BPA-RELATED RISKS

- **BPA scientific monitoring since May 2009: An overall assessment**
- **Key Findings from January to March 2012**

Réseau Environnement Santé

148 rue du Faubourg Saint-Denis
75010 PARIS
FRANCE

A/ BPA scientific monitoring since May 2009: An overall assessment

Number of studies on humans and animals

Showing effects: 256 (94 %)

- **On animals: 163 (45 of which are *in vivo* studies that used a BPA dose < ADI (EFSA))**
- **On humans: 93 (Health effects: 43 ; *In vitro* effects : 50)**

Showing no effect: 15

- **On animals: 8**
- **On humans: 7**

B/ BPA scientific monitoring from January to March 2012: A comprehensive overview

EFFECTS ON HUMANS

Adverse pathophysiological effects:

- Associations between higher BPA exposure and incident coronary artery disease CAD during >10 years of follow-up in UK showed trends similar to previously reported cross-sectional findings in the more highly exposed NHANES respondents.
- Based on the examination of 1 380 subjects from the National Health and Nutritional Examination Survey 2003-2004, urinary BPA levels are associated with hypertension, independent of traditional risk factors.
- Altered DNA methylation at various CpG sites in women undergoing in vitro fertilization was associated with exposure to mercury, lead or BPA. Further studies are needed to confirm these associations.
- The presence of unconjugated BPA (uBPA) in 152 cord blood samples suggests placental transfer and fetal exposure but similar uBPA levels in control and cryptorchid groups make the participation of fetal exposure to uBPA in the physiopathology of undescended testes unlikely.
- Low doses of bisphenol-A induce rapid reduction in the K(ATP) channel activity and insulinotropic effect in pancreatic ß-cells and islets of Langerhans in humans and rodents, with stronger actions in human islets. The results suggest that BPA behaves as a strong estrogen via nuclear ERß and indicate that results obtained with BPA in mouse ß-cells (insulin release) may be extrapolated to humans

In vitro effects:

- BPA can potentiate leptin action (cell proliferation) in human ovarian cancer cells by creating more binding sites for leptin and extending the time of leptin-induced Stat3, ERK1/2 and Akt phosphorylation.
- Low doses of bisphenol-A induce rapid reduction in the K(ATP) channel activity and insulinotropic effect in pancreatic ß-cells and islets of Langerhans in humans and rodents, with stronger actions in human islets. The results suggest that BPA behaves as a strong estrogen via nuclear ERß and indicate that results obtained with BPA in mouse ß-cells (insulin release) may be extrapolated to humans

EFFECTS ON ANIMALS

Rats:

- A nanomolar dose of bisphenol A (10nM) has rapid effects on the spinogenesis of adult rat hippocampal neurons.
- Developmental exposure of male rats to environmental doses of BPA impacts androgen secretion which, in turn, is alleviated by an increase in Leydig cell numbers. BPA causes biological effects at environmentally relevant exposure levels and its presence in consumer products potentially has implication for public health
- Perinatal exposure to low doses of BPA or DES resulted in long-lasting effects in femal rats, including delayed mammary gland differentiation, altered milk yield and modified milk composition.
- Perinatal exposure to BPA affects offspring phenotype and epigenetic regulation across multiple doses, indicating the need to evaluate dose effects in human clinical and population studies.
- Fetal exposure to plastic mixture (bisphenol A and phthalates), dioxin (TCDD) or jet fuel induce transgenerational negative effects on reproduction. The authors have identified exposure-specific epigenetic biomarkers that may allow for the assessment of ancestral environmental exposures associated with adult onset disease.

Mice:

- Prenatal exposures to BPA, followed by postnatal allergic sensitization and challenges, promote the development of experimental allergic asthma in mice.
- Environmental estrogen contaminants, such as bisphenol A, can have a detrimental effect on the developmental lumbar bone growth and mineralization in mice.

ENVIRONMENTAL EXPOSURE

Human impregnation studies:

- People with lower incomes have higher body burdens of BPA; the reverse was true for PFCs.

Environmental contamination:

- Migration tests performed on 277 baby bottles found that bottles made of PP and silicones showed a greater number of substances in the migration solutions and in greater quantity. Some substances found were not included in the Community positive list. Phtalates were also detected in silicone bottles (DiBP, DBP ans DEHP). The presence of components potentially coming from inks was also detected (potentially coming from instructions leaflets in the bottles) as well as BPA which was quantified in baby bottles made of PA, but limited to one brand (although labeled BPA free).

BPA: A GENERAL REVIEW

- Review that focuses on the developmental effects of estrogenic endocrine disrupting chemicals (EDCs), and more specifically on effects of exposure to the estrogenic EDC bisphenol A (BPA) (obesity, reproductive capacity, fetal growth).
- The report of a working group from the National Toxicology Program (NTP) concluded that type 2 diabetes and obesity could be linked to exposures to environmental chemicals.
- The available data from biomonitoring studies clearly indicate that the general population is at risk from internal exposure to unconjugated BPA and that the two toxicokinetic studies which suggested human BPA exposure is negligible have significant deficiencies and are not reliable for risk assessment.

BPA-RELATED RISKS

PEER-REVIEWED PAPERS (JANUARY-MARCH 2012)
SOURCE: PubMed

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PAPER ANALYSES

A. EFFECTS ON HUMANS

1. ADVERSE PATHOPHYSIOLOGICAL EFFECTS:

- **Asthma**

Spanier AJ, Kahn RS, Kunselman AR, Hornung R, Xu Y, Calafat AM, Lanphear BP. **Prenatal Exposure to Bisphenol A and Child Wheeze from Birth to Three Years. Environ Health Perspect.** 2012 Feb 14. [Epub ahead of print] *Penn State Hershey Medical Center*.
http://www.ncbi.nlm.nih.gov/pubmed/22334053

This prospective birth cohort study of 398 mother-infant pairs found that there is an association between wheeze from six months to three years and log-transformed BPA concentration at 16 weeks gestation only.

- **Breast cancer**

A TD, Bl S, J W, Jm H, Dsm B, E AB, G S, E B, J H, C H. **Phenol xenoestrogens and mammographic breast density**. Cancer Epidemiol Biomarkers Prev. 2012 Mar;21(3):561-2. Epub 2012 Feb 15.
http://www.ncbi.nlm.nih.gov/pubmed/22337547

This study suggests that higher serum BPA levels in postmenopausal women ages 55-70 years are associated with a clinically-relevant 5% greater breast density. Further investigation into the potential influence of BPA on breast cancer risk using human populations is warranted.

- **Coronary disease**

Melzer D, Osborne NJ, Henley WE, Cipelli R, Young A, Money C, McCormack P, Luben R, Khaw KT, Wareham NJ, Galloway TS. **Urinary bisphenol a concentration and risk of future coronary artery disease in apparently healthy men and women.** Circulation. 2012 Mar 27;125(12):1482-90. Epub 2012 Feb 21. *MB, Epidemiology and Public Health Group, Peninsula College of Medicine and Dentistry, Barrack Road, Exeter EX2 5DW, United Kingdom.*
http://www.ncbi.nlm.nih.gov/pubmed/22354940

Associations between higher BPA exposure and incident coronary artery disease CAD during >10 years of follow-up in UK showed trends similar to previously reported cross-sectional findings in the more highly exposed NHANES respondents.

- **Hypertension**

Shankar A, Teppala S. **Urinary bisphenol A and hypertension in a multiethnic sample of US adults**. J Environ Public Health. 2012;2012:481641. Epub 2012 Jan 27. *Department of Community Medicine, West Virginia University School of Medicine, Morgantown, WV 26506-9190, USA.*
http://www.ncbi.nlm.nih.gov/pubmed/22363351

Based on the examination of 1 380 subjects from the National Health and Nutritional Examination Survey 2003-2004, urinary BPA levels are associated with hypertension, independent of traditional risk factors.

