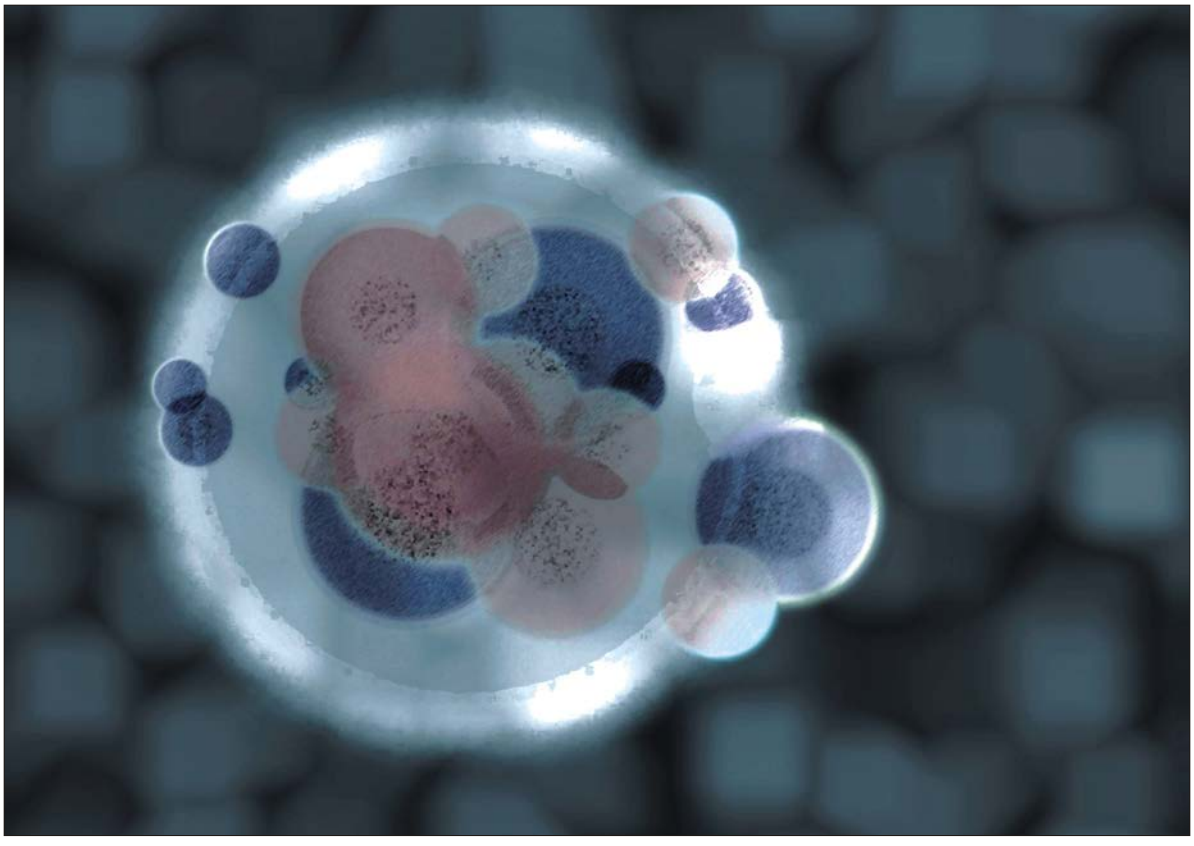

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Determination of the Amount of Environmental Hormone Contamination in Raw Materials and Products of Bandar-e-Imam Petrochemical Complex

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Abstract: Environmental hormone pollutants are synthetic chemicals which can disturb endocrine systems in human and wildlife if they enter body. Many diseases have been related to environmental hormones ranging from hormone dependent cancers to low sperm quality and quantity, infertility, wildlife population decline, developmental abnormalities and many more disruptions. Many of these pollutants are generally originated from oil and petroleum products. Therefore, estimating the amount of environmental hormone contaminations in raw materials and products of petrochemical complexes can illustrate the amount of society exposure to those dangerous pollutants. This study has looked at one of the biggest petrochemical complex, Bandar-e-Imam petrochemical complex, in Iran in order to determination of the extent of environmental hormones' contamination in material used and produced there. Bandar-e-Imam petrochemical complex produces 6.1 million tons of different products (3.5 million tons such as light and heavy chains polyethylene, polypropylene, PVC, artificial plastic, aromatic compounds (benzene, xylene) etc) every year. From 158 ingredients or products (7546928.47 tons) studied in this paper, 30 of them (3871447.8 tons) possess at least one environmental hormone pollutant. The most and the least percentage of the number of environmental hormones belong respectively to used and produced materials in CA unit (50%) and EDU unit (8%). No significant difference ($p>0.05$) were observed between raw materials used and final products made in petrochemical complex regarding to environmental hormone pollution.

