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Introduction

The plastic world: Sources, amounts, ecological impacts and effects on development, reproduction, brain and behavior in aquatic and terrestrial animals and humans

1. The Ettore Majorana International Centre for Scientific Culture

The following set of papers concerning contaminants in plastic were presented at a workshop held in association with the International Seminars on Planetary Emergencies, 36th Session, Erice, Sicily, 19th–24th August, 2006 (Ragiani, 2006). The World Federation of Scientists was founded in 1973, and since then the Erice International Seminars on Nuclear War and Planetary Emergencies have been held annually in Erice, Sicily, under the direction of Professor Antonino Zichichi. The seminars are held at the Ettore Majorana International Centre for Scientific Culture, which is named after an outstanding Italian physicist, Ettore Majorana. Embracing 114 schools, covering all branches of science, the Center is situated in the pre-medieval city of Erice, where three restored monasteries provide an appropriate setting for high intellectual endeavor. The World Federation of Scientists is the only group in the world engaged in the study of planetary emergencies, both theoretically and experimentally, via the implementation of pilot projects. The World Federation of Scientists has identified 63 planetary emergencies, and meetings consist of seminars and associated workshops, which are sponsored by panels devoted to studying these planetary emergencies. The workshop on "The Plastic World" was co-sponsored by the permanent panels on Water Quality and Endocrine Disrupting Chemicals.

2. Endocrine disrupting chemicals (EDCs) in plastic

As discussed in the following article by Charles Moore (2008), 30 years ago the prevailing attitude of the plastic industry was that "plastic litter is a very small proportion of all litter and causes no harm to the environment except as an eyesore". However, between 1970 and 2003, plastic has become the fastest growing segment of the US municipal waste stream with a nine-fold increase, and marine litter is now 60–80% of plastic, reaching 90–95% in some areas.

While often presented to the public as being inert, a number of chemicals used in plastic products are classified as "endocrine disrupting chemicals" (EDCs), since they disrupt hormones and other components of the endocrine system, which coordinates both the development, and subsequently, the functioning of all organ systems in the adult body (Colborn et al., 1993). In addition, Jorg Oehlmann (2008) discusses how endocrine disruption is recognized as an important issue in ecology; his review focuses on adverse consequences of the global distribution of these contaminants for aquatic organisms.

The following six articles are based on presentations made at the workshop. The focus is primarily on the ecological and health effects of chemicals in plastic that are contaminating the entire world, and are found in virtually everyone who is monitored for the presence of these contaminants. The focus of the workshop with regard to health effects of these chemicals was on developmental effects. Since the effects caused by developmental exposure are permanent, the effects are, by definition, adverse.

The EDCs in plastic that were the focus of the workshop are (1) bisphenol A (BPA), which is the chemical used to make polycarbonate (PC) plastic; BPA is also used as a plasticizer, since it is added to polyvinyl chloride (PVC) plastic. (2) Phthalates are plasticizers (additives) in plastic. PVC plastic cannot be made without phthalates, which make the PVC less brittle. The softer the product (such as a "rubber" duck made from PVC), the greater the amount of phthalate that is present; phthalates are also used in many other products such as cosmetics and pills. PVC also contains other EDCs, such as BPA, tributyl tin, and lead. (3) Flame retardants are added to plastic and many other common household products. Both polybrominated diphenyl ethers (PBDEs) and tetrabromo-bisphenol A (TB-BPA) are flame retardants; the focus here is on PBDEs.

Phthalates are not chemically bonded to PVC, and as a result, they "off-gas" from PVC plastic. All polycarbonate products leach some amount of BPA, with the rate of leaching increasing with repeated use, due to washing, exposure to heat, and contact with acidic or basic substances. PBDEs are also released from products, resulting in virtually ubiquitous exposure. Thus, virtually all wildlife and humans, as well as plant species, are exposed to these chemicals.

The presence of the recycling symbol containing a number (1–7) provides a mechanism to identify the monomer used to create the main polymer in plastic (Table 1), although the use of these codes is voluntary, and many plastic products are manufactured without any indication of the type of polymer used to make the plastic. In addition, the plasticizers that are added are protected from disclosure to the public under product confidentiality legislation; this limits the ability to recycle the plastic, since the recyclers do not know what chemicals are present. Not all plastics are able to be recycled for re-use; the chemical bond in thermoset plastic (such as polycarbonate) products makes them unable to be recycled for use in making the same product.