- **Reproduction**

Hanna CW, Bloom MS, Robinson WP, Kim D, Parsons PJ, Vom Saal FS, Taylor JA, Steuerwald AJ, Fujimoto VY. **DNA methylation changes in whole blood is associated with exposure to the environmental contaminants, mercury, lead, cadmium and bisphenol A, in women undergoing ovarian stimulation for IVF**. Hum Reprod. 2012 Feb 29. [Epub ahead of print] *Department of Medical Genetics, University of British Columbia, Vancouver, BC V6T 1Z3, Canada.*
http://www.ncbi.nlm.nih.gov/pubmed/22381621

The authors found that altered DNA methylation at various CpG sites in women undergoing in vitro fertilization was associated with exposure to mercury, lead or BPA. Further studies are needed to confirm these associations.

- **Reproduction (cryptorchidism)**

Fénichel P, Déchaux H, Harthe C, Gal J, Ferrari P, Pacini P, Wagner-Mahler K, Pugeat M, Brucker-Davis F. **Unconjugated bisphenol A cord blood levels in boys with descended or undescended testes**. Hum Reprod. 2012 Apr;27(4):983-90. Epub 2012 Jan 20. Department of Reproductive Endocrinology, University Hospital of Nice, *06602 Nice, France.*
http://www.ncbi.nlm.nih.gov/pubmed/22267833

The presence of unconjugated BPA (uBPA) in 152 cord blood samples suggests placental transfer and fetal exposure but similar uBPA levels in the control and cryptorchid groups make the participation of fetal exposure to uBPA in the physiopathology of undescended testes unlikely.

- **Cardiovascular disease**

Olsén L, Lind L, Lind PM. **Associations between circulating levels of bisphenol A and phthalate metabolites and coronary risk in the elderly**. Ecotoxicol Environ Saf. 2012 Mar 13. [Epub ahead of print] Department of Medical Sciences, Occupational and Environmental Medicine, Uppsala University, Uppsala, Sweden.
http://www.ncbi.nlm.nih.gov/pubmed/22421452

There is a significant association between some phthalate metabolites, but not BPA, and some risk factors for coronary heart disease in subjects aged 70 years.

2. IN VITRO EFFECTS:

- **Cancer**

Qin XY, Fukuda T, Yang L, Zaha H, Akanuma H, Zeng Q, Yoshinaga J, Sone H. **Effects of bisphenol A exposure on the proliferation and senescence of normal human mammary epithelial cells.** National Institute for Environmental Studies; Tsukuba, Japan. Cancer Biol Ther. 2012 Mar 1;13(5). [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/22258036

The study suggests that the genetic and epigenetic alterations by BPA might damage human mammary epithelial cells function and result in complex activities related to cell proliferation and senescence, playing a role in mammary carcinogenesis.

Lee HR, Hwang KA, Park MA, Yi BR, Jeung EB, Choi KC. **Treatment with bisphenol A and methoxychlor results in the growth of human breast cancer cells and alteration of the expression of cell cycle-related genes, cyclin D1 and p21, via an estrogen receptor-dependent signaling pathway.** Int J Mol Med. 2012 May;29(5):883-90. doi: 10.3892/ijmm.2012.903. Epub 2012 Feb 3. *Laboratory of Veterinary Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University, Cheongju, Chungbuk 361-763, Republic of Korea.*
http://www.ncbi.nlm.nih.gov/pubmed/22307313

This study confirms the carcinogenicity of bisphenol A (BPA) and methoxychlor in vitro.

Ptak A, Gregoraszczuk EL. B**isphenol A induces leptin receptor expression, creating more binding sites for leptin, and activates the JAK/Stat, MAPK/ERK and PI3K/Akt signalling pathways in human ovarian cancer cell.** Toxicol Lett. 2012 May 5;210(3):332-7. Epub 2012 Feb 10. *Department of Physiology and Toxicology of Reproduction, Chair of Animal Physiology, Institute of Zoology, Jagiellonian University, Krakow, Poland.*
http://www.ncbi.nlm.nih.gov/pubmed/22343039

This study shows that BPA creates more binding sites for leptin (cell proliferation) and extends the time of leptin-induced Stat3, ERK1/2 and Akt phosphorylation, which may potentiate leptin action in cancer cells. Confirmation required by in vivo study.

- **Structural biology**

Liu X, Matsushima A, Nakamura M, Costa T, Nose T, Shimohigashi Y. **Fine spatial assembly for construction of the phenol-binding pocket to capture bisphenol A in the human nuclear receptor estrogen-related receptor γ.** J Biochem. 2012 Apr;151(4):403-15. Epub 2012 Jan 31. *Department of Chemistry, Laboratory of Structure-Function Biochemistry, Faculty and Graduate School of Sciences, Risk Science Research Center, Kyushu University, Fukuoka 812-8581, Japan, and Laboratorio di Farmacologia, Istituto Superiore di Sanità, Viale Regina Elena 299, Roma, Italy.*
http://www.ncbi.nlm.nih.gov/pubmed/22298789

The authors demonstrated that human estrogen-related receptor γ (ERRγ) residues are essential structural elements for the strong binding of BPA to ERRγ.

- **Hormone metabolism**

Watanabe M, Ohno S, Nakajin S. **Effects of bisphenol A on the expression of cytochrome P450 aromatase (CYP19) in human fetal osteoblastic and granulosa cell-like cell lines**. Toxicol Lett. 2012 Apr 5;210(1):95-9.

Epub 2012 Feb 4. *Department of Biochemistry, Hoshi University School of Pharmacy and Pharmaceutical Sciences, Japan.*
http://www.ncbi.nlm.nih.gov/pubmed/22327052

> *Bisphenol A (BPA) suppresses aromatase (CYP19) activity in a dose-dependent fashion in human osteoblastic (SV-HFO) and ovarian granulosa-like (KGN) cell lines.*

- **Genotoxicity**

Blasiak J, Synowiec E, Tarnawska J, Czarny P, Poplawski T, Reiter RJ. **Dental methacrylates may exert genotoxic effects via the oxidative induction of DNA double strand breaks and the inhibition of their repair**. Mol Biol Rep. 2012 Feb 12. [Epub ahead of print] *Department of Molecular Genetics, University of Lodz, Pomorska 141/143, 90-236, Lodz, Poland*
http://www.ncbi.nlm.nih.gov/pubmed/22327778

> *Dental adhesive consisting of 45% 2-hydroxyethyl methacrylate (HEMA) and 55% bisphenol A-diglycidyl dimethacrylate (Bis-GMA) induces DNA double strand breaks in cultured primary human gingival fibroblasts through oxidative mechanisms. Vitamin C or melatonin may reduce the detrimental effects induced by methacrylates applied in dentistry.*

- **Metabolic disorders**

Soriano S, Alonso-Magdalena P, García-Arévalo M, Novials A, Muhammed SJ, Salehi A, Gustafsson JA, Quesada I, Nadal A. **Rapid insulinotropic action of low doses of bisphenol-A on mouse and human islets of Langerhans: role of estrogen receptor ß.**PLoS One. 2012;7(2):e31109. Epub 2012 Feb 8. *Instituto Bioingeniería and CIBER de Diabetes y Enfermedades Metabólicas Asociadas, Universidad Miguel Hernández de Elche, Elche, Alicante, Spain.*
http://www.ncbi.nlm.nih.gov/pubmed/22347437

> *Low doses of bisphenol-A induce rapid reduction in the K(ATP) channel activity and insulinotropic effect in pancreatic ß-cells and islets of Langerhans in humans and rodents, with stronger actions in human islets. The results suggest that BPA behaves as a strong estrogen via nuclear ERß and indicate that results obtained with BPA in mouse ß-cells (insulin release) may be extrapolated to humans.*

- **Effects on genes**

Hwang KA, Hyun SH, Jeung EB, Choi KC. B**isphenol a and 17-Beta-oestradiol resulted in the gene alterations in oestrogen-receptor positive bg-1 ovarian cancer cells**. Reprod Fertil Dev. 2011 Dec;24(1):188.
Laboratory of Veterinary Biochemistry and Immunology, College of Veterinary Medicine, Chungbuk National University, Cheongju, Chungbuk 361-763 Republic of Korea.
http://www.ncbi.nlm.nih.gov/pubmed/22394875

> *The results indicate that BPA may have an oestrogenic effect by regulating E2-responsive genes in ER-positive BG-1 ovarian cancer cells and that BG-1 cells would be the best in vitro model to detect these oestrogenic endocrine disrupting chemicals.*

- **Gene expression**

Sui Y, Ai N, Park SH, Rios-Pilier J, Perkins JT, Welsh WJ, Zhou C. **Bisphenol a and its analogues activate human pregnane x receptor.** Environ Health Perspect. 2012 Mar;120(3):399-405. Epub 2012 Jan 3. *Graduate Center for Nutritional Sciences, University of Kentucky, Lexington, Kentucky, USA.*
http://www.ncbi.nlm.nih.gov/pubmed/22214767

BPA and several of its analogues are potent agonists for human PXR (hPXR) but do not affect mouse PXR activity. Activation of PXR by BPA may explain some of the adverse effects of BPA in humans.

