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NUTRITIONAL ENDOCRINE DISRUPTORS

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ABSTRACT

This review focuses on nutritional endocrine disruptors found in food that may be responsible for the increasing incidence of infertility in males. These testicular function altering compounds are found in food sources such as artificial sweetness, food additives, plastic food and drink containers as well as pesticide and insecticides, industrial and agricultural chemicals, polycarbonated drinks, phytoestrogen and preservatives. Awareness into such endocrine disruptors may help reduce the incidence of male infertility.

It was discovered that there is a significant increase in the incidence of male infertility, raising the question about causes and effects of these maladies. As a result of the literature search, artificial sweetness, food additives, plastic food and drink containers, pesticide and insecticides, industrial and agricultural chemicals, polycarbonated drinks, phytoestrogen and preservatives are main NED that cause male infertility.

Keywords: Endocrine disruptors, nutrition, male infertility.

INTRODUCTION

Nutritional endocrine disruptors are chemicals in food which interfere with endocrine system or function and produce adverse effects in humans, and wildlife. These chemicals affect growth, reproduction, biochemical and physiological functions. For example, endocrine disruptors increase incidence or progression of some diseases such as diabetics, cancer e.t.c. [2] However, NED may not only affect the individual directly exposed , but also affect future generations.[3][4] Research has revealed that NED pose the greatest risk during prenatal and early postnatal periods which entails the development various organs and neural systems .[5] The effects of nutrition on endocrine system are largely undetermined and knowledge of

exogenous factors affecting the testicular function is still limited. The rate at which NED affects various organs of the body is alarming. These hazards could cause anomalies that are irreversible, if unprevented.[6] Researchers have hypothesized chemicals in food that are potentially hazardous on male reproductive axis resulting to infertility and other hormonal dependent reproductive functions causing reproductive dysfunctions. Besides infertility and erectile dysfunction, testicular and prostate cancers, abnormal sexual development, alteration in pituitary and thyroid gland function, immune suppression and neurobehavioral effects have also bee attributed to adverse effects of these endocrine disruptors in males. [6] Endocrine disruption is on the agenda of many expert groups, steering committees and panels of governmental organizations, industry and academic throughout the world. Because the disturbance of the endocrine system is sensitive, and scientific findings orobservations are controversially discussed among scientists, environmentalists, and authorities. [8] Hence, the aim of this review is to provide a scientific basis of chemical factors that cause endocrine disruption.

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MATERIALS AND METHODS

The current study reviewed the specialized literatures and scientific publications on substances present in foods that have the potential to disrupt the endocrine systems of males that may eventually lead to male infertility.

Table 1: REVIEW OF NUTRITIONAL ENDOCRINE DISRUPTOR

	NUTRITIONAL ENDOCRINE DISRUPTORS	FOOD SOURCES	MANIFESTATION
1	Aspartame, Cyclamate, Saccharin [7]	Artificial Sweetners [7]	Cancer, testicular atrophy and impaired Spermatogenesis [7]
2	Monosodium Glutamate (MSG)	Food additives such as monosodium Glutamate	Irreversible lesion in the arcuate nucleus of the brain.
3	Beverages container	Phthalates[15]	Testicular Atrophy and reduced fertility [15]
4.	Aerosol	Pesticide, insecticide Herbicide, fertilizer [8]	Low sperm count, motility and abnormal morphology [8]

5	Heavy metals	Such as Mercury, cadmium and lead [10],[12],[13]	Low sperm count, and abnormal morphology [10],[12],[13]
6	Polyethanol [14]	Alcohol [14]	Decreased testicular LH [14]
7	Carbonated drink [7]	Coca cola [7]	Cancer [7]
8.	Phytoestrogens	Soya beans	Reduction in LH and FSH levels
9	Preservative	Bromate [9]	Cancer [9]