Key words: Environmental hormone, Bandar-e-Imam, petrochemical complex, pollution

INTRODUCTION

Recently, there are many concerns about disrupting effects of some pollutants on human and wildlife health via interfering with the endocrine system (Grun and Blumberg, 2006; Whitehead and Rice, 2006). It has been shown that not only some synthetic but also natural compounds can disrupt normal endocrine functions through either competing or blocking hormone receptors (Bogi *et al*., 2003; McMullin *et al*., 2004). Different names have been used to identify them such as: environmental hormone, endocrine disrupting chemicals, xenoestrogens and environmental estrogens (Kelce *et al*., 1994; Kodama and Kodama, 1998; Niyachi *et al*., 2000; Gulledge *et al*., 2001; Newbold *et al*., 2007a). Many abnormalities including reproductive and evolutional difficulties have increased the number of infertiles (Cheek and McLachlan, 1998; Golden *et al*., 1998), increase in hormone dependent cancer incidences (Golden *et al*., 1998; Kodama *et al*., 2000) and others have been related to more exposure of populations to these chemicals which are widespread. We applied the term of environmental hormones in this paper (Moller, 2001; Morrison *et al*., 2003; Lind *et al*., 2004).

It has been shown environmental hormones when attach to hormones' receptors can either mimic natural hormones activity (over-stimulating the receptors) or block them so, no normal hormones can bind to the receptors (Kovacs *et al*., 1983; Birrell *et al*., 2007) meanwhile, some environmental hormones may bind to the receptors and induce other activities than normal procedures (Atanassova *et al*., 2000; Jobling *et al*., 2003). Due to disruption of normal hormone-receptor binding and activity, it would be no surprise to see that some hormone related diseases such as developmental and reproductive abnormalities, hormone dependent cancers, diminished sperm quality and quantity, reproductive system anomalies and population changes in wildlife are increasing either sharply or steadily in communities with higher exposures to environmental hormones (Holmes *et al*., 2004; Lemaire *et al*., 2004). Well-known relation have been reported between sharp declining in

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population of alligators in great lakes of Florida with increased exposure and contamination with pesticides such as DDT, dicophole, toxaphene (pesticides having environmental hormone properties) (Drbohlav *et al*., 2004). The same reports have been cited for increased abnormalities in birds' reproduction and decreased egg laying potential whom fed from contaminated fish of polluted lakes (Dhooge *et al*., 2001; Dorner *et al*., 2001). In addition, there is deleterious effects in development of nervous system in embryos of pregnant women consumed fish from the same lakes (Giesy *et al*., 2003).

Before World War I, about half of the industrial products in industrial countries including the United States, were made from renewable resources, such as plant-, wood and animal-based materials (Imaida and Shirai, 2000; Henson and Chedrese, 2004; Newbold *et al*., 2007b). In 1920s and 1930s, oil and chemical companies like Union Carbide, Shell and Dow expanded their interest in petrochemical manufacturing (Whaley *et al*., 2001; Takeyoshi *et al*., 2002). The petrochemical industry, strengthened immensely by World War II, replaced by renewable materials with synthetic organic compounds made from the by-products of oil and natural gas. For instance, synthetic rubber, chemical detergents and polyester replaced with natural rubber, animal-based soaps and cotton, respectively. In the 1950s and 1960s, the thriving plastics industry accelerated the shift even more. In doing so, today, 92% of the materials used for example in US products and production processes are nonrenewable (Whaley *et al*., 2001; Takeyoshi *et al*., 2002).

One of the largest industrial establishments in Iran is located on the northwest coast of the Persian Gulf. This location has been chosen owing to its easy access to feed stocks, the main national roads, railway network, as well as international waterway. In the early seventies, a 50-50 joint venture agreements was signed between National Petrochemical Company (NPC) of Iran and a consortium of Japanese firms, head by Mitsui and Co., In order to constructing this colossal petrochemical complex, under the name of Iran-Japan Petrochemical Company (IJPC). Preliminary and basic activities, including back filling, site grading, construction of buildings and warehouses, installation of power, water and steam facilities and construction jetties began in 1974. At this stage, the resumption of sit activities began with the cooperation of national and international contractors and complex units came on stream, one bye one from 1990 through 1994. The complex is now working less than total capacity but it is one of the biggest petrochemical complexes in Iran which producing many products which feed downstream factories.