B. EFFECTS ON ANIMALS

a) RATS:

- **Cancer: signalisation**

Watson CS, Jeng YJ, Hu G, Wozniak A, Bulayeva N, Guptarak J. **Estrogen- and xenoestrogen-induced ERK signaling in pituitary tumor cells involves estrogen receptor-α interactions with G protein-αi and caveolin I.** Steroids. 2012 Apr;77(5):424-32. Epub 2011 Dec 30. *Dept. of Biochemistry & Molecular Biology, Univ. of Texas Medical Branch, Galveston, TX 77555-0645, USA.*
http://www.ncbi.nlm.nih.gov/pubmed/22230296

This study shows that Xenoestrogens, like physiologic estrogens, can evoke downstream kinase signaling involving selective interactions of ERa with G(□i) and caveolin I, which could explain their disruptive actions.

- **Genotoxicity**

Tiwari D, Kamble J, Chilgunde S, Patil P, Maru G, Kawle D, Bhartiya U, Joseph L, Vanage G. **Clastogenic and mutagenic effects of bisphenol A: An endocrine disruptor.** Mutat Res. 2012 Mar 18;743(1-2):83-90. Epub 2012 Jan 9. National Center for Preclinical Reproductive and Genetic Toxicology, National Institute for Research in Reproductive Health, J.M. Street, Parel, Mumbai 400012, India.
http://www.ncbi.nlm.nih.gov/pubmed/22245107

In this study, adult male and female rats were orally administered with various doses of BPA (2.4µg, 10µg, 5mg and 50mg/kgbw) once a day for six consecutive days. Then, in-vivo and in-vitro assays were performed to determine genotoxic and mutagenic effects of BPA. The data obtained clearly documents that BPA is not mutagenic but exhibits genotoxic activity and oxidative stress could be one of the mechanisms leading to genetic toxicity.

- **Nervous system**

Tanabe N, Yoshino H, Kimoto T, Hojo Y, Ogiue-Ikeda M, Shimohigashi Y, Kawato S. **Nanomolar dose of bisphenol A rapidly modulates spinogenesis in adult hippocampal neurons.** Mol Cell Endocrinol. 2012 Apr 4;351(2):317-25. Epub 2012 Jan 16. *Department of Biophysics and Life Sciences, Graduate School of Arts and Sciences, The University of Tokyo, Komaba 3-8-1, Meguro, Tokyo 153-8902, Japan.*
http://www.ncbi.nlm.nih.gov/pubmed/22281313

This study demonstrates that a nanomolar dose of bisphenol A (10nM) has rapid effects on the spinogenesis of adult rat hippocampal neurons.

- **Hormone disruption mechanism**

Quignot N, Arnaud M, Robidel F, Lecomte A, Tournier M, Cren-Olivé C, Barouki R, Lemazurier E. **Characterization of endocrine-disrupting chemicals based on hormonal balance disruption in male and female adult rats.** Reprod Toxicol. 2012 Jan 21. [Epub ahead of print] *Experimental Toxicology Unit, INERIS, Parc Technologique ALATA, 60550 Verneuil-en-Halatte, France.*
http://www.ncbi.nlm.nih.gov/pubmed/22285353

This study shows that atrazine, vinclozolin, methoxychlor, and bisphenol A have different aromatase regulation profiles between animals with similar estrogen-to-androgen ratios but with different chemical treatments. The measurement of many endpoints is necessary for good risk assessment.

- **Reproduction**

Nanjappa MK, Simon L, Akingbemi BT. **The Industrial Chemical Bisphenol A (BPA) Interferes with Proliferative Activity and Development of Steroidogenic Capacity in Rat Leydig Cells**. Biol Reprod. 2012 Feb 1. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/22302688

Developmental exposure of male rats to environmental doses of BPA impacts androgen secretion which, in turn, is alleviated by an increase in Leydig cell numbers. BPA causes biological effects at environmentally relevant exposure levels and its presence in consumer products potentially has implication for public health.

- **Effects on mammary gland**

Kass L, Altamirano GA, Bosquiazzo VL, Luque EH, Muñoz-de-Toro M. **Perinatal exposure to xenoestrogens impairs mammary gland differentiation and modifies milk composition in Wistar rats**. Reprod Toxicol. 2012 Feb 13. [Epub ahead of print] *Laboratorio de Endocrinología y Tumores Hormonodependientes, Facultad de Bioquimica y Ciencias Biologicas, Universidad Nacional del Litoral (UNL), Santa Fe, Argentina.*
http://www.ncbi.nlm.nih.gov/pubmed/22349186

This study found that perinatal exposure to low doses of BPA or DES resulted in long-lasting effects in femal rats, including delayed mammary gland differentiation, altered milk yield and modified milk composition.

- **Développement**

Jones BA, Watson NV. **Perinatal BPA exposure demasculinizes males in measures of affect but has no effect on water maze learning in adulthood**. Horm Behav. 2012 Apr;61(4):605-10. Epub 2012 Feb 17.
http://www.ncbi.nlm.nih.gov/pubmed/22370244

Perinatal BPA exposure interferes with the normal development of affective behaviors in a non-linear, dose-dependent manner, which corresponds to behavioral demasculinization of adult males.

- **Transgenerational effects**

Anderson OS, Nahar MS, Faulk C, Jones TR, Liao C, Kannan K, Weinhouse C, Rozek LS, Dolinoy DC. **Epigenetic responses following maternal dietary exposure to physiologically relevant levels of bisphenol A.** Environ Mol Mutagen. 2012 Mar 29. doi: 10.1002/em.21692. [Epub ahead of print] *Department of Environmental Health Sciences, University of Michigan, Ann Arbor, Michigan.*
http://www.ncbi.nlm.nih.gov/pubmed/22467340

Perinatal exposure to BPA affects offspring phenotype and epigenetic regulation across multiple doses, indicating the need to evaluate dose effects in human clinical and population studies.

- Tran**sgenerational effects (reproduction)**

Manikkam M, Guerrero-Bosagna C, Tracey R, Haque MM, Skinner MK. **Transgenerational actions of environmental compounds on reproductive disease and identification of epigenetic biomarkers of ancestral exposures.** PLoS One. 2012;7(2):e31901. Epub 2012 Feb 28. *Center for Reproductive Biology, School of Biological Sciences, Washington State University, Pullman, Washington, United States of America.*
http://www.ncbi.nlm.nih.gov/pubmed/22389676

Fetal exposure to plastic mixture (bisphenol A and phthalates), dioxin (TCDD) or jet fuel induce transgenerational negative effects on reproduction. The authors have identified exposure-specific epigenetic biomarkers that may allow for the assessment of ancestral environmental exposures associated with adult onset disease.

- **Modelisation /cocktail effect on human**

Christiansen S, Kortenkamp A, Axelstad M, Boberg J, Scholze M, Jacobsen PR, Faust M, Lichtensteiger W, Schlumpf M, Burdorf A, Hass U. **Mixtures of endocrine disrupting contaminants modelled on human high end exposures: an exploratory study in rats**. Int J Androl. 2012 Feb 28. doi: 10.1111/j.1365-2605.2011.01242.x. [Epub ahead of print] *National Food Institute, Technical University of Denmark, Division of Toxicology and Risk Assessment, Søborg, Denmark Institute for the Environment, Brunel University, Kingston Lane, Uxbridge, Middlesex, UK F+B Environmental Consulting, Bremen, Germany GREEN Tox and University of Zurich, Zurich, Switzerland Department of Public Health, Erasmus MC, Rotterdam, The Netherlands.*
http://www.ncbi.nlm.nih.gov/pubmed/22372636

This study suggests that women of reproductive age may not be protected sufficiently against the combined effects of chemicals that affect the hormonal milieu required for normal male sexual differentiation.

b) MICE :

- **Cytotoxicity and genotoxicity (*in vitro)***

Li YC, Kuan YH, Huang FM, Chang YC. **The role of DNA damage and caspase activation in cytotoxicity and genotoxicity of macrophages induced by bisphenol-A-glycidyldimethacrylate**. Int Endod J. 2012 Jan 14. doi: 10.1111/j.1365-2591.2011.02001.x. [Epub ahead of print] *Department of Pharmacology, Chung Shan Medical University Department of Dentistry, Chung Shan Medical University Hospital School of Dentistry, Chung Shan Medical University, Taichung, Taiwan.*
http://www.ncbi.nlm.nih.gov/pubmed/22242562

BisGMA demonstrated a cytotoxic and genotoxic effects on murine macrophage cell line RAW264.7 which are mediated by DNA damage and caspase activation.