DISCUSSION

The problem of human reproductive system has led to a variety of undesired outcomes such as complete or partial infertility. In an attempt to prevent these phenomenon question about food eaten need to be assessed. Is it purely coincidence that sperm quality has diminished over the past 50 years or increasing amounts of synthetic chemicals and hormones introduced to the environment and food supply? Perhaps one should consider decreased fertility in men as a physiological early warning system, a ' canary in the mine+; so to speak, which is acting as a sensitive indicator of nutritional disruption and imbalances. [6]

However, male infertility is a multifactoral disease process with a number of potential contributory causes. The majority of male infertility cases are due to deficient sperm production of unknown origin. Various nutritional or dietary choices have been investigated which have a negative impart on testicular function. [8] NED compounds encompass a variety of

chemicals including hormones, plant constituents, pesticides, compounds used in the plastics industry, consumer products and other industrial by-products and pollutants. Some are pervasive and widely dispersed in the environment. Some are persistent organic pollutants (POP's), and can be transported long distances across national boundaries and have been found in virtually all regions of the world. Others are rapidly degraded in the environment or human body or may be present for only short periods of time.[16] Health effects attributed to NEDS include a range of reproductive problems (reduced fertility, male and female reproductive tract abnormalities, and skewed male/female sex ratios, loss of fetus, menstrual problems); changes in hormone levels; early puberty; brain and behavioral problems; impaired immune functions; and various cancers.).[17]

Recognizing that a synthetic chemical has the potential to cause harm reveals a "hazard."The "risk" of this chemical to induce a biological effect depends on the properties of the chemical, but will occur only when exposure reaches a particular level, and this can be determined by standard toxicological methods. The relationship between human diseases of the endocrine system and the exposure to environmental contaminants, however, is poorly understood and scientifically controversial.[18]

There are many causes of infertility in men, although, sperm count does not equate by any means precisely infertility, it is recognized that men with very low sperm counts often have fertility problems. There has been some speculation that a decrease in sperm count may be a direct result of increasing human exposure to NED. Many factors may interact to influence sperm count; it is therefore difficult to identify any a single cause of an observed effect. It is not possible, based on present evidence, either to refute or confirm the possibility of a connection between human exposure to EDCs and the disputed fall in sperm count.

NED known as an exogenous agent that interferes with synthesis, secretion, transport, metabolism, binding action, or elimination of natural blood-borne hormones present in the body are responsible for homeostasis, reproduction, and developmental process. Thus, from a

physiological perspective, an endocrine-disrupting substance is a compound, either natural or synthetic, which, through environmental or inappropriate developmental exposures, alters the hormonal and homeostatic systems that enable the organism to communicate with and respond to its environment. It is a synthetic chemical that when absorbed into the body either mimics or blocks hormones and disrupts the body's normal functions. The first endocrine disruptors identified were synthetic chemicals that had weak intrinsic hormonal or anti-hormonal activity, usually estrogenic or anti-androgenic activity. Such compounds, when in the body, have the potential to interact with oestrogen or androgen signaling mechanisms [16]. The group of molecules identified as endocrine disruptors is highly heterogeneous and includes synthetic chemicals used as industrial solvents/lubricants and their byproducts [polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), dioxins], plastics [bisphenol A (BPA)], plasticizers (phthalates), pesticides [methoxychlor, chlorpyrifos, dichlorodiphenyltrichloroethane (DDT)], fungicides (vinclozolin), and pharmaceutical agents [diethylstilbestrol (DES)].

Natural chemicals found in human and animal food *e.g.*, xenoestrogens and phytoestrogens (genistein and coumestrol) can also act as endocrine disruptors. These substances generally thought to have relatively low binding affinity to estrogen receptors (ERs), are widely consumed and are components of infant formula[19].A recent study revealed that urinary concentrations of the phytoestrogens genistein and daidzein were about 500-fold higher in infants fed soy formula compared with those fed cowôs milk formula [20]. Therefore, the potential for endocrine disruptions by phytoestrogens was considered.

