Center for Hormonforstyrrende Stoffer

Litteraturgennemgang for perioden 1. juli – 26. september 2012

Humane studier ved Afd. for Vækst og Reproduktion, Rigshospitalet

Søgning er udført på PubMed og dækker perioden 1 juli – 26 september 2012

Følgende søgeprofil er benyttet:

Bisphenol A
Phthalat*
Paraben*
(perfluor* OR polyfluor*)
Triclocarban
Triclosan
(Flame retardant)
tributyltin
endocrine disrupters

kombineret med nedenstående tekst:

AND expos* AND (human OR men OR women OR child* OR adult* OR adolescen* OR infan*)

Limits: title/abstract, English language

For udvalgte artikler har vi i denne omgang valgt at fokusere på **kildeidentifikation**, idet der var mange relevante artikler om emnet. De engelske abstracts for øvrige relevante artikler er dog medtaget.

Udvalgte publikationer

Environ Health Perspect. 2012 Jul;120(7):935-43. Epub 2012 Feb 21.
Endocrine disruptors and asthma-associated chemicals in consumer products.
Dodson RE, Nishioka M, Standley LJ, Perovich LJ, Brody JG, Rudel RA.
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BACKGROUND: Laboratory and human studies raise concerns about endocrine disruption and asthma resulting from exposure to chemicals in consumer products. Limited labeling or testing information is available to evaluate products as exposure sources. OBJECTIVES: We analytically quantified endocrine disruptors and asthma-related chemicals in a range of cosmetics, personal care products, cleaners, sunscreens, and vinyl products. We also evaluated whether product labels provide information that can be used to select products without these chemicals. METHODS: We selected 213 commercial products representing 50 product types. We tested 42 composited samples of high-market-share products, and we tested 43 alternative products identified using criteria expected to minimize target compounds. Analytes included parabens, phthalates, bisphenol A (BPA), triclosan, ethanolamines, alkylphenols, fragrances, glycol ethers, cyclosiloxanes, and ultraviolet (UV) filters. RESULTS: We detected 55 compounds, indicating a wide range of exposures from common products. Vinyl products contained > 10% bis(2-ethylhexyl) phthalate (DEHP) and could be an important source of DEHP in homes. In other products, the highest concentrations and numbers of detects were in the fragranced products (e.g., perfume, air fresheners, and dryer sheets) and in sunscreens. Some products that did not contain the well-known endocrine-disrupting phthalates contained other less-studied phthalates (dicyclohexyl phthalate, diisononyl phthalate, and di-n-propyl phthalate; also endocrine-disrupting compounds), suggesting a substitution. Many detected chemicals were not listed on product labels. CONCLUSIONS: Common products contain complex mixtures of EDCs and asthma-related compounds. Toxicological studies of these mixtures are needed to understand their biological activity. Regarding epidemiology, our findings raise concern about potential confounding from co-occurring chemicals and misclassification due to variability in product composition. Consumers should be able to avoid some target chemicals-synthetic fragrances, BPA, and regulated active ingredients-using purchasing criteria. More complete product labeling would enable consumers to avoid the rest of the target chemicals.

Environ Int. 2012 Nov 1;48:102-8. Epub 2012 Aug 9.

Phthalates dietary exposure and food sources for Belgian preschool children and adults.

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Numerous studies have indicated that for phthalates, the intake of contaminated foods is the most important exposure pathway for the general population. Up to now, data on dietary phthalate intake are scarce and - to the authors' knowledge - not available for the Belgian population. Therefore, the purpose of this study was: (1) to assess the long-term intake of the Belgian population for eight phthalates considering different exposure scenarios (benzylbutyl phthalate (BBP); di-n-butyl phthalate (DnBP); dicyclohexyl phthalate (DCHP); di(2-ethylhexyl) phthalate (DEHP); diethyl phthalate (DEP); diisobutyl phthalate (DiBP); dimethyl phthalate (DMP), di-n-octyl phthalate (DnOP)); (2) to evaluate the intake of BBP, DnBP, DEP and DEHP against tolerable daily intake (TDI) values; and (3) to assess the contribution of the different food groups to the phthalate intake. The intake assessment was performed using two Belgian food consumption databases, one with consumption data of preschool children (2.5 to 6.5years old) and another of adults (≥15years old), combined with a database of phthalate concentrations measured in over 550 food products sold on the Belgian market. Phthalate intake was calculated using the 'Monte Carlo Risk Assessment' programme (MCRA 7.0). The intake of DEHP was the highest, followed by DiBP. The intake of BBP, DnBP and DEP was far below the TDI for both children and adults. However, for DEHP, the 99th percentile of the intake distribution of preschoolers in the worst case exposure scenario was equal to 80% of the TDI, respectively. This is not negligible, since other exposure routes of DEHP exist for children as well (e.g. mouthing of toys). Bread was the most important contributor to the DEHP intake and this may deserve further exploration, since the origin of this phthalate in bread remains unclear.

Food Chem Toxicol. 2012 Oct;50(10):3725-40. doi: 10.1016/j.fct.2012.07.059. Epub 2012 Aug 4.

A review of dietary and non-dietary exposure to bisphenol-A.

Geens T, Aerts D, Berthot C, Bourguignon JP, Goeyens L, Lecomte P, Maghuin-Rogister G, Pironnet AM, Pussemier L, Scippo ML, Van Loco J, Covaci A.

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Due to the large number of applications of bisphenol-A (BPA), the human exposure routes are multiple. We aimed to review shortly the food and non-food sources of BPA, and to evaluate their contribution to the human exposure. Food sources discussed here include epoxy resins, polycarbonate and other applications, such as paperboard and polyvinylchloride materials. Among the non-food sources, exposures through dust, thermal paper, dental materials, and medical devices were summarized. Based on the available data for these exposure sources, it was concluded that the exposure to BPA from non-food sources is generally lower than that from exposure from food by at least one order of magnitude for most studied subgroups. The use of urinary concentrations from biomonitoring studies was evaluated and the back-calculation of BPA intake seems reliable for the overall exposure assessment. In general, the total exposure to BPA is several orders of magnitude lower than the current tolerable daily intake of 50μg/kgbw/day. Finally, the paper concludes with some critical remarks and recommendations on future human exposure studies to BPA.

Chemosphere. 2012 Sep;88(11):1276-82. Epub 2012 Apr 30.

Occurrence of alternative flame retardants in indoor dust from New Zealand: indoor sources and human exposure assessment.

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Due to worldwide restrictions on polybrominated diphenyl ethers (PBDEs), the demand for alternative flame retardants (AFRs), such as organophosphate flame retardants (OPFRs), novel brominated FRs (NBFRs) and hexabromocyclododecanes (HBCDs), has recently increased. Little is known about human exposure to NBFRs

and OPFRs and that their levels in dust have been scarcely evaluated worldwide. To increase the knowledge regarding these chemicals, we measured concentrations of five major NBFRs, ten OPFRs and three HBCD isomers in indoor dust from New Zealand homes. Dust samples were taken from living room floors (n=34) and from mattresses of the same houses (n=16). Concentrations (ngg(-1)) of NBFRs were: 1,2-bis(2,4,6-tribromophenoxy)ethane (BTBPE) (<2-175), decabromodiphenyl ethane (DBDPE) (<5-1430), 2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB) (<2-2285) and bis(2-ethylhexyl)-3,4,5,6-tetrabromophthalate (TBPH) (<2-640). For OPFRs, concentrations (ngg(-1)) ranged between: tri-ethyl-phosphate (TEP) (<10-235), tri-n-butyl-phosphate (TnBP) (<20-7545), tris-(2-chloroethyl)-phosphate (TCEP) (<20-7605), tris-(1-chloro-2-propyl) phosphate (TCPP) (20-7615), tri-(2-butoxyethyl)-phosphate (TBEP) (50-27325), tris-(2,3-dichloropropyl)-phosphate (TDCPP) (20-16560), tri-phenyl-phosphate (TPhP) (20-35190), and tri-cresyl-phosphate (TCP) (<50-3760). HBCD concentrations fell in the range <2-4100ngg(-1). BTBPE, DBDPE, TBPH, TBEP, and TnBP showed significant positive correlation ($p<0.05$) between their concentrations in mattresses and the corresponding floor dust (n=16). These data were used to derive a range of plausible exposure scenarios. Although the estimated exposure is well below the corresponding reference doses (RfDs), caution is needed given the likely future increase in use of these FRs and the currently unknown contribution to human exposure by other pathways such as inhalation and diet.

J Environ Monit. 2012 Sep 22;14(9):2482-7. Epub 2012 Aug 1.

Concentrations of organophosphate esters and brominated flame retardants in German indoor dust samples.

