

## Latest research and recommendations regarding endocrine disrupting chemicals



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## Presentation overview

**The Prague declaration on endocrine disruption**

**Highlight some of the latest research findings**

**Regulatory shortcomings and recommendations**

## Endocrine disruption: the problem

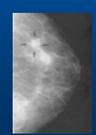
- Seals in the Baltic and North Sea have suffered reproductive failure and population declines attributed to PCBs and dioxins
- Male fish developed eggs in the testes, poorer sperm quality and reduced reproductive capacity due to oestrogens in sewage effluent
- Female molluscs developed male sex organs resulting in population decline due to tributyl tin applied to the hulls of ships in antifouling paints



Female mudsnail electron micrograph images: Jörg Oehlmann

## Human health concerns

- Geographical variation in the incidence of certain congenital malformations in children
- Cryptorchidism (testis maldescent) and hypospadias are the two most common affecting 2-4% and 0.3-0.7% of newborn boys
- Low sperm count affects approx. 20% of young men in many European countries
- Increasing incidence of hormone related cancers (such as breast and testicular cancer)



## Human health concerns

- Hormone action is important in the development of all of these disorders
- It is plausible that chemicals which interfere with the endocrine system, so called endocrine disrupters, may be involved
- Contribution of endocrine disrupters to these human abnormalities is uncertain



## Prague declaration - origin

- May 2005 - experts and scientists came together in Prague to discuss the health risks associated with these chemicals
- Many results came from large research projects on endocrine disruption funded by the European Commission
  - See [www.credocluster.info](http://www.credocluster.info)



## Prague declaration - objectives

- *The Prague declaration on endocrine disruption* is intended to
  - inform citizens, policy makers and regulators about research progress
  - highlight shortcomings in current regulation
  - and to make suggestions... that might lead to better protection of human and wildlife health
- To date over 200 scientists have signed the Prague declaration



## Human health concerns

- “There is serious concern about the high prevalence of reproductive disorders in European boys and young men and about the rise in cancers of reproductive organs, such as breast and testis”
- “Lifestyle, diet and environmental contamination play a role in the observed regional differences of these disorders and their changes with time”
- “Endocrine disruptors may be involved, but there are inherent difficulties in establishing such causal links in humans”



## Latest research

- Phthalates are widely used in makeup, shampoo, soaps, plastics, paints, and some pesticide formulations
- Genital development in male rodents is known to be altered by phthalates
  - which act as anti-androgens
- A similar syndrome of reproductive disorders is seen in newborn boys and young men



## Latest research - phthalates

- Swan *et al.* measured anogenital distance
  - a sensitive marker of anti-androgen action
- Found a significant decrease in anogenital distance among baby boys whose mothers were exposed to certain phthalates
- First evidence of an association between phthalate exposure of mothers and hormonal dysfunction in their baby boys

### Reference

Swan *et al.* Environ Health Perspect. 2005 Aug;113(8):1056-61

## Latest research - phthalates

- This does not prove that phthalates caused a decrease in anogenital distance
- The association is highly plausible and may provide a link between exposure to phthalates and disorders in human males
- The effects were observed at phthalate levels below those found in 25% of women in the US

### Reference

Swan *et al.* Environ Health Perspect. 2005 Aug;113(8):1056-61

## Linking cause and effect

- “There is a serious gap of knowledge regarding the effects of endocrine disruptive compounds on other serious human diseases such as obesity, neuronal disorders etc.”
- “Identification of causative chemicals is complicated by the possibility that disorders may become manifest long after exposure has taken place. By this time, causative agents may have disappeared”

## Latest research

- Vinclozolin used as a fungicide in the wine industry and methoxychlor used as a pesticide to replace DDT
- Anway *et al.* looked at rodents briefly exposed to these chemicals at a key time during pregnancy
- Found a decreased sperm count in nearly all the male offspring exposed in the womb...

