Endocrine Disruption The problem European Commission 2003

Concern over fertility trends
Observations in humans and wildlife over the last 40 years show a worrying trend of adverse effects on the development of reproductive systems. There is already evidence of decreased fertility in birds, fish, and mammals; reduced hatching success in fish, birds, and turtles; the feminization of male fish and birds; the masculinization of female fish, gastropods, and birds. In humans, decreased sperm numbers, an increasing incidence of certain congenital malformations in children and hormone-related cancers (such as breast and testicular cancer) have been observed.

Meta-analysis of studies supports a significant decline in sperm density in Europe and the United States. However, there are large intraregional differences.
(Data from Swan et al. 1997. Picture adapted with permission from www.ourstolenfuture.org).

For a number of years now, expert scientists have hypothesised that these trends may result from the effects of low levels of chemicals in the environment which interfere with or alter the body's own chemical messaging or endocrine system. These chemicals are known as endocrine disrupting chemicals (EDCs).

What are endocrine disruptors?
The endocrine system regulates many essential bodily functions, including reproduction and development, through the production of hormones which serve as chemical messengers. Hormones, such as oestrogens and androgens, are released into the blood stream by endocrine glands and circulate around the body at very low concentrations. Once within their target cells, the hormones bind to, and activate specific receptors that respond to hormone signals and influence changes in bodily functions and organs.

EDCs are synthetic chemicals and natural plant products which interfere with or alter the development or function of the endocrine system. Certain EDCs are known to mimic the effects of natural hormones by triggering their specific receptors, these are termed agonists. Some endocrine disruptors bind to hormone receptors and block the action of the natural hormones, these are termed antagonists. However, there are other ways that EDCs can alter the endocrine system. They can also interfere with the production, transport, metabolism or excretion of naturally occurring hormones. What these EDCs have in common, is that they have the potential to interfere with wildlife and human health.

Where do endocrine disruptors come from?
EDCs come from a wide variety of sources. Many EDCs are synthetic chemicals produced specifically for their biological properties and are used as pesticides, herbicides or pharmaceuticals. Other EDCs are used in a diverse array of products, including cosmetics, sunscreens and plastic formulations. There are also a large number of

synthetic chemicals in production which have not been tested for endocrine disrupting activity, and whether they have the potential to act as EDCs is not known.

As EDCs are released into the environment they may be carried by air, water or in the food chain. Many of the known EDCs are now ubiquitous environmental contaminants, which has resulted in widespread exposure of both humans and wildlife. For example, EDCs have been detected in the fat of polar bears in the polar region where these chemicals have never been used.

Widespread wildlife effects

Studies of wildlife and laboratory animals have shown that EDCs have the potential to interfere with the development of the endocrine system, including the reproductive tract. For example, male fish living downstream of sewage treatment plants in southern England have been found to have high concentrations of the female egg-yolk protein, vitellogenin, not normally present in males. Some affected male fish also have female-like oocytes within their testis resulting in gonads that are intermediate between male and female. These effects have been shown to result from synthetic oestrogenic chemicals which are released into the aquatic environment via the sewage treatment plant effluent.

Scanning electron micrograph images showing the effects of tributyltin in female mudsnails (Hydrobia ulvae) producing abnormal penis, sperm canal and blocking of the oviduct (PP, Vd and OvL), lower picture. Normal in top picture.

Perhaps the clearest evidence of endocrine disruption resulting from a chemical pollutant comes from marine gastropods. Widespread development of a male sexual organ in female marine snails, such as the dog whelk has been observed. This condition, called 'imposex', results in sterilization of the females and has led to a population decline in many harbours and coastal waters. The cause of this phenomenon is attributed to a chemical called tributyltin (TBT), which is a constituent of marine anti-fouling paints. TBT inhibits the steroidogenic enzyme, aromatase that transforms androgens into oestrogens in gastropods and is now known to be responsible for these effects.

Concentration-response relationship between the masculinisation index and tributyltin (TBT) concentrations of ambient sea water in the dog whelk, Nucella lapillus.

Uncertain human health effects

A number of adverse human health effects have been observed in which EDCs may be implicated. However, a causal relationship between the human health observations and exposure to EDCs has not been established. Some studies have found statistical evidence for declining sperm counts and decreasing quality of semen during the past 50 years but others have not detected any change. What is clear is that there is geographical variation

in the incidence of certain congenital malformations e.g. undescended testes (cryptorchidism) and hypospadias (an abnormality where the opening of the urethra is not at the tip of the penis). These findings coincide with an increase in many hormone-related cancers, including germ cell cancer of the testis, and breast cancer in women. However, contribution of EDCs to these abnormalities remains uncertain and will be confounded by other factors.

Age-standardised incidence rates for testicular cancer in Europe per 100,000 (1995). Picture based on Bray et al., 2002. Adapted with permission from www.encr.com.fr.

Questions and uncertainty

There are many questions about EDCs which remain unanswered.

There are a large number of synthetic chemicals in the environment to which humans and wildlife are exposed which have never been tested for endocrine disrupting activity. Which of these chemicals have the potential for endocrine disruption remains to be determined. Furthermore, we do not know enough about our exposure to these EDCs.
What could be the effects of long term exposure to low concentrations of endocrine disruptors?
What are the effects of exposure to the complex mixture of endocrine disruptors which are present in the environment and how may they interact in biological systems?
Does the life stage at which humans and wildlife are exposed to EDCs influence the effect on the organism?
Some species are likely to be more sensitive than others. Identifying these 'sentinel' species will not only help us to protect them but will also better enable us to determine where there is cause for alarm and take timely action.

The ramshorn snail, Marisa cornuarietis, is one of the test species applied to identify endocrine disrupters.