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While it is known that the ingestion of indoor dust contributes substantially to human exposure to the recently restricted polybrominated diphenyl ethers (PBDEs), the situation for one class of potential replacements, i.e. organophosphate esters (OPEs), used in a variety of applications including as flame retardants has yet to be fully characterised. In this study, surface dust from twelve different cars from various locations throughout Germany were analysed for eight OPEs, decabromodiphenyl ethane (DBDPE), and eight PBDEs. In five cars, tris-(1,3-dichloro-2-propyl) phosphate (TDCPP) was the dominant compound with concentrations up to 620 μg g(-1) dust. High concentrations of tri-cresyl phosphate (TCP) (up to 150 μg g(-1)) were also detected in two samples of car dust. Dust from ten offices in the same building in Ludwigsburg, Germany was also analysed. In these samples, tri (2-butoxyethyl) phosphate (TBEP) predominated with an average concentration of 7.0 μg g(-1) dust, followed by tris (1-chloro-2-propyl) phosphate (TCPP) at 3.0 μg g(-1) and triphenyl phosphate (TPhP) at 2.5 μg g(-1) dust. Although caution must be exercised given the relatively small database reported here; this study provides evidence that cars and offices from Germany are significantly more contaminated with OPEs than PBDEs. Average concentrations of ΣOPEs were ten times higher in car than in office dust. This is the first study to provide data on a wide range of OPE concentrations in German indoor dust samples.

Environ Int. 2012 Aug 24;49C:1-8. [Epub ahead of print]

Country specific comparison for profile of chlorinated, brominated and phosphate organic contaminants in indoor dust. Case study for Eastern Romania, 2010.

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We have evaluated the levels and specific profiles of several organohalogenated contaminants, including organochlorine pesticides (OCPs), polychlorinated biphenyls (PCBs), and flame retardants (FRs), such as polybrominated diphenyl ethers (PBDEs), hexabromocyclododecanes (HBCDs), novel brominated FRs (NBFRs), and organophosphate FRs (OPFRs), in 47 indoor dust samples collected in 2010 from urban locations from Iasi, Eastern Romania. The dominant contaminants found in the samples were OPFRs (median sum OPFRs 7890ng/g). Surprisingly, OCPs were also measured at high levels (median 1300ng/g). Except for BDE 209 (median 275ng/g), PBDEs were present in dust samples at relatively low levels (median sum PBDEs 8ng/g). PCBs were also measured at low levels (median sum PCBs 35ng/g), while NBFRs were only occasionally detected, showing a low usage in goods present on

the Romanian market. The results of the present study evidence the existence of a multitude of chemical formulations in indoor dust. FRs are usually associated to human exposure via ingestion of dust, but other chemicals, such as OCPs, are not commonly reported in such matrix. Although OCPs were found at comparable levels with OPFRs in Romanian dust, OCPs possess a higher risk to human health due to their considerably lower reference dose (RfD) values. Indeed, the OCP exposure calculated for various intake scenarios was only 2-fold lower than the corresponding RfD. Therefore, the inclusion of OCPs as target chemicals in the indoor environment becomes important for countries where elevated levels in other environmental compartments have been previously shown.

J Expo Sci Environ Epidemiol. 2012 Jul 4. doi: 10.1038/jes.2012.67. [Epub ahead of print]

Associations between serum levels of polybrominated diphenyl ether (PBDE) flame retardants and environmental and behavioral factors in pregnant women.

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Polybrominated diphenyl ethers (PBDE) are flame retardants that were previously used in upholstery, fabrics, and household appliances. PBDEs have been linked to adverse health outcomes, including neurotoxicity, thyroid hormone dysregulation, endocrine disruption, and poor semen quality. Because PBDEs pass into placental circulation, maternal exposures can approximate fetal exposures. Our objectives were to determine whether diet and specific human behaviors were significantly associated with PBDE exposures in a cohort of pregnant women. Women between the 34th and 38th week of pregnancy were given a questionnaire about behavioral, environmental, and dietary factors and asked to provide blood samples. Serum PBDE levels were measured using GS-MS and lipid adjusted. An adjusted ordinary least squares regression model was run to identify potential associations between behaviors and serum PBDE levels. Serum concentrations of BDEs 47, 99, 100, and 153 were found above the limit of detection in at least 50% of study participants and used in our models. Associations with serum PBDEs were observed with self-reported hand-to-mouth behaviors, including biting nails and licking fingers. Serum BDE levels of 47, 99, 153, and total PBDEs were also significantly higher in those individuals owning a large-screen TV compared with those who did not. Serum PBDE levels were comparable to levels reported in the general population. Hand-to-mouth behaviors may influence serum PBDE concentrations in adults. Household electronics such as large-screen TVs appear to serve as a significant source of PBDEs in pregnant women. Together, hand-to-mouth behaviors and TV ownership may serve as a route of exposure to PBDEs in adults.

Environ Sci Technol. 2012 Aug 21;46(16):9071-9. Epub 2012 Aug 10.

Perfluorinated Alkyl Acids in Blood Serum from Primiparous Women in Sweden: Serial Sampling during Pregnancy and Nursing, And Temporal Trends 1996-2010.

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We investigated temporal trends of blood serum levels of 13 perfluorinated alkyl acids (PFAAs) and perfluorooctane sulfonamide (FOSA) in primiparous women (N = 413) from Uppsala County, Sweden, sampled 3 weeks after delivery 1996-2010. Levels of the short-chain perfluorobutane sulfonate (PFBS) and perfluorohexane sulfonate (PFHxS) increased 11%/y and 8.3%/y, respectively, and levels of the long-chain perfluorononanoate (PFNA) and perfluorodecanoate (PFDA) increased 4.3%/y and 3.8%/y, respectively. Concomitantly, levels of FOSA (22%/y), perfluorooctane sulfonate (PFOS, 8.4%/y), perfluorodecane sulfonate (PFDS, 10%/y), and perfluorooctanoate (PFOA, 3.1%/y) decreased. Thus, one or several sources of exposure to the latter compounds have been reduced or eliminated, whereas exposure to the former compounds has recently increased. We explored if maternal levels of PFOS, PFOA, and PFNA during the early nursing period are representative for the fetal development period, using serial maternal serum samples, including cord blood (N = 19). PFAA levels in maternal serum sampled during pregnancy and the nursing period as well as in cord blood were strongly correlated. Strongest correlations between cord blood levels and maternal levels were observed for maternal serum sampled shortly before or after the delivery (r = 0.70-0.89 for PFOS and PFOA). A similar pattern was observed for PFNA, although the correlations were less strong due to levels close to the method detection limit in cord blood.

PLoS One. 2012;7(8):e42474. Epub 2012 Aug 3.

Perfluorinated compounds in umbilical cord blood and adverse birth outcomes.

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BACKGROUND: Previous animal studies have shown that perfluorinated compounds (PFCs) have adverse impacts on birth outcomes, but the results have been inconclusive in humans. We investigated associations between prenatal exposure to perfluorooctanoic acid (PFOA), perfluorooctyl sulfonate (PFOS), perfluorononanoic acid (PFNA), and perfluoroundecanoic acid (PFUA) and birth outcomes. METHODS: In total, 429 mother-infant pairs were recruited from the Taiwan Birth Panel Study (TBPS). Demographic data were obtained by interviewing mothers using a structured questionnaire and birth outcomes were extracted from medical records. Cord blood was collected for PFOA, PFOS, PFNA, and PFUA analysis by ultra-high-performance liquid chromatography/tandem mass spectrometry. RESULTS: The geometric mean (standard deviation) levels of PFOA, PFOS, PFNA, and PFUA in cord blood plasma were 1.84 (2.23), 5.94 (1.95), 2.36(4.74), and 10.26 (3.07) ng/mL, respectively. Only PFOS levels were found to be inversely associated with gestational age, birth weight, and head circumference [per ln unit: adjusted β (95% confidence interval, CI) = -0.37 (-0.60, -0.13) wks, -110.2 (-176.0, -44.5) gm and -0.25 (-0.46, -0.05) cm]. Additionally, the odds ratio of preterm birth, low birth weight, and small for gestational age increased with PFOS exposure [per ln unit: adjusted odds ratio (OR) (95%CI) = 2.45 (1.47, 4.08), 2.61(0.85, 8.03) and 2.27 (1.25, 4.15)]. When PFOS levels were divided into quartiles, a dose-response relation was observed. However, PFOA, PFNA, and PFUA were not observed to have any convincing impact on birth outcomes. CONCLUSIONS: An adverse dose-dependent association was observed between prenatal PFOS exposure and birth outcomes. However, no associations were found for the other examined PFCs.

Environ Health Perspect. 2012 Aug 30. [Epub ahead of print]

Maternal Concentrations of Polyfluoroalkyl Compounds during Pregnancy and Fetal and Postnatal Growth in British Girls.

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Background. Prenatal exposures to polyfluoroalkyl compounds (PFCs) may be associated with adverse changes in fetal and postnatal growth. Objective. To explore associations of prenatal serum concentrations of perfluorooctane sulfonate (PFOS), perfluorooctanoate (PFOA), and perfluorohexane sulfonate (PFHxS) with fetal and postnatal growth in girls. Methods. We studied a sample of 447 singleton girls and their mothers participating in the Avon Longitudinal Study of Parents and Children. Data on weight and length were obtained at birth, 2, 9, and 20 months. Serum samples were obtained in 1991-1992, from mothers, during pregnancy. We explored associations between prenatal PFC concentrations and weight at birth as well as longitudinal changes in weight-for-age SD scores between birth and 20 months. Results. PFOS (median 19.6 ng/mL), PFOA (median 3.7 ng/mL), and PFHxS (median 1.6 ng/mL) were detected in 100% of samples. On average, girls born to mothers with prenatal concentrations of PFOS in the upper tertile weighed 140 grams less (95% confidence interval [CI]: -238,-42) at birth than girls born to mothers with concentrations in the lower tertile in adjusted models. Similar patterns were seen for PFOA (-133 g; 95% CI: -237, -30) and PFHxS (-108 g; 95% CI: -206, -10). At 20 months, however, girls born to mothers with prenatal concentrations of PFOS in the upper tertile weighed 580 g more (95% CI: 301, 858) when compared to those in the lower tertile. No differences in weight were found for PFOA and PFHxS. Conclusions. Girls with higher prenatal exposure to each of the PFCs examined were smaller at birth than those with lower exposure. In addition, those with higher exposure to (PFOS) were larger at 20 months.