As many environmental hormones are products of petrochemical factories and regarding to the role of Bandar-e-Imam complex and importance in Iran, this study looked at contamination of raw materials used (incomes) and products made (outcomes) of the complex with environmental hormones.

MATERIALS AND METHODS

Research samples were taken from Bandar-Imam-Petrochemical complex. The complex is composed of ten separated units working together (gas dissociation unit (NF), Olefin unit (OL), Aromatic unit (AR), Heavy chain polyethylene unit (HD), Light chain polyethylene unit (LD), Propylene unit (PP), Butadiene and artificial plastics unit (BD/SR), Alkaline chloride unit (CA), Ethylene dichloride unit (EDC), Vinyl chloride monomer (VCM) and Water power (UT)). Each unit consumes some raw materials and produces some products. In a cross-sectional study and by using questioners and interview as data gathering tools, all different kinds of raw materials and products in every unit, the amount of raw materials and products (tons), their chemical structures and chemical prosperities were determined. After defining chemical structure and property of each material used or produced in the complex, their environmental hormones potential were calculated with scientific database (Environmental Protection Agency-EPA-guidelines and experiments were used as standard criteria to define environmental hormones property of each compound) and finally data were categorized by means of SPSS v. 14 (SPSS Inc., 444 N. Michigan Avenue, Chicago, Illinois 60611, USA) software and presented afterward.

RESULTS

Raw materials needed for petrochemical complex includes 3.2 million tons of liquid gas, 120 million cubic feet of natural gas, 400 thousand tons of salt, 1 million tons of NAFTA and 7800 thousand tons of monostyrene per year. Most natural gas comes from nearby Ahwaz and Maron gas fields. Different unites are working together in Bandar-e-Imam complex. The final and proposed capacity of complex is 6.1 million tons of different products: meanwhile, at the time of this study, it was working with 5.3 million tons capacity of producing different products such as light and heavy polyethylene, polypropylene, PVC, artificial plastic, aromatic compounds, liquid gas, HCl, NaOH and ethylene dichloride. Most of these products used as fuel materials (4.358 million tons 81.72%) and other products are chemical substances (946.1 million tons 83.36%), polymers (425 million tons, 97.7%) and aromatics (550 million tons 10.31%) (Table 1).

Table 1: Weights of different products produced in Bandar-e-Imam petrochemical complex (tons)

Types of products	Amount (tons)	Percent
Chemical	964.1	83.36
Polymers	425.0	97.70
Aromatic	550.0	10.31
Fuel	4358.0	81.72
Total	7297.1	

Table 2: The percentage of environmental hormone pollutants in each operating unit of Bandar-e-Imam petrochemical complex

Bandar-e-Imam petrochemical complex units	Percent
Alkaline chloride unit (CA)	50.0
Vinyl Chloride Monomer (VCM)	25.0
UT	17.0
Butadiene and artificial plastics unit (BD/SR)	15.8
Gas dissociation unit (NF)	31.0
Heavy chain polyethylene unit (HD)	13.0
EDU	8.0
Aromatic unit (AR)	27.0
Propylene unit (PP)	22.0
Light chain polyethylene unit (LD)	22.0
Olefin unit (OL)	19.0
Poly Vinyl Chloride (PVC)	13.0
Total	908.0

The results showed that 158 different ingredients (either as raw materials or products) are being dealt with in Bandar-e-Imam petrochemical complex (Table 3) with the most and least number were in BD/SR unit (15.8%) and EDC unit (1.3%), respectively. From 7546280.47 tons of materials used or produced in the complex, 19.3% (1460448.5 tons) were incomes and 81.7% (6106480 tons) as outcomes. OL unit with 1434305.2 tons (19%) and UT unit with 473.5 tons (0.006%) were the most and the least consumers of incomes and outcomes materials.

This research demonstrated that in 158 different types of materials either used or produced in Bandar-e-Imam petrochemical complex, 30 (18.98%) possess environmental hormone activity. Of all of those materials, about 3871447.8 tons (51.3%) had environmental hormone activity. The maximum amount of environmental hormone pollutants belong to OL, PP and BD/SR units (4 in every unit, 13%) and the minimum belong to CA, LDPE and EDC (1 in every unit, 3.3%) (Table 2). The maximum and minimum amount of products with environmental hormone activity found in PVC unit (180000 tons, 28.15%) and in NF and AR units (0 tons), respectively (Table 2). The maximum and minimum of products including environmental hormone agents were in NT unit (1908040 tone, 59.04%) and LDPE, EDC, HDPE, BD/SR and UT units (0 tone), respectively. Maximum numbers of incomes and outcomes in different units of Bandar-e-Imam petrochemical complex observed in BD/SR unit (25) and minimum was in CA unit (2) and the maximum amount of environmental hormones contaminant measured in NF and BD/SR units (4) and the minimum numbers seen in OL, EDU and CA units (1). The most and the least percentage of the number of environmental hormones than total used and produced materials were in CA unit (50%) and EDU unit (8%), respectively (Table 2).