- **Protective Effects of Ginsenosides**

Wang L, Hao J, Hu J, Pu J, Lü Z, Zhao L, Wang Q, Yu Q, Wang Y, Li G. **Protective Effects of Ginsenosides against Bisphenol A-Induced Cytotoxicity in 15P-1 Sertoli Cells via Extracellular Signal-Regulated Kinase 1/2 Signalling and Antioxidant Mechanisms.** Basic Clin Pharmacol Toxicol. 2012 Jan 23. doi: 10.1111/j.1742-7843.2012.00857.x. [Epub ahead of print] *Institute of Life Sciences, Chongqing Medical University, Chongqing, China.*
http://www.ncbi.nlm.nih.gov/pubmed/22269103

Ginsenosides have protective effects against BPA-induced cell damage.

- **Mutagenic, genotoxic and reproductive effects**

Dobrzyńska MM, Radzikowska J. **Genotoxicity and reproductive toxicity of bisphenol A and X-ray/bisphenol A combination in male mice.** Drug Chem Toxicol. 2012 Jan 21. [Epub ahead of print] Department of Radiation Protection and Radiobiology, National Institute of Public Health-National Institute of Hygiene , Warsaw , Poland.
http://www.ncbi.nlm.nih.gov/pubmed/22263531

Both X-rays and BPA administered alone to male mice decreased sperm count and quality. X-rays induced DNA strand breaks in spleen cells, whereas BPA induced DNA strand breaks in lymphocytes and in cells from spleen, kidneys, and lung and in germ cells. Results confirmed the mutagenic ability of BPA which is genotoxic and reprotoxic.

- **Diabetes**

Batista TM, Alonso-Magdalena P, Vieira E, Amaral ME, Cederroth CR, Nef S, Quesada I, Carneiro EM, Nadal A. **Short-term treatment with bisphenol-a leads to metabolic abnormalities in adult male mice**. PLoS One. 2012;7(3):e33814. Epub 2012 Mar 28. *Departamento de Anatomia, Biologia Celular, Fisiologia e Biofísica, Instituto de Biologia, Universidade Estadual de Campinas, UNICAMP, Campinas, Sao Paulo, Brazil.*
http://www.ncbi.nlm.nih.gov/pubmed/22470480

Short-term treatment with low doses of BPA slows down whole body energy metabolism and disrupts insulin signaling in peripheral tissues in mice. These findings support the notion that BPA can be considered a risk factor for the development of type 2 diabetes.

- **Cytotoxicity of dental materials (BisGMA)**

Kuan YH, Li YC, Huang FM, Chang YC. **The upregulation of tumour necrosis factor-α and surface antigens expression on macrophages by bisphenol A-glycidyl-methacrylate**. Int Endod J. 2012 Jan 23. doi: 10.1111/j.1365-2591.2012.02017.x. [Epub ahead of print] *Department of Pharmacology, Chung Shan Medical University, Taichung Department Dentistry, Chung Shan Medical University Hospital, Taichung School of Dentistry, Chung Shan Medical University, Taichung, Taiwan.*
http://www.ncbi.nlm.nih.gov/pubmed/22268514

BisGMA is cytotoxic to murine macrophage cell line RAW264.7. When exposed to BisGMA, the ability of macrophages to induce an appropriate immune response has the potential to upregulate tumour necrosis factor-a production and expression of surface antigens.

- **Asthma**

Nakajima Y, Goldblum RM, Midoro-Horiuti T. **Fetal exposure to bisphenol A as a risk factor for the development of childhood asthma: an animal model study.** Environ Health. 2012 Feb 21;11:8. *Departments of Pediatrics and Biochemistry and Molecular Biology, The University of Texas Medical Branch, 301 University Boulevard, Galveston, TX, 77555-0366, USA.*
http://www.ncbi.nlm.nih.gov/pubmed/22353195

Prenatal exposures to BPA, followed by postnatal allergic sensitization and challenges, promote the development of experimental allergic asthma in mice.

- **Reproduction**

Nah WH, Park MJ, Gye MC. **Effects of early prepubertal exposure to bisphenol A on the onset of puberty, ovarian weights, and estrous cycle in female mice**. Clin Exp Reprod Med. 2011 Jun;38(2):75-81. Epub 2011 Jun 30. *Department of Life Sciences and Institute for Natural Sciences, Hanyang University, Seoul, Korea.*
http://www.ncbi.nlm.nih.gov/pubmed/22384422

Early prepubertal exposure to BPA accelerated the onset of puberty but decreased reproductive parameters in female mice.

Karavan JR, Pepling ME. **Effects of estrogenic compounds on neonatal oocyte development.** Reprod Toxicol. 2012 Mar 3. [Epub ahead of print] *Syracuse University, Syracuse, NY, United States.*
http://www.ncbi.nlm.nih.gov/pubmed/22406039

Exposure of neonatal mice to synthetic estrogens, diethylstilbestrol, ethinyl estradiol and bisphenol A altered cyst breakdown, oocyte survival and follicle development.

- **Effects on the musculoskeletal system**

Al Rowas S, Haddad R, Gawri R, Al Ma'awi A, Chalifour L, Antoniou J, Mwale F. **Effect of in utero exposure to diethystilbesterol on lumbar and femoral bone, articular cartilage and the intervertebral disc in male and female adult mice progeny with and without swimming exercise**. Arthritis Res Ther. 2012 Jan 23;14(1):R17. [Epub ahead of print]
http://www.ncbi.nlm.nih.gov/pubmed/22269139

This study suggests that environmental estrogen contaminants can have a detrimental effect on the developmental lumbar bone growth and mineralization in mice. Further studies measuring the impact of environmental estrogen mimics, such as bisphenol A, are then warranted.

- **Nervous system**

Komada M, Asai Y, Morii M, Matsuki M, Sato M, Nagao T. **Maternal bisphenol A oral dosing relates to the acceleration of neurogenesis in the developing neocortex of mouse fetuses**. Toxicology. 2012 May

16;295(1-3):31-8. Epub 2012 Mar 7. *Division of Cell Biology and Neuroscience, Department of Morphological and Physiological Sciences, Faculty of Medical Sciences, University of Fukui, Eiheiji-cho, Fukui 910-0337, Japan; Research and Education Program for Life Science, University of Fukui, Fukui, Fukui 910-8507, Japan.*

> *Maternal oral exposure to BPA related to the disruption of the cell cycle in fetal intermediate progenitor cells (IPCs) and the effects of neurogenesis in the developing neocortex.*

- **Uterine infection**

Kendziorski JA, Kendig EL, Gear RB, Belcher SM. **Strain specific induction of pyometra and differences in immune responsiveness in mice exposed to 17α-ethinyl estradiol or the endocrine disrupting chemical bisphenol A.** Reprod Toxicol. 2012 Mar 10. [Epub ahead of print] *Department of Pharmacology and Cell Biophysics, University of Cincinnati College of Medicine, Cincinnati, OH 45267-0575, United States.*
http://www.ncbi.nlm.nih.gov/pubmed/22429997

> *Exposure to low doses of 17a-éthinyl oestradiol (EE) or BPA induces pyometra (uterine infection) in C57BL/6 mice but not in CD1 mice.*