Environ Health Perspect. 2012 Jul 23. [Epub ahead of print]

Phthalate Excretion Pattern and Testicular Function: A Study of 881 Healthy Danish Men.

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Background: In animals, some phthalates impair male reproductive development and function. Epidemiological studies have reported inconsistent evidence of associations between phthalates and markers of human testicular function. Objectives: To provide estimates of the effects of phthalate exposure on reproductive hormone levels and semen quality in healthy men. Methods: 881 men gave urine, serum and semen samples. Serum levels of testosterone (T), estradiol (E), sex hormone-binding globulin (SHBG), luteinizing hormone (LH), follicle-stimulating hormone (FSH) and inhibin-B; semen quality; and urinary concentrations of 14 phthalate metabolites, including metabolites of di-(2-ethylhexyl) phthalate (DEHP) and di-iso-nonyl phthalate (DiNP), were assessed. The proportions of DEHP and DiNP excreted as their respective primary metabolites [mono(2-ethylhexyl) phthalate, MEHP, and mono-iso-nonyl phthalate, MiNP], were calculated and expressed as %MEHP and %MiNP. Results: Free androgen index was 15% lower (95% CI: -23, -8%) for men in the highest %MiNP quartile compared to the lowest quartile ($p<0.001$) after adjusting for confounders, and 9% lower (95% CI: -16, -1%) in the highest %MEHP quartile ($p=0.02$). %MEHP and %MiNP were negatively associated with the ratio of T to LH, and FSH. %MEHP was negatively associated with total T, free T and ratio of T to E. %MiNP was positively associated with SHBG. There was little evidence of associations between urinary phthalate metabolites or sums of phthalates with reproductive hormones or semen quality Conclusion: Our data suggest that both T production and pituitary-hypothalamic feedback may be compromised in individuals excreting a high proportion of primary metabolites of long-chained phthalates relative to the proportion of secondary metabolites.

JAMA. 2012 Sep 19;308(11):1113-21.

Association between urinary bisphenol A concentration and obesity prevalence in children and adolescents.

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CONTEXT: Bisphenol A (BPA), a manufactured chemical, is found in canned food, polycarbonate-bottled liquids, and other consumer products. In adults, elevated urinary BPA concentrations are associated with obesity and incident coronary artery disease. BPA exposure is plausibly linked to childhood obesity, but evidence is lacking to date. OBJECTIVE: To examine associations between urinary BPA concentration and body mass outcomes in children. DESIGN, SETTING, AND PARTICIPANTS: Cross-sectional analysis of a nationally representative subsample of 2838 participants aged 6 through 19 years randomly selected for measurement of urinary BPA concentration in the 2003-2008 National Health and Nutrition Examination Surveys. MAIN OUTCOME MEASURES: Body mass index (BMI), converted to sex- and age-standardized z scores and used to classify participants as overweight (BMI ≥85th percentile for age/sex) or obese (BMI ≥95th percentile). RESULTS: Median urinary BPA concentration was 2.8 ng/mL (interquartile range, 1.5-5.6). Of the participants, 1047 (34.1% [SE, 1.5%]) were overweight and 590 (17.8% [SE, 1.3%]) were obese. Controlling for race/ethnicity, age, caregiver education, poverty to income ratio, sex, serum cotinine level, caloric intake, television watching, and urinary creatinine level, children in the lowest urinary BPA quartile had a lower estimated prevalence of obesity (10.3% [95% CI, 7.5%-13.1%]) than those in quartiles 2 (20.1% [95% CI, 14.5%-25.6%]), 3 (19.0% [95% CI, 13.7%-24.2%]), and 4 (22.3% [95% CI, 16.6%-27.9%]). Similar patterns of association were found in multivariable analyses examining the association between quartiled urinary BPA concentration and BMI z score and in analyses that examined the logarithm of urinary BPA concentration and the prevalence of obesity. Obesity was not associated with exposure to other environmental phenols commonly used in other consumer products, such as sunscreens and soaps. In stratified analysis, significant associations between urinary BPA concentrations and obesity were found among whites ($P < .001$) but not among blacks or Hispanics. CONCLUSIONS: Urinary BPA concentration was significantly associated with obesity in this cross-sectional study of children and adolescents. Explanations of the association cannot rule out the possibility that obese children ingest food with higher BPA content or have greater adipose stores of BPA.

Environ Health Perspect. 2012 Sep;120(9):1307-13. Epub 2012 Jun 1.

Urinary Phthalate Metabolite Concentrations and Diabetes among Women in the National Health and Nutrition Examination Survey (NHANES) 2001-2008.

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Background: Previous studies have shown that women have higher urinary concentrations of several phthalate metabolites than do men, possibly because of a higher use of personal care products. Few studies have evaluated the association between phthalate metabolites, diabetes, and diabetes-related risk factors among women.Objective: We explored the association between urinary phthalate metabolite concentrations and diabetes among women who participated in a cross-sectional study.Methods: We used urinary concentrations of phthalate metabolites, analyzed by the Centers for Disease Control and Prevention, and self-reported diabetes of 2,350 women between 20 and 79 years of age who participated in the NHANES (2001-2008). We used multiple logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) and adjusted for urinary creatinine, sociodemographic characteristics, dietary factors, and body size. A secondary analysis was conducted for women who did not have diabetes to evaluate the association between phthalate metabolite concentrations and fasting blood glucose (FBG), homeostasis model assessment-estimated insulin resistance, and glycosylated hemoglobin A1c.Results: After adjusting for potential confounders, women with higher levels of mono-n-butyl phthalate (MnBP), mono-isobutyl phthalate (MiBP), monobenzyl phthalate (MBzP), mono-(3-carboxypropyl) phthalate (MCPP), and three di-(2-ethylhexyl) phthalate metabolites (ΣDEHP) had an increased odds of diabetes compared with women with the lowest levels of these phthalates. Women in the highest quartile for MBzP and MiBP had almost twice the odds of diabetes [OR = 1.96 (95% CI: 1.11, 3.47) and OR = 1.95 (95% CI: 0.99, 3.85), respectively] compared with women in the lowest quartile. Nonmonotonic, positive associations were found for MnBP and ΣDEHP, whereas MCPP appeared to have a threshold effect. Certain phthalate metabolites were positively associated with FBG and insulin resistance.Discussion: Urinary levels of several phthalates were associated with prevalent diabetes. Future prospective studies are needed to further explore these associations to determine whether phthalate exposure can alter glucose metabolism and increase the risk of insulin resistance and diabetes.

Bruttoliste

Søgning: (bisphenol a) AND expos* AND (human OR men OR women OR child* OR adult* OR adolescen* OR infan*) udført den 4 sept (28/6 – 26/9)

Trasande L, Attina TM, Blustein J. Association between urinary bisphenol A concentration and obesity prevalence in children and adolescents. JAMA. 2012 Sep 19;308(11):1113-21.

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CEHOS Litteratur update *in vitro* og *in vivo* Juli –September 2012

DTU-Fødevareinstituttet

***In vitro* studier ved DTU-FOOD**

Søgt i Pubmed med følgende kriterier:

" Endocrine disrupt* AND in vitro*" samt "Endocrine disrupt* AND expose* AND in vitro*",

"Paraben* AND in vitro*,"perfluor* OR polyfluor* AND in vitro*" og "Phthalat* AND in vitro*".

Publiceret fra i perioden 2012/06/30 to 2012/12/31 (Juli 2012 og indtil nu)

Efter at have fjernet gengangere, fra forrige litteraturopdateringslister, gav litteratursøgningen, med de angivne søgekriterier, tilsammen en liste med i alt 46 artikler:

Udvalgte publikationer:

To artikler er blevet udvalgt til nærmere beskrivelse baseret på, at de beskrevne resultater bidrager til ny eller mere viden omkring effekterne eller virkningsmekanismerne for den eller de beskrevede hormonforstyrrende stoffer.

Effects of Selected **Phytoestrogens** and Their Mixtures on the Function of the Thyroid Hormone and the Aryl Hydrocarbon Receptor.
Long M, Krüger T, Ghisari M, Bonefeld-Jørgensen EC.
Abstract:

Phytoestrogens (PEs) are natural plant components, which can induce biologic responses in vertebrates by mimicking or blocking the actions of natural hormones or influencing the hormone production in the body. This study investigated the effect of different mixtures composed of food-relevant PEs on the thyroid hormone (TH) system assessing the proliferation of the 3,3',5-triiodi-L-thryonine (T3) dependent rat pituitary GH3 cells using the T-screen assay, and the effect on the aryl hydrocarbon receptor (AhR) transactivation using an AhR-luciferase reporter gene assay. Most tested PEs and their mixtures showed effect on both the TH and AhR system. Single isoflavonoid metabolites and their mixture and coumestrol induced GH3 cell growth and AhR transactivity dose-dependently. Isoflavonoid metabolites elicited an additive effect on the T3-dependent GH3 cell growth, and a synergistic effect on the AhR transactivity. In conclusion, nutrition-relevant PEs, alone and in mixture may possess endocrine-disrupting potential by interfering with TH and AhR functions, which need to be considered when assessing the effects on human health.

