

# Neuro-endocrinology

## 1 BRIEFINGS

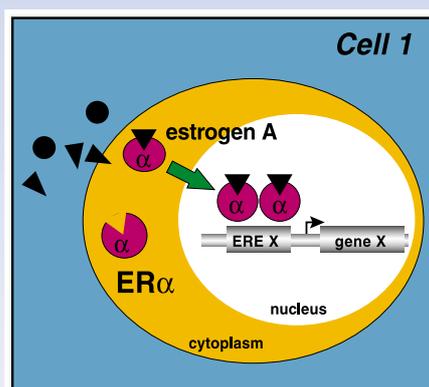
### ENVIRONMENTAL ESTROGENS: A HAZARD TO HUMAN REPRODUCTIVE HEALTH?

#### SUMMARY

During our everyday life we are continuously exposed to a cocktail of chemicals which can mimic the actions of the female hormone, estrogen. There is concern that these chemicals, known as environmental estrogens, may have adverse effects on reproductive health in humans and wildlife. Researchers have a key role to play in understanding how these chemicals control the reproductive system, so that we are better able to judge if they really are a hazard to human reproductive health.

#### The perceived threat – scare or reality?

Declining sperm counts in men, an increased incidence in breast cancer, feminised fish, alligators with small phalluses; these are just some of the adverse changes in reproductive health, reported to have taken place in the past few years, and with one thing in common; they can all be caused by the female hormone estrogen. Recent research has shown that many man made chemicals can act as weak estrogens,

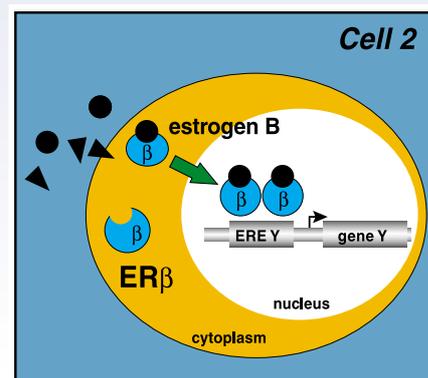


mimicking in part the actions of our own natural hormones. These chemicals are present throughout our daily life. They can be found in the plastic lining of food cans, in pesticides, in plastics and in paints. The question is – are these chemicals actually responsible for the increased level of adverse reproductive effects? Is this a scare or reality?

#### The uncertainty

Researchers have known for some time now that if the body is exposed to excessive amounts of estrogen at certain stages in development, this can have adverse reproductive effects. For example, females exposed to estrogens during critical periods of brain sexual development are unable to ovulate as adults, and exhibit male patterns of sexual behaviour. Could environmental estrogens mimic these adverse effects? Another example is found in an intriguing hypothesis to explain how human sperm counts may have

*Tissue differences in the types and amounts of estrogen receptor may explain how natural, synthetic and environmental estrogens could have specific effects in the body. ER $\alpha$  which predominates in Cell 1, prefers to bind a particular type of estrogen (estrogen A) whereas ER $\beta$  located in Cell 2, prefers another (estrogen B). Following interaction of these estrogens with their receptors the receptors pair up and bind to estrogen response elements (ERE) in the target genes. These genes may contain ERE's which also have a preference for each of the receptors. These many and complex control mechanisms would allow different types of estrogen (perhaps environmental estrogenic chemicals) to act in a particular part of the body to change the activity of a specific target gene.*



## Neuro-endocrinology Briefing 1:

# Environmental estrogens: a hazard to human reproductive health?

declined in the past 50 years. A man's capacity to produce sperm is determined by the number of specialised cells in the testis, called Sertoli cells. Sertoli cell number is regulated by follicle stimulating hormone (FSH) which is secreted from the pituitary gland, but FSH can only do this during a critical period in fetal and early neonatal life. If animals are exposed to a synthetic estrogen called diethylstilbestrol during this critical period, this reduces the amount of FSH produced in the fetal pituitary gland and the testes in the male offspring are smaller, with fewer Sertoli cells.

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*“Testes in the male offspring are smaller, with fewer Sertoli cells.”*

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These animals produce less sperm when they reach adulthood. Can environmental estrogens have similar effects? Researchers have recently shown that when pregnant animals are exposed to a chemical called octylphenol, the secretion of FSH in the fetus is reduced. Octylphenol is a break-down product of a group of chemicals which are used in the manufacture of some detergents and paints. If exposure to this chemical were to take place for long enough during the sensitive period, then this may lead to smaller testes and reduced sperm counts. But a word of caution. We are still uncertain as to the extent to which the human body is actually exposed to chemicals such as octylphenol, and as yet there is no direct proof that there is any link between chemical exposure and changes in sperm counts in man.

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*“Estrogen receptors are promiscuous. They allow many hundreds of different chemicals to bind to them”*

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## Unravelling the mystery – the role of research

In order for estrogenic hormones to exert their many effects in the body of humans, they must first bind to an estrogen receptor, a specialised protein located in target cells, which recognises the hormone and allows it to regulate specific estrogen responsive genes within the cell. Estrogen receptors are promiscuous. They allow many hundreds of different chemicals to bind to them. In some cases the chemicals have structures which are so dissimilar to that of the body's natural hormone estradiol, that they would never normally be thought of as having hormonal activity. These chemicals are very weak estrogens by comparison with naturally occurring hormones, but if given in high enough amounts they can activate estrogen receptors in much the same way as natural hormones do. Until recently, it was thought that there was only one estrogen receptor. However, researchers have now discovered a second estrogen receptor (ER $\beta$ ) which prefers to bind certain environmental and natural estrogens compared with the original estrogen receptor (ER $\alpha$ ). This new receptor is located in higher amounts in specific tissues in the body, such as the prostate, ovary and brain. Scientists now believe that this combination of different types of estrogen receptor and differing tissue distribution, may be crucial in determining if a particular part of

the body is likely to be affected by natural or environmental estrogens (see figure).

## Where to from now?

The topic of environmental estrogens is of growing interest. Government agencies in the US and in Europe are eager to introduce methods for testing and interpreting data to allow an assessment of the threat to human health from exposure to endocrine disruptors. Even with a variety of different tests in place, human hazard assessment will be a challenging task. Researchers have an exciting time ahead, as they unravel the many complex ways in which natural and environmental estrogens interact with the reproductive system.

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<http://units.ox.ac.uk/departments/anatomy/BNG.html>

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