affecting the reproductive system in men and women have also raised the question of whether this could be due to exposure to EDCs. The difficulty in finding conclusive evidence on what is happening globally is compounded when researchers try to compare and integrate data about trends in human health from different sources collected at different times, and often using different methods under varying conditions.

Another major problem is the lack of information on EDC exposure during critical periods of early human development, which influence the way the body functions in later life. What is more, the amounts of hormones we naturally produce – and the strength of their effects – in our bodies are generally greater than those of foreign chemicals. However, overall, the biological plausibility of possible damage to certain human functions (particularly reproductive and developing systems) from exposure to EDCs seems strong when viewed against the background of known influences of endogenous and exogenous hormones on many of these processes. Therefore, despite the difficulties and uncertainties, concern remains about the possible role of exposure to EDCs in adverse health effects in humans. The examples in 4.1. illustrate these concerns.

4.1 What are the possible reproductive effects of EDCs in humans?

4.1.1 **Reproductive effects:**

- **Sperm quality**: A number of studies report a decline (since the 1930s) in sperm quality – i.e. sperm count, proportion of normal sperm, semen volume – in several countries, which might be expected to affect fertility. But not everyone agrees with these results. Several surveys refute this downward trend in human sperm quality. Even if there is not a worldwide decline in sperm quality, there are clearly variations in sperm quality, both within and between countries. From what is known about testis development and function, it is plausible that endocrine-active chemicals could affect sperm quality. But so far, no research has studied the relationship between exposure to endocrine disrupting chemicals and sperm quality.

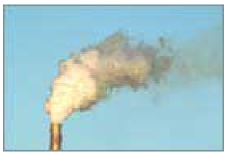
- **Fertility**: Some human and experimental animal studies have shown that occupational or environmental exposure to high levels of certain chemicals, such as pesticides and PCBs, can impair fertility and increase the rate of miscarriages, but any relationship to endocrine disruption remains speculative.
- **Sex ratio**: In a number of regions and countries, fewer boys than girls are being born. There is evidence that unidentified external influences are associated with such changes, but it is not known whether endocrine disruptors are involved.
- **Abnormalities of male sex organs**: Increased numbers of birth defects in male sex organs have been reported. The abnormalities are cryptorchidism, a condition in which the testes remain inside the abdominal area instead of dropping down, and hypospadias, which is a malformation where the opening is on the underside of the penis instead of the end. The possible role of EDC exposure in these human malformations has not been investigated. However, experimental animal studies clearly show that a number of EDCs can disrupt development of the male reproductive system.

4.1.2 **Endometriosis**: This is a disease affecting women where uterine tissue appears in parts of the abdomen other than the uterus, causing pain and infertility. The disease is made worse by oestrogens. Some reports have linked development of endometriosis in women to exposure to EDCs, such as dioxins. However, these findings are debatable.

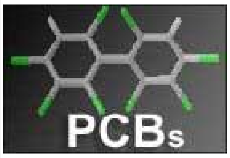
4.1.3 **Precocious puberty**: Some studies have raised concerns about the possible influence of EDCs on the timing of puberty, or the process of sexual maturation. There is evidence from population studies that the age at which puberty normally occurs is becoming younger, but the reasons for this and the role of other factors, such as nutrition, need to be clarified.

4.2 What are other possible effects of EDCs?

4.2.1 **Nervous system function**: Information from human and experimental animal studies clearly shows that exposure to certain endocrine disrupting chemicals (EDCs), such as PCBs – particularly before birth – can harm the development of the nervous system, neuroendocrine function, and behaviour. Some of these effects appear to result from alterations in thyroid function or in the activity of the chemicals which carry messages between nerve cells. In the majority of cases, however, it has not been demonstrated that these effects are due to endocrine disruption. Similar effects can also result from exposure to chemicals that influence nervous system development, but have no known action on the endocrine system.