The **endocrine disruptor** monoethyl-hexyl-phthalate promotes adipocyte differentiation and induces obesity in mice.
Hao C, Cheng X, Xia H, Ma X.
Abstract:
The environmental obesogen hypothesis proposes that exposure to endocrine disruptors during developmental "window" contributes to adipogenesis and the development of obesity. Monoethyl-hexyl-phthalate (MEHP), a metabolite of the widespread plasticizer diethyl-hexyl-phthalate (DEHP), has been found in exposed organisms and identified as a selective peroxisome proliferator-activated receptor (PPAR) γ modulator. However, implication of MEHP on adipose tissue development has been poorly investigated. Here we showed the dose-dependent effects of MEHP on adipocyte differentiation and glycerol-3-phosphate dehydrogenase (GPDH) activity in the murine 3T3-L1 cell model. MEHP induced the expression of PPARγ as well as its target genes required for adipogenesis in vitro. Moreover, MEHP perturbed key regulators of adipogenesis and lipogenic pathway in vivo. In utero exposure to low dose of MEHP significantly increased body weight and fat pads weight in male offspring at postnatal day (PND) 60. In addition, serum cholesterol, triglyceride and glucose levels were also significantly elevated. These results suggest that perinatal exposure to MEHP may be expected to increase the incidence of obesity in a sex-dependent manner and can act as a potential chemical stressor for obesity and obesity-related disorders.

Bruttolisten *in vitro*

1.

An **in vitro** investigation of **endocrine disrupting** effects of trichothecenes deoxynivalenol (DON), T-2 and HT-2 toxins.
Ndossi DG, Frizzell C, Tremoen NH, Fæste CK, Verhaegen S, Dahl E, Eriksen GS, Sørlie M, Connolly L, Ropstad E.
Toxicol Lett. 2012 Sep 12. pii: S0378-4274(12)01301-X. doi: 10.1016/j.toxlet.2012.09.005.

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Brominated flame retardants stimulate mouse immune cells **in vitro**.
Koike E, Yanagisawa R, Takigami H, Takano H.
J Appl Toxicol. 2012 Sep 12. doi: 10.1002/jat.2809. [Epub ahead of print]

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Calbindin-D9k as a sensitive molecular biomarker for evaluating the synergistic impact of estrogenic chemicals on GH3 rat pituitary cells.
Vo TT, An BS, Yang H, Jung EM, Hwang I, Jeung EB.
Int J Mol Med. 2012 Nov;30(5):1233-40. doi: 10.3892/ijmm.2012.1122. Epub 2012 Sep 6.

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Effect of di-(2-ethylhexyl) phthalate and mono-(2-ethylhexyl) phthalate on **in vitro** developmental competence of bovine oocytes.
Grossman D, Kalo D, Gendelman M, Roth Z.
Cell Biol Toxicol. 2012 Sep 8. [Epub ahead of print]

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The **endocrine disruptor** monoethyl-hexyl-phthalate promotes adipocyte differentiation and induces obesity in mice.
Hao C, Cheng X, Xia H, Ma X.
Biosci Rep. 2012 Sep 7. [Epub ahead of print]

6.

Low-level Phenolic Estrogen Pollutants Impair Islets Morphology and β-Cells Function in Isolated Rat Islets.
Song L, Xia W, Zhou Z, Li Y, Lin Y, Wei J, Wei Z, Xu B, Shen J, Li W, Xu S.
J Endocrinol. 2012 Sep 3. [Epub ahead of print]

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Laccase-Mediated Transformations of **Endocrine Disrupting** Chemicals Abolish Binding Affinities to Estrogen Receptors and Their Estrogenic Activity in Zebrafish.

Torres-Duarte C, Viana MT, Vazquez-Duhalt R.
Appl Biochem Biotechnol. 2012 Sep 2. [Epub ahead of print]

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Endocrine disruptors and female fertility: focus on (bovine) ovarian follicular physiology.
Petro EM, Leroy JL, Van Cruchten SJ, Covaci A, Jorssen EP, Bols PE.
Theriogenology. 2012 Aug 25. [Epub ahead of print]

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Targeting the pregnane X receptor in liver injury.
Li T, Yu RT, Atkins AR, Downes M, Tukey RH, Evans RM.
Expert Opin Ther Targets. 2012 Aug 23. [Epub ahead of print]

10.

Developing **in vitro** reporter gene assays to assess the hormone receptor activities of chemicals frequently detected in drinking water.
Sun H, Si C, Bian Q, Chen X, Chen L, Wang X.
J Appl Toxicol. 2012 Aug;32(8):635-41.

11.

Alkylphenols-potential modulators of the allergic response.
Suen JL, Hung CH, Yu HS, Huang SK.
Kaohsiung J Med Sci. 2012 Jul;28(7 Suppl):S43-8. Epub 2012 Jul 4.

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JNK pathway decreases thyroid hormones via TRH receptor: A novel mechanism for disturbance of thyroid hormone homeostasis by PCB153.
Liu C, Ha M, Cui Y, Wang C, Yan M, Fu W, Quan C, Zhou J, Yang K.
Toxicology. 2012 Dec 8;302(1):68-76. Epub 2012 Aug 4.

13.

Reconstitution studies of pesticides and surfactants exploring the cause of estrogenic activity observed in surface waters of the san francisco bay delta.
Schlenk D, Lavado R, Loyo-Rosales JE, Jones W, Maryoung L, Riar N, Werner I, Sedlak D.
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Photochemical induced changes of in vitro estrogenic activity of steroid hormones.
Whidbey CM, Daumit KE, Nguyen TH, Ashworth DD, Davis JC, Latch DE.
Water Res. 2012 Oct 15;46(16):5287-96. Epub 2012 Jul 24.

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Transcriptional responses of the brain-gonad-liver axis of fathead minnows exposed to untreated and ozone-treated oil sands process-affected water.
He Y, Wiseman SB, Wang N, Perez-Estrada LA, El-Din MG, Martin JW, Giesy JP.
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Environmental **endocrine disruptors** in farm animal reproduction: research and reality.
Magnusson U.
Reprod Domest Anim. 2012 Aug;47 Suppl 4:333-7. doi: 10.1111/j.1439-0531.2012.02095.x.

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Effects of maternal diet and exposure to bisphenol a on sexually dimorphic responses in conceptuses and offspring.
Rosenfeld C.
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Estrogen receptor alpha as a key target of organochlorines to promote angiogenesis.
Clere N, Lauret E, Malthiery Y, Andriantsitohaina R, Faure S.
Angiogenesis. 2012 Jul 25.

19.

Environmental exposure to arsenic may reduce human semen quality: associations derived from a Chinese cross-sectional study.
Xu W, Bao H, Liu F, Liu L, Zhu YG, She J, Dong S, Cai M, Li L, Li C, Shen H.
Environ Health. 2012 Jul 9;11:46.

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Bisphenol A modulates germ cell differentiation and retinoic acid signaling in mouse ES cells.
Aoki T, Takada T.
Reprod Toxicol. 2012 Nov;34(3):463-70. Epub 2012 Jun 23.

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DNA strand breaks detected in embryos of the adult snails, Potamopyrgus antipodarum, and in neonates exposed to genotoxic chemicals.
Vincent-Hubert F, Revel M, Garric J.
Aquat Toxicol. 2012 Oct 15;122-123:1-8. Epub 2012 May 22.

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The **endocrine disruptor** diethylstilbestrol induces adipocyte differentiation and promotes obesity in mice.
Hao CJ, Cheng XJ, Xia HF, Ma X.
Toxicol Appl Pharmacol. 2012 Aug 15;263(1):102-10. Epub 2012 Jun 15.

23.

Additive mixture effects of estrogenic chemicals in human cell-based assays can be influenced by inclusion of chemicals with differing effect profiles.
Evans RM, Scholze M, Kortenkamp A.
PLoS One. 2012;7(8):e43606. Epub 2012 Aug 17.

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(19)F MRI tracer preserves **in vitro** and in vivo properties of hematopoietic stem cells.

Helfer BM, Balducci A, Sadeghi Z, O'Hanlon C, Hijaz A, Flask CA, Wesa A.

Cell Transplant. 2012 Aug 2. [Epub ahead of print]

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Fluorine-19 magnetic resonance angiography of the mouse.

van Heeswijk RB, Pilloud Y, Flögel U, Schwitter J, Stuber M.

PLoS One. 2012;7(7):e42236. Epub 2012 Jul 27.

26.

Disruption of phosphatidylcholine monolayers and bilayers by **perfluorobutane** sulfonate.

Oldham ED, Xie W, Farnoud AM, Fiegel J, Lehmler HJ.

J Phys Chem B. 2012 Aug 23;116(33):9999-10007. Epub 2012 Aug 13.

