Endocrine Disruptors

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Citation

K Bharti, K Sanjay, K Amit, S Amit. *Endocrine Disruptors*. The Internet Journal of Family Practice. 2012 Volume 10 Number 1.

Abstract

This paper reviews the available literature on environmental endocrine disruptors or toxins, and puts in perspective the deleterious effects that these chemicals have on hormonal health. It concludes with simple measures describing how we can reduce our exposure to environmental endocrine disruptor chemicals (EDCs).

DEFINITION OF ENDOCRINE DISRUPTORS

Endocrine disruptor chemicals (EDCs) are exogenous agents which interfere with the synthesis, secretion, transport, binding, action or elimination of natural hormones in the body, which are responsible for the maintenance of homeostasis, reproduction, development or behaviour[1]

They may be either natural or synthetic chemicals.

CLASSIFICATION OF EDCS

EDCs are chemicals which are usually present in

A. Plastic & plastic components, e.g., phthalates

B. Pesticides, including fungicides, herbicides, eg, organochlorine pesticides, atrazine, trifluralin, permethrin.

C. Industrial chemicals, eg polychlorinated dioxins, polychlorinated biphenyls

D. Paints, eg, organotins, found in antifoultants used to paint hulls of ship:tributylin.

E. Detergents, eg, alkylphenolics (surfactant) : nonylphenol

F. Heavy metals e.g. mercury, cadmium and lead.

G. Natural products

-Phytoestrogens e.g. genistein, equol

-Fungal estrogens e.g. zearalenone

SYSTEMS AFFECTED BY ENDOCRINE DISRUPTORS:

Systems affected by endocrine disruptors are summarized in Table 1.

SUBSTANCES WHICH DISRUPT ENDOCRINE SYSTEMS

CLINICAL EFFECTS

Endocrine disruptors affect various glands and systems in the human body (Table 3) However, many of the causal relationships are uncertain.

Exposure to EDCs occurs through food, ground water, combustion sources, contaminated consumer products, pesticides (including agricultural and domestic use of chemicals) and plastic.

DECLINE IN SEMEN QUALITY

A hypothesis was put forwarded by Sharpe and Skakkeback in 1993 that agents which interfere with normal development of the reproductive system could be linked to the increase in human male reproductive system disorders, all of which were expressions of the testicular dysgenesis syndrome. [3]

While there is controversy regarding the temporal trends in sperm count, metaanalysis reported in 1980, [4] and again in 1992, [5] 1997 [6] and 2000, [7] have shown significant declines in semen quality. Whether this is due to endocrine disruptor chemicals alone, or due to other factors, is debatable.

Studies however, have demonstrated negative correlation between sperm count and motility, and PCB (polychlorinated biphenyls) concentrations in men. [8]

IMPAIRED FERTILITY

Studies are also available on the adverse effect of EDCs on fertility and fecundity. Reduced fertility has been noted in male fruit growers exposed to pesticides[9]. Similar findings have been seen in men exposed to aromatic solvents[10],

women with recent consumption of PCB- contaminated fish[11], and men with high intake of sport fish containing PCBs and mercury[12].

High isoflavone intake has led to a prolongation of the follicular phase[13], while flaxseed ingestion has been noted to prolong the luteal phase, in healthy women[14].

INCREASES IN RATE OF SPONTANEOUS ABORTION

Paternal exposure to 2, 4- dichlorophenoxyacetic acid, a phenoxyherbicide, increases the risk of abortion[15], as does exposure to other organochlorine pesticides. Paternal exposure to thiocarbamates, carbaryl and unclassified pesticides has been demonstrated to increase the spontaneous abortion rate in Canadian farmers' wives. The same study, which analysed 3984 pregnancies in 1898 couples, reported a higher risk of preterm delivery with atrazine and 2, 4-D[16].

DECLINE IN SEX RATIO (FEWER MALE BIRTHS)

Medical, occupational and environmental factors are known to impact the sex ratio. Workplace exposure to organochlorines[9], vinclozolin[17], anaesthetic gases[18], aluminium industry[19], smelters, steel foundries, incinerators [20] have been shown to reduce the number of male births.

INCREASES IN DEVELOPMENT ANOMALIES

Male reproductive anomalies such as hypospadias and cryptorchidism are more frequent in boys born on farms where pesticides are used[21]. An increased rate of orchipexy has also been reported in areas where pesticides are used intensively[22]. An endocrine disruptors- mediated mechanism has been proposed for prostatic inflammation or lateral prostatitis, based on animal studies.

ENDOMETRIOSIS

An association has been noticed between endometriosis and PCB[23], as well as dioxin [24] concentration by some, but not by other workers. The human data at present neither confirms nor refutes the role of endocrine disruptors in the pathogenesis endometriosis.

PRECOCIOUS PUBERTY

Phthalate levels have been found to be linked to premature breast development in girls. High DDE levels have been noted to be associated with precocious puberty in girls with shortened lactation period in women. [25]

DEVELOPMENTAL NEUROBEHAVIOURS

Central and peripheral nervous system symptoms, such as headache, amnesia and hypoesthesia or neuralgia have been reported in people exposed to high levels of PCBs (polychlorinated biphenyls) through contaminated rice oil. Children born to mother exposed during two mass poisoning events at Yusho, Japan (1968) and Yu-Cheng, Taiwan (1979) have demonstrated lower IQs, reduced cognition, behavioral disorders and increased activity[26].Exposure to PCBs in breast milk has also been related to a negative impact on mental and motor development.

It is possible that these effects are mediated through the hypothyroid effect of PCB.

IMMUNE SYSTEM

Immunotoxicity due to environmental toxin may be a direct effect or EDC – mediated.

