Assessment of Potential Exposure and Health Risks from Exposure to Environmental Estrogen Among Helwan University Students

Thesis

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Samar Mahmoud Abbas

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List of Abbreviations

Abb.	Full term
4-NP	*4-nonylphenol*
AR	*Androgen receptor*
BHA	*Butylated hydroxyanisole*
BHT	*Butylated hydroxytoluene*
BPA	*Bisphenol-A*
Cd	*Cadmium*
CDC	*Centers for Disease Control and Prevention*
CFCT	*Consumers' Foundation, Chinese Taipei*
DDT	*Dichlorodiphenyltrichloroethane*
DDT	*Dichlorodiphenyltrichloroethane*
DEHP	*di-2-ethylhexyl phthalate, diethylhexyl phthalate,*
DES	*Diethylstilbestrol*
DMDD	*Dimethoxydiphenyl-dichloroethane*
DMDE	*1,1-bis(4-methoxyphenyl)-2,2-dichloroethene*
EA	*Estrogenic activity*
EC	European Commission
EDCs	*Endocrine disrupting chemicals*
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EE2	*17α-ethinylestradiol*
EPA	*Environmental Protection Agency*
ERα	*Estrogen Receptor α*
EU	*European Union*
FDA	*Food and Drug Administration*
FSH	*Follicle-stimulating hormone*
HCB	*Hexachlorbenzol*
HCH or BHC	*Hexachloro-cyclohexane*

List of Abbreviations (Cont…)

Abb.	Full term
HHDN	*1,2,3,4,10, l0-hexachloro-1,4,4a,5,8,8a-hexahydro-exo-1,4-endo-5,8-dimethanonapthalene*
HPG	*Hypothalamic–pituitary–gonadal*
IDF	*International Diabetes Federation*
IGRs	*Insect growth regulators*
IPCS	*International Programme on Chemical Safety*
IVF	*In vitro fertilization*
LCAPs	*Long chain alkylphenols"*
LH	*Luteinizing hormone*
MBP	*Metabolite of dibutyl phthalate*
NCTR	*National Center for Toxicological Research*
NHANES	*National Health and Nutrition Examination Survey*
NOAEL	*No-observed-adverse-effect level*
NIEHS	*National Institute of Environmental Health Sciences*
NTP	*National Toxicology Program*
OBELIX	*OBesogenic Endocrine disrupting chemicals: Linking prenatal eXposure to the development of obesity later in life*
OECD CF	*Organization for Economic Co-operation and Development Conceptual Framework*
OECD	*Organization for Economic Co-operation and Development*

List of Abbreviations (Cont…)

Abb.	Full term
OSE	*Ovarian surface epithelium*
PAHs	*Polycyclic aromatic hydrocarbons*
PBB	*Polybrominated biphenyl*
PBDEs	*Polybrominated diphenyl ethers*
PBT	*Persistent, bioacculumative, and toxic*
PCAHs	*Polycyclic aromatic hydrocarbons*
PCBs	*Polychlorinated biphenyls*
PCDDs	*Polychlorinated dibenzodioxins*
PCDFs	*Polychlor-inated dibenzofurans*
PCNs	*Polychlorinated naphthalenes*
PCOS	*Polycystic ovarian syndrome*
PCP	*Pentachlorophenol*
PBDEs	*Polybrominated diphenyl ethers*
PFC	*Perfluorinated chemical*
PFOS	*Perfluorooctane sulfonate*
PIN	*Prostatic intraepithelial hyperplasias*
PMS	*Pre Menstrual Tension Syndrome.*
POF	*Premature Ovarian Failure*
POPs	*Persistent organic pollutants*
PPPR	*Plant Protection Products Regulation*
PVC	*Poly vinyl chloride*
REACH	*Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals.*
RMMs	*Risk Management Measures*
SCCO	*Scientific Committee on Consumer Products*
STWs	*Sewage Treatment Works*

List of Abbreviations (Cont…)

Abb.	Full term
TBT	*Tributyltin*
TCDD	*Tetrachlorodibenzo-p-dioxin*
TEF	*Toxic equivalency factor*
TDCs	*Thyroid-disrupting chemicals*
TDS	*Testicular dysgenesis syndrome*
TSH	*Thyroid stimulating hormone*
UNEP	*United Nations Environmental Programme*
UNIDO	*United Nations Industrial Development Organization*
USEPA	*United States Environmental Protection Agency*
WHO	*World Health Organization*
WWTP	*Waste water treatment plant*
WWTP	*Municipal waste water treatment plant*

INTRODUCTION

For many years humans have been adding chemicals and pollutants to the environment. Some of these chemicals can alter endocrine function e.g. can alter the synthesis, catabolism and action of natural hormones and their corresponding receptors. These substances are often termed environmental estrogens or "xenoestrogens" but are also sometimes referred to as endocrine disruptors or endocrine modulators. Many of these chemicals (which include pesticides, plasticizers, household products and detergents, pharmaceuticals and industrial chemicals) are now present in nature. In addition, humans are exposed to these chemicals through the food chain via bioaccumulation ***(Crane et al., 2008).***