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Evaluation of (18)F-labeled targeted **perfluorocarbon**-filled albumin microbubbles as a probe for microUS and microPET in tumor-bearing mice.

Liao AH, Wu SY, Wang HE, Weng CH, Wu MF, Li PC.

Ultrasonics. 2012 Jul 7. [Epub ahead of print]

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In vitro and in vivo studies of the toxic effects of **perfluorononanoic** acid on rat hepatocytes and Kupffer cells.

Fang X, Gao G, Xue H, Zhang X, Wang H.

Environ Toxicol Pharmacol. 2012 Jul 1;34(2):484-494. [Epub ahead of print]

29.

Changes in thyroid peroxidase activity in response to various chemicals.

Song M, Kim YJ, Park YK, Ryu JC.

J Environ Monit. 2012 Aug 27;14(8):2121-6. Epub 2012 Jun 15.

30.

Kupffer cells suppress **perfluorononanoic** acid-induced hepatic peroxisome proliferator-activated receptor α expression by releasing cytokines.

Fang X, Zou S, Zhao Y, Cui R, Zhang W, Hu J, Dai J.

Arch Toxicol. 2012 Oct;86(10):1515-25. Epub 2012 May 31.

31.

Interaction between **perfluorcarbon** liquid and heavy silicone oil: risk factor for "sticky oil" formation.

Romano MR, Vallejo-Garcia JL, Parmeggiani F, Vito R, Vinciguerra P.

Curr Eye Res. 2012 Jul;37(7):563-6. Epub 2012 May 11.

32.

Long-circulating **perfluorooctyl** bromide nanocapsules for tumor imaging by 19FMRI.

Diou O, Tsapis N, Giraudeau C, Valette J, Gueutin C, Bourasset F, Zanna S, Vauthier C, Fattal E.

Biomaterials. 2012 Aug;33(22):5593-602. Epub 2012 May 9.

33.

Quantitative analysis of **perfluorinated** chemicals in media for **in vitro** fertilization and related samples.

Iwasaki Y, Terayama E, Kato A, Ito R, Saito K, Makino T, Nakazawa H.

Chemosphere. 2012 Jul;88(4):445-9. Epub 2012 Mar 21.

34.

Effects of per- and **polyfluorinated** compounds on adult rat testicular cells following **in vitro** exposure.

Lindeman B, Maass C, Duale N, Gützkow KB, Brunborg G, Andreassen A.

Reprod Toxicol. 2012 Jul;33(4):531-7. Epub 2011 Apr 17.

35.

Polycyclic aromatic hydrocarbons and dibutyl **phthalate** disrupt dorsal-ventral axis determination via the Wnt/β-catenin signaling pathway in zebrafish embryos.

Fairbairn EA, Bonthius J, Cherr GN.

Aquat Toxicol. 2012 Aug 28;124-125C:188-196. doi: 10.1016/j.aquatox.2012.08.017.

36.

Epigenetic effects of environmental chemicals bisphenol a and **phthalates**.

Singh S, Li SS.

Int J Mol Sci. 2012;13(8):10143-53. Epub 2012 Aug 15.

37.

Developing **in vitro** reporter gene assays to assess the hormone receptor activities of chemicals frequently detected in drinking water.

Sun H, Si C, Bian Q, Chen X, Chen L, Wang X.

J Appl Toxicol. 2012 Aug;32(8):635-41.

38.

n-Butyl Benzyl **Phthalate** Promotes Breast Cancer Progression by Inducing Expression of Lymphoid Enhancer Factor 1.

Hsieh TH, Tsai CF, Hsu CY, Kuo PL, Hsi E, Suen JL, Hung CH, Lee JN, Chai CY, Wang SC, Tsai EM.

PLoS One. 2012;7(8):e42750. Epub 2012 Aug 8.

39.

Species specific differences in the **in vitro** metabolism of the flame retardant mixture, Firemaster(®) BZ-54.

Bearr JS, Mitchelmore CL, Roberts SC, Stapleton HM.

Aquat Toxicol. 2012 Jul 5;124-125C:41-47. [Epub ahead of print]

40.

Effects of **Phthalates** on the Human Corneal Endothelial Cell Line B4G12.

Krüger T, Cao Y, Kjærgaard SK, Knudsen LE, Bonefeld-Jørgensen EC.

Int J Toxicol. 2012 Aug;31(4):364-71. Epub 2012 Jun 21.

41.

Compound-specific effects of diverse neurodevelopmental toxicants on global gene expression in the neural embryonic stem cell test (ESTn).

Theunissen PT, Robinson JF, Pennings JL, van Herwijnen MH, Kleinjans JC, Piersma AH.

Toxicol Appl Pharmacol. 2012 Aug 1;262(3):330-40. Epub 2012 May 23.

42.

Phthalates Stimulate the Epithelial to Mesenchymal TransitionThrough an HDAC6-Dependent Mechanism in Human BreastEpithelial Stem Cells.

Hsieh TH, Tsai CF, Hsu CY, Kuo PL, Lee JN, Chai CY, Hou MF, Chang CC, Long CY, Ko YC, Tsai EM.

Toxicol Sci. 2012 Aug;128(2):365-76. Epub 2012 May 2.

43.

Phthalates and bisphenol do not accumulate in human follicular fluid.

Krotz SP, Carson SA, Tomey C, Buster JE.

J Assist Reprod Genet. 2012 Aug;29(8):773-7. Epub 2012 Apr 27.

44.

DEHP: Genotoxicity and potential carcinogenic mechanisms-A review.

Caldwell JC.

Mutat Res. 2012 Oct;751(2):82-157. Epub 2012 Apr 3.

45.

Development and validation of an **in vitro** micronucleus assay platform in TK6 cells.

Sobol Z, Homiski ML, Dickinson DA, Spellman RA, Li D, Scott A, Cheung JR, Coffing SL, Munzner JB, Sanok KE, Gunther WC, Dobo KL, Schuler M.

Mutat Res. 2012 Jul 4;746(1):29-34. Epub 2012 Mar 13.

46.

Exploratory **in vitro** study of red blood cell storage containers formulated with an alternative plasticizer.

Dumont LJ, Baker S, Dumont DF, Herschel L, Waters S, Calcagni K, Sandford C, Radwanski K, Min K, David RM, Otter R.

Transfusion. 2012 Jul;52(7):1439-45. doi: 10.1111/j.1537-2995.2011.03506.x. Epub 2011 Dec 30.

Herudover er der yderligere 1 artikel, som ikke blev fanget af de valgte søgekriterier:

Effects of Selected **Phytoestrogens** and Their Mixtures on the Function of the Thyroid Hormone and the Aryl Hydrocarbon Receptor.
Long M, Krüger T, Ghisari M, Bonefeld-Jørgensen EC.
Nutr Cancer. 2012 Sep 11. [Epub ahead of print]

In Vivo studier ved DTU - FOOD

Søgning er udført på PubMed og dækker perioden 21/6 2012 – 24/9 2012

(juli- september 2012)

Følgende søgeprofil er benyttet: ”(endocrine disrupt*) AND (rat OR mice OR mammal*)” og ”(endocrine disrupt*) AND(in vivo*). Derudover er der også søgt på ”(endocrine disrupt*) AND(Paraben*)”, ”(endocrine disrupt*) AND(Phthalat*), Endocrine disrupt* AND (antiandrogen) samt ”(endocrine disrupt*) AND(behaviour/behavior*).

Efter at have fjernet gengangere fra dem vi havde med på den forrige litteraturopdateringsliste samt in vitro, human eller SDU relevante artikler, gav litteratursøgningen en liste med i alt 16 artikler (Bruttolisten)

Tre artikler er blevet udvalgt til nærmere beskrivelse. Disse 3 er valgt fordi vi mener de bidrager til ny viden om clorpyrifos (review, Venerosi et al.), BPA og Adfærd (Matsuda et al.) samt effekter hos rotter efter eksponering for prochloraz.

Ud fra bruttolisten (se længere nede i dokumentet) er udvalgt følgende 3 artikler til engelsk abstrakt:

Udvalgte publikationer:

Sex dimorphic behaviors as markers of neuroendocrine disruption by environmental chemicals: The case of chlorpyrifos.

Venerosi A, Ricceri L, Tait S, Calamandrei G.
Neurotoxicology. 2012 Aug 29. pii: S0161-813X(12)00205-7. doi: 10.1016/j.neuro.2012.08.009. [Epub ahead of print] *Dette er et review og derfor bringes kun et abstract.*

Abstract

The complexity of the neuroendocrine level of investigation requires the assessment of behavioral patterns that extend beyond the reproductive functions, which are age- and sex-specific in rodents, described by defined clusters of behavioral items regulated by genetic, hormonal, and epigenetic factors. The study of social behavior in laboratory rodents reveals sex-dimorphic effects of environmental chemicals that may be undetected either by a traditional neurotoxicological approach or referring to the classical definition of endocrine disrupting chemicals. Here we review data on the neurobehavioral effects of developmental exposure to the non-persistent organophosphorus insecticide chlorpyrifos, whose neurotoxic activity at low doses is currently a matter of concern for

children's health. In mice exposed to chlorpyrifos in utero and/or in early development social/emotional responses are differently affected in the two sexes in parallel with sex-dependent interference on hypothalamic neuroendocrine pathways regulating social behaviors (vasopressin, oxytocin, and steroid regulated systems). Through the analysis of complex sex-dimorphic behavioral patterns we show that neurotoxic and endocrine disrupting activities of CPF overlap. This widely diffused organophosphorus pesticide might thus be considered as a neuroendocrine disruptor possibly representing a risk factor for sex-biased neurodevelopmental disorders in children.