Table 3: The number of environmental hormone pollutants in each operating unit of Bandar-e-Imam petrochemical complex comparing to the total number of products produced in that unit

Bandar-e-Imam petrochemical complex units	No. of environmental hormone pollutants	Total No. of products
Alkaline chloride unit (CA)	1	2
Vinyl Chloride Monomer (VCM)	3	12
UT	2	12
Butadiene and artificial plastics unit (BD/SR)	4	25
Gas dissociation unit (NF)	4	13
Heavy chain polyethylene unit (HD)	2	16
EDU	1	12
Aromatic unit (AR)	3	11
Propylene unit (PP)	4	18
Light chain polyethylene unit (LD)	2	9
Olefin unit (OL)	1	12
Poly Vinyl Chloride (PVC)	2	16
Total	29	158

DISCUSSION

Since the publication of Rachel Carson's *Silent Spring* (Daston *et al*., 2003), there has been increasing awareness that chemicals in the environment can exert profound and deleterious effects on wildlife populations which is inextricably linked to the health of the environment (Cheek and McLachlan, 1998; Niyachi *et al*., 2000; Gilbert and Fausto-Sterling, 2003; Newbold *et al*., 2007a). The last three decades in particular have witnessed a growing scientific concern, public debate and media attention over the probable deleterious influences in humans and wildlife which are possibly owing to chemicals exposure having potential to interfering with the endocrine system (Saenz de Rodriguez, 1984; Kobayashi *et al*., 2001; Newbold *et al*., 2007a).

Environmental hormones encompass a variety of chemical classes, including natural and synthetic hormones (Kobayashi *et al*., 2001), plant constituents (Krazeisen *et al*., 2001; Vollmer *et al*., 2002), pesticides (Guillette and Moore, 2006; Bretveld *et al*., 2007; Lurling and Scheffer, 2007), compounds used in the plastics industry and consumer products (Skakkebaek *et al*., 1998; Kodama *et al*., 1999) and other industrial by-products and pollutants. They are often pervasive and widely dispersed in the environment and mainly come from oil and petrochemical products (Harvey *et al*., 1981; Peakall *et al*., 1981). Some of which are persistent (Steinhardt, 2004; Grun and Blumberg, 2006; Grun *et al*., 2006; Newbold *et al*., 2007b) able to scatter in long distances across national boundaries and also have been found in virtually all regions of the world (Arukwe, 2001;

Hanselman *et al*., 2003). Others are rapidly degraded in the environment or human body or may be present for only short periods of time but at critical periods of development.

Many abnormalities have been related to environmental hormones contamination in a range from increasing cancers ratio to developmental defects, reducing in sperm quality and quantity and even wildlife populations' decline (Allen *et al*., 1997; Ahmed, 2000; Aoki, 2001; Danzo *et al*., 2002; Jobling *et al*., 2003; Jobling and Tyler, 2003; Morrison *et al*., 2003; Chung *et al*., 2004; Helbing *et al*., 2007).

In developed countries, tough regulations are being implemented to lessen the human and wildlife exposure to these pollutants: meanwhile, in developing countries, the lacking of the necessary infrastructure to monitor and evaluate these chemicals expressed a particular need for an objective international assessment. One major source of contamination comes from refinery and petrochemical products so that. this study looked at the extent of contamination of Bandar-e-Imam petrochemical complex. The result showed that more than 51% of raw materials and products of Bandar-e-Imam petrochemical complex have at least one environmental hormone pollutants. In some units which are producing some especial products (such as PVC unit or units which produce heavy and light chain aromatics), nearly all products have environmental hormone agents. Regarding to the huge capacity of this petrochemical complex for producing different kinds of products and also the extent of society exposures to these products (nearly all populations are in close contact with petrochemical products either directly or indirectly) (Sonnenschein and Soto, 1998; Ohlson and Hardell, 2000; Kumar, 2004), it is clear that those contaminated products will insert their deleterious impacts on Iranian populations in short and long terms exposure. It should also be considered that many petrochemical products are themselves raw materials for other factories and the extent of population exposure would be even more and more. The danger would also be higher for laborers who are in touch more closely with those pollutant raw materials and products inside the petrochemical complex (Sonnenschein and Soto, 1998; Hanaoka *et al*., 2002; Fossi *et al*., 2003; Kumar, 2004).

