Center for Hormonforstyrrende Stoffer

Litteraturgennemgang for perioden 11/12 2010 - 30/3 2011

Indholdsfortegnelse **Side**

Humane studier ved Afdeling for Vækst og Reproduktion, Rigshospitalet

Søgning er udført på PubMed og dækker perioden 11/12/2010 - 30/3/2011

Følgende søgeprofil er benyttet: (endocrine disrupt*) AND expos* AND (human OR men OR women OR child* OR adult* OR adolescen* OR infan*)

(Bemærkning: * i slutningen af et ord betyder at man søger på alle tænkelige endelser for det givne ord. For child* betyder det for eksempel at man søger på childhood, children og child)

Limits: title/abstract, English language

Brutto resultat: der blev fundet 63 artikler via denne søgning. Af disse er 5 udvalgt til nærmere gennemgang. Herudover har vi ad andre kanaler stiftet bekendtskab med yderligere 7 artikler, som vi finder relevante.

Som ønsket har vi søgt specielt efter artikler vedrørende parabener, men har kun fundet en enkelt. Denne omhandler eksponeringsniveuaer af 4 forskellige parabener hos spanske gravide og børn.

De udvalgte studier har blandt andet fokus på eksponeringsniveauer, sædkvalitetsdata og kvindelig reproduktion.

Int J Androl. 2011 Mar 2. doi: 10.1111/j.1365-2605.2010.01133.x. [Epub ahead of print]
Recent adverse trends in semen quality and testis cancer incidence among Finnish men.
Jørgensen N, Vierula M, Jacobsen R, Pukkala E, Perheentupa A, Virtanen HE, Skakkebaek NE, Toppari J.
University Department of Growth and Reproduction, Rigshospitalet, Copenhagen, Denmark Department of Physiology, University of Turku, Turku, Finland Institute of Public Health, Epidemiology, University of Southern Denmark, Odense, Denmark Finnish Cancer Registry, Institute for Statistical and Epidemiological Cancer Research, Helsinki, Finland Department of Obstetrics and Gynaecology, University of Turku, Turku, Finland Department of Paediatrics, University of Turku, Turku, Finland.

Impaired semen quality and testicular cancer may be linked through a testicular dysgenesis syndrome of foetal origin. The incidence of testis cancer has been shown to increase among Finnish men, whereas there is no recent publication describing temporal trends in semen quality. Therefore, we carried out a prospective semen quality study and a registry study of testis cancer incidence among Finnish men to explore recent trends. A total of 858 men were investigated in the semen quality study during 1998-2006. Median sperm concentrations were 67 million/mL, 60 (51-71) and 48 (39-60) for birth cohorts 1979-81, (95% CI 57-80) million, 202 (170-240) and 165 1982-83 and 1987; total sperm counts 227 (189-272) million, (132-207); total number of morphologically normal spermatozoa 18 (14-23) years at the time of diagnosis with 15 (12-19) and 11 (8-15). Men aged 10-59 years at the time of diagnosis with testicular cancer during 1954-2008 were included in the registry study, which confirmed the increasing incidence of testicular cancer in recent cohorts. These simultaneous and rapidly occurring adverse trends suggest that the underlying causes are environmental and, as such, preventable. Our findings necessitate not only further surveillance of male reproductive health but also research to detect and remove the underlying factors.

Fertil Steril. 2011 Feb;95(2):625-30.e1-4. Epub 2010 Oct 29
Urine bisphenol-A (BPA) level in relation to semen quality
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OBJECTIVE: To determine whether urine bisphenol-A (BPA) levels are associated with lower semen quality. DESIGN: Cohort study. SETTING: Four regions in China where high exposure to BPA in the workplace existed. PATIENT(S): 218 men with and without BPA exposure in the workplace. INTERVENTION(S): None. MAIN OUTCOME MEASURE(S): Semen parameters. RESULT(S): After adjustment for potential confounders using linear regression, increasing urine BPA level was statistically significantly associated with [1] decreased sperm concentration, [2] decreased total sperm count, [3] decreased sperm vitality, and [4] decreased sperm motility. Compared with men who did not have detectable urine BPA levels, those with detectable urine BPA had more than three times the risk of lowered sperm concentration and lower sperm vitality, more than four times the risk of lower sperm count, and more than twice the risk of lower sperm motility. The urine BPA level was not associated with semen volume or abnormal sperm morphology. Similar dose-response associations were observed among men with environmental BPA exposure at levels comparable with those in the U.S population. Despite a markedly reduced sample size, the inverse correlation between increased urine BPA levels and decreased sperm concentration and total sperm count remained statistically significant. CONCLUSION(S): These results provide the first epidemiologic evidence of an adverse effect of BPA on semen quality.

Environ Health. 2011 Jan 14;10(1):3.
Parental occupational exposure to endocrine disrupting chemicals and male genital malformations: a study in the Danish National Birth Cohort study.
Morales-Suárez-Varela MM, Toft GV, Jensen MS, Ramlau-Hansen C, Kaerlev L, Thulstrup AM, Llopis-González A, Olsen J, Bonde JP.
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BACKGROUND: Sex hormones closely regulate development of the male genital organs during fetal life. The hypothesis that xenobiotics may disrupt endogenous hormonal signalling has received considerable scientific attention, but human evidence is scarce. OBJECTIVES: We analyse occurrence of hypospadias and cryptorchidism according to maternal and paternal occupational exposure to possible endocrine disrupting
chemicals. METHODS: We conducted a follow-up study of 45,341 male singleton deliveries in the Danish National Birth Cohort during 1997-2009. Information on work during pregnancy was obtained by telephone interviews around gestational week 16. Parents' job titles were classified according to DISCO-88. A job exposure matrix for endocrine disrupting chemicals (EDCs) was implemented to assess occupational exposures. The Medical Birth and National Hospital Register provided data on congenital anomalies diagnosed at birth or during follow-up, which ended in 2009. Crude and adjusted hazard ratios (HR) were obtained from Cox regression models. RESULTS: Among all pregnancies, 6.3% were classified as possibly or probably exposed to EDCs. The most prevalent occupations conferring possible exposure were cleaners, laboratory technicians, hairdressers and agricultural workers (58% of all potentially exposed). The final cumulative incidence of cryptorchidism in boys was 2.2% (1002 cases), and of hypospadias 0.6% (262 cases). The occurrence of hypospadias increased when mothers were probably [HRa = 1.8 (95% CI 1.0-2.6)] or possibly exposed to one or more EDCs [HRa = 2.6 (95% CI 1.8-3.4). Possible paternal exposure to heavy metals increased the risk of hypospadias [HRa 2.2 (95% CI: 1.0-3.4)] and cryptorchidism [HRa 1.9 (95% CI: 1.1-2.7)]. None of the exposure groups reached statistical significance. CONCLUSION: The study provides some but limited evidence that occupational exposure to possible endocrine disrupting chemicals during pregnancy increases the risk of hypospadias.