See also GreenFacts' Digest on Dioxins [see https://www.greenfacts.org/en/dioxins/index.htm]



See also GreenFacts' Digest on Polychlorinated biphenyls [see https://www.greenfacts.org/en/pcbs/index.htm]

4.2.2 **Immune Function**: The immune system is involved in fighting infections and in allergic reactions. Exposure to environmental chemicals – including certain EDCs, such as DES, a powerful synthetic oestrogen, or PCBs and dioxins – has been shown to alter human and animal immunity. But it is not clear whether this occurs via endocrine disruption.

4.3 Do EDCs cause cancer in humans?

4.3.1 **Cancer**: The occurrence of certain cancers at hormonally sensitive sites in the body has been increasing over time in many industrialised countries. Although some of the apparent increases may be due to improvement in our ability to detect cancer, it does not explain all of the increases. This has led to suggestions that the general population's widespread exposure to endocrine disrupting chemicals (EDCs) could be damaging human health. One argument is that the increases are roughly linked in time with the increased use and release of industrial chemicals into the environment.

4.3.2 **Breast Cancer**: Numerous studies have examined whether environmental EDCs, particularly organochlorine contaminants such as DDT and PCBs, may increase breast cancer risk in women, but the current scientific evidence does not support such a conclusion. All the studies have the same weakness in that they measured current EDC levels in women both with and without breast cancer, but they had no data on exposure during other potentially important periods in their lives, such as while they were in the womb, or during childhood and adolescence. During the mid-twentieth century, organochlorine contaminants were more widespread, making the absence of this early exposure information a major problem.

4.3.3 **Endometrial Cancer**: There are very few studies on endometrial cancer, which is cancer of the lining of the womb, and exposure to EDCs. Although exposure to oestrogen is known to increase the risk of this cancer, the number of women developing endometrial cancer is not increasing. The limited experimental and human studies available on this subject fail to draw a link between EDCs and endometrial cancer.

4.3.4 **Testicular Cancer**: Cancer of the testis is the most common cancer in young men. A number of countries have reported increases of this form of cancer, but with considerably varying rates. The rate started rising around 1910 in the Nordic countries – even earlier in England and Wales – which means it cannot be attributed solely to chemicals introduced in the mid- or late twentieth century. Some evidence suggests that male sex organ abnormalities (see 4.1.) may be linked to testicular cancer, both because they have a similar geographical distribution and because they may have a common origin if sex hormone levels are disturbed during early development. However, no studies have examined the relationship between testicular cancer and EDC exposure during critical periods of development.

4.3.5 **Prostate Cancer**: Prostate cancer occurs mainly in older men and is the most common male cancer. Much of the increase in prostate cancer is due to improved diagnosis. It is known that male sex hormones cause growth of prostate cancers and oestrogens reduce the size of prostate cancers. Exposure to certain pesticides and organochlorines has been linked to increases in the incidence of prostate cancer in a few limited studies. Other studies have found no association between EDC exposure and this form of cancer.

4.3.6 **Thyroid Cancer**: It is known from experimental animal studies that some chemicals, such as certain pesticides, can disturb the part of the brain that controls thyroid hormone release, or can increase the destruction rate of thyroid hormones in the liver, thereby causing thyroid tumours. Yet so far no relationship between exposure to EDCs and thyroid cancer in humans has been shown.

4.4 What other factors must be considered regarding human health?

Three kinds of evidence have to be considered in reaching tentative conclusions about EDCs and human health at this point in time:

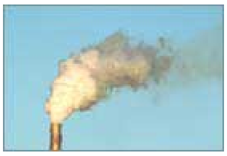
- **knowledge about hormones and the endocrine system**: overall, the biological plausibility of possible damage to certain human functions from exposure to EDCs seems strong, particularly for reproduction and development;
- **evidence from other species**: adverse effects found in wildlife and laboratory animals exposed to EDCs support concerns about possible similar effects in humans;
- **evidence from humans**: changes in certain human health trends are also worrying enough to make this area a high research priority.

Both the possible roles of EDCs and non-EDC mechanisms need to be explored. Above all, the links between human exposure to low environmental levels of EDCs and health effects needs to be investigated.