Regarding the results of this study about Bandar-e-Imam petrochemical complex contamination with environmental hormones pollutants, multiplying by the number of active petrochemical complexes in Iran (the number of workers in each unit), it would be fairly simple to imagine the extent of society exposure to these contaminants. As many of these pollutants are lipophilic (Bogh *et al*., 2001; Goralczyk *et al*., 2002; Christensen *et al*., 2005), then, they can accumulate in body fats (Adelsbach and Tjeerdema, 2003; Kumar, 2004; Lemaire *et al*., 2004; Correa-Reyes *et al*., 2007), so that their side effects would be obvious mainly in a long term period (Guenther *et al*., 2002; Silbergeld *et al*., 2002). Even now in many industrial countries, environmentally hormones dependent diseases are so high that concerned many scientist and environmentalist (Elswick *et al*., 2000; Bogh *et al*., 2001; McMaster *et al*., 2001; Fuerhacker, 2003; Kumar, 2004). Therefore, seeking for products which are safer and more trustable in order to substituting with current contaminated products is extremely recommended.

REFERENCES

Adelsbach, T.L. and R.S. Tjeerdema, 2003. Chemistry and fate of fenvalerate and esfenvalerate. Rev. Environ. Contam. Toxicol., 176: 137-154.

Ahmed, S.A., 2000. The immune system as a potential target for environmental estrogens (endocrine disrupters): A new emerging field. Toxicology, 150: 191-206.

Allen, R.H.M., E. Gottlieb, M.J. Clute, J. Pongsiri, Sherman and G.I. Obrams, 1997. Breast cancer and pesticides in Hawaii: The need for further study. Environ. Health Perspect., 105: 679-683.

Aoki, Y., 2001. Polychlorinated biphenyls, polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans as endocrine disrupters-what we have learned from Yusho disease. Environ. Res., 86: 2-11.

Arukwe, A., 2001. Cellular and molecular responses to endocrine-modulators and the impact on fish reproduction. Mar. Pollut. Bull., 42: 643-655.

Atanassova, N.C., K.J. McKinnell, M. Turner, J.S. Walker, M. Fisher, M.R. Morley, M.N.P. Groome and R.M. Sharpe, 2000. Comparative effects of neonatal exposure of male rats to potent and weak (environmental) estrogens on spermatogenesis at puberty and the relationship to adult testis size and fertility: Evidence for stimulatory effects of low estrogen levels. Endocrinology, 141: 3898-3907.

Birrell, S.N.L.M., J.M. Butler, G. Harris, Buchanan and W.D. Tilley, 2007. Disruption of androgen receptor signaling by synthetic progestins may increase risk of developing breast cancer. Faseb J. (In Press).

Bogh, I.B.P., V. Christensen, M. Dantzer, I.C. Groot, R.K. Thofner, R.M Schmidt and T. Greve, 2001. Endocrine disrupting compounds: Effect of octylphenol on reproduction over three generations. Theriogenology, 55: 131-150.

Bogi, C.J., H. Schwaiger, U. Ferling, C. Mallow, F. Steineck, W. Sinowatz, R.D. Kalbfus N.I. Lutz and W. Kloas, 2003. Endocrine effects of environmental pollution on *Xenopus laevis* and *Rana temporaria*. Environ. Res., 93: 195-201.

Bretveld, R.M., B.I. Ebisch and N. Roeleveld, 2007. Influence of pesticides on male fertility. Scand J. Work Environ. Health, 33: 13-28.

Cheek, A.O. and J.A. McLachlan, 1998. Environmental hormones and the male reproductive system. J. Androl., 19: 5-10.

Christensen, J.R.J.S., C.A. Richardson, B.B. Pauli and J. Elliott, 2005. Effects of nonylphenol on rates of tail resorption and metamorphosis in Rana catesbeiana tadpoles. J. Toxicol. Environ. Health A, 68: 557-572.

Chung, H.W.S.W., J.B. Park, J.K. Chung, J.W. Kang, H.S. Kim, W.J. Kim, S.H. Hyung, Noh and S.Y. Song, 2004. Differences in genetic expression profiles between young-age and old-age gastric adenocarcinoma using cDNA microarray for endocrine disruptor study. Oncol Rep., 12: 33-39.