Environ Health Perspect. 2011 Mar 1. [Epub ahead of print]
Shorter Anogenital Distance Predicts Poorer Semen Quality in Young Men in Rochester, New York
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Background: In male rodents, anogenital distance (AGD) provides a sensitive and continuous correlate of androgen exposure in the intrauterine environment and predicts later reproductive success. Some endocrine disrupting chemicals can alter male reproductive tract development, including shortening AGD, in both rodents and humans. Whether AGD is related to semen quality in human is unknown. Objectives: To examine associations between AGD and semen parameters in adult males. Methods: We used multiple regression analyses to model the relationships between sperm parameters and two alternative measures of AGD (anus to the posterior base of the scrotum [AGDAS], and to the cephalad insertion of the penis [AGDAP]), in 126 volunteers in Rochester, NY. Results: AGDAS, but not AGDAP, was associated with sperm concentration, motility, morphology, total sperm count and total motile count (p-values 0.002-0.048). Men with AGDAS below (compared to above) the median were 7.3 times more likely (95% CI 2.5, 21.6) to have a low sperm concentration (<20x106/ml). For a typical study participant, sperm concentrations were 34.7 x106/ml and 51.6 x106/ml at the 25th and 75th percentiles of (adjusted) AGDAS. Conclusions: In our population, AGDAS was a strong correlate of all semen parameters and a predictor of low sperm concentration. In animals, male AGD at birth reflects androgen levels during the masculinization programming window and predicts adult AGD and reproductive function. Our results suggest, therefore, that the androgenic environment during early fetal life exerts a fundamental influence on both AGD and adult sperm counts in humans, as demonstrated in rodents.

Int J Hyg Environ Health. 2011 Mar 1. [Epub ahead of print]

Exposure to phthalates in 5-6 years old primary school starters in Germany-A human biomonitoring study and a cumulative risk assessment.

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We determined the internal exposure of 111 German primary school starters by analyzing urinary metabolites of six phthalates: butyl benzyl phthalate (BBzP), di-iso-butyl phthalate (DiBP), di-n-butyl phthalate (DnBP), di (2-ethylhexyl) phthalate (DEHP), di-iso-nonyl phthalate (DiNP) and di-iso-ecylphthalate (DiDP). From the urinary metabolite levels, we calculated daily intakes and related these values to Tolerable Daily Intake (TDI) values. By introducing the concept of a relative cumulative Tolerable Daily Intake (TDI(cum)) value, we tried to account for the cumulative exposure to several of the above-mentioned phthalates. The TDI(cum) was derived as follows: the daily intake (DI) calculated from the metabolite level was divided by the TDI for each phthalate; this ratio was multiplied by 100% indicating the TDI percentage for which the DI accounted. Finally the % TDIs of the different phthalates were totalled to get the TDI(cum). A TDI(cum) above 100% is a potential cause for concern. We confirmed the ubiquitous exposure of the children to all phthalates investigated. Exposures were within range of levels previously reported for GerES, albeit slightly lower. Regarding daily intakes, two children exceeded the TDI for DnBP, whereas one child closely approached the TDI for DEHP. 24% of the children exceeded the TDI(cum) for the three most critical phthalates: DEHP, DnBP and DiBP. Furthermore, 54% of the children had total exposures that used up more than 50% the TDI(cum). Therefore, the overall exposure to a number of phthalates, and the knowledge that these phthalates (and other anti-androgens) act in a dose-additive manner, urgently warrants a cumulative risk assessment approach.

Environ Res. 2011 Mar 21. [Epub ahead of print]

Urinary excretion of phthalate metabolites in 129 healthy Danish children and adolescents: Estimation of daily phthalate intake.

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BACKGROUND: Phthalates are a group of chemicals with widespread use in the industrial production of numerous consumer products. They are suspected to be involved in male reproductive health problems and have also been associated with several other health problems in children including obesity and asthma.
OBJECTIVES: To study the urinary excretion of phthalate metabolites in Danish children recruited from the general population, and to estimate the daily intake of phthalates in this segment of the population.
METHOD: One 24h urine sample and to consecutive first morning urine samples were collected from 129 healthy Danish children and adolescents (range 6-21yrs). The concentrations of 11 phthalate metabolites of 5 different phthalate diesters were analyzed by liquid chromatography-tandem mass spectrometry.
RESULTS: The analyzed metabolites were detectable in almost all 24h urine samples. The median concentrations of monoethyl phthalate (MEP), monobenzyl phthalate (MBzP) and the sums of the two monobutyl phthalate isoforms (∑MBP(i+n)), metabolites of di-(2-ethylhexyl) phthalate (∑DEHPm) and of di-iso-nonyl phthalate (∑DiNPm) were 29, 17, 111, 107 and 31ng/mL, respectively. The youngest children were generally more exposed to phthalates than older children and adolescents (except diethyl phthalate (DEP)). Boys were more exposed than girls. The median estimated daily intake of phthalate diesters was: 4.29 (dibutyl phthalate isoforms (DBP(i+n))), 4.04 (DEHP), 1.70 (DiNP), 1.09 (DEP) and 0.62 (butylbenzyl phthalate (BBzP)), all calculated as µg/kg body weight/24h. Between 40% and 48% of the absolute amount of phthalate metabolites excreted over 24h were excreted in first morning urine voids.
CONCLUSION: Danish children are exposed simultaneously to multiple phthalates. The highest exposure levels were found for DBP(i+n) and DEHP, which in animal models are the known most potent anti-androgenic phthalates. The combined exposure to the two isoforms of DBP, which have similar endocrine-disrupting potencies in animal models, exceeded the TDI for di-n-butyl phthalate (DnBP) in several of the younger children.

Environ Int. 2011 Mar 24. [Epub ahead of print]
Urinary concentrations of phthalates and phenols in a population of Spanish pregnant women and children.
Casas L, Fernández MF, Llop S, Guxens M, Ballester F, Olea N, Irurzun MB, Rodríguez LS, Riaño I, Tardón A, Vrijheid M, Calafat AM, Sunyer J; On behalf of the INMA Project.
Centre for Research in Environmental Epidemiology, Dr Aiguader 88, 08003 Barcelona, Catalonia, Spain; Hospital del Mar Research Institute (IMIM), Dr Aiguader 88, 08003 Barcelona, Catalonia, Spain; CIBER Epidemiología y Salud Pública (CIBERESP), Spain.

BACKGROUND: Phthalate and phenol exposure is prevalent among the general population and of potential concern for pregnant women and children because of their suspected susceptibility to endocrine effects. OBJECTIVES: To evaluate the extent of exposure to several phthalates and phenols in a sample of Spanish pregnant women - according to their individual characteristics (age, social class, education, and body mass index) - and children who participated in the INMA - Infancia y Medio Ambiente (Environment and Childhood) project. METHODS: One spot urine sample was taken during the third trimester of pregnancy from 120 pregnant women and from 30 4-year old children belonging to 5 Spanish birth cohorts, and analyzed for 11 phthalate metabolites and 9 phenols. RESULTS: Three metabolites of di(2-ethylhexyl) phthalate, mono-2-ethyl-5-carboxypentyl phthalate, mono-2-ethyl-5-hydroxyhexyl phthalate, and mono-2-ethyl-5-oxohexyl phthalate; two metabolites of dibutyl phthalates, mono-isobutyl phthalate and mono-n-butyl phthalate; monoethyl phthalate (MEP), the main metabolite of diethyl phthalate; and two phenols, methyl paraben (M-PB) and 2,5-dichlorophenol were detected in the urine samples of all women. The highest urinary concentrations were for MEP and M-PB. Urinary concentrations of all phthalate metabolites and of 2,4-dichlorophenol, 2,5-dichlorophenol, and bisphenol A were lower in the pregnant women than in the children. Among women, a positive relationship with social class and education was shown for most of the phthalate metabolites and phenols. Almost all phthalate metabolites varied by region even after adjusting for social class and education. CONCLUSIONS: Phthalate and phenol exposures are prevalent in a group of pregnant women and young children, two susceptible populations, and these exposures might be positively related to social class.