- **Calcic absorption**

Otsuka H, Sugimoto M, Ikeda S, Kume S. **Effects of bisphenol A administration to pregnant mice on serum Ca and intestinal Ca absorption.** Anim Sci J. 2012 Mar;83(3):232-7. doi: 10.1111/j.1740-0929.2011.00947.x. Epub 2011 Sep 12. *Graduate School of Agriculture, Kyoto University, Sakyo, Kyoto, Japan.*
http://www.ncbi.nlm.nih.gov/pubmed/22435627

> *This study shows that BPA administration at 20mg/kg body weight/day during pregnancy decreases serum calcium (Ca) in pre-delivery mice, which may be partly due to decreased paracellular Ca absorption.*

c) MONKEY

- **Effects on thyroid hormone (*In vitro*)**

Sheng ZG, Tang Y, Liu YX, Yuan Y, Zhao BQ, Chao XJ, Zhu BZ. **Low concentrations of bisphenol a suppress thyroid hormone receptor transcription through a nongenomic mechanism**. Toxicol Appl Pharmacol. 2012 Feb 15;259(1):133-42. Epub 2011 Dec 28. *State Key Laboratory of Environmental Chemistry and Ecotoxicology, Research Center for Eco-Environmental Science, Chinese Academy of Sciences, 18 Shuangqing Road, Beijing 100085, PR China.*
http://www.ncbi.nlm.nih.gov/pubmed/22227104

> *The results of this study indicate that low concentrations of BPA suppress the thyroid hormone receptor (TR) transcription by disrupting physiologic concentrations of T3/T4-mediated β3 integrin/c-Src/MAPK/TR-β1 pathways, followed by recruiting N-CoR/SMRT to TR-β1, providing a novel insight regarding the TH disruption effects of low concentration BPA.*

d) FOWL

➢ **Feminization**

Oshima A, Yamashita R, Nakamura K, Wada M, Shibuya K. **In ovo exposure to nonylphenol and bisphenol A resulted in dose-independent feminization of male gonads in Japanese quail (Coturnix japonica) embryos**. Environ Toxicol Chem. 2012 Mar 2. doi: 10.1002/etc.1787. [Epub ahead of print] Nippon Institute for Biological Science, Ome, Tokyo, Japan.
http://www.ncbi.nlm.nih.gov/pubmed/22447559

Injection of BPA or nonylphenol into the eggs of Japanese quail just before incubation revealed that both substances have a dose-independent potential of ovotestis induction (feminization of the male gonad) in the Japanese quail embryo.

E) FISH AND AMPHIBIANS

➢ **Thyroid metabolism**

Pelayo S, Oliveira E, Thienpont B, Babin PJ, Raldúa D, André M, Piña B. **Triiodothyronine-induced changes in the zebrafish transcriptome during the eleutheroembryonic stage: Implications for bisphenol A developmental toxicity**. Aquat Toxicol. 2012 Apr;110-111:114-22. Epub 2011 Dec 31. *Institute of Environmental Assessment and Water Research (IDAEA-CSIC), Jordi Girona, 18, 08034 Barcelona, Spain.*
http://www.ncbi.nlm.nih.gov/pubmed/22281776

The results suggest that BPA disrupts thyroid function by potentiating the effect of endogenous T3 in early development.

➢ **Ecotoxicology**

Chow WS, Chan WK, Chan KM**. Toxicity assessment and vitellogenin expression in zebrafish (Danio rerio) embryos and larvae acutely exposed to bisphenol A, endosulfan, heptachlor, methoxychlor and tetrabromobisphenol A.** J Appl Toxicol. 2012 Feb 21. doi: 10.1002/jat.2723. [Epub ahead of print] *Biochemistry Program, School of Life Sciences, Faculty of Science, The Chinese University of Hong Kong, Sha Tin, N.T., Hong Kong, SAR, China.*
http://www.ncbi.nlm.nih.gov/pubmed/22351617

The use of vitellogenin mRNA induction in zebrafish embryos and larvae was found to be a sensitive biomarker of exposure to organochlorine pesticides tetrabromobisphenol A (flame retardant), and its precursor compound bisphenol A.

a) INSECTS / WATER SNAILS

➢ **Ecotoxiclogy**

Martínez-Guitarte JL, Planelló R, Morcillo G. **Overexpression of long non-coding RNAs following exposure to xenobiotics in the aquatic midge Chironomus riparius**. Aquat Toxicol. 2012 Apr;110-111:84-90. Epub 2012 Jan 5. *Grupo de Biología y Toxicología Ambiental, Facultad de Ciencias, Universidad Nacional de Educación a Distancia, UNED, Senda del Rey 9, 28040 Madrid, Spain.*
http://www.ncbi.nlm.nih.gov/pubmed/22277249

This study shows that Bisphenol A has the ability to activate non-coding sequences mainly located at telomeres and centromeres. It provides evidence that xenobiotics can induce specific responses in ncRNAs derived from repetitive sequences that could be relevant in the toxic response.

- **Ecotoxicology**

Sánchez-Argüello P, Aparicio N, Fernández C. **Linking embryo toxicity with genotoxic responses in the freshwater snail Physa acuta: Single exposure to benzo(a)pyrene, fluoxetine, bisphenol A, vinclozolin and exposure to binary mixtures with benzo(a)pyrene**. Ecotoxicol Environ Saf. 2012 Mar 12. [Epub ahead of print] *Laboratory for Ecotoxicology, Department of the Environment, INIA, Crta, A Coruña km 7, 28040 Madrid, Spain.*
http://www.ncbi.nlm.nih.gov/pubmed/22417675

The authors developed assays on the freshwater snail Physa acuta to address correlations between embryo toxicity and genotoxicity following waterborne pollutant exposure. The results found that benzo(a)pyrene, fluoxetine and BPA are toxic to embryos. The authors conclude that the embryo toxicity test is a starting point for the development of a life cycle test with freshwater snails even for undertaking multigeneration studies.

C. ENVIRONMENTAL EXPOSURE

HUMAN IMPREGNATION STUDIES:

- **Impregnation during pregnancy**

Braun JM, Smith KW, Williams PL, Calafat AM, Berry K, Ehrlich S, Hauser R. **Variability of Urinary Phthalate Metabolite and Bisphenol A Concentrations before and during Pregnancy**. Environ Health Perspect. 2012 Jan 19. [Epub ahead of print] Harvard University.
http://www.ncbi.nlm.nih.gov/pubmed/22262702

The study found that urinary phthalate metabolites and BPA concentrations were variable before and during pregnancy, but the magnitude of variability was biomarker specific. A single spot-urine sample adequately classified MBP and MEP concentrations during pregnancy. The present results should be replicated in other pregnancy cohorts.

- **Impregnation and social disparities**

Nelson JW, Scammell MK, Hatch EE, Webster TF. **Social disparities in exposures to bisphenol A and polyfluoroalkyl chemicals: a cross-sectional study within NHANES 2003-2006**. Environ Health. 2012 Mar 6;11:10. *Boston University School of Public Health, Department of Environmental Health, 715 Albany Street, T4W, Boston, Massachusetts 02118, USA.*
http://www.ncbi.nlm.nih.gov/pubmed/22394520

People with lower incomes had higher body burdens of BPA; the reverse was true for PFCs. For both BPA and PFCs there was smaller and less consistent associations with education and occupation.

- **Maternal and fetal impregnation / ethnicity**

Unal ER, Lynn T, Neidich J, Salazar D, Goetzl L, Baatz JE, Hulsey TC, Van Dolah R, Guillette LJ Jr, Newman R. **Racial disparity in maternal and fetal-cord bisphenol A concentrations**. J Perinatol. 2012 Mar 8. doi: 10.1038/jp.2012.12. [Epub ahead of print] *Department of Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Medical University of South Carolina, Charleston, SC, USA.*
http://www.ncbi.nlm.nih.gov/pubmed/22402483

The authors found significant racial/ethnic differences in maternal/fetal BPA concentrations. African-Americans had the highest maternal serum concentrations; Hispanics had higher fetal concentrations than non-Hispanics.