Effects of perinatal exposure to low dose of bisphenol A on anxiety like behavior and dopamine metabolites in brain.
Matsuda S, Matsuzawa D, Ishii D, Tomizawa H, Sutoh C, Nakazawa K, Amano K, Sajiki J, Shimizu E. Prog Neuropsychopharmacol Biol Psychiatry. 2012 Jul 1. [Epub ahead of print]
Abstract
Bisphenol A (BPA), an endocrine-disrupting chemical, is widely present in the environment. It has been reported that perinatal exposure to low doses of BPA that are less than the tolerable daily intake level (50μg/kg/day) affects anxiety-like behavior and dopamine levels in the brain. Although the dopaminergic system in the brain is considered to be related to anxiety, no study has reported the effects of low-dose BPA exposure on the dopaminergic system in the brain and on anxiety-like behavior using the same methods of BPA exposure. To investigate the relationship between alterations in anxiety-like behavior and changes in the dopaminergic system in the brain induced by BPA, we examined the effects of BPA on anxiety-like behavior using an open field test in juvenile and adult mice and measured DA and DOPAC levels and the DOPAC/DA ratio in the dorsal hippocampus (HIP), amygdala (AMY), and medulla oblongata (MED) using high-performance liquid chromatography (HPLC) in adult mice. In males, BPA decreased the time spent in the center area of the open field in both juveniles and adults. In addition, BPA increased DA levels in the dorsal HIP and MED and decreased the DOPAC/DA ratio in the dorsal HIP, AMY, and MED in adults. The activity of monoamine oxidase (MAO)-B, the enzyme that metabolizes DA into DOPAC, was reduced in the MED. In females, those changes were not observed. These results suggest that an increase in anxiety-like behavior induced by perinatal exposure to BPA may be related to decreases in DA metabolites in the brain, and there are sex differences in those BPA effects.
Konklusion

Prenatal prochloraz treatment significantly increases pregnancy length and reduces offspring weight but does not affect social-olfactory memory in rats.
Dmytriyeva O, Klementiev B, Berezin V, Bock E.
Exp Toxicol Pathol. 2012 Jun 21. [Epub ahead of print]

Metabolites of the commonly used imidazole fungicide prochloraz are androgen receptor antagonists. They have been shown to block androgen-driven development and compromise reproductive function. We tested the effect of prochloraz on cognitive behavior following exposure to this fungicide during the perinatal period. Pregnant Wistar rats were administered a 200mg/kg dose of prochloraz on gestational day (GD) 7, GD11, and GD15. The social recognition test (SRT) was performed on 7-week-old male rat offspring. We found an increase in pregnancy length and a

significantly reduced pup weight on PND15 and PND40 but no effect of prenatal prochloraz exposure on social investigation or acquisition of social-olfactory memory.

Bruttolisten *in vivo*

1. Endocrine-disrupting chemicals: associated disorders and mechanisms of action.

De Coster S, van Larebeke N.

J Environ Public Health. 2012;2012:713696. Epub 2012 Sep 6.

2. Exposure to diethyl hexyl phthalate (DEHP) to adult male rat is associated with insulin resistance in adipose tisssue: Protective role of antioxidant vitamins (C & E).

Rajesh P, Sathish S, Srinivasan C, Selvaraj J, Balasubramanian K.

J Cell Biochem. 2012 Sep 18. doi: 10.1002/jcb.24399. [Epub ahead of print]

3. Di-(2-ethylhcxyl) phthalate reduces progesterone levels and induces apoptosis of ovarian granulosa cell in adult female ICR mice.

Li N, Liu T, Zhou L, He J, Ye L.

Environ Toxicol Pharmacol. 2012 Sep 1. pii: S1382-6689(12)00129-9. doi: 10.1016/j.etap.2012.08.013. [Epub ahead of print]

4. Anogenital distance and the risk of prostate cancer.

Castaño-Vinyals G, Carrasco E, Lorente JA, Sabaté Y, Cirac-Claveras J, Pollán M, Kogevinas M.

BJU Int. 2012 Sep 18. doi: 10.1111/j.1464-410X.2012.11516.x. [Epub ahead of print]

5. The endocrine disruptor monoethyl-hexyl-phthalate promotes adipocyte differentiation and induces obesity in mice.

Hao C, Cheng X, Xia H, Ma X.

Biosci Rep. 2012 Sep 7. [Epub ahead of print]

6. The association between some endocrine disruptors and hypospadias in biological samples.

Choi H, Kim J, Im Y, Lee S, Kim Y.

J Environ Sci Health A Tox Hazard Subst Environ Eng. 2012 Nov;47(13):2173-9.

7. Phthalate exposure changes the metabolic profile of cardiac muscle cells.

Posnack NG, Swift LM, Kay MW, Lee NH, Sarvazyan N.

Environ Health Perspect. 2012 Sep;120(9):1243-51. Epub 2012 Jun 6.

8. The metabonomics of combined dietary exposure to phthalates and polychlorinated biphenyls in mice.

Zhang J, Yan L, Tian M, Huang Q, Peng S, Dong S, Shen H.

J Pharm Biomed Anal. 2012 Jul;66:287-97. Epub 2012 Apr 3.

9. Does perinatal exposure to endocrine disruptors induce autism spectrum and attention deficit hyperactivity disorders? Review.

de Cock M, Maas YG, van de Bor M.

Acta Paediatr. 2012 Aug;101(8):811-8. doi: 10.1111/j.1651-2227.2012.02693.x. Epub 2012 May 7.

10. The endocrine disruptor 4-nonylphenol promotes adipocyte differentiation and induces obesity in mice.

Hao CJ, Cheng XJ, Xia HF, Ma X.

Cell Physiol Biochem. 2012;30(2):382-94. Epub 2012 Jul 3.

11. The endocrine disruptor diethylstilbestrol induces adipocyte differentiation and promotes obesity in mice.

Hao CJ, Cheng XJ, Xia HF, Ma X.

Toxicol Appl Pharmacol. 2012 Aug 15;263(1):102-10. Epub 2012 Jun 15.

12. Parabens inhibit the early phase of folliculogenesis and steroidogenesis in the ovaries of neonatal rats.

Ahn HJ, An BS, Jung EM, Yang H, Choi KC, Jeung EB.

Mol Reprod Dev. 2012 Sep;79(9):626-36. doi: 10.1002/mrd.22070. Epub 2012 Jul 26.

13. Sex dimorphic behaviors as markers of neuroendocrine disruption by environmental chemicals: The case of chlorpyrifos **Abstract**.

Venerosi A, Ricceri L, Tait S, Calamandrei G.

Neurotoxicology. 2012 Aug 29. pii: S0161-813X(12)00205-7. doi: 10.1016/j.neuro.2012.08.009. [Epub ahead of print]

14. Effects of perinatal exposure to low dose of bisphenol A on anxiety like behavior and dopamine metabolites in brain **udvalgt**.

Matsuda S, Matsuzawa D, Ishii D, Tomizawa H, Sutoh C, Nakazawa K, Amano K, Sajiki J, Shimizu E.

Prog Neuropsychopharmacol Biol Psychiatry. 2012 Jul 1. [Epub ahead of print]

15. Bisphenol A alters the development of the rhesus monkey mammary gland.

Tharp AP, Maffini MV, Hunt PA, VandeVoort CA, Sonnenschein C, Soto AM.

Proc Natl Acad Sci U S A. 2012 May 22;109(21):8190-5. Epub 2012 May 7.

16. Prenatal prochloraz treatment significantly increases pregnancy length and reduces offspring weight but does not affect social-olfactory memory in rats.**udvalgt**

Dmytriyeva O, Klementiev B, Berezin V, Bock E.

Exp Toxicol Pathol. 2012 Jun 21. [Epub ahead of print]

Wildlife studier ved Biologisk Institut, Syddansk Universitet (SDU)

Søgningen er udført på Web of Science og dækker perioden 27/6 2011 – 23/9 2011.

Søgeprofilen kombinerer:	Endocrine disrupt*	og	Fish* Amphibia* Bird* OR Avia* Invertebrat* Mollus* Gastropod* Insect* Crustacea* Echinoderm* Ursus Reptil* OR Alligator Whal* OR seal OR dolphin

Fra bruttolisten (længere nede i dokumentet) er udvalgt 3 artikler til medtagelse af abstract.

Artikel 1:

Title: Adverse effects in wild fish living downstream from pharmaceutical manufacture discharges
Author(s): Sanchez Wilfried; Sremski William; Piccini Benjamin; et al.
Source: ENVIRONMENT INTERNATIONAL Volume: 37 Issue: 8 Pages: 1342-1348

Abstract: A set of biochemical and histological responses was measured in wild gudgeon collected upstream and downstream of urban and pharmaceutical manufacture effluents. These individual end-points were associated to fish assemblage characterisation. Responses of biotransformation enzymes, neurotoxicity and endocrine disruption biomarkers revealed contamination of investigated stream by a mixture of pollutants. Fish from sampled sites downstream of the industrial effluent exhibited also strong signs of endocrine disruption including vitellogenin induction, intersex and male-biased sex-ratio. These individual effects were associated to a decrease of density and a lack of sensitive fish species. This evidence supports the hypothesis that pharmaceutical compounds discharged in stream are involved in recorded endocrine disruption effects and fish population disturbances and threaten disappearance of resident fish species. Overall, this study gives argument for the utilisation of an effect-based monitoring approach to assess impacts of pharmaceutical manufacture discharges on wild fish populations.