### Reference

Anway *et al.* Science. 2005 Jun 3;308(5727):1466-9



## Latest research - inheritance

- But... also found a decreased sperm count in all subsequent generations tested, down to the great-great-grandsons
  - even though only the first mother was exposed
- Effects were inheritance by changes in gene expression
  - by altered patterns of DNA methylation

### Reference

Anway *et al.* Science. 2005 Jun 3;308(5727):1466-9



## Latest research - inheritance

- First report of endocrine disrupting effects passed down multiple generations without altering DNA sequence
- Indicates fertility may be affected by exposure of previous generations
- Work needs to confirm the cause of the effects and whether or not this takes place at lower, environmentally relevant levels

### Reference

Anway *et al.* Science. 2005 Jun 3;308(5727):1466-9



## Wildlife effects

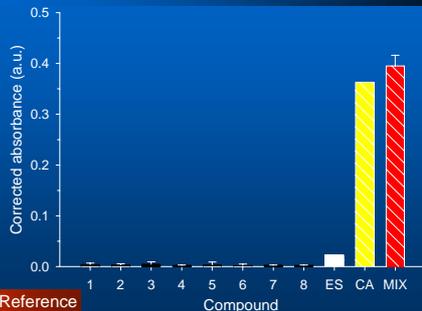
- “Causality is well established for detrimental effects in wildlife as a direct consequence of exposure to endocrine disrupters”
- “The severity of endocrine disrupting effects observed in the laboratory indicates that these substances may pose a threat for wildlife biodiversity”



## Mixture effects

- “Europeans are exposed to low levels of a large number of endocrine disrupters”
- “Mixture effects can occur even when each component is present at a dose that individually does not produce effects”
- “A dose of a single chemical judged to be safe after testing in isolation may give a false sense of security when exposure includes large numbers of other endocrine active chemicals which may interact”

## Mixture effects



Reference  
Silva *et al.* Environ Sci Technol. 2002 Apr 15;36(8):1751-6.

## Regulatory shortcomings

- “Testing does not account for the effects of simultaneous exposure to many chemicals and may lead to serious underestimations of risk”
- “The current safety testing guidelines are based on reproductive effects, and do not take into account the deleterious effects of endocrine disruptors in other tissues”



## Latest research

- Wozniak *et al.* studied an important signalling system that controls calcium flow in cells
- Exposed pituitary tumour cells in culture to oestradiol or individual xenoestrogens at extremely low doses
- Organochlorine pesticides (dieldrin, endosulfan, *o,p'*-DDE), industrial chemicals (nonylphenol, bisphenol A), a plant and a synthetic oestrogen (coumestrol, diethylstilbestrol)

Reference  
Wozniak *et al.* Environ Health Perspect. 2005 Apr;113(4):431-9.

*o,p'*-DDE: *o,p'*-dichlorodiphenylethylene

## Latest research

- Xenoestrogens and oestradiol all rapidly increased calcium flow into the cells
- The effect was seen even at the lowest concentrations tested - parts per trillion
- Some xenoestrogens had greater effects than oestradiol at the same concentration

Reference  
Wozniak *et al.* Environ Health Perspect. 2005 Apr;113(4):431-9.

## Latest research

- Effects of the pesticides were seen below the levels deemed safe by regulatory standards
- The xenoestrogens worked through mechanisms other than classical oestrogen receptors
- These effects are likely to be missed by routine safety testing based on classical oestrogen receptors

Reference  
Wozniak *et al.* Environ Health Perspect. 2005 Apr;113(4):431-9.

## Recommendations

- “Endocrine disruptors require a long-term commitment to monitoring and research dedicated to characterising human and wildlife exposure”
- “Steps should be taken to restrict the use of persistent chemicals in order to halt their build-up in humans and the environment”

## Recommendations

- “Endocrine disrupting chemicals should be subject to the authorisation procedure in the proposed European chemicals regulation – REACH”
- “In view of the magnitude of the potential risks associated with endocrine disrupters, scientific uncertainty should not delay precautionary action on reducing the exposures to and the risks from endocrine disrupters”

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Thank you for your attention!



For more information

[www.edenresearch.info/declaration.html](http://www.edenresearch.info/declaration.html)