- **Swedish population**

Gyllenhammar I, Glynn A, Darnerud PO, Lignell S, van Delft R, Aune M. **4-Nonylphenol and bisphenol A in Swedish food and exposure in Swedish nursing women**. Environ Int. 2012 Mar 29;43C:21-28. [Epub ahead of print] *National Food Agency, P.O. Box 622, 751 26 Uppsala, Sweden.*
http://www.ncbi.nlm.nih.gov/pubmed/22466019

This study found that food is a source of BPA and 4-Nonylphenol (NP) in the general Swedish population and that there is a continuous source of exposure to those pollutants that is high enough for free NP and BPA to be detected in some consumers.

- **Dental composite fillings**

Chung SY, Kwon H, Choi YH, Karmaus W, Merchant AT, Song KB, Sakong J, Ha M, Hong YC, Kang D. **Dental composite fillings and bisphenol A among children: a survey in South Korea**. Int Dent J. 2012 Apr;62(2):65-69. doi: 10.1111/j.1875-595X.2011.00089.x. *Department of Preventive Dentistry, School of Dentistry, Kyungpook National University, Daegu, South Korea Department of Preventive Medicine, College of Medicine, Dankook University, Choongnam, South Korea Department of Epidemiology and Biostatistics, Arnold School of Public Health, University of South Carolina, Columbia, SC, USA*
http://www.ncbi.nlm.nih.gov/pubmed/22420473

This study, conducted on a total of 495 children aged 8-9 years, found that having many dental composite filling surfaces on teeth may increase the urinary BPA concentration in children.

- **Bioaccumulation**

Geens T, Neels H, Covaci A. **Distribution of bisphenol-A, triclosan and n-nonylphenol in human adipose tissue, liver and brain.** Chemosphere. 2012 May;87(7):796-802. Epub 2012 Jan 24. *Toxicological Centre, Department of Pharmaceutical Sciences, University of Antwerp, Belgium.*
http://www.ncbi.nlm.nih.gov/pubmed/22277880

BPA could be detected in almost all adipose tissue, liver and brain samples from 11 individuals. Its potential for bioaccumulation is low though. The reported concentrations of free BPA in the various tissues are in slight disagreement with pharmacokinetic models in humans and rats.

ENVIRONMENTAL CONTAMINATION

- **Baby bottles**

Simoneau C, Van den Eede L, Valzacchi S. **Identification and quantification of the migration of chemicals from plastic baby bottles used as substitutes for polycarbonate**. Food Addit Contam Part A Chem Anal Control Expo Risk Assess. 2012;29(3):469-80. doi: 10.1080/19440049.2011.644588. Epub 2012 Jan 18. *European Commission, Joint Research Centre, Institute for Health and Consumer Protection, Unit Chemical Assessment and Testing, Italy.*
http://www.ncbi.nlm.nih.gov/pubmed/22257226

> *Migration tests performed on 277 baby bottles found that bottles made of PP and silicones showed a greater number of substances in the migration solutions and in greater quantity (alkanes and benzene derivatives). Some substances found were not included in the Community positive list. Phtalates were also detected in silicone bottles (DiBP, DBP ans DEHP). The presence of components potentially coming from inks was also detected (potentially coming from instructions leaflets in the bottles) as well as BPA which was quantified in baby bottles made of PA, but limited to one brand (although labeled BPA free) .*

- **Food**

Gyllenhammar I, Glynn A, Darnerud PO, Lignell S, van Delft R, Aune M. **4-Nonylphenol and bisphenol A in Swedish food and exposure in Swedish nursing women**. Environ Int. 2012 Mar 29;43C:21-28. [Epub ahead of print] *National Food Agency, P.O. Box 622, 751 26 Uppsala, Sweden.*
http://www.ncbi.nlm.nih.gov/pubmed/22466019

> *This study found that food is a source of BPA and 4-Nonylphenol (NP) in the general Swedish population and that there is a continuous source of exposure to those pollutants that is high enough for free NP and BPA to be detected in some consumers.*

- **Dentistery**

Michelsen VB, Kopperud HB, Lygre GB, Björkman L, Jensen E, Kleven IS, Svahn J, Lygre H. **Detection and quantification of monomers in unstimulated whole saliva after treatment with resin-based composite fillings in vivo.** Eur J Oral Sci. 2012 Feb;120(1):89-95. doi: 10.1111/j.1600-0722.2011.00897.x. Epub 2012 Jan 25. *Department of Clinical Dentistry, University of Tromsø, Tromsø, Norway.*
http://www.ncbi.nlm.nih.gov/pubmed/22288926

> *Monomers from resin-based composite materials used in dentistry such as bisphenol-A diglycidyl methacrylate (Bis-GMA) are detected in the saliva of patients shortly after restorative therapy. One week after treatment, no monomers could be detected in patients' saliva samples.*

Hsu WY, Wang VS, Lai CC, Tsai FJ. **Simultaneous determination of components released from dental composite resins in human saliva by liquid chromatography/multiple-stage ion trap mass spectrometry**. Electrophoresis. 2012 Feb;33(4):719-25. doi: 10.1002/elps.201100571. *Department of Medical Research, China Medical University Hospital, Taichung, Taiwan.*
http://www.ncbi.nlm.nih.gov/pubmed/22451066

This study was able to successfully quantify monomers (TEGDMA, UDMA, et Bis-GMA) and their principal biodegradation products from dental composite resins in human saliva.

- **Consumer Products**

Dodson RE, Nishioka M, Standley LJ, Perovich LJ, Brody JG, Rudel RA**. Endocrine Disruptors and Asthma-Associated Chemicals in Consumer Products.** Environ Health Perspect. 2012 Mar 8. [Epub ahead of print] *Silent Spring Institute.*
http://www.ncbi.nlm.nih.gov/pubmed/22398195

The authors found 55 endocrine disruptors and asthma-related chemicals in a range of cosmetics, personal care products, cleaners, sunscreens, and vinyl products, many of which were not listed on labels.

- **Seawater**

Salgueiro-González N, Concha-Graña E, Turnes-Carou I, Muniategui-Lorenzo S, López-Mahía P, Prada-Rodríguez D. **Determination of alkylphenols and bisphenol A in seawater samples by dispersive liquid-liquid microextraction and liquid chromatography tandem mass spectrometry for compliance with environmental quality standards (Directive 2008/105/EC).** J Chromatogr A. 2012 Feb 3;1223:1-8. Epub 2011 Dec 9. *Department of Analytical Chemistry, University of A Coruña, Campus da Zapateira, Rúa da Fraga 10, E-15008 A Coruña, Spain.*
http://www.ncbi.nlm.nih.gov/pubmed/22227360

A new sensitive and green analytical chemistry method was used to detect the presence of BPA (0.035 μg L^{-1}) and nonylphenol (0.14 μg L^{-1}) in seawater samples from different sites of A Coruña (Northwest of Spain).

- **Seawater and** outfall **discharges (Spain)**

de los Ríos A, Juanes JA, Ortiz-Zarragoitia M, López de Alda M, Barceló D, Cajaraville MP. **Assessment of the effects of a marine urban outfall discharge on caged mussels using chemical and biomarker analysis**. Mar Pollut Bull. 2012 Mar;64(3):563-73. Epub 2012 Jan 31. *Laboratory of Cell Biology and Histology, Science and Technology Faculty, University of the Basque Country, Sarriena z/g, Leioa, Basque Country, Spain.*
http://www.ncbi.nlm.nih.gov/pubmed/22296624

There were no significant differences in contamination levels by EDs between the environmental mixing zone of the outfall of the Santander sanitation system and control sites except for 4-tert-octylphenol which was higher in the outfall site.

- **Source waters (Spain)**

Bono-Blay F, Guart A, de la Fuente B, Pedemonte M, Pastor MC, Borrell A, Lacorte S. **Survey of phthalates, alkylphenols, bisphenol A and herbicides in Spanish source waters intended for bottling.** Environ Sci Pollut Res Int. 2012 Mar 16. [Epub ahead of print] *Department of Environmental Chemistry, IDAEA-CSIC, Jordi Girona 18-26, 08034, Barcelona, Catalonia, Spain.*
http://www.ncbi.nlm.nih.gov/pubmed/22421799

Bisphenol a, triazine herbicides, alkylphenols, and phthalates were detected in a very low concentration in a few water sources intended for bottling in Spain. Spring water intended for consumption remains of good quality.