Recent reports, not only of feminized wildlife, but also of the possibility of a precipitous fall in sperm counts of people and of the rise in hormone-related cancers, such as breast cancer, have brought popular attention to environmental hormones—estrogen, in particular. But the so-called ecoestrogen may be only the most obvious of the chemical mimics in the environment. Observation of the effects of environmental estrogens is paving the way for what will undoubtedly turn out to be a larger phenomenon of environmental signaling. We believe that environmental estrogens are the paradigm for a new understanding of the health effects of external signals in the environment ***(Daftary and Taylor, 2006).***

One of the biggest health threats facing humans today is the excess estrogen assault from our environment. Detection of estrogens in the environment has raised concerns in recent years because of their

potential to affect both wildlife and humans. In recent years there has been a growing evidence that exposure to chemicals in the environment poses a serious threat to human and animals reproduction via disrupting effects on endocrine function. Despite the fact that these substances are persistent, they may be metabolized into more toxic compounds than the parent molecule in endocrine organs. This endocrine disrupting chemicals (EDCs) adversely affect health and reproduction even at very low concentrations and may exert their effects on the embryo and fetus ***(Crane et al., 2008).***

One of the critical points of concern in relation to EDCs is the potential time lag between exposure and the manifestations of the clinical disorders. In humans, this period may be years or decades and hence consequences of developmental exposure may be manifested in adulthood or during aging process. Also the timing of exposure to EDC is the key to human diseases; exposure of an adult to an EDC may have very different consequences than a developing fetus or infant ***(Parron et al., 2010).***

The complexity and diversity of factors belonging to EDCs, its direct action on the ovary and sperms and disorders of the reproductive function indicate that the impact of environmental pollution as an important determinant factor in fertility should not be minimized. In addition, attention should be directed towards dose-response relationships in environmental toxicology. Such studies can provide useful information that might have a significant impact on the strategies for risk assessment of toxic substance ***(Ewa et al., 2013)***

Rates of endocrine diseases and disorders, such as some reproductive and developmental harm in human populations, have changed in line with the growth of the chemical industry, leading to concerns that these factors may be linked. For example, the current status of semen quality in few European countries where studies have been systematically conducted is very poor: fertility in approximately 40 % of men is impaired. There is also evidence of reproductive and developmental harm linked to impairments in endocrine function in a number of wildlife species, particularly in environments that are contaminated by cocktails of chemicals that are in everyday use. Based on the human and wildlife evidence, many scientists are concerned about chemical pollutants being able to interfere with the normal functioning of hormones, so-called endocrine-disrupting chemicals (EDCs) that could play a causative role in these diseases and disorders. Then these 'early warnings' signal a failure in environmental protection that should be addressed. In wildlife, particularly some fish species, the evidence linking exposure to chemicals with reproductive disorders and dysfunction is strong; in humans research is still sparse, largely due to the length, cost and methodological difficulties of such studies ***(EEA, 2012).***

The realization that chemicals can disrupt the normal development and function of the male reproductive system has led to much more investigation of the possible effects of EDCs on other endocrine diseases and disorders: exposure to estrogen or to estrogenic EDCs is an accepted risk factor for breast cancer, endometriosis, fibroids and polycystic ovarian syndrome (PCOS) in women. There are now limited data to support a role of xenoestrogens in the disease processes behind some of

these disorders. Moreover, studies associating precocious puberty in girls with high levels of persistent dichlorodiphenyltrichloroethane (DDT) derivative p, p'-DDE (immigrant children) and polybrominated biphenyl (PBB) also exist. The increased incidence of diseases and disorders of the thyroid, immune, digestive, cardiovascular, and metabolic systems, together with laboratory studies suggesting that EDCs could affect these systems, have led to further investigation of these areas ***(Evanthia et al., 2009)***.

We have realized that there are characteristics typical of EDCs that make risk assessment processes difficult, such as critical time for exposure, the long latency between exposure and effect, and the realization that every similarly acting EDC in a combination contributes to the overall mixture effect. In particular, the latter challenges the traditional risk assessment paradigm of a threshold dose which a chemical fails to produce effects ***(Feki et al., 2009).***

In the 1996 Weybridge meeting on EDCs ('European Workshop on the Impact of Endocrine Disrupters on Human Health and Wildlife', European Environmental Agency (EEA)/Directorate-General for Research, 1996), the problem of endocrine disrupters was first comprehensively discussed by both European and United States regulatory authorities. Since then, substantial European Union (EU) funds (i.e. over EUR 150 million spent until 2011 have been allocated to research into endocrine disrupters and their effects, and the World Health Organization (WHO) ***(EEA, 2012).***

The Organization for Economic Co-operation and Development (OECD) have addressed the problem in many ways. At the Weybridge meeting in 1996, much focus was placed on estrogenic compounds, and especially on receptor-mediated effects. Scientific progress over the last decade or so has expanded the scope considerably: it includes EDCs with new modes of action, e.g. inhibitors of endogenous hormone production or metabolism; and target tissues for EDCs other than those in the reproductive system, such as the brain and cardiovascular system ***(EEA, 2012).***

There are enormous gaps in our knowledge. Further research in this area is needed; this seems only a tip of the iceberg phenomenon, as many of these processes still remain poorly understood, the unfortunate part being that this is all a creation of so called modern civilization. Hence, Xenoestrogens is "The Curse of Civilization". Further extensive research is required to elucidate potential interactions between these endocrine disrupting substances and well being of mankind ***(Evanthia et al., 2009)***.