Correa-Reyes, G., M.T. Viana, F.J. Marquez-Rocha, A.F. Licea, E. Ponce and R. Vazquez-Duhalt, 2007. Nonylphenol algal bioaccumulation and its effect through the trophic chain. Chemosphere (In Press).

Danzo, B.J., H.W. Shappell, A. Banerjee and D.L. Hachey, 2002. Effects of nonylphenol, 1,1-dichloro-2,2-bis(p-chlorophenyl)ethylene (p,p'-DDE) and pentachlorophenol on the adult female guinea pig reproductive tract. Reprod. Toxicol., 16: 29-43.

Daston, G.P., J.C. Cook and R.J. Kavlock, 2003. Uncertainties for endocrine disrupters: Our view on progress. Toxicol. Sci., 74: 245-252.

Dhooge, W., F. Eertmans and F. Comhaire, 2001. Estrogen receptor based *in vitro* assays for the evaluation of endocrine disrupters. Folia Histochem Cytobiol, 39: 44-45.

Dorner, G., F. Gotz, W. Rohde, A. Plagemann, R. Lindner, H. Peters and Z. Ghanaati, 2001. Genetic and epigenetic effects on sexual brain organization mediated by sex hormones. Neuroendocrinol. Lett., 22: 403-409.

Drbohlav, P., V. Bencko, J. Masata and S. Jirsova, 2004. Effect of toxic substances in the environment on reproduction. Ceska Gynekol., 69: 20-26.

Elswick, B., A.F. Welsch and D.B. Janszen, 2000. Effect of different sampling designs on outcome of endocrine disruptor studies. Reprod. Toxicol., 14: 359-367.

Fossi, M.C., L. Marsili, G. Neri, A. Natoli, E. Politi and S. Panigada, 2003. The use of a non-lethal tool for evaluating toxicological hazard of organochlorine contaminants in Mediterranean cetaceans: New data 10 years after the first paper published in MPB. Mar. Pollut. Bull., 46: 972-982.

Fuerhacker, M., 2003. Bisphenol A emission factors from industrial sources and elimination rates in a sewage treatment plant. Water Sci. Technol., 47: 117-122.

Giesy, J.P., E.M. Snyder, K.M. Nichols, S.A. Snyder, S.A. Villalobos, P.D. Jones and S.D. Fitzgerald, 2003. Examination of reproductive endpoints in goldfish (*Carassius auratus*) exposed in situ to municipal sewage treatment plant effluent discharges in Michigan, USA. Environ. Toxicol. Chem., 22: 2416-2431.

Gilbert, S.F. and A. Fausto-Sterling, 2003. Educating for social responsibility: Changing the syllabus of developmental biology. Int. J. Dev. Biol., 47: 237-244.

Golden, R.J., K.L. Noller, L. Titus-Ernstoff, R.H. Kaufman, R. Mittendorf, R. Stillman and E.A. Reese, 1998. Environmental endocrine modulators and human health: An assessment of the biological evidence. Crit. Rev. Toxicol., 28: 109-227.

Goralczyk, K., P. Strucinski, K. Czaja, A. Hernik and J.K. Ludwicki, 2002. Flame retardants-use and hazards for human. Rocz Panstw Zakl Hig., 53: 293-305.

Grun, F. and B. Blumberg, 2006. Environmental obesogens: Organotins and endocrine disruption via nuclear receptor signaling. Endocrinology, 147: S50-55.

Grun, F., H. Watanabe, Z. Zamanian, L. Maeda, K. Arima, R. Cubacha, D.M. Gardiner, J. Kanno, T. Iguchi and B. Blumberg, 2006. Endocrine-disrupting organotin compounds are potent inducers of adipogenesis in vertebrates. Mol. Endocrinol., 20: 2141-2155.

Guenther, K., V. Heinke, B. Thiele, E. Kleist, H. Prast and T. Raecker, 2002. Endocrine disrupting nonylphenols are ubiquitous in food. Environ. Sci. Technol., 36: 1676-1680.

Guillette, L.J. and B.C. Moore, 2006. Environmental contaminants, fertility and multioocytic follicles: A lesson from wildlife? Semin. Reprod. Med., 24: 134-141.

Gulledge, C.C., M.E. Burow and J.A. McLachlan, 2001. Endocrine disruption in sexual differentiation and puberty. What do pseudohermaphroditic polar bears have to do with the practice of pediatrics? Pediatr. Clin. North Am., 48: 1223-1240.

Hanaoka, T., N. Kawamura, K. Hara and S. Tsugane, 2002. Urinary bisphenol A and plasma hormone concentrations in male workers exposed to bisphenol A diglycidyl ether and mixed organic solvents. Occup. Environ. Med., 59: 625-628.