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Table 1
Types of monomers used to make plastic as indicated by the recycling code (located in the recycling triangle), and plasticizers (additives) that are also found in plastic

Code	Types of plastic materials
#1	PET: polyethylene terephthalate (contains antimony)—soda and water bottles
#2	HDPE: high density polyethylene—milk and water jugs, detergent bottles
#3	PVC: polyvinyl chloride (contains phthalates)—children's toys, meat plastic wrap
#4	LDPE: low density polyethylene—grocery and trash bags
#5	PP: polypropylene—food storage containers
#6	PS: polystyrene (contains PBDEs—flame retardant)—fast food containers and cups
#7	Other: usually (not always) polycarbonate (bisphenol A)—baby bottles, can lining, dental sealants/fillings

From: "Report of the Berkeley Plastics Task Force", April 8, 1996 [http://www.ecologycenter.org/ptf/report1996/report1996_toc.html].

Recycling PVC is problematic due to the presence of chlorine, which can lead to formation of dioxin as a by-product of recycling. Lack of knowledge of the chemicals that are in plastic also makes it impossible for consumers to know which products have the potential to leach EDCs.

PBDEs act as EDCs by interfering with normal thyroid hormone function, and thus disrupt development of the brain and reproductive systems. BPA is an estrogen-mimicking chemical at very low doses, while at higher doses it interferes with the binding of testosterone to androgen receptors and thyroid hormone to thyroid hormone receptors. The phthalates (and their *in vivo* metabolites) discussed in the following articles act as inhibitors of the synthesis of testosterone.

The reason that BPA, PBDEs, and phthalates were chosen for discussion at the workshop in Erice is that there are similarities in effects caused by developmental exposure to BPA and to specific phthalates, such as DEHP, and PBDEs, such as PBDE 99. For example, BPA (Akingbemi et al., 2004), DEHP (Andrade et al., 2006b), and PBDE-99 (Canton et al., 2005) all have been reported to inhibit the enzyme aromatase, which converts testosterone to estradiol, and thus plays an important role in sexual differentiation. As pointed out in the articles that follow, each of these chemicals interferes with many aspects of normal sexual differentiation, with studies having focused on sex differences in the brain, behavior, and in reproductive organ development and function.

The effects of BPA on development of the reproductive system have been well documented (Markey et al., 2005; Richter et al., 2007; vom Saal and Welshons, 2006), but the largest number of published papers concerns effects of BPA on the development of brain. A consensus statement from an US NIH-sponsored meeting was published, and based on a review of the published literature, 38 expert scientists were confident that "prenatal and/or neonatal exposure to low doses of BPA results in organizational changes in…brain structure and chemistry, and behavior of laboratory animals" (vom Saal et al., 2007). The emphasis of the review by Paola Palanza (2008) is thus on neurobehavioral effects due to developmental exposure to BPA, and the focus of the review of PBDEs by Chris Talsness (2008) is also on neurobehavioral effects due to developmental exposure. There is limited epidemiological evidence for human effects of BPA and BPDEs. However, Chris Talsness (2008) points out that BPDEs show many similarities to polychlorinated biphenyls (PCBs), for which there is a fairly large and consistent literature showing neurobehavioral effects associated with exposure during critical periods in brain development.

Exposure to all of these chemicals is ubiquitous, and studies in experimental animals lead to the prediction that combined exposure to these chemicals could have unexpected synergistic effects on the brain, reproductive system, and other systems that are impacted by gonadal steroids and thyroid hormone. The levels of BPA (Calafat et al., 2007; Vandenberg et al., 2007), phthalates (Silva et al., 2004), and BPDEs (Schecter et al., 2007; Schecter et al., 2006) in human populations have been reported. As pointed out by Chris Talsness (2008) in her review, biomonitoring studies show that levels of PBDEs are high and increasing, and Shanna Swan (2008) describes the ubiquitous exposure to many types of phthalates. In contrast, limiting the use of BPA in some products in Japan has been suggested to be the basis for a decrease in BPA levels in urine in Japan (Matsumoto et al., 2003).