Environmental Health Perspectives doi: 10.1289/ehp.1003170 (available at http://dx.doi.org/) Online 30 March 2011
Food Packaging and Bisphenol A and Bis(2-Ethyhexyl) Phthalate Exposure: Findings from a Dietary Intervention
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Abstract
BACKGROUND: Bisphenol A (BPA) and bis(2-ethylhexyl) phthalate (DEHP) are high production-volume chemicals used in plastics and resins for food packaging. They have been associated with endocrine disruption in animals and in some human studies. Human exposure sources have been estimated, but the relative contribution of dietary exposure to total intake has not been studied empirically. OBJECTIVES: To evaluate the contribution of food packaging to exposure, we measured urinary BPA and phthalate metabolites before, during and after a “fresh foods” dietary intervention. METHODS: We selected 20 participants in five families based on self-reported use of canned and packaged foods. Participants ate their usual diet, followed by three days of “fresh foods” that were not canned or packaged in plastic, and then returned to their usual diet. We collected evening urine samples over eight days in January 2010 and composited them into preintervention, intervention, and post-intervention samples. We used mixed effects models for repeated measures and Wilcoxon signed rank tests to assess change in urinary levels across time. RESULTS: Urine levels of BPA and DEHP metabolites decreased significantly during the fresh foods intervention (e.g., BPA geometric mean 3.7 ng/mL pre-intervention and 1.2 ng/mL during intervention; MEHHP geometric mean 57 ng/mL vs 25 ng/mL). The intervention reduced geometric mean concentrations of BPA by 66% and DEHP metabolites by 53-56%. Maxima were reduced by 76% for BPA and 93-96% for DEHP metabolites. CONCLUSIONS: BPA and DEHP exposures were substantially reduced when participants’ diets were restricted to food with limited packaging.

Environ Health Perspect. 2011 Jan 14. [Epub ahead of print]
Environmental Chemicals in Pregnant Women in the US: NHANES 2003-2004.
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Background: We analyzed biomonitoring data from the National Health and Nutritional Examination Survey (NHANES) to characterize both individual and multiple chemical exposures in U.S. pregnant women. Methods: We analyzed data for 163 chemical analytes in 12 chemical classes for subsamples of 268 pregnant women from NHANES 2003-2004, a nationally representative sample of the U.S. population. For each chemical analyte, we calculated descriptive statistics. We calculated the number of chemicals detected within the following chemical classes; polybrominated diphenyl ethers (PBDEs), perfluorinated compounds (PFCs), organochlorine pesticides, and phthalates, and across multiple chemical classes. We compared chemical analyte concentrations for pregnant and non-pregnant women using least square geometric means, adjusting for demographic and physiological covariates. Results: The percent of pregnant women with detectable levels of an individual chemical ranged from 0 to 100 percent. Certain PCBs, organochlorine pesticides, PFCs, phenols, PBDEs, phthalates, polycyclic aromatic hydrocarbons (PAHs) and perchlorate were detected in 99 to 100% of pregnant women. The median number of detected chemicals by chemical class ranged from 4 (out of 12 PFCs) to 9 (out of 13 phthalates). Across chemical classes, median number ranged from 8 (out of 17 chemical analytes) to 50 (out of 71 chemical analytes). We found, generally, levels in pregnant women were similar or lower than levels in non-pregnant women, adjustment for covariates tended to increase levels in pregnant women compared to non-pregnant women. Conclusions: Pregnant women in the U.S. are exposed to multiple chemicals. Further efforts are warranted to understand sources of exposure and implications for policy-making.

J Clin Endocrinol Metab. 2011 Mar 16. [Epub ahead of print]
Implications of Early Menopause in Women Exposed to Perfluorocarbons.
Knox SS, Jackson T, Javins B, Frisbee SJ, Shankar A, Ducatman AM.
Departments of Community Medicine (S.S.K., B.J., S.J.F., A.S., A.M.D.) and Medicine (T.J.) and Center for Cardiovascular and Respiratory Sciences (S.J.F.), West Virginia University School of Medicine, Morgantown, West Virginia 26506.

Context: Perfluorocarbons (PFC) are man-made chemicals used in numerous household products. They have a long half-life in humans and complex animal toxicity, and accumulating evidence points toward associations with multiple human health endpoints. Objective: Our objective was to investigate whether PFC are associated with endocrine disruption in women. Design: Cross-sectional analyses were made between quintiles of serum PFC, serum estradiol, and menopause onset. Setting: The C8 Health Project, with cohort of 69,030 adults and children, was conducted due to PFC contamination of drinking water from six water districts in two states. Participants: Participants included 25,957 women aged 18-65 yr. Main Outcome Measures: Serum estradiol levels and onset of menopause were assessed. The survey was the result of a class action suit, and survey designers (an independent corporation) had no a priori hypotheses. All hypotheses have been formulated by other investigators after data collection. Results: After excluding women who reported hysterectomy and adjusting for age within the group, smoking, alcohol consumption, body mass index, and exercise, the odds of having experienced menopause were significantly higher in the highest quintile relative to the lowest quintile of perfluorooctanoate (PFOA) and perfluorooctane sulfonate (PFOS) in the perimenopausal [PFOS odds = 1.4, confidence interval (CI) = 1.1-1.8; PFOA odds =1.4, CI = 1.1-1.8] and menopausal age groups (PFOS odds = 2.1, CI=1.6-2.8; PFOA odds = 1.7, CI = 1.3-2.3). After appropriate exclusions and adjustment for covariates, there was a significant inverse association between PFOS and estradiol in perimenopausal ($\beta = -3.65$; $P < 0.0001$) and menopausal age groups ($\beta = -0.83$; $P = 0.007$) but not between PFOA and estradiol. Conclusions: These data suggest that PFC are associated with endocrine disruption in women and that further research on mechanisms is warranted.

J Clin Endocrinol Metab. 2011 Mar;96(3):E480-4. Epub 2010 Dec 30.