Hanselman, T.A., D.A. Graetz and A.C. Wilkie, 2003. Manure-borne estrogens as potential environmental contaminants: A review. Environ. Sci. Technol., 37: 5471-5478.

Harvey, S., H. Klandorf and J.G. Phillips, 1981. Reproductive performance and endocrine responses to ingested petroleum in domestic ducks (Anas platyrhynchos). Gen. Comp. Endocrinol., 45: 372-380.

Helbing, C.C.L., Ji.C.M. Bailey, N. Veldhoen, F. Zhang, G.W. Holcombe, P.A. Kosian, J. Tietge, J.J. Korte and S.J. Degitz, 2007. Identification of gene expression indicators for thyroid axis disruption in a *Xenopus laevis* metamorphosis screening assay Part 2. Effects on the tail and hindlimb. Aquat. Toxicol. (In Press).

Henson, M.C. and P.J. Chedrese, 2004. Endocrine disruption by cadmium, a common environmental toxicant with paradoxical effects on reproduction. Exp. Biol. Med. (Maywood), 229: 383-392.

Holmes, P., P. Rumsby and P.T. Harrison, 2004. Endocrine disrupters and menopausal health. J. Br. Menopause Soc., 10: 54-59.

Imaida, K. and T. Shirai, 2000. Endocrine disrupting chemicals and carcinogenesis-breast, testis and prostate cancer. Nippon. Rinsho., 58: 2527-2532.

Jobling, S. and C.R. Tyler, 2003. Endocrine disruption, parasites and pollutants in wild freshwater fish. Parasitology, 126: S103-108.

Jobling, S., D. Casey, T. Rodgers-Gray, J. Oehlmann, U. Schulte-Oehlmann, S. Pawlowski, T. Baunbeck, A.P. Turner and C.R. Tyler, 2003. Comparative responses of molluscs and fish to environmental estrogens and an estrogenic effluent. Aquat. Toxicol., 65: 205-220.

Kelce, W.R., E. Monosson, M.P. Gamcsik, S.C. Laws and L.E. Gray, 1994. Environmental hormone disruptors: Evidence that vinclozolin developmental toxicity is mediated by antiandrogenic metabolites. Toxicol. Applied Pharmacol., 126: 276-285.

Kobayashi, S., T. Sugaya, N. Sakata, M. Uebayasi, K. Sameshima and A. Tanaka, 2001. Prediction of endocrine disruptors based on a new structure-activity relationship for sex and environmental hormones using chemical hardness concept. Chem. Pharm. Bull. (Tokyo), 49: 680-688.

Kodama, M. and T. Kodama, 1998. Comparative epidemiology of cancers of the testis, lung, bladder and stomach with special reference to the possible implication of environmental hormones in the recent risk changes of the 4 neoplasia types. Int. J. Mol. Med., 2: 705-714.

Kodama, M., M. Murakami and T. Kodama, 1999. Topological transition of the parametric expression site of tumor suppressor inactivation as a marker evidence of environmental hormone-oriented cancer risk increase. Int. J. Mol. Med., 4: 153-161.

Kodama, M., T. Kodama and M. Murakami, 2000. Oncogene activation and tumor suppressor gene inactivation find their sites of expression in the changes in time and space of the age-adjusted cancer incidence rate. *In vivo*, 14: 725-734.

Kovacs, W.J., J.E. Griffin and J.D. Wilson, 1983. Transformation of human androgen receptors to the deoxyribonucleic acid-binding state. Endocrinology, 113: 1574-1581.

Krazeisen, A., R. Breitling, G. Moller and J. Adamski, 2001. Phytoestrogens inhibit human 17beta-hydroxysteroid dehydrogenase type 5. Mol. Cell Endocrinol., 171: 151-162.

Kumar, S., 2004. Occupational exposure associated with reproductive dysfunction. J. Occup. Health, 46: 1-19.

Lemaire, G., B. Terouanne, P. Mauvais, S. Michel and R. Rahmani, 2004. Effect of organochlorine pesticides on human androgen receptor activation *in vitro*. Toxicol. Applied Pharmacol., 196: 235-246.

Lind, P.M., M.R. Milnes, R. Lundberg, D. Bermudez, J.A. Orberg and L.J. Guillette, 2004. Abnormal bone composition in female juvenile American alligators from a pesticide-polluted lake (Lake Apopka, Florida). Environ. Health Perspect, 112: 359-362.

Lurling, M. and M. Scheffer, 2007. Info-disruption: Pollution and the transfer of chemical information between organisms. Trends. Ecol. Evol. (In Press).