- **Sediments (Germany)**

Schmitt S, Reifferscheid G, Claus E, Schlüsener M, Buchinger S. **Effect directed analysis and mixture effects of estrogenic compounds in a sediment of the river Elbe.** Environ Sci Pollut Res Int. 2012 Mar 16. [Epub ahead of print] *Federal Institute of Hydrology, Am Mainzer Tor 1, 56068, Koblenz, Germany.*
http://www.ncbi.nlm.nih.gov/pubmed/22421800

A sediment sample from the river Elbe/Germany was found to be contaminated with xenoestrogens: 17β-estradiol, estrone, 4-iso-nonylphenols, bisphenol A, stigmasterol and chlorophene.

- **Sediments (China)**

Li Y, Hu XF, Oh K, Motegi M, Ohtsuka N, Hosono S, Du Y, Jiang Q, Li S, Feng JW. [**Spatial distribution of three endocrine disrupting chemicals in sediments of the Suzhou Creek and their environmental risks**]. Huan Jing Ke Xue. 2012 Jan;33(1):239-46. [Article in Chinese] Department of Environmental Science and Engineering, School of Environmental and Chemical Engineering, Shanghai University, Shanghai 200444, China.

Detection of endocrine disrupting chemicals (nonylphenol (NP), octylphenol (4-t-OP) and bisphenol A (BPA)), in sediments of the Suzhou Creek (China) and its branches. The accumulation of pollutants closely related to the intensity of anthropogenic activities.

- **Surface water and sediment (China)**

Wang B, Huang B, Jin W, Wang Y, Zhao S, Li F, Hu P, Pan X. **Seasonal distribution, source investigation and vertical profile of phenolic endocrine disrupting compounds in Dianchi Lake, China.** J Environ Monit. 2012 Apr 1;14(4):1274-81. Epub 2012 Mar 15. Faculty of Environment Science and Engineering, Kunming University of *Science and Technology, Kunming 650500, China.*
http://www.ncbi.nlm.nih.gov/pubmed/22421980

Pollution of Dianchi Lake, China, with phenolic endocrine disrupting compounds including nonylphenol-di-, nonylphenol-mono-ethoxylate, 4-nonylphenol, bisphenol A, 4-cumylphenol and 4-tert-octylphenol. This pollution comes mainly from industry, agriculture and daily life.

Wang G, Ma P, Zhang Q, Lewis J, Lacey M, Furukawa Y, O'Reilly SE, Meaux S, McLachlan J, Zhang S. **Endocrine disrupting chemicals in New Orleans surface waters and Mississippi Sound sediments.** J Environ Monit. 2012 Mar 22. [Epub ahead of print] *Department of Chemistry, Xavier University of Louisiana, New Orleans, LA 70125, U.S.A. gwang@xula.edu.*
http://www.ncbi.nlm.nih.gov/pubmed/22438038

Sediment from the Gulf of Mexico, New Orleans surface water, and the influent and effluent of a New Orleans municipal sewage treatment plant are contaminated with EDCs, including organochlorine pesticides, polychlorinated biphenyls, bisphenol A and steroid hormones.

Mortazavi S, Riyahi Bakhtiari A, Sari AE, Bahramifar N, Rahbarizade F. **Phenolic endocrine disrupting chemicals (EDCs) in Anzali Wetland, Iran: Elevated concentrations of 4-nonylphenol, octhylphenol and bisphenol A.** Mar Pollut Bull. 2012 Mar 27. [Epub ahead of print] Environmental Forensic Laboratory, Department of Env*ironmental Sciences, Faculty of Natural Resource and Marine Science, Tarbiat Modares University, P.O. Box 46414 356, Noor, Mazandaran, Iran.*
http://www.ncbi.nlm.nih.gov/pubmed/22459496

This study found that sediments from Anzali Wetland, Iran, are contaminated with 4-nonylphenol (4-NP), octylphenol (OP) and bisphenol A (BPA). High levels of alkylphenols and BPA were also found near urban areas.

- **Sewage sludge (California)**

Yu Y, Wu L. **Analysis of endocrine disrupting compounds, pharmaceuticals and personal care products in sewage sludge by gas chromatography-mass spectrometry**. Talanta. 2012 Jan 30;89:258-63. Epub 2011 Dec 17. Department of Environmental Sciences, University of California, Riverside, CA 92521, USA.
http://www.ncbi.nlm.nih.gov/pubmed/22284489

High concentrations of EDCs (bisphenol A, estrone, nonylphenol and octylphenol) and personal care products (acetylsalicylic acid, carbamazepine, clofibric acid, diclofenac, gemfibrozil, ibuprofen, ketoprofen, naproxen, paracetamol and triclosan) were found in sewage sludge, from sewage treatment plants in southern California.

D. METABOLISM AND BIOMONITORING

- **Excretion via sweat**

Genuis SJ, Beesoon S, Birkholz D, Lobo RA. **Human excretion of bisphenol A: blood, urine, and sweat (BUS) study.** J Environ Public Health. 2012;2012:185731. Epub 2011 Dec 27. Faculty of Medicine, University of Alberta, Edmonton, Canada.
http://www.ncbi.nlm.nih.gov/pubmed/22253637

The study shows that BPA can be found in human sweat, even in individuals with no BPA detected in their serum or urine samples. The authors conclude that Biomonitoring of BPA through blood and/or urine testing may underestimate the total body burden of this potential toxicant and that sweat analysis should be considered as an additional method for monitoring bioaccumulation of BPA in humans.

- **Pharmacokinetics**

Doerge DR, Twaddle NC, Vanlandingham M, Fisher JW. **Pharmacokinetics of bisphenol A in serum and adipose tissue following intravenous administration to adult female CD-1 mice**. Toxicol Lett. 2012 Mar 20. [Epub ahead of print] Division of Biochemical Toxicology, National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, AR 72079, United States.
http://www.ncbi.nlm.nih.gov/pubmed/22465602

The study of BPA pharmacokinetics in mice shows that less than 0.01% of the administered dose remains in adipose tissue after 24h. The authors underscore the non-persistent nature of BPA.

- **US and Canadian population exposure**

Lakind JS, Levesque J, Dumas P, Bryan S, Clarke J, Naiman DQ. **Comparing United States and Canadian population exposures from National Biomonitoring Surveys: Bisphenol A intake as a case study.** J Expo Sci Environ Epidemiol. 2012 Feb 15. doi: 10.1038/jes.2012.1. [Epub ahead of print] 1] *LaKind Associates, LLC, Catonsville, Maryland, USA [2] Department of Epidemiology and Public Health, University of Maryland School of Medicine, Baltimore, Maryland, USA [3] Department of Pediatrics, Pennsylvania State University College of Medicine, Hershey, Pennsylvania, USA.*
http://www.ncbi.nlm.nih.gov/pubmed/22333730

This study compares human exposure to BPA in the US and Canada using biomonitoring data from the American NHANES and Canadian CHMS. After they have examined CHMS and NHANES methodologies, the authors conclude that BPA intakes for both countries are below health-based guidance values set by the US, Canada and the European Food Safety Authority.

E. BPA: A GENERAL REVIEW

- **Autism**

de Cock M, Maas YG, van de Bor M. **Does perinatal exposure to endocrine disruptors induce autism spectrum and attention deficit hyperactivity disorders? Review.** Acta Paediatr. 2012 Mar 28. doi: 10.1111/j.1651-2227.2012.02693.x. [Epub ahead of print] *Department of Health and Life Sciences, VU University, Amsterdam, Netherlands.*
http://www.ncbi.nlm.nih.gov/pubmed/22458970

Perinatal exposure to EDCs such as BPA, pesticides, phthalates, PCBs etc. appears to be associated with the occurrence of autism spectrum (ASD) as well as attention deficit hyperactivity (ADHD) disorders.

- **Alternative mechanisms**

Alonso-Magdalena P, Ropero AB, Soriano S, García-Arévalo M, Ripoll C, Fuentes E, Quesada I, Nadal_A. **Bisphenol-A acts as a potent estrogen via non-classical estrogen triggered pathways.** Mol Cell Endocrinol. 2011 Dec 31. [Epub ahead of print] *Instituto de Bioingeniería and CIBERDEM, Universidad Miguel Hernández de Elche, 03202 Elche, Spain.*
http://www.ncbi.nlm.nih.gov/pubmed/22227557

This review analyzes with substantiated scientific evidence the strong estrogenic activity of BPA at very low concentrations when it acts through alternative mechanisms of action at least in certain cell types.