While mixture studies with combinations of BPA, PBDEs, phthalates, and other components of plastic have not been conducted, initial studies with mixtures discussed by Kembra Howdeshell and colleagues (2008), as well as Chris Talsness (2008) in her article, suggest that at least additive and potentially even synergistic effects will be found. This type of research is becoming recognized to be of great importance due to the increasing body burden of these chemicals, particularly in USA and Europe.

For phthalates, there is now enough epidemiological evidence that is consistent with results from animal studies for there to be a high level of concern that "the phthalate syndrome" described in rodents exposed during development of the reproductive system to the anti-androgenic phthalates (discussed by Kembra Howdeshell and colleagues, 2008) also occurs in humans, as discussed in the article by Shanna Swan (2008). The adverse reproductive effects of phthalates need to be considered in relation to the adverse effects on development of the reproductive system caused in laboratory animals by very low doses of BPA (Richter et al., 2007) that lead to blood and tissue levels of BPA that are below median levels found in every study in humans (Vandenberg et al., 2007). In addition, they need to be considered in relation to findings for phthalates such as DEHP (Andrade et al., 2006a, c) and others discussed by Kembra Howdeshell and colleagues (2008). The phthalate esters discussed here (DEHP, DBP, BBP, and DINP) have in common that they interfere with the synthesis of testosterone as well as insulin-like growth factor 3 (Insl 3), and are thus of particular concern with regard to exposure of males during sexual differentiation. While less studied, effects on female sexual differentiation cannot be ruled out.

3. Workshop presentations

The degree to which plastic products can now be discussed as global pollutants is the subject of the first article "Synthetic polymers in the marine environment: A rapidly increasing, long term threat" by Charles Moore (2008). Moore provides evidence that billions of pounds of raw plastic pellets are being globally distributed in the oceans, and additional billions of pounds of post-production plastics are contaminating virtually every ecosystem in the world. Most readers will be surprised to learn that a region of the Pacific Ocean known as the Northern Pacific Gyre has experienced a dramatic increase in plastic debris over the last decade, and that there is now a far greater amount of plastic relative to living organisms in this large and expanding area of the Pacific Ocean. Of additional concern is that highly reactive non-persistent chemicals in some plastic, such as BPA, bind to persistent organic pollutants (POPs), such as dioxin and PCBs, about which much has been written with regard to the threats they pose (NRC, 1999). Water or are exposed to chemicals via trans-dermal exposure.

The second article "A critical evaluation of the environmental risk assessment for plasticizers in the freshwater environment in Europe, with special emphasis on BPA and endocrine disruption" by Jörg Oehlmann (2008) and colleagues discusses further the amounts and impacts of phthaltes, PBDEs, and BPA in aquatic ecosystems. This article also includes a discussion of the ecological risk assessment process for these chemicals conducted by the European Union, and identifies disturbing aspects of the decision making process involved in establishing safety standards for these chemicals. In addition, they discuss the impacts on aquatic species of exposure to these chemicals.

The third article "Effects of developmental exposure to bisphenol A on brain and behavior in mice" by Paola Palanza and colleagues (2008) concerns an ethotoxicological analysis of the effects on development of the brain and behavior of exposure to very low doses of BPA that result in blood levels of biologically active unconjugated BPA in mice that are within the range found in studies of BPA levels in human blood (Taylor et al., 2008; Vandenberg et al., 2007).

The fourth article "Overview of toxicological aspects of polybrominated diphenyl ethers: a flame retardant additive in several consumer products" by Chris Talsness (2008) discusses the neurobehavioral effects of BPDEs and draws attention to the similarities between PBDEs and PCBs. In contrast to BPA and phthalates, PBDEs are highly persistent environmental contaminants, and are thus labeled as POPs, which bioaccumulate and pose a long-term threat to the environment. This is also discussed in the article by Jean-François Debroux.

The fifth article "Mechanisms of action of phthalate esters, individually and in combination, to induce abnormal reproductive development in male laboratory rats" by Kembra Howdeshell and colleagues (2008) describes the developmental effects of two of the most highly used phthalates, DEHP and DBP, both of which inhibit testosterone synthesis. In addition, these phthalates inhibit the production in the fetal testicular Leydig cells of the protein insulin-like growth factor 3 (Insl 3), which is required for normal testicular descent. The range of effects identified in the studies described in rats is very similar to a complex of abnormalities in human males referred to as the "testicular dysgenesis syndrome", which includes cryptorchidism, hypospadias, and decreased sperm count. Although the exposures in humans are generally lower than the doses used in the animal studies, some people have been reported to have very high levels of these phthalates in their bodies. Findings are also described for mixtures of these two phthalates, since humans are exposed to large numbers of these chemicals, but regulatory agencies examine their potential health effects one at a time. Evidence is presented for dose additivity, which is expected for mixtures of two chemicals that act through the same mechanism.