Artikel 2:

Title: Selective uptake and biological consequences of environmentally relevant antidepressant pharmaceutical exposures on male fathead minnows
Author(s): Schultz Melissa M.; Painter Meghan M.; Bartell Stephen E.; et al.
Source: AQUATIC TOXICOLOGY Volume: 104 Issue: 1-2 Pages: 38-47

Abstract: Antidepressant pharmaceuticals have been reported in wastewater effluent at the nanogram to low microgram-per-liter range, and include bupropion (BUP), fluoxetine (FLX), sertraline (SER), and venlafaxine (VEN). To assess the effects of antidepressants on reproductive anatomy, physiology, and behavior, adult male fathead minnows (Pimephales promelas) were exposed for 21 days either to a single concentration of the antidepressants FLX, SER, VEN, or BUP, or to an antidepressant mixture. The data demonstrated that exposure to VEN (305 ng/L and 1104 ng/L) and SER (5.2 ng/L) resulted in mortality.

Anatomical alterations were noted within the testes of fish exposed to SER and FLX, both modulators of the neurotransmitter serotonin. Additionally, FLX at 28 ng/L induced vitellogenin in male fish—a common endpoint for estrogenic endocrine disruption. Significant alterations in male secondary sex characteristics were noted with single exposures. Effects of single compound exposures neither carried over, nor became additive in the antidepressant mixtures, and reproductive behavior was not affected. Analysis of brain tissues from the exposed fish suggested increased uptake of FLX, SER and BUP and minimal uptake of VEN when compared to exposure water concentrations. Furthermore, the only metabolite detected consistently in the brain tissues was norfluoxetine. Similar trends of uptake by brain tissue were observed when fish were exposed to antidepressant mixtures. The present study demonstrates that anatomy and physiology, but not reproductive behavior, can be disrupted by exposure to environmental concentrations of some antidepressants. The observation that antidepressant uptake into fish tissues is selective may have consequences on assessing the mode-of-action and effects of these compounds in future studies.

Artikel 3:

Title: The synthetic gestagen levonorgestrel impairs metamorphosis in Xenopus laevis by disruption of the thyroid system
Author(s): Lorenz Claudia; Contardo-Jara Valeska; Pflugmacher Stephan; et al.
Source: TOXICOLOGICAL SCIENCES Volume: 123 Issue: 1 Pages: 94-102

Abstract: Synthetic gestagens, including levonorgestrel (LNG), are active compounds in contraceptives, and several studies report their occurrence in surface waters. However, information about endocrine-disrupting effects in nontarget organisms is scarce. The present study investigated effects of LNG exposure on thyroid hormone–dependent metamorphosis of Xenopus laevis. Premetamorphic X. laevis tadpoles at Nieuwkoop and Faber (NF) stage 48 were exposed in a flow-through culture system to four LNG concentrations (10211, 10210, 1029, and 1028M) over the period of metamorphosis. At NF 58 and 66, tadpoles were examined sex specifically. Developmental time and organismal responses were recorded and correlated with molecular and histopathological endpoints. Exposure to 1028M LNG caused an inhibition of metamorphosis resulting in developmental arrest at early climax stages as giant tadpoles or tailed frogs. In brain-pituitary tissue of NF 58 tadpoles, gene expression of thyroid-stimulating hormone (b-subunit; TSHb), TH receptor b (TRb), and deiodinase type 3 (D3) was not changed. Instead, prolactin (PRL) messenger RNA (mRNA) was significantly increased by 1029M LNG in females and by 1028M LNG in both sexes. In NF 66 tadpoles, mRNA levels of TSHb mRNA were significantly increased in the 1029 and 1028M LNG treatment groups indicating a hypothyroid state. No changes of TRb, D3, and PRL gene expression were detected. Histopathological evaluation of thyroid gland sections revealed no typical sign of hypothyroidism but rather an inactivated appearance of the thyroid. In conclusion, our data demonstrate for the first time a completely new aspect of thyroid system disruption caused by synthetic gestagens in developing amphibians.

Bruttoliste:

Title: Adverse effects in wild fish living downstream from pharmaceutical manufacture discharges
Author(s): Sanchez Wilfried; Sremski William; Piccini Benjamin; et al.
Source: ENVIRONMENT INTERNATIONAL Volume: 37 Issue: 8 Pages: 1342-1348

Title: Thyroid axis disruption in juvenile brown trout (Salmo trutta) exposed to the flame retardant beta-tetrabromoethylcyclohexane (beta-TBECH) via the diet
Author(s): Park Bradley J.; Palace Vince; Wautier Kerry; et al.

Source: ENVIRONMENTAL SCIENCE & TECHNOLOGY Volume: 45 Issue: 18 Pages: 7923-7927

Title: Decreased vitellogenin inducibility and 17 beta-estradiol levels correlated with reduced egg production in killifish (Fundulus heteroclitus) from Newark Bay, NJ
Author(s): Bugel Sean M.; White Lori A.; Cooper Keith R.
Source: AQUATIC TOXICOLOGY Volume: 105 Issue: 1-2 Pages: 1-12

Title: Bezafibrate, a lipid-lowering pharmaceutical, as a potential endocrine disruptor in male zebrafish (Danio rerio)
Author(s): Velasco-Santamaria Yohana M.; Korsgaard Bodil; Madsen Steffen S.; et al.
Source: AQUATIC TOXICOLOGY Volume: 105 Issue: 1-2 Pages: 107-118

Title: Generation of fluorescent zebrafish to study endocrine disruption and potential crosstalk between thyroid hormone and corticosteroids
Author(s): Terrien Xavier; Fini Jean-Baptiste; Demeneix Barbara A.; et al.
Source: AQUATIC TOXICOLOGY Volume: 105 Issue: 1-2 Pages: 13-20

Title: Low-dose exposure to alkylphenols adversely affects the sexual development of Atlantic cod (Gadus morhua): Acceleration of the onset of puberty and delayed seasonal gonad development in mature female cod
Author(s): Meier Sonnich; Morton H. Craig; Andersson Eva; et al.
Source: AQUATIC TOXICOLOGY Volume: 105 Issue: 1-2 Pages: 136-150

Title: The anti-estrogenic activity of sediments from agriculturally intense watersheds: Assessment using in vivo and in vitro assays
Author(s): Jeffries Marlo K. Sellin; Conoan Nicholas H.; Cox Marc B.; et al.
Source: AQUATIC TOXICOLOGY Volume: 105 Issue: 1-2 Pages: 189-198

Title: 17 alpha-Ethinyl estradiol affects anxiety and shoaling behavior in adult male zebra fish (Danio rerio)
Author(s): Reyhanian Nasim; Volkova Kristina; Hallgren Stefan; et al.
Source: AQUATIC TOXICOLOGY Volume: 105 Issue: 1-2 Pages: 41-48

Title: Short-term exposure to a treated sewage effluent alters reproductive behaviour in the three-spined stickleback (Gasterosteus aculeatus)
Author(s): Sebire Marion; Katsiadaki Ioanna; Taylor Nick G. H.; et al.
Source: AQUATIC TOXICOLOGY Volume: 105 Issue: 1-2 Pages: 78-88

Title: Ligula intestinalis infection is associated with alterations of both brain and gonad aromatase expression in roach (Rutilus rutilus)
Author(s): Boulange-Lecomte C.; Geraudie P.; Forget-Leray J.; et al.
Source: JOURNAL OF HELMINTHOLOGY Volume: 85 Issue: 3 Pages: 339-344

Title: Transcriptional regulatory dynamics of the hypothalamic-pituitary-gonadal axis and its peripheral pathways as impacted by the 3-beta HSD inhibitor trilostane in zebrafish (Danio rerio)
Author(s): Wang Rong-Lin; Bencic David; Lazorchak Jim; et al.
Source: ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY Volume: 74 Issue: 6 Pages: 1461-1470

Title: Early life-stage and multigeneration toxicity study with bisphenol A and fathead minnows (Pimephales promelas)
Author(s): Staples Charles A.; Hall A. Tilghman; Friederich Urs; et al.