- **Brain Development**

Itoh K, Yaoi T, Fushiki S. **Bisphenol A, an endocrine-disrupting chemical, and brain development. Neuropathology.** 2012 Jan 12. doi: 10.1111/j.1440-1789.2011.01287.x. [Epub ahead of print] *Department of*

Pathology & Applied Neurobiology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Japan.
http://www.ncbi.nlm.nih.gov/pubmed/22239237

This review focuses on the effects of prenatal and lactational exposure to low doses of BPA on brain development in mice. Functionally, BPA exposure disturbs murine behavior accompanied with a disrupted neurotransmitter system, in the postnatal development period and in adult mice. Epigenetic alterations in promoter-associated CpG islands might underlie some of the effects on brain development.

- **Inventory of the situation in Israel**

Berman T, Amitai Y, Almog S, Richter ED. **Human biomonitoring in Israel: past, present, future. Int J Hyg Environ Health.** 2012 Feb;215(2):138-41. Epub 2012 Jan 2. P*ublic Health Services, Israel Ministry of Health, King David Street 20, Jerusalem, Israel.*
http://www.ncbi.nlm.nih.gov/pubmed/22218107

This article reports on human biomonitoring studies carried out in Israel.

- **Obesity - diabetes**

Vom Saal FS, Nagel SC, Coe BL, Angle BM, Taylor JA. **The estrogenic endocrine disrupting chemical bisphenol A (BPA) and obesity. Mol Cell Endocrinol.** 2012 May 6;354(1-2):74-84. Epub 2012 Jan 10. Division of Biological *Sciences, University of Missouri - Columbia, Columbia, MO 65211, USA.*
http://www.ncbi.nlm.nih.gov/pubmed/22249005

This review focuses on the developmental effects of estrogenic endocrine disrupting chemicals (EDCs), and more specifically on effects of exposure to the estrogenic EDC bisphenol A (BPA) (obesity, reproductive capacity, fetal growth).

Thayer KA, Heindel JJ, Bucher JR, Gallo MA. **Role of Environmental Chemicals in Diabetes and Obesity: A National Toxicology Program Workshop Report.** Environ Health Perspect. 2012 Feb 1. [Epub ahead of print] *NIEHS.*
http://www.ncbi.nlm.nih.gov/pubmed/22296744

The report of a working group from the National Toxicology Program (NTP) concluded that type 2 diabetes and obesity could be linked to exposures to environmental chemicals.

García-Mayor RV, Larrañaga Vidal A, Docet Caamaño MF, Lafuente Giménez A. **Endocrine disruptors and obesity: obesogens.** Endocrinol Nutr. 2012 Jan 31. [Epub ahead of print] *Unidad de Investigación Compartida «Obesógenos» Sergas, Servicio de Endocrinología, Diabetes, Nutrición y Metabolismo, Universidad de Vigo, Vigo, España.*
http://www.ncbi.nlm.nih.gov/pubmed/22300604

There is evidence of the obesogenic effect of polluting chemical substances (DES, genistein, bisphenol A, organotins, and phthalates) in tissues and experimental animals, but few data are available in humans.

- **Human exposure**

Vandenberg LN, Chahoud I, Heindel JJ, Padmanabhan V, Paumgartten FJ, Schoenfelder G. **Urinary, circulating, and tissue biomonitoring studies indicate widespread exposure to bisphenol A.** Cien Saude Colet. 2012 Feb;17(2):407-34. Tufts Center for Regenerative and Developmental Biology, Department of Biology, Tufts University, Medford, MA 02155, USA.
http://www.ncbi.nlm.nih.gov/pubmed/22267036

This review concludes that available data from biomonitoring studies clearly indicate that the general population is at risk from internal exposure to unconjugated BPA and that the two toxicokinetic studies which suggested human BPA exposure is negligible have significant deficiencies and are not reliable for risk assessment.

- **Dermal exposure**

Weschler CJ, Nazaroff WW. **SVOC exposure indoors: fresh look at dermal pathways**. Indoor Air. 2012 Feb 7. doi: 10.1111/j.1600-0668.2012.00772.x. [Epub ahead of print] Environmental and Occupational Health *Sciences Institute, UMDNJ-Robert Wood Johnson Medical School and Rutgers University, Piscataway, NJ, USA International Centre for Indoor Environment and Energy, Technical University of Denmark, Lyngby, Denmark*
http://www.ncbi.nlm.nih.gov/pubmed/22313149

This paper argues that human exposure to indoor pollutants through the dermal pathway is underestimated. Health consequences vary with exposure pathway. For example, an SVOC that enters the blood through the skin does not encounter the same detoxifying enzymes that an ingested SVOC.

- **Reproduction**

Mruk DD, Cheng CY. **Environmental contaminants: Is male reproductive health at risk?** Spermatogenesis. 2011 Oct;1(4):283-290. Epub 2011 Oct 1. *The Mary M. Wohlford Laboratory for Male Contraceptive Research; Center for Biomedical Research; The Population Council; New York, NY USA.*
http://www.ncbi.nlm.nih.gov/pubmed/22332111

The authors of this review discuss how environmental toxicants (cadmium, bisphenol A and lead) may affect reproductive function and how toxicant-induced damage may be effectively managed so that fertility can be maintained.

- **Cardiovascular disease**

Lind L, Lind PM. **Can persistent organic pollutants and plastic-associated chemicals cause cardiovascular disease?** J Intern Med. 2012 Feb 28. doi: 10.1111/j.1365-2796.2012.02536.x. [Epub ahead of print] From the Department of Medical Sciences Occupational and Environmental Medicine; Uppsala University, Uppsala, Sweden.
http://www.ncbi.nlm.nih.gov/pubmed/22372998

This review of the scientific literature reports that there exist associations between plastic-associated chemicals (BPA, phthalates), persistent organic pollutants, and overt cardiovascular disease.

- **Cell Signaling**

Marino M, Pellegrini M, La Rosa P, Acconcia F. **Susceptibility of estrogen receptor rapid responses to xenoestrogens: Physiological outcomes**. Steroids. 2012 Mar 5. [Epub ahead of print] *Department of Biology, University Roma TRE, viale G. Marconi, 446, I-00146 Rome, Italy.*
http://www.ncbi.nlm.nih.gov/pubmed/22410438

> *Extra-nuclear ER signals are highly susceptible to different ligands such as BPA that, by unbalancing E2-induced cell functions, drive cells to different functional endpoints.*

F. METHODOLOGY

- **Reproduction: antigestagenic effects**

Fischer L, Deppert WR, Pfeifer D, Stanzel S, Weimer M, Hanjalic-Beck A, Stein A, Straßer M, Zahradnik HP, Schaefer WR. **Potential hazards to embryo implantation: A human endometrial in vitro model to identify unwanted antigestagenic actions of chemicals**. Toxicol Appl Pharmacol. 2012 Mar 6. [Epub ahead of print] *Department of Obstetrics & Gynecology, University Hospital Freiburg, Germany.*
http://www.ncbi.nlm.nih.gov/pubmed/22414680

> *The authors developped a flexible in vitro model based on human endometrial Ishikawa cells to study quantitatively effects of antiprogestin-like chemicals on endometrial target genes. Assays found, inter alia, that 4-nonylphenol, bisphenol A and apigenin have antagonistic effects on progesterone.*

- **Potentiel de perturbation endocrinienne**

Lee HK, Kim TS, Kim CY, Kang IH, Kim MG, Kyung Jung K, Kim HS, Han SY, Yoon HJ, Rhee GS. **Evaluation of in vitro screening system for estrogenicity: comparison of stably transfected human estrogen receptor-α transcriptional activation (OECD TG455) assay and estrogen receptor (ER) binding assay**. J Toxicol Sci. 2012;37(2):431-7. *Health Effects Analysis Team, National Institute of Food and Drug Safety Evaluation, Korea.*
http://www.ncbi.nlm.nih.gov/pubmed/22467034

> *According to OECD test guideline 455(TG455), the estrogenic activity of BBP, BPA and NP are weaker than 17β-estradiol whereas DEHP, DBP and DEP did not show any estrogenicity activity in a STTA assay.*