PCBs (polychlorinated biphenyls), PCDFs (polychlorinated dibenzofurans) and PCDDs (polychlorinated dibenzo dioxins) cause toxicity through, AhR binding, affecting hormones of the thymus[27].

DES has endocrine – disrupting mechanism if exposure occurs in utero, it has a direct chemical interaction with thymocytes, which release soluble immunoregulatory factors.

CANCER

An increase in incidence of hormonal malignancies of the breast, uterus, prostate and testis has been noted in the developed world. This can not be explained by availability of improved diagnostic methods alone.

EDCs with estrogenic activity are thought to act as tumour promoters.[28]

BREAST CANCER

The etiology of estrogens is proven beyond doubt. The role of EDCs, including phytoestrogens, DDT and dieldrin has been studied extensively. The timing of exposure is important, and exposure in the perinatal period, puberty, and the period between menarche and first full term pregnancy is important [28]

ENDOMETRIAL CANCER

The limited human data available does not support an association between organochlorine exposure and endometrial cancer[29], through the endometrial tissue is very

responsive to endocrine manipulation.

TESTICULAR AND PROSTATE CANCER

While there is ample potential for EDC effects on the testis and prostate, enough data is not available to implicate any particular EDC in the etiopathogenesis of male endocrine cancers.[28]

ACTION

The potential impact of EDCs on human (and animal) health is enormous. While scientists seem to be aware of the gradual increase in morbidity due to excessive use of chemicals, pesticides and fertilizers, no action seems to have been taken by clinical endocrinologists to sensitize patients, society and opinion leaders about this impending catastrophe.

At an individual and community level, however one can take action to reduce exposure to EDCs. As endocrinologists, we should encourage our patients to take the following steps.

FOOD - RELATED EXPOSURE

Consume foodstuffs grown by organic farming, i.e. without fertilizers/ pesticides

In case this is not possible, use vegetables which need less pesticide spray e.g. roots and tubers.

Crops which need comparatively more chemical help to grow, eg, ladyfinger, bitter gourd, tomato, should be avoided

Remove a thick layer of skin or rind while peeling vegetables

Immerse vegetables in lukewarm or salty water for 10 – 15 minutes prior to cutting or cooking

PLASTIC - RELATED EXPOSURE

Reduce the amount of plastic you consume or buy

Store food stuffs and water in glass, steel or bone china containers, rather than plastic containers

Do not reuse plastic containers e.g., disposable mineral water bottles

Thinner and softer plastic will have more chemicals, and thus more EDCs than thick, less malleable plastic, and should be avoided.

Change plastic utensils used for storage or microwaving of food frequently

CHEMICAL - RELATED EXPOSURE

Investigate the chemicals in your cosmetics, insect spray, lotion and toiletries and mosquito repellants.

Use less perfumes, deodorants in spray form. Patronize traditional powder-based or essence based perfumes, eg. sandal wood, rose essence.

If you swim, choose a swimming pool that uses non chlorine based disinfectants.

Open your windows to air the house out instead of spraying the air freshener.

WATER- RELATED EXPOSURE

Know your water supply

Read your water quality reports

If you drink purified water out of plastic bottles, do not leave the bottles in you car or hot sun for any length of time; heat activates the molecules in plastic, which increases the rate at which the polycarbons leach into the water.

Do not reuse plastic bottles in which mineral water or soft drinks are supplied.

Figure 1

Table 1

A. Reproductive system
B. Adrenal gland
C. Thyroid gland
D. Growth hormone axis
E. Neural function
F. Immune function
G. Endocrine malignancies

Figure 2

Table 2: Sources, category, and examples of substances that have been reported as potential endocrine disruptors.

Sources	Category (Example of Uses)	Examples of Substances
Incineration, landfill	Polychlorinated Compounds (from industrial production or by-products of mostly banned substances)	Polychlorinated dioxins, polychlorinated biphenyls
Agricultural runoff / Atmospheric transport	Organochlorine Pesticides (found in insecticides, many now phased out)	DDT, dieldrin , lindane
Agricultural runoff	Pesticides currently in use	Atrazine, trifluralin, permethrin
Harbours	Organotins (found in antifoulants used to paint the hulls of ships)	Tributyltin
Industrial and municipal effluents	Alkylphenolics (Surfactants – certain kinds of detergents used for removing oil – and their metabolites)	Nonylphenol
Industrial effluent	Phthalates (found in placticisers)	Dibutyl phthalate, butylbenzyl phthalate
Municipal effluent and agricultural runoff	Natural Hormones (produced naturally by animals); synthetic steroids (found in contraceptives)	17-b-estradiol, estrone, Testosterone; ethynyl estradiol
Pulp mill effluents	Phytoestrogens (found in plant material)	Isoflavones, ligans, coumestans

Figure 3

Table 3

1. The Reproductive system
   a. Decline in semen quality
   b. Impaired fertility
   c. Increases in rate of spontaneous abortion
   d. Decline in sex ratio (fewer male births)
   e. Increases in development anomalies
      i. Cryptorchidism
      ii. Hypospadias
   f. Endometriosis
   g. Precocious puberty
2. Neural function
   a. Neurological development
   b. Neuroendocrine function
   c. Behaviour
3. Immune function
   a. Altered immune function
4. Cancer
   a. Breast cancer
   b. Endometrial cancer
   c. Testicular cancer
   d. Prostate cancer
5. Thyroid system

CONCLUSION

Concerted action should be taken by endocrinologists and physians to sensitize the public (and themselves), to the actual and potential dangers of EDCs. A public health awareness and action plan should be launched to minimize exposure to EDCs, and to reduce unwanted effects on our health.

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