Seeking answers

Scientific research has been gathering increasing evidence about how EDCs can affect both wildlife and human health. Unravelling the complexity of this issue will require co-ordinated wildlife studies, clinical human health and exposure assessments and laboratory experiments. The integrated approach of CREDO to human health and environmental research will enable us to better predict the effects of EDCs.

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Endocrine Disruption: The problem

Concern over fertility trends

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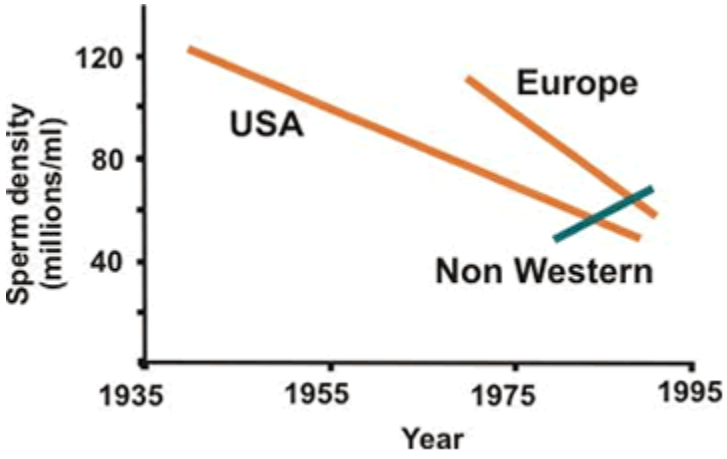

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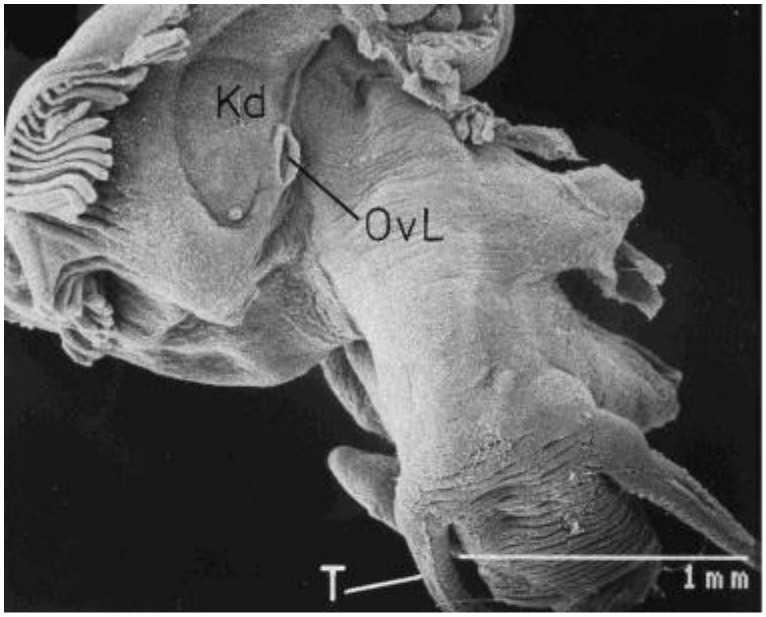

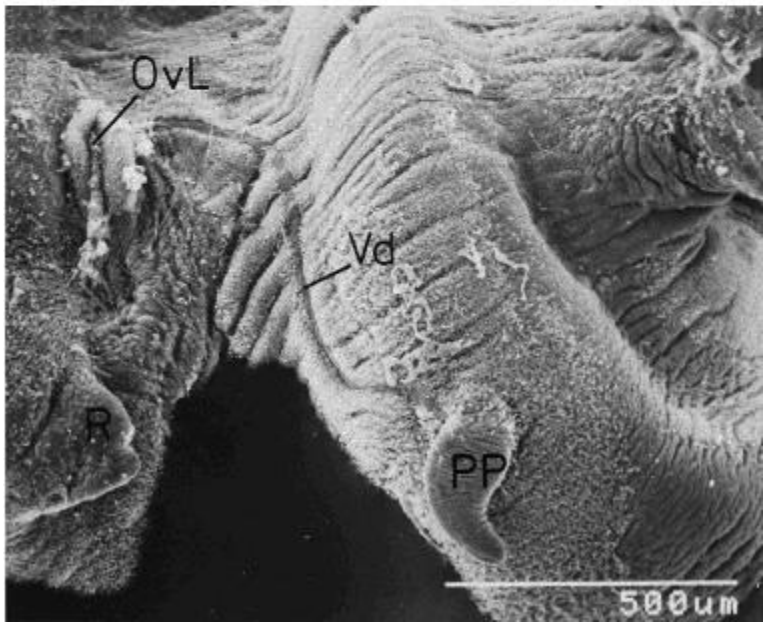

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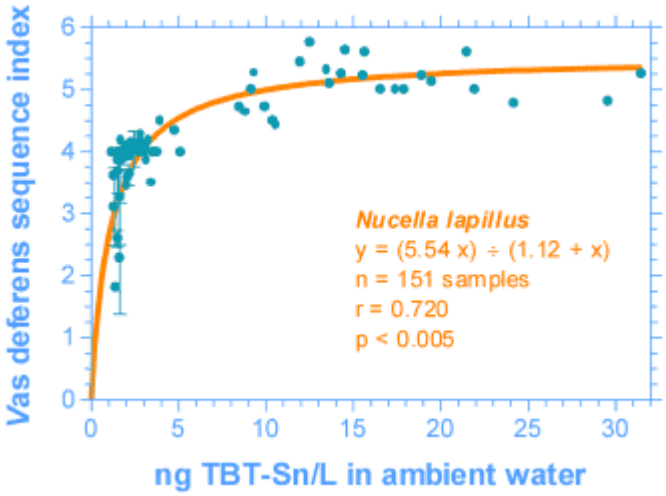

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