Endocrine Disruptors and Polycystic Ovary Syndrome (PCOS): Elevated Serum Levels of Bisphenol A in Women with PCOS

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Context: Bisphenol A (BPA) is a widespread industrial compound used in the synthesis of polycarbonate plastics. In experimental animals, neonatal exposure to BPA results in a polycystic ovary-like syndrome (PCOS) in adulthood. A bidirectional interaction between androgens and BPA levels has been disclosed. Objective: To determine BPA levels in PCOS women as well as the association between BPA and hormonal/metabolic parameters compared to a control group. Design, Setting, and Participants: Cross-sectional study of 71 PCOS (National Institutes of Health criteria) and 100 normal women, age- and body mass index-matched, in a University hospital setting. Main Outcome Measures: Anthropometric, hormonal, metabolic parameters and BPA blood levels were determined. Patients (PCOS) and controls (C) were further subdivided according to body mass index into lean and overweight subgroups, respectively. Results: BPA levels were significantly higher in the total PCOS group compared with the controls (1.05±0.56 vs. 0.72±0.37ng/ml, $P < 0.001$). PCOS women, lean (PCOS-L) and overweight (PCOS-OW), had higher BPA levels compared to the corresponding control group lean (C-L) and overweight (C-OW): (PCOS-L = 1.13±0.63 vs. C-L = 0.70±0.36, $P < 0.001$) (PCOS-OW = 0.96 ± 0.46 vs. C-OW = 0.72 ± 0.39, $P < 0.05$). A significant association of testosterone ($r = 0.192$, $P < 0.05$) and androstenedione ($r = 0.257$, $P < 0.05$) with BPA was observed. Multiple regression analysis for BPA showed significant correlation with the existence of PCOS ($r = 0.497$, $P < 0.05$). BPA was also positively correlated with insulin resistance (Matsuda index) in the PCOS group ($r = 0.273$, $P < 0.05$). Conclusions: Higher BPA levels in PCOS women compared to controls and a statistically significant positive association between androgens and BPA point to a potential role of this endocrine disruptor in PCOS pathophysiology.

Science. 2011 Mar 4;331(6021):1136.

Assessing chemical risk: societies offer expertise

American Society of Human Genetics; American Society for Reproductive Medicine; Endocrine Society; Genetics Society of America; Society for Developmental Biology; Society for Pediatric Urology; Society for the Study of Reproduction; Society for Gynecologic Investigation.

Der er intet abstract

Bruttoliste

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In Vitro studier ved DTU - FOOD

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*" og "Paraben* AND in vitro*"

Limits Activated: published in the last 180 days (Januar-marts 2011)

Efter at have fjernet genganger fra dem vi havde med på den forrige litteraturopdateringsliste, gav litteratursøgningen med de to søgekriterier tilsammen en liste med i alt 19 artikler: (Bruttolisten):

Ud fra bruttolisten (se længere nede i dokumentet) er udvalgt følgende 3 artikler til engelsk abstrakt og i nogle tilfælde dansk konklusion og kommentarer.

Udvalgte publikationer:

Widely Used Pesticides with Previously Unknown Endocrine Activity Revealed as in Vitro Anti-Androgens.

Orton F, Rosivatz E, Scholze M, Kortenkamp A.

Environ Health Perspect. 2011 Feb 10. [Epub ahead of print]

Abstract

Background: Evidence suggests that there is widespread decline in male reproductive health and anti-androgenic pollutants may play a significant role. There is also a clear disparity between pesticide exposure and endocrine disrupting data, with the majority of the published literature focused on pesticides that are no longer registered for use in developed countries. Objective: The aim of this study was to utilise estimated human exposure data to select pesticides to test for anti-androgenic activity, focusing on highest use pesticides. Methods: We used European databases to select 134 candidate pesticides based on highest exposure, followed by a filtering step according to known or predicted receptor mediated anti-androgenic potency, based on a previously published quantitative structure-activity relationship (QSAR) model. In total, 37 pesticides were tested for in vitro androgen receptor (AR) antagonism. Of these, 14 were previously reported to be AR antagonists ("active"), 4 were predicted AR antagonists using the QSAR, 6 were predicted to not be AR antagonists ("inactive"), and 13 with unknown activity, which were "out of domain" and therefore could not be classified with the QSAR ("unknown"). Results: All 14 pesticides with previous evidence of AR antagonism were confirmed as anti-androgenic in our assay and 9 previously untested pesticides were identified as anti-androgenic (dimethomorph, fenhexamid, quinoxyfen, cyprodinil, λ-cyhalothrin, pyrimethanil, fludioxonil, azinphos-methyl, pirimiphos-methyl). In addition, 7 compounds were classified as androgenic. Conclusions: Due to estimated anti-androgenic potency, current use, estimated exposure, and lack of previous data, we strongly recommend that dimethomorph, fludioxonil, fenhexamid, imazalil, ortho-phenylphenol and pirimiphos-methyl be tested for anti-androgenic effects in vivo. The lack of human biomonitoring data for environmentally relevant pesticides presents a barrier to current risk assessment of pesticides on humans.

Effect of bisphenol A on human endometrial stromal fibroblasts in vitro.

Aghajanova L, Giudice LC.

Reprod Biomed Online. 2011 Mar;22(3):249-56. Epub 2010 Dec 23.

Abstract

This study evaluated the effects of bisphenol A (BPA) on human endometrial stromal fibroblast (ESF) differentiation and expression of genes involved in oestrogen metabolism. Human ESF from eight hysterectomy specimens were cultured and treated with 5-100μmol/l of BPA±oestradiol or 8-br-cAMP for 48h. mRNA expression was analysed by real-time reverse-transcription PCR. 8-br-

cAMP-induced human ESF decidualization was confirmed by expression of insulin-like growth factor binding protein-1 (IGFBP1) and prolactin secretion. Short-term exposure (48h) decreased human ESF proliferation (P<0.04) not due to apoptosis. High doses of BPA significantly induced IGFBP1 mRNA and protein, decreased P450scc mRNA, reversed the 8-br-cAMP-induced increase in HSD17B2 (oestradiol to oestrone conversion) in a dose-dependent manner and down-regulated HSD17B1 expression (oestrone to oestradiol conversion; P□0.03). 8-br-cAMP significantly potentiated this effect (P=0.028). BPA had no significant effect on aromatase and PPAR γ expression. The oestrogen-receptor antagonist ICI had no effect on gene expression in BPA-treated cells, and oestrogen receptor α, but not oestrogen receptor β, was significantly down-regulated by high doses of BPA (P=0.028). BPA has an endocrine-disrupting effect on human ESF function and gene expression but the underlying mechanisms appear not to involve oestrogen-mediated pathways. Studies of the effects of bisphenol A (BPA), an endocrine disruptor, on the endometrium, a steroid hormone-sensitive tissue in which an embryo implants to establish pregnancy, are limited. Herein, we evaluated the effects of BPA on human endometrial stromal fibroblast (ESF) differentiation and expression of several genes involved in oestrogen metabolism. Human ESF were isolated from eight hysterectomy specimens, free from endometriosis or adenomyosis. They were cultured and treated with 5-100μmol/l of BPA with or without oestradiol or 8-br-cAMP (a decidualization/differentiation stimulus) for 48h. mRNA expression was analysed by real-time reverse-transcription PCR. 8-br-cAMP-induced human ESF decidualization (started 48h prior to BPA) was confirmed by insulin-like growth factor binding protein 1 and prolactin secretion. Short-term exposure (48h) of endometrial stromal cells to BPA significantly decreased human ESF proliferation, which was not due to increased apoptosis. High doses of BPA significantly induced differentiation in a dose-dependent manner to the same extent as 8-br-cAMP and significantly potentiated its effect. BPA had a significant effect on the expression of the enzyme that makes oestrogen, although the oestrogen-receptor antagonist had no effect on gene expression in BPA-treated cells. Interestingly, the main receptor that mediates oestrogen signalling, oestrogen receptor α, was significantly down-regulated by high doses of BPA. BPA thus has an endocrine-disrupting effect on human ESF function and gene expression. The effects on subsequent endometrial function remain to be determined.