The sixth article "Environmental phthalate exposure in relation to reproductive outcomes and other health endpoints in humans" by Shanna Swan (2008) discusses recent epidemiological findings relating levels of phthalates and the biologically active metabolites found in urine with adverse outcomes on the reproductive system in human male fetuses and in adult men. She reports on findings supporting the prediction that it is critical to look at combinations of chemicals, rather than one at a time, in determining the adverse effects of exposure during both development and in adulthood. Of great importance, the epidemiological findings discussed for phthalates lead to the conclusion that while studies relating adverse health effects to differences in exposure to BPA and PBDEs in people are needed, given the extensive evidence from studies with experimental animals for adverse effects of BPA and PBDEs, it would be unwise to wait for extensive evidence from human studies of these chemicals before taking regulatory action.

References

Akingbemi, B.T., Sottas, C.M., Koulova, A.I., Klinefelter, G.R., Hardy, M.P., 2004. Inhibition of testicular steroidogenesis by the xenoestrogen bisphenol A is associated with reduced pituitary luteinizing hormone secretion and decreased steroidogenic enzyme gene expression in rat Leydig cells. Endocrinology 145, 592–603.

Andrade, A.J., Grande, S.W., Talsness, C.E., Gericke, C., Grote, K., Golombiewski, A., Sterner-Kock, A., Chahoud, I., 2006a. A dose response study following in utero and lactational exposure to di-(2-ethylhexyl) phthalate (DEHP): reproductive effects on adult male offspring rats. Toxicology 228, 85–97.

Andrade, A.J., Grande, S.W., Talsness, C.E., Grote, K., Chahoud, I., 2006b. A dose–response study following in utero and lactational exposure to di-(2-ethylhexyl)-phthalate (DEHP): non-monotonic dose-response and low dose effects on rat brain aromatase activity. Toxicology 227, 185–192.

Andrade, A.J., Grande, S.W., Talsness, C.E., Grote, K., Golombiewski, A., Sterner-Kock, A., Chahoud, I., 2006c. A dose–response study following in utero and lactational exposure to di-(2-ethylhexyl) phthalate (DEHP): effects on androgenic status, developmental landmarks and testicular histology in male offspring rats. Toxicology 225, 64–74.

Calafat, A.M., Ye, X., Wong, L.-Y., Reidy, J.A., Needham, L.L., 2007. Exposure of the US population to bisphenol A and 4-tertiary-octylphenol: 2003–2004. Environ. Health Perspect. (Online 24 October 2007).

Canton, R.F., Sanderson, J.T., Letcher, R.J., Bergman, A., van den Berg, M., 2005. Inhibition and induction of aromatase (CYP19) activity by brominated flame retardants in H295R human adrenocortical carcinoma cells. Toxicol. Sci. 88, 447–455.

Colborn, T., vom Saal, F.S., Soto, A.M., 1993. Developmental effects of endocrine-disrupting chemicals in wildlife and humans. Environ. Health Perspect. 101, 378–384.

Howdeshell, K.L., Rider, C.V., Wilson, V.S., Gray, L.E., 2008. Mechanisms of action of phthalate esters, individually and in combination, to induce abnormal reproductive development in male laboratory rats. Environ. Res. 108, 168–176.

Markey, C.M., Wadia, P.R., Rubin, B.S., Sonnenschein, C., Soto, A.M., 2005. Long-term effects of fetal exposure to low doses of the xenoestrogen bisphenol-A in the female mouse genital tract. Biol. Reprod. 72, 1344–1351.

Matsumoto, A., Kunugita, N., Kitagawa, K., Isse, T., Oyama, T., Foureman, G.L., Morita, M., Kawamoto, T., 2003. Bisphenol A levels in human urine. Environ. Health Perspect. 111, 101–104.