5. What are potential sources of EDC exposure?

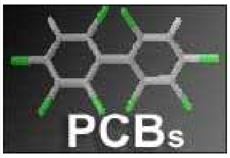
Lack of scientifically sound data about the frequency, length and levels of exposure to endocrine disrupting chemicals (EDCs) is the weak link in the argument that they have harmful effects on human and animal health. Most of the information on EDC exposure has focused on the presence of persistent organic pollutants, such as PCBs, dioxins, DDT and other chlorine-containing pesticides, in Europe and North America. Exposures to other non-persistent EDCs have not been investigated in any depth.

Another shortcoming is the lack of information on exposure during critical periods of human or animal development. Moreover, the available information relates mostly to EDCs present in the environment – such as in the air, food and water – rather than to levels in blood and tissues in the body. Limited exceptions are human breast milk and fat tissue samples, which have been screened for potential EDCs, such as organochlorines.



See also GreenFacts' Digest on Dioxins [see https://www.greenfacts.org/en/pcbs/index.htm]

Generally, exposure to potential EDCs occurs through contaminated food and groundwater, gas emissions from industrial sources and the burning of waste, and contaminants in consumer products.



and on Polychlorinated biphenyls [see https://www.greenfacts.org/en/dioxins/index.htm]

Despite a heavy investment of money, time and effort worldwide, information comparing human and wildlife EDC exposures in different countries is still sorely needed. Such information, obtained through field studies on wildlife and studies in human populations - epidemiological studies - on diseases or other observations like sperm quality or outcomes of pregnancy, is essential to establish causal relationships between exposure and response. Exposure information is also essential to produce a credible risk assessment of this problem.

6. Conclusions

Studies carried out to date have focused on North America and Europe, so conclusions about endocrine disrupting chemical (EDCs) effects worldwide cannot be drawn, especially not for developing countries where very little information is available.

6.1 What conclusions can be drawn concerning EDC effects in humans?

Although it is known from laboratory and wildlife studies that certain environmental chemicals can disrupt normal endocrine function, evidence suggesting that human health has been affected remains weak. There are some signs that humans are vulnerable to endocrine disrupting chemicals (EDCs) at high levels of exposure, but effects from long-term and low-level EDC exposure have yet to be proven. This statement is not meant to downplay the potential effects of EDCs; rather, it highlights the need for more rigorous studies, especially those examining the possible effects from exposure to EDCs at sensitive stages in early life.

6.2 What conclusions can be drawn concerning EDC effects in wildlife?

Evidence about the effects of endocrine disrupting chemicals (EDCs) on wildlife is more extensive than for humans, showing that EDCs have, indeed, harmed wildlife. Of course, the ability to study wildlife species both in the laboratory and in the field has been helpful.

Many of the studies showing adverse effects in wildlife have been undertaken in areas where pollution was reported to be high, particularly in aquatic ecosystems, where persistent environmental chemicals accumulate.

A big challenge in this area is to broaden the research to cover more thoroughly more species in the wild, and to develop a better understanding of their biology and their different endocrine systems. This way, more can be learned about the many species that could potentially be affected by EDCs.

6.3 What are the future research needs identified by the IPCS report?

It is clear that too little is known about the link between exposures to potential endocrine disrupting chemicals (EDCs) and their effects on health – both humans and wildlife. Nevertheless, some progress has been made in identifying potential EDCs and studying the ways in which they work by using laboratory animals. Research has mainly focused on chemicals that persist in the environment and accumulate in living organisms, but less persistent chemicals also require attention. International collaboration is needed in some broad research areas, such as in:

- understanding how endocrine disruption interferes with normal biological processes,
- clarify the relationships between effects observed in the laboratory and those observed in the wild
- developing improved methods for detecting EDCs,
- increasing monitoring of organisms in the wild and monitoring of potentially relevant trends in human health,
- identifying EDCs most likely to have substantial effects in populations at low environmental concentrations,
- identifying any 'hot spots' of high exposure to EDCs,
- investigating life stages or species that might be particularly vulnerable to EDCs, and
- assembling global information on EDCs into usable and shared databases.

This research is a priority because of the endocrine system' s key role in many aspects of normal human - and animal - development and function. More information about how EDC exposure may impair or damage this vital system is therefore paramount.