QSAR models for anti-androgenic effect - a preliminary study.

Jensen GE, Nikolov NG, Wedebye EB, Ringsted T, Niemela JR.

SAR QSAR Environ Res. 2011 Mar;22(1):35-49.

AbstractThree modelling systems (MultiCase®, LeadScope® and MDL® QSAR) were used for construction of androgenic receptor antagonist models. There were 923-942 chemicals in the training sets. The models were cross-validated (leave-groups-out) with concordances of 77-81%, specificity of 78-91% and sensitivity of 51-76%. The specificity was highest in the MultiCase® model and the sensitivity was highest in the MDL® QSAR model. A complementary use of the models may be a valuable tool when optimizing the prediction of chemicals for androgenic receptor antagonism. When evaluating the fitness of the model for a particular application, balance of training sets, domain definition, and cut-offs for prediction interpretation should also be taken into account. Different descriptors in the modelling systems are illustrated with hydroxyflutamide and dexamethasone as examples (a non-steroid and a steroid anti-androgen, respectively). More research concerning the mechanism of anti-androgens would increase the possibility for further optimization of the QSAR models. Further expansion of the basis for the models is in progress, including the addition of more drugs.

Brutto søgeresultat in vitro

1. Cadmium-mediated disruption of cortisol biosynthesis involves suppression of corticosteroidogenic genes in rainbow trout.
Sandhu N, Vijayan MM.
Aquat Toxicol. 2011 Feb 18;103(1-2):92-100. [Epub ahead of print]

2. The consequences of feminization in breeding groups of wild fish.
Harris CA, Hamilton PB, Runnalls TJ, Vinciotti V, Henshaw A, Hodgson D, Coe TS, Jobling S, Tyler CR, Sumpter JP.
Environ Health Perspect. 2011 Mar;119(3):306-11.

3. In vitro transformation of MCF-10A cells by sera harvested from heifers two months post-Zeranol implantation.
Ye W, Xu P, Zhong S, Jen R, Threlfall WR, Frasure CV, Feng E, Li H, Lin SH, Liu JY, Lin YC.
Int J Oncol. 2011 Apr;38(4):985-92. doi: 10.3892/ijo.2011.941. Epub 2011 Feb 11.

4. Widely Used Pesticides with Previously Unknown Endocrine Activity Revealed as in Vitro Anti-Androgens.
Orton F, Rosivatz E, Scholze M, Kortenkamp A.
Environ Health Perspect. 2011 Feb 10. [Epub ahead of print]

5. Modulation of steroidogenic gene expression and hormone synthesis in H295R cells exposed to PCP and TCP.
Ma Y, Liu C, Lam PK, Wu RS, Giesy JP, Hecker M, Zhang X, Zhou B.
Toxicology. 2011 Apr 11;282(3):146-53. Epub 2011 Feb 4.

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Aghajanova L, Giudice LC.
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Liu J, Yang Y, Yang Y, Zhang Y, Liu W.
Toxicology. 2011 Mar 28;282(1-2):47-55. Epub 2011 Jan 18.

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Borgert CJ, Mihaich EM, Quill TF, Marty MS, Levine SL, Becker RA.
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Mohamed el-SA, Park YJ, Song WH, Shin DH, You YA, Ryu BY, Pang MG.
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Kamata R, Shiraishi F, Nakajima D, Kageyama S.
Aquat Toxicol. 2011 Jan 25;101(2):430-7. Epub 2010 Dec 4.

11.Effects of perfluoroalkyl compounds (PFCs) on mRNA expression levels of thyroid hormone-responsive genes in primary cultures of avian neuronal cells.
Vongphachan V, Cassone CG, Wu D, Chiu S, Crump D, Kennedy SW.
Toxicol Sci. 2011 Jan 6. [Epub ahead of print]

12.Estrogen receptors in medaka (Oryzias latipes) and estrogenic environmental contaminants: an in vitro-in vivo correlation.
Chakraborty T, Katsu Y, Zhou LY, Miyagawa S, Nagahama Y, Iguchi T.
J Steroid Biochem Mol Biol. 2011 Feb;123(3-5):115-21. Epub 2010 Dec 9.

13. The environmental endocrine disruptor, bisphenol A, affects germination, elicits stress response and alters steroid hormone production in kiwifruit pollen.
Speranza A, Crosti P, Malerba M, Stocchi O, Scoccianti V.
Plant Biol (Stuttg). 2011 Jan;13(1):209-17. doi: 10.1111/j.1438-8677.2010.00330.x.

14. Computational estimation of rainbow trout estrogen receptor binding affinities for environmental estrogens.
Shyu C, Cavileer TD, Nagler JJ, Ytreberg FM.
Toxicol Appl Pharmacol. 2011 Feb 1;250(3):322-6. Epub 2010 Nov 12.

15. Viable skin efficiently absorbs and metabolizes bisphenol A.
Zalko D, Jacques C, Duplan H, Bruel S, Perdu E.
Chemosphere. 2011 Jan;82(3):424-30. Epub 2010 Oct 27.

16.Assessing estrogenic activity in surface water and sediment of the Liao River system in northeast China using combined chemical and biological tools.
Wang L, Ying GG, Zhao JL, Liu S, Yang B, Zhou LJ, Tao R, Su HC.
Environ Pollut. 2011 Jan;159(1):148-56. Epub 2010 Oct 15.

17.The implementation of a battery of in vivo and in vitro bioassays to assess river water for estrogenic endocrine disrupting chemicals.
Swart JC, Pool EJ, van Wyk JH.
Ecotoxicol Environ Saf. 2011 Jan;74(1):138-43.

18.The effect of valproate and levetiracetam on steroidogenesis in forskolin-stimulated H295R cells.
von Krogh K, Harjen H, Almås C, Zimmer KE, Dahl E, Olsaker I, Taubøll E, Ropstad E, Verhaegen S.
Epilepsia. 2010 Nov;51(11):2280-8. doi: 10.1111/j.1528-1167.2010.02702.x. Epub 2010 Aug 17.

19.Identification of Personal Lubricants That Can Cause Rectal Epithelial Cell Damage and Enhance HIV Type 1 Replication in Vitro.
Begay O, Jean-Pierre N, Abraham CJ, Chudolij A, Seidor S, Rodriguez A, Ford BE, Henderson M, Katz D, Zydowsky T, Robbiani M, Fernández-Romero JA.
AIDS Res Hum Retroviruses. 2011 Mar 8. [Epub ahead of print]

Herudover er der yderligere en artikel, som ikke blev fanget af de valgte søgekriterier:
QSAR models for anti-androgenic effect - a preliminary study.
Jensen GE, Nikolov NG, Wedebye EB, Ringsted T, Niemela JR.
SAR QSAR Environ Res. 2011 Mar;22(1):35-49.

In Vivo studier ved DTU - FOOD

Søgning er udført på PubMed samt DTU Digital Library og dækker perioden 1/1/2011-23/3
(januar – marts 2011)
Følgende søgeprofil er benyttet: ”(endocrine disrupt*) AND utero* AND (rat OR mice OR mammal*)” samt ”(endocrine disrupt*) AND (rat OR mice OR mammal*)”. Derudover er der også søgt på ”Paraben* AND in vivo*”
Efter at have fjernet genganger fra dem vi havde med på den forrige litteraturopdateringsliste, gav litteratursøgningen tilsammen en liste med i alt 28 artikler: (Bruttolisten):
De udvalgte studier har fokus på en phthalat (Dipentyl phthalat), bisphenol A, PCB samt en OECD test H295 (**in vitro**) (sidste 2 vises kun abstract).