Moore, C.J., 2008. Synthetic polymers in the marine environment: A rapidly increasing, long term threat. Environ. Res. 108, 131–139.

NRC, 1999. Hormonally Active Agents in the Environment. National Academy Press, Washington, DC.

Oehlmann, J., Oetken, M., Schulte-Oehlmann, U., 2008. A critical evaluation of the environmental risk assessment for plasticizers in the freshwater environment in Europe, with special emphasis on BPA and endocrine disruption. Environ. Res. 108, 140–149.

Palanza, P., Gioiosa, L., vom Saal, F.S., Parmigiani, S., 2008. Effects of developmental exposure to BPA on brain and behavior in mice. Environ. Res. 108, 150–157.

Ragiani, R., (Ed.), 2006. Proceedings of Conference International Seminar on Nuclear War and Planetary Emergencies, 27th Session, Erice, Sicily, Italy, August 19–24, 2006. World Scientific, Singapore.

Richter, C.A., Birnbaum, L.S., Farabollini, F., Newbold, R.R., Rubin, B.S., Talsness, C.E., Vandenbergh, J.G., Walser-Kuntz, D.R., vom Saal, F.S., 2007. In vivo effects of bisphenol A in laboratory rodent studies. Reprod. Toxicol. 24, 199–224.

Schecter, A., Papke, O., Harris, T.R., Tung, K.C., Musumba, A., Olson, J., Birnbaum, L., 2006. Polybrominated diphenyl ether (PBDE) levels in an expanded market basket survey of US food and estimated PBDE dietary intake by age and sex. Environ. Health Perspect. 114, 1515–1520.

Schecter, A., Johnson-Welch, S., Tung, K.C., Harris, T.R., Papke, O., Rosen, R., 2007. Polybrominated diphenyl ether (PBDE) levels in livers of US human fetuses and newborns. J. Toxicol. Environ. Health A 70, 1–6.

Silva, M.J., Barr, D.B., Reidy, J.A., Malek, N.A., Hodge, C.C., Caudill, S.P., Brock, J.W., Needham, L.L., Calafat, A.M., 2004. Urinary levels of seven phthalate metabolites in the US population from the national health and nutrition examination survey (NHANES) 1999–2000. Environ. Health Perspect. 112, 331–338.

Swan, S.H., 2008. Environmental phthalate exposure in relation to reproductive outcomes and other health endpoints in humans. Environ. Res. 108, 177–184.

Talsness, C.E., 2008. Overview of toxicological aspects of polybrominated diphenyl ethers: a flame retardant additive in several consumer products. Environ. Res. 108, 158–167.

Taylor, J.A., Welshons, W.V., vom Saal, F.S., 2008. No effect of route of exposure (oral; subcutaneous injection) on plasma bisphenol A throughout 24 h after administration in neonatal female mice. Reprod. Toxicol. 25, 169–176.

Vandenberg, L.N., Hauser, R., Marcus, M., Olea, N., Welshons, W.V., 2007. Human exposure to bisphenol A (BPA). Reprod. Toxicol. 24, 139–177.

vom Saal, F.S., Welshons, W.V., 2006. Large effects from small exposures. II. The importance of positive controls in low-dose research on bisphenol A. Environ. Res. 100, 50–76.

vom Saal, F.S., Akingbemi, B.T., Belcher, S.M., Birnbaum, L.S., Crain, D.A., Eriksen, M., Farabollini, F., Guillette Jr., L.J., Hauser, R., Heindel, J.J., Ho, S.M., Hunt, P.A.,

Iguchi, T., Jobling, S., Kanno, J., Keri, R.A., Knudsen, K.E., Laufer, H., Leblanc, G.A., Marcus, M., McLachlan, J.A., Myers, J.P., Nadal, A., Newbold, R.R., Olea, N., Prins, G.S., Richter, C.A., Rubin, B.S., Sonnenschein, C., Soto, A.M., Talsness, C.E., Vandenbergh, J.G., Vandenberg, L.N., Walser-Kuntz, D.R., Watson, C.S., Welshons, W.V., Wetherill, Y., Zoeller, R.T., 2007. Chapel Hill bisphenol A expert panel consensus statement: integration of mechanisms, effects in animals and potential to impact human health at current levels of exposure. Reprod. Toxicol. 24, 131–138.

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