This disruption can occur by altering normal hormone levels, halting or stimulating the production of hormones, or changing the way hormones travel through the body, thus affecting the functions that these hormones control. Endocrine-disrupting chemicals (EDCs) were originally thought to exert actions primarily through nuclear hormone receptors, including estrogen receptors (ERs), androgen receptors (ARs), progesterone receptors, thyroid receptors (TRs), and retinoid receptors, among others.

Today, basic scientific research shows that the mechanisms are much broader than originally recognized. Thus, endocrine disruptors act via nuclear receptors, nonnuclear steroid hormone receptors (*e.g.*, membrane ERs), non-steroid receptors (*e.g.*, neurotransmitter receptors such as the serotonin receptor, dopamine receptor, norepinephrine receptor), orphan receptors [*e.g.*, aryl hydrocarbon receptor (AhR)ð an orphan receptor], enzymatic pathways involved in steroid biosynthesis and/or metabolism, and numerous other mechanisms that converge upon endocrine and reproductive systems. Some EDCs were designed to have long half-lives and because these substances do not decay easily, they may not be metabolized, or they may be metabolized or broken down into more toxic compounds than the parent molecule.

Nevertheless, in very broad terms, EDCs such as dioxins, PCBs, PBBs, and pesticides often contain halogen group substitutions by chlorine and bromine. They often have a phenolic moiety that is thought to mimic natural steroid hormones and enable EDCs to interact with steroid hormone receptors as analogs or antagonists. Even heavy metals and metalloids may have estrogenic activity, suggesting that these compounds are EDCs as well as more generalized toxicants.

Diet is a major source of pollutant exposure. Diet is thought to account for up to 90% of a person's PCB and DDT body burden.[21] Many endocrine disruptors are persistent in the environment and accumulate in fat, so the greatest exposures come from the consumption of fatty foods and fish from contaminated water. In a study of 32 different common food products from three grocery stores in Dallas fish and other animal products were found to be contaminated with PBDE[22] . Since these compounds are fat soluble, it is likely they are accumulating from the environment in the fatty tissue of animals. Some fish consumption is a major source of many environmental contaminates.

A challenge to understanding the relationship between EDCs and health abnormalities is that EDCs are a 'moving target': Individuals and populations are exposed to ever-changing patterns of production and use

of these compounds. They also tend to be released into the environment as mixtures, rather than individual chemicals. Therefore, it is important to understand the effects of coexposures to these chemicals, which may interact additively, multiplicatively (synergistically), or antagonistically[23]. There are limited data on the interactions between chemicals within a class or across classes of chemicals. Presently, there are good analytical methods for measuring exposures to a variety of endocrine disruptors in humans. An increased understanding of the potential human health risks of exposure to mixtures of EDC is important but remains much understudied.

Hence, measurement of body burden of the most prevalent xenobiotics would probably be the best strategy for finding a link between exposure and effect. Once known, this could be related to mechanistic studies in laboratory models, and future experiments could be designed to evaluate the effects of combinations of common EDCs in the laboratory, with the obvious caveat that it will not be possible to mimic every possible combination and dose. Despite these challenges, evolving and innovative technologies designed to improve the assessment of human exposure and reproductive and endocrine health endpoints should provide enhanced opportunities for improving our understanding of these relationships.

REFERENCES

1. OLiva A, Spira A, Multigner L: Contribution of environmental factors to the risk of male infertility. Human Reproduction (2003) 43: 1768-1776.

2, Michal F, More S, Ase P: Impact of the environment on reproductive Health óExecutive Summaryó Environmental Health perspective (1993) 101: 159 ï 167.

3 Price TM, Morphy SK, Younglai EV: Perspective: The possible influence of assisted reproductive technologies on Trans generational reproductive effects of environmental endocrine disruptors. Toxicological sciences. Journal of the society of Toxicology, (2007)69: 218 ï 226.

4. Anway MD, Cupp AS, Uzumcu M, Skinner MK: Epigenetic trans generational actions of endocrine dIsrupctors and male fertility. Science (2005) 308: 1466 ï 1669.