Source: ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY Volume: 74 Issue: 6 Pages: 1548-1557

Title: Use of sex ratio of bream (Abramis brama L.) as an indicator of endocrine effects: Results from the German Environmental Specimen Bank
Author(s): Teubner Diana; Tarricone Kathrin; Veith Michael; et al.
Source: ECOLOGICAL INDICATORS Volume: 11 Issue: 5 Pages: 1487-1489

Title: Toxic influence of endocrine disruptor, carbendazim, on brain biochemical and haematological changes in the fresh water fish, Cyprinus carpio
Author(s): Govindassamy P.; Tiroumavalavane M.; Marcelline S. O.; et al.
Conference: 47th Congress of the European-Societies-of-Toxicology Location: Paris, FRANCE Date: AUG 28-31, 2011
Sponsor(s): European Soc Toxicol
Source: TOXICOLOGY LETTERS Volume: 205 Supplement: 1 Pages: S125-S125

Title: Low-dose effects and biphasic effect profiles: Is trenbolone a genotoxicant?
Author(s): Boettcher Melanie; Kosmehl Thomas; Braunbeck Thomas
Source: MUTATION RESEARCH-GENETIC TOXICOLOGY AND ENVIRONMENTAL MUTAGENESIS Volume: 723 Issue: 2 Pages: 152-157

Title: Towards a system level understanding of non-model organisms sampled from the environment: A network biology approach
Author(s): Williams Tim D.; Turan Nil; Diab Amer M.; et al.
Source: PLOS COMPUTATIONAL BIOLOGY Volume: 7 Issue: 8 Article Number: e1002126

Title: Accumulation and debromination of decabromodiphenyl ether (BDE-209) in juvenile fathead minnows (Pimephales promelas) induces thyroid disruption and liver alterations
Author(s): Noyes Pamela D.; Hinton David E.; Stapleton Heather M.
Source: TOXICOLOGICAL SCIENCES Volume: 122 Issue: 2 Pages: 265-274

Title: Organochlorine concentrations in franciscana dolphins, Pontoporia blainvillei, from Brazilian waters
Author(s): Lailson-Brito Jose; Dorneles Paulo Renato; Azevedo-Silva Claudio Eduardo; et al.
Source: CHEMOSPHERE Volume: 84 Issue: 7 Pages: 882-887

Title: Health status of native fish (Percilia gillissi and Trichomycterus areolatus) downstream of the discharge of effluent from a tertiary-treated elemental chlorine-free pulp mill in Chile
Author(s): Chiang Gustavo; McMaster Mark E.; Urrutia Roberto; et al.
Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 8 Pages: 1793-1809

Title: Cloning and expression of the translocator protein (18 kDa), voltage-dependent anion channel, and diazepam binding inhibitor in the gonad of largemouth bass (Micropterus salmoides) across the reproductive cycle
Author(s): Doperalski Nicholas J.; Martyniuk Christopher J.; Prucha Melinda S.; et al.
Source: GENERAL AND COMPARATIVE ENDOCRINOLOGY Volume: 173 Issue: 1 Pages: 86-95

Title: Bisphenol A modulates expression of sex differentiation genes in the self-fertilizing fish, Kryptolebias marmoratus
Author(s): Rhee Jae-Sung; Kim Bo-Mi; Lee Chang Joo; et al.
Source: AQUATIC TOXICOLOGY Volume: 104 Issue: 3-4 Pages: 218-229

Title: Effect of the organochlorine pesticide endosulfan on GnRH and gonadotrope cell populations in fish larvae
Author(s): Piazza Yanina G.; Pandolfi Matias; Lo Nostro Fabiana L.
Source: ARCHIVES OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY Volume: 61 Issue: 2 Pages: 300-310

Title: Vitellogenin-like gene expression in freshwater amphipod Gammarus fossarum (Koch, 1835): functional characterization in females and potential for use as an endocrine disruption biomarker in males
Author(s): Xuereb Benoit; Bezin Laurent; Chaumot Arnaud; et al.
Source: ECOTOXICOLOGY Volume: 20 Issue: 6 Pages: 1286-1299

Title: A review of studies on androgen and estrogen exposure in fish early life stages: effects on gene and hormonal control of sexual differentiation
Author(s): Leet Jessica K.; Gall Heather E.; Sepulveda Maria S.
Source: JOURNAL OF APPLIED TOXICOLOGY Volume: 31 Issue: 5 Pages: 379-398

Title: Use of GC x GC/TOF-MS and LC/TOF-MS for metabolomic analysis of Hyalella azteca chronically exposed to atrazine and its primary metabolite, desethylatrazine
Author(s): Ralston-Hooper Kimberly J.; Adamec Jiri; Jannash Amber; et al.
Source: JOURNAL OF APPLIED TOXICOLOGY Volume: 31 Issue: 5 Pages: 399-410

Title: Drifting towards the surface: A shift in newborn pipefish's vertical distribution when exposed to the synthetic steroid ethinylestradiol
Author(s): Sarria M. P.; Santos M. M.; Reis-Henriques M. A.; et al.
Source: CHEMOSPHERE Volume: 84 Issue: 5 Pages: 618-624

Title: Development of enzyme-linked immunosorbent assays for plasma vitellogenin in Chinese rare minnow (Gobiocypris rarus)
Author(s): Luo Wenru; Zhou Qunfang; Jiang Guibin
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Title: Selective uptake and biological consequences of environmentally relevant antidepressant pharmaceutical exposures on male fathead minnows
Author(s): Schultz Melissa M.; Painter Meghan M.; Bartell Stephen E.; et al.
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Author(s): Yamamoto Yoji; Luckenbach J. Adam; Goetz Frederick W.; et al.
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Title: Apparent rapid loss of endocrine disruptors from wetlands used to store either tertiary treated sewage effluent or stormwater runoff
Author(s): Norris Andrew; Burgin Shelley
Source: WATER AIR AND SOIL POLLUTION Volume: 219 Issue: 1-4 Pages: 285-295

Title: Occurrence of sexual hormones in sediments of mangrove in Brazil
Author(s): Froehner Sandro; Machado Karina Scurupa; Stefen Elisa; et al.
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Title: Genotoxic effects in erythrocytes of Oreochromis niloticus exposed to nanograms-per-liter concentration of 17 beta-estradiol (E(2)): An assessment using micronucleus test and comet assay
Author(s): Sponchiado Graziela; Fortunato de Lucena Reynaldo Eliana Mara; de Andrade Any Caroline B.; et al.
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Title: Effects of a short-term exposure to the fungicide prochloraz on endocrine function and gene expression in female fathead minnows (Pimephales promelas)
Author(s): Skolness Sarah Y.; Durhan Elizabeth J.; Garcia-Reyero Natalia; et al.
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Title: Demasculinization of male fish by wastewater treatment plant effluent
Author(s): Vajda Alan M.; Barber Larry B.; Gray James L.; et al.
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Author(s): Karmaus Wilfried; Osuch Janet Rose; Landgraf Jeff; et al.
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Title: Antiestrogenicity and estrogenicity in leachates from solid waste deposits
Author(s): Svenson Anders; Sjoholm Sofia; Allard Ann-Sofie; et al.
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Author(s): Wada Haruka; Bergeron Christine M.; McNabb F. M. Anne; et al.
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Title: The synthetic gestagen levonorgestrel impairs metamorphosis in Xenopus laevis by disruption of the thyroid system
Author(s): Lorenz Claudia; Contardo-Jara Valeska; Pflugmacher Stephan; et al.
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Title: The Fungicide chlorothalonil is nonlinearly associated with corticosterone levels, immunity, and mortality in amphibians
Author(s): McMahon Taegan A.; Halstead Neal T.; Johnson Steve; et al.
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Title: Effects of 4-tert-octylphenol on Xenopus tropicalis in a long term exposure
Author(s): Porter Karen L.; Olmstead Allen W.; Kumsher David M.; et al.
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Title: Cloning of estrogen receptor alpha and aromatase cDNAs and gene expression in turtles (Chrysemys picta and Pseudemys scripta) exposed to different environments
Author(s): Marquez Emily C.; Traylor-Knowles Nikki; Novillo-Villajos Apolonia; et al.
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Title: Effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) on steroid concentrations in blood and gonads of chicken embryo
Author(s): Sechman Andrzej; Hrabia Anna; Lis Marcin W.; et al.
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Title: Behavioural responses to human-induced environmental change
Author(s): Tuomainen Ulla; Candolin Ulrika
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Title: Effects of the pharmaceuticals gemfibrozil and diclofenac on the marine mussel (Mytilus spp.) and their comparison with standardized toxicity tests
Author(s): Schmidt Wiebke; O'Rourke Kathleen; Hernan Robert; et al.
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Title: Two-generation effects of the chitin synthesis inhibitor, teflubenzuron, on the aquatic midge Chironomus riparius
Author(s): Tassou Koffi T.; Schulz Ralf
Source: ECOTOXICOLOGY AND ENVIRONMENTAL SAFETY Volume: 74 Issue: 5 Pages: 1203-1209

Title: The effects of organotin on female gastropods
Author(s): Titley-O'Neal Cassander P.; Munkittrick Kelly R.; MacDonald Bruce A.
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Title: Comparative effects of butyl benzyl phthalate (BBP) and di(2-ethylhexyl) phthalate (DEHP) on the aquatic larvae of Chironomus riparius based on gene expression assays related to the endocrine system, the stress response and ribosomes
Author(s): Planello Rosario; Herrero Oscar; Luis Martinez-Guitarte Jose; et al.
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Title: Occurrence and concentrations of pharmaceutical compounds in groundwater used for public drinking-water supply in California
Author(s): Fram Miranda S.; Belitz Kenneth
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Author(s): Verderame Mariailaria; Prisco Marina; Andreuccetti Piero; et al.
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Author(s): Stoker C.; Repetti M. R.; Garcia S. R.; et al.
Source: CHEMOSPHERE Volume: 84 Issue: 3 Pages: 311-317