McMaster, M.E., J.J. Jardine, G.T. Ankley, W.H. Benson, M.S. Greeley, T.S. Gross, L.J. Guillette, D.L. MacLatchy, E.F. Orlando, G.J. Van Der Kraak and K.R. Munkittrick, 2001. An interlaboratory study on the use of steroid hormones in examining endocrine disruption. Environ. Toxicol. Chem., 20: 2081-2087.

McMullin, T.S., M.E. Andersen, A. Nagahara, T.D. Lund, T. Pak, R.J. Handa and W.H. Hanneman, 2004. Evidence that atrazine and diaminochlorotriazine inhibit the estrogen/progesterone induced surge of luteinizing hormone in female Sprague-Dawley rats without changing estrogen receptor action. Toxicol. Sci., 79: 278-286.

Moller, H., 2001. Hormones and endocrine disrupters in food and water: Possible impact on human health. Proceedings from an international workshop. Copenhagen, Denmark, May 27-30, 2000. APMIS, 103: S1-571.

Morrison, A.G., J.J. Callanan, N.P. Evans, T.C. Aldridge and T. Sweeney, 2003. Effects of endocrine disrupting compounds on the pathology and oestrogen receptor alpha and beta distribution in the uterus and cervix of ewe lambs. Domest. Anim. Endocrinol., 25: 329-343.

Newbold, R.R., E. Padilla-Banks, R.J. Snyder, T.M. Phillips and W.N. Jefferson, 2007a. Developmental exposure to endocrine disruptors and the obesity epidemic. Reprod. Toxicol. (In Press).

Newbold, R.R., W.N. Jefferson, S.F. Grissom, E. Padilla-Banks, R.J. Snyder and E.K. Lobenhofer, 2007b. Developmental exposure to diethylstilbestrol alters uterine gene expression that may be associated with uterine neoplasia later in life. Mol. Carcinog. (In Press).

Niyachi, Y., T. Ichijo and N. Yamamoto, 2000. Endocrine-disrupting chemical substances (so-called environmental hormones). Nippon Naika Gakkai Zasshi, 89: 361-367.

Ohlson, C.G. and L. Hardell, 2000. Testicular cancer and occupational exposures with a focus on xenoestrogens in polyvinyl chloride plastics. Chemosphere, 40: 1277-1282.

Peakall, D.B., J. Tremblay, W.B. Kinter and D.S. Miller, 1981. Endocrine dysfunction in seabirds caused by ingested oil. Environ. Res., 24: 6-14.

Saenz de Rodriguez, C.A., 1984. Environmental hormone contamination in Puerto Rico. N. Eng. J. Med., 310: 1741-1742.

Silbergeld, E.K., J.A. Flaws and K.M. Brown, 2002. Organizational and activational effects of estrogenic endocrine disrupting chemicals. Cad Saude Publica, 18: 495-504.

Skakkebaek, N.E., E. Rajpert-De Meyts, N. Jorgensen, E. Carlsen, P.M. Petersen, A. Giwercman, A.G. Andersen, T.K. Jensen, A.M. Andersson and J. Muller, 1998. Germ cell cancer and disorders of spermatogenesis: An environmental connection? Apmis, 106: 3-11; Discussion 12.

Sonnenschein, C. and A.M. Soto, 1998. An updated review of environmental estrogen and androgen mimics and antagonists. J. Steroid. Biochem. Mol. Biol., 65: 143-150.

Steinhardt, G.F., 2004. Endocrine disruption and hypospadias. Adv. Exp. Med. Biol., 545: 203-215.

Takeyoshi, M., K. Yamasaki, M. Sawaki, M. Nakai, S. Noda and M. Takatsuki, 2002. The efficacy of endocrine disruptor screening tests in detecting anti-estrogenic effects downstream of receptor-ligand interactions. Toxicol. Lett., 126: 91-98.

Vollmer, G., S. Starcke, J. Wober and O. Zierau, 2002. Endocrine modulation and the fragile balance of homeostasis. An overview. Neuroendocrinol. Lett., 23: 37-42.

Whaley, D.A., D. Keyes and B. Khorrami, 2001. Incorporation of endocrine disruption into chemical hazard scoring for pollution prevention and current list of endocrine disrupting chemicals. Drug. Chem. Toxicol., 24: 359-420.

Whitehead, S.A. and S. Rice, 2006. Endocrine-disrupting chemicals as modulators of sex steroid synthesis. Best Pract. Res. Clin. Endocrinol. Metab., 20: 45-61.