5. Colborn T, Vom Saal FS, Soto AM: Developmental effects of endocrine disrupting chemicals in wildlife and humans. Environmental health perspectives (1993) 101: 378- 384.

6. Moline JM, Golden AL, Bar ï chama N, Smith E, Rauch ME, Chapin RE, Perreault SD, Schrader SM, Suk WA, Landrigan PJ: Exposure to hazardous substances and male reproductive health a research frame work. Environmental health perspective (2000) 108: 803 ï 813.

7. Mercola J: Nutrasweet Lowers sperm counts. Tokyo Mainniche

daily news (2003) 1-2.

8. Fleming LE, Gomez ï Marin O, Zheng D, Ma F, Lee D: National Health interview survey mortality among US formers and pesticide applicators. A m J ind med (2003) 43:227 ï 233.

9. Demstra T: Global Assessment on the state of the endocrine disruptors (2002) WHO publication No. WHO/ PLS / EDS/ 02.2.2 98 ï 301.

10. Sharpe R.M, Skakkebaek: Environmental endocrine disruptors of testicular function (1993) 341: 1392- 1395.

11. Boscolo P, Sacchettoni- Logroscino G, Ranelletti FO, Gioia A, Mazor M: The effects of Long term cadmium exposure on the testis of rabbits|, Ultra structural study. Toxicology (1985) 24: 145 ï 149.

12. Lancranjam I: Reproductive ability of workmen occupationally exposed to lead.Environmental health (1975) 30: 396 ï 401.

13. Hendry WF, AôHern RP, Cole PJ: Was youngôs syndrome caused by exposure to mercury in childhood? BMJ (1993) 307: 1579 ï 1582.

14. Melnick RL: Introduction workshop on characterizing the effects of endocrine disruptors on human health at environmental exposure level. Environmental health perspectives (1999) 107:603 ï 604

15. Wams TJ: Diethylehxypthalate as an environmental container: a review. Science total environmental (1987) 66: 1 ï 16.

16. Damstra T, Barlow S, Bergman A, Kavlock R, Van Der Kraak G, eds. Global assessment of the state-of-the-science of endocrine disruptors. International Programme on Chemical Safety, 2002.

17. Harrison PTC, Humfrey CDN, Litchfield M, Peakall D, Shuker LK (1995). "Environmental oestrogens: consequences to human health and wildlife". *IEH assessment*. Medical Research Council, Institute for Environment and Health.

http://www.cranfield.ac.uk/health/researchareas/environmenthealth/ieh/ieh%20publications/a1.pdf. Retrieved 2009-03-14.

18 Kavlock R, Cummings A 2005 Mode of action: inhibition of androgen receptor functionð vinclozolin-induced malformationsin reproductive development. Crit Rev Toxicol 35:721ï 726

19. Kuiper GG, Lemmen JG, Carlsson B, Corton JC, Safe SH,van der Saag PT, van der Burg B, Gustafsson JA 1998 Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor _. Endocrinology 139:4252ï 4263

20. Cao Y, Calafat AM, Doerge DR, Umbach DM, Bernbaum JC, Twaddle NC, Ye X, Rogan WJ 2009 Isoflavones in urine, saliva and blood of infantsð data from a pilot study on the estrogenic activity of soy formula. J Expo Sci Environ Epidemiol 19:223ï 234

21. Fürst P (October 2006). "Dioxins, polychlorinated biphenyls and other organohalogen compounds in human milk. Levels, correlations, trends and exposure through breastfeeding". *Mol Nutr Food Res* 50 (10): 922ï 33. doi:10.1002/mnfr.200600008. PMID 17009213.

22. Schecter A, Päpke O, Tung KC, Staskal D, Birnbaum L (October 2004). "Polybrominated diphenyl ethers contamination of United States food". *Environ. Sci. Technol.* 38 (20): 5306ï 11. doi:10.1021/es0490830. PMID 15543730.

23. Kortenkamp A 2008Lowdose mixture effects of endocrine disrupters: implications for risk assessment and epidemiology. Int J Androl 31:233ï 240