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

Udvalgte publikationer in vivo:
Dipentyl Phthalate Dosing during Sexual Differentiation Disrupts Fetal Testis Function and Postnatal Development of the Male Sprague-Dawley Rat with Greater Relative Potency than Other Phthalates (Toxicol Sci — 2011, Volume 120, Issue 1, pp. 184-193)
Bethany R. Hannas*, Johnathan Furr†, Christy S. Lambright†, Vickie S. Wilson†, Paul M. D. Foster‡ and L. Earl Gray Jr†
Abstract: Phthalate esters (PEs) constitute a large class of plasticizer compounds that are widely used for many consumer product applications. Ten or more members of the PE class of compounds are known to induce male fetal endocrine toxicity and postnatal reproductive malformations by disrupting androgen production during the sexual differentiation period of development. An early study conducted in the rat pubertal model suggested that dipentyl phthalate (DPeP) may be a more potent testicular toxicant than some more extensively studied phthalates. Regulatory agencies require dose-response and potency data to facilitate risk assessment; however, very little data are currently available for DPeP. The goal of this study was to establish a more comprehensive data set for DPeP, focusing on dose-response and potency information for fetal and postnatal male reproductive endpoints. We dosed pregnant rats on gestational day (GD) 17 or GD 14–18 and subsequently evaluated fetal testicular testosterone (T) production on GD 17.5 and GD 18, respectively. We also dosed pregnant rats on GD 8–18 and evaluated early postnatal endpoints in male offspring. Comparison of these data to data previously obtained under similar conditions for di (2-ethylhexyl) phthalate indicates that DPeP is approximately eightfold more potent in reducing fetal T production and two- to threefold more potent in inducing development of early postnatal male reproductive malformations. Additionally, fetal testicular T production was more sensitive to inhibitory effects of DPeP exposure than was gene expression of target genes involved in male reproductive development, supporting the use of this endpoint as a critical effect in the risk assessment process.

Horm Behav. 2011 Feb;59(2):246-51. Epub 2010 Dec 23.
Pre- and postnatal bisphenol A treatment results in persistent deficits in the sexual behavior of male rats, but not female rats, in adulthood.
Jones BA, Shimell JJ, Watson NV.

Abstract: Perinatal administration of the endocrine disruptor bisphenol A (BPA) reportedly inhibits the sexual behavior of sexually naïve adult male rats. In order to evaluate the effects of BPA administration during early development on later reproductive behavior, we administered one of five doses of bisphenol A daily to pregnant female rats throughout gestation and lactation, and quantified the appetitive and consummatory sexual behaviors of the resultant male and female offspring over multiple sexual encounters in adulthood. Males receiving low dose perinatal BPA (50 μg/kg bw/day) showed persistent deficits in sexual behavior in adulthood. Males receiving the highest dose (5 mg/kg bw/day), however, were indistinguishable from controls with respect to consummatory sexual behaviors but showed decreased latencies to engage in those behaviors when sexually naïve, with significant non-linear, or U-shaped, dose-response relationships observed on the first and last day of testing. Adult female sexual behavior was not affected by early BPA administration at any dose tested. These results are consistent with previous reports that BPA exerts behavioral effects especially at low doses, and further indicates that BPA can cause lasting impairment of sexual behavior in males, but does not alter the normal development of female appetitive or consummatory sexual behaviors. To our knowledge, this is the first report indicating that adult sexual performance is impaired in sexually experienced animals following perinatal exposure to bisphenol A.

Environ Sci Pollut Res Int. 2011 Mar;18(3):503-15. Epub 2010 Oct 3.

OECD Validation (kun abstract vises) – DTU Fødevareinstituttet har deltaget i dette arbejde.

The OECD validation program of the H295R steroidogenesis assay: Phase 3. Final inter-laboratory validation study.

Hecker M, Hollert H, Cooper R, Vinggaard AM, Akahori Y, Murphy M, Nellemann C, Higley E, Newsted J, Laskey J, Buckalew A, Grund S, Maletz S, Giesy J, Timm G.

Abstract

BACKGROUND, GOALS, AND SCOPE: In response to increasing concerns regarding the potential of chemicals to interact with the endocrine system of humans and wildlife, various national and international programs have been initiated with the aim to develop new guidelines for the screening and testing of these chemicals in vertebrates. Here, we report on the validation of an in vitro assay, the H295R steroidogenesis assay, to detect chemicals with the potential to inhibit or induce the production of the sex steroid hormones testosterone (T) and 17β-estradiol (E2) in preparation for the development of an Organization for Economic Cooperation and Development (OECD) test guideline. METHODS: A previously optimized and pre-validated protocol was used to assess the potential of 28 chemicals of diverse structures and properties to validate the H295R steroidogenesis assay. These chemicals are comprised of known endocrine-active chemicals and "negative" chemicals that were not expected to have effects on the targeted endpoints, as well as a

number of test chemicals with unknown modes of action at the level of the steroidogenic pathway. A total of seven laboratories from seven countries participated in this effort. In addition to effects on hormone production, confounding factors, such as cell viability and possible direct interference of test substances with antibody-based hormone detection assays, were assessed. Prior to and during the conduct of exposure experiments, each laboratory had to demonstrate that they were able to conduct the assay within the margin of predefined performance criteria. RESULTS: With a few exceptions, all laboratories met the key quality performance parameters, and only 2% and 7% of all experiments for T and E2, respectively, were excluded due to exceedance of these parameters. Of the 28 chemicals analyzed, 13 and 14 tested affected production of T and E2, respectively, while 11 and 8 did not result in significant effects on T and E2 production, respectively. Four and six chemicals produced ambiguous results for effects on T and E2 production, respectively. However, four of these cases each for T and E2 were associated with only one laboratory after a personnel change occurred. Significant interference of test chemicals with some of the antibody-based hormone detection systems occurred for four chemicals. Only one of these chemicals, however, significantly affected the ability of the detection system to categorize the chemical as affecting E2 or T production. DISCUSSION AND CONCLUSIONS: With one exception, the H295R steroidogenesis assay protocol successfully identified the majority of chemicals with known and unknown modes of interaction as inducers or inhibitors of T and E2 production. Thus it can be considered a reliable screen for chemicals that can alter the production of sex steroid hormones. One of the remaining limitations associated with the H295R steroidogenesis assay protocol is the relatively small basal production of E2 and its effect on quantifying the decreased production of this hormone with regard to the identification of weak inhibitors. An initial comparison of the data produced in this study with those from in vivo studies from the literature demonstrated the potential of the H295R steroidogenesis assay to identify chemicals affecting hormone homeostasis in whole organisms. Particularly promising was the lack of any false negatives during the validation and the very low number of false positives (1 out of 28 chemicals for each T and E2).PERSPECTIVES: Based on the results obtained during this validation study and the accordingly revised test protocols, an OECD draft test guideline was developed and submitted to the OECD working group of the national coordinators of the test guidelines program (WNT) for comments in December 2009.

Endocrine disruption of brain sexual differentiation by developmental PCB exposure.

Dickerson SM, Cunningham SL, Patisaul HB, Woller MJ, Gore AC.
Division of Pharmacology and Toxicology and Center for Molecular and Cellular Toxicology, The University of Texas at Austin, Texas 78712-0125, USA.

Abstract
In mammals, sexual differentiation of the hypothalamus occurs during prenatal and early postnatal development due in large part to sex differences in hormones. These early organizational processes are critically important for the attainment and maintenance of adult reproductive functions. We tested the hypothesis that perinatal exposure to polychlorinated biphenyls (PCBs) that disrupt hormonal pathways would perturb reproductive maturation and the sexually dimorphic development of neuroendocrine systems in the preoptic area (POA). Pregnant Sprague-Dawley rats were injected on gestational d 16 and 18 with vehicle (dimethylsulfoxide), Aroclor 1221 (A1221, an estrogenic PCB mix), a reconstituted PCB mixture representing those highest in human body burden (PCBs 138, 153, 180), or estradiol benzoate, an estrogenic control. Male and female pups were monitored for somatic and reproductive development. In adulthood, some rats were perfused and used for

immunohistochemistry of estrogen receptor α, kisspeptin, and coexpression of Fos in GnRH neurons. Other rats were used to obtain fresh-frozen POA dissections for use in a PCR-based 48-gene expression array. Pubertal onset was advanced and estrous cyclicity irregular in endocrine-disrupted females. Furthermore, sexual differentiation of female neuroendocrine systems was masculinized/defeminized. Specifically, in the adult female anteroventral periventricular nucleus, estrogen receptor α-cell numbers and kisspeptin fiber density were significantly decreased, as was GnRH-Fos coexpression. PCR analysis identified androgen receptor, IGF-I, N-methyl-d-aspartate receptor subunit NR2b, and TGFβ1 mRNAs as significantly down-regulated in endocrine-disrupted female POAs. These data suggest that developmental PCBs profoundly impair the sexual differentiation of the female hypothalamus.

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5. Endocrine disrupting properties of perfluorooctanoic acid.
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23. Endocrine disruption of brain sexual differentiation by developmental PCB exposure.
Dickerson SM, Cunningham SL, Patisaul HB, Woller MJ, Gore AC.
Endocrinology. 2011 Feb;152(2):581-94. Epub 2010 Dec 29. **(kun abstract vises)**

Herudover kommer yderligere 5 artikler som ikke blev fanget på Pubmed men på DTU Library (ny søgemaskine):

24. Dipentyl Phthalate Dosing during Sexual Differentiation Disrupts Fetal Testis Function and Postnatal Development of the Male Sprague-Dawley Rat with Greater Relative Potency than Other Phthalates A (Toxicol Sci — 2011, Volume 120, Issue 1, pp. 184-193)
Hannas, Bethany R. • Furr, Johnathan • Lambright, Christy S. • Wilson, Vickie S. • Foster, Paul M. D. • Gray, L. Earl, Jr **(denne er udvalgt)**

25.Urinary and serum metabolites of di-n-pentyl phthalate in rats (Chemosphere — 2011, Volume 82, Issue 3, pp. 431-436)Silva, Manori J. • Furr, Johnathan • Samandar, Ella • Preau, James L., Jr. • Gray, L. Earl • Needham, Larry L. • Calafat, Antonia M.
26. Endocrine Disruption: Historical Perspectives and Its Impact on the Future of Toxicology Testing (Toxicol Sci — 2011, Volume 120, Issue suppl_1, pp. S93-S108) Marty, Mary Sue • Carney, Edward W. • Rowlands, Justin Craig (review)

27. The OECD validation program of the H295R steroidogenesis assay: Phase 3. Final inter-laboratory validation study. (Environ Sci Pollut Res Int. 2011 Mar;18(3):503-15. Epub 2010 Oct 3.) Hecker M, Hollert H, Cooper R, Vinggaard AM, Akahori Y, Murphy M, Nellemann C, Higley E, Newsted J, Laskey J, Buckalew A, Grund S, Maletz S, Giesy J, Timm G. **(kun abstract vises)**

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Wildlife studier ved Biologisk Institut, Syddansk Universitet (SDU)

Søgningen er udført på Web of Science og dækker perioden 10/12 2010 – 27/3 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

Desuden er der efter ønske fra MST søgt på "parabens", men ingen af de fundne artikler fra det seneste kvartal relaterer til "wildlife".

Fra bruttolisten (længere nede i dokumentet) er udvalgt 3 artikler til medtagelse af abstract og yderligere kommentarer. Artikel 1 og 2 omhandler begge feminisering af skaller og kommenteres samlet.

Artikel 1:

Title: The Consequences of Feminization in Breeding Groups of Wild Fish
Author(s): Harris CA, Hamilton PB, Runnalls TJ, et al.
Source: ENVIRONMENTAL HEALTH PERSPECTIVES Volume: 119 Issue: 3 Pages: 306-311

Abstract: BACKGROUND: The feminization of nature by endocrine-disrupting chemicals (EDCs) is a key environmental issue affecting both terrestrial and aquatic wildlife. A crucial and as yet unanswered question is whether EDCs have adverse impacts on the sustainability of wildlife populations. There is widespread concern that intersex fish are reproductively compromised, with potential population-level consequences. However, to date, only in vitro sperm quality data are available in support of this hypothesis.
OBJECTIVE: The aim of this study was to examine whether wild endocrine-disrupted fish can compete successfully in a realistic breeding scenario.
METHODS: In two competitive breeding experiments using wild roach (Rutilus rutilus), we used DNA micro-satellites to assign parentage and thus determine reproductive success of the adults.
RESULTS: In both studies, the majority of intersex fish were able to breed, albeit with varying degrees of success. In the first study, where most intersex fish were only mildly feminized, body length was the only factor correlated with reproductive success. In the second study, which included a higher number of more severely intersex fish, reproductive performance was negatively correlated with severity of intersex. The intersex condition reduced reproductive performance by up to 76% for the most feminized individuals in this study, demonstrating a significant adverse effect of intersex on reproductive performance.
CONCLUSION: Feminization of male fish is likely to be an important determinant of reproductive performance in rivers where there is a high prevalence of moderately to severely feminized males.

Artikel 2:

Title: Implications of Persistent Exposure to Treated Wastewater Effluent for Breeding in Wild Roach (Rutilus rutilus) Populations
Author(s): Lange A, Paull GC, Hamilton PB, et al.
Source: ENVIRONMENTAL SCIENCE & TECHNOLOGY Volume: 45 Issue: 4 Pages: 1673-1679

Abstract: Feminized responses are widespread in wild populations of roach, Rutilus rutilus, living in UK rivers, and some of these responses have been shown to arise as a consequence of exposure to wastewater treatment works (WwTW) effluent discharges and the endocrine disrupting chemicals (EDCs) they contain. The causation of the ovotestis condition in wild roach, however, has yet to be established. Furthermore, the impact of long-term exposure to WwTW effluents on the reproductive fitness of wild fish populations is not known, and this information is crucial for population level effect assessments. We undertook a chronic exposure of roach to a treated estrogenic wastewater effluent for up to 3.5 years to assess principally for effects on subsequent reproductive fitness, as determined through parentage analysis on offspring from a competitive breeding study. In generating the fish for the breeding study we found that exposure to full strength WwTW effluent until sexual maturity resulted in sex reversal in almost all males in the population; 98% of the exposed fish were phenotypic females, containing ovaries. Furthermore, fish exposed to a 50% dilution of WwTW effluent contained ovotestis (21% of the male roach) that was absent from the control population. In competitive breeding studies, and applying DNA microsatellites to assess parentage, we show that presumptive females exposed to sexual maturity to WwTW effluent bred normally, albeit in the absence of nonexposed females, but putative sex-reversed males breeding as females contributed poorly, if at all, in a breeding population, depending on the competition. These novel findings on sex reversal add a new dimension for impact assessments of exposure to WwTW effluents on fish populations.

Artikel 3:

Title: Exposure to 17 alpha-ethynylestradiol causes dose and temporally dependent changes in intersex, females and vitellogenin production in the Sydney rock oyster
Author(s): Andrew MN, O'Connor WA, Dunstan RH, et al.
Source: ECOTOXICOLOGY Volume: 19 Issue: 8 Pages: 1440-1451

Abstract: Although mounting evidence suggests exposure to estrogenic contaminants increases vitellogenin production in molluscs, demonstration of dose-response relationships and knowledge of the temporal nature of the vitellogenin response with continual exposure is currently lacking for biomarker utility. To address this knowledge gap, adult Sydney rock oysters, Saccostrea glomerata, were exposed to a range of environmentally relevant concentrations of 17 alpha-ethynylestradiol (EE2) (0, 6.25, 12.5, 25 or 50 ng/l) in seawater under laboratory conditions. Vitellogenin induction and gonadal development was assessed following 4, 21 and 49 days exposure to EE2. Vitellogenin was found to increase in a dose dependent manner with EE2 exposure for females (4 and 49 days) and males (4 and 21 days). Histological examination of gonads revealed a number of individuals exhibited intersex (ovotestis) in 50 ng/l EE2 (after 21 days) and in 6.25 and 12.5 ng/l EE2 (after 49 days). Furthermore, a significant shift towards females was observed following 49 days exposure at 50 ng/l EE2 suggesting estrogenic exposure is capable of facilitating a progression for protandric males from male-intersex-female gametal status. Increases in female vitellogenin (4 days) were predictive of later increases in female developmental stages at 21 days and increases in oocyte area following 49 days. Male vitellogenin (4 days) was predictive of decreased male percentages and lower male developmental stages at 49 days. Vitellogenin in S. glomerata is a predictive biomarker of estrogenic exposure and effect if sampled soon after exposure and at the commencement of a gonadal development cycle.

Bruttoliste:

Title: Specific profiles of polybrominated diphenylethers (PBDEs) and polychlorinated biphenyls (PCBs) in fish and tucuxi dolphins from the estuary of Paraiba do Sul River, Southeastern Brazil
Author(s): Quinete N, Lavandier R, Dias P, et al.
Source: MARINE POLLUTION BULLETIN Volume: 62 Issue: 2 Pages: 440-446

Title: Endocrine Modulation in Atlantic Cod (Gadus morhua L.) Exposed to Alkylphenols, Polyaromatic Hydrocarbons, Produced Water, and Dispersed Oil
Author(s): Tollefsen KE, Sundt RC, Beyer J, et al.
Conference Information: 3rd Norwegian Environmental Toxicology Symposium, APR 14-16, 2010 Univ Bergen, Bergen, NORWAY
Source: JOURNAL OF TOXICOLOGY AND ENVIRONMENTAL HEALTH-PART A-CURRENT ISSUES Volume: 74 Issue: 7-9 Pages: 529-542

Title: Implications of Persistent Exposure to Treated Wastewater Effluent for Breeding in Wild Roach (Rutilus rutilus) Populations
Author(s): Lange A, Paull GC, Hamilton PB, et al.
Source: ENVIRONMENTAL SCIENCE & TECHNOLOGY Volume: 45 Issue: 4 Pages: 1673-1679

Title: Effects of chronic bisphenol A exposure on hepatic antioxidant parameters in medaka (Oryzias latipes)
Author(s): Wu MH, Xu H, Yang M, et al.
Source: TOXICOLOGICAL AND ENVIRONMENTAL CHEMISTRY Volume: 93 Issue: 2 Pages: 270-278

Title: The endocrine disrupting potential of sediments from the Upper Danube River (Germany) as revealed by in vitro bioassays and chemical analysis
Author(s): Grund S, Higley E, Schonenberger R, et al.
Source: ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH Volume: 18 Issue: 3 Pages: 446-460

Title: Global Gene Expression Profiling in Larval Zebrafish Exposed to Microcystin-LR and Microcystis Reveals Endocrine Disrupting Effects of Cyanobacteria
Author(s): Rogers ED, Henry TB, Twiner MJ, et al.
Source: ENVIRONMENTAL SCIENCE & TECHNOLOGY Volume: 45 Issue: 5 Pages: 1962-1969

Title: The Consequences of Feminization in Breeding Groups of Wild Fish
Author(s): Harris CA, Hamilton PB, Runnalls TJ, et al.
Source: ENVIRONMENTAL HEALTH PERSPECTIVES Volume: 119 Issue: 3 Pages: 306-311

Title: The thyroid-disrupting effects of long-term perfluorononanoate exposure on zebrafish (Danio rerio)
Author(s): Liu Y, Wang JS, Fang XM, et al.
Source: ECOTOXICOLOGY Volume: 20 Issue: 1 Pages: 47-55

Title: Recent Progress in Understanding the Causes of Endocrine Disruption Related to Pulp and Paper Mill Effluents
Author(s): van den Heuvel MR
Conference Information: 7th International Conference on Fata and Effects of Pulp and Paper Mill Effluents Returned to Canada/9th International-Water-Assocation Symposium on Forest Industry Wastewaters, 2009 Fredericton, CANADA
Source: WATER QUALITY RESEARCH JOURNAL OF CANADA Volume: 45 Issue: 2 Pages: 137-144

Title: Summary of a Decade of Research on the Effects of a New Zealand Pulp and Paper Mill on Reproduction in Fishes
Author(s): van den Heuvel MR, Slade AH, Landman MJ
Conference Information: 7th International Conference on Fata and Effects of Pulp and Paper Mill Effluents Returned to Canada/9th International-Water-Assocation Symposium on Forest Industry Wastewaters, 2009 Fredericton, CANADA
Source: WATER QUALITY RESEARCH JOURNAL OF CANADA Volume: 45 Issue: 2 Pages: 123-135

Title: Effects of Neutral Sulfite Semichemical Pulp Mill Effluent in the Mummichog (Fundulus heteroclitus) Adult Fish Reproductive Test
Author(s): Bosker T, Hewitt LM, Doyle MA, et al.
Conference Information: 7th International Conference on Fata and Effects of Pulp and Paper Mill Effluents Returned to Canada/9th International-Water-Assocation Symposium on Forest Industry Wastewaters, 2009 Fredericton, CANADA
Source: WATER QUALITY RESEARCH JOURNAL OF CANADA Volume: 45 Issue: 2 Pages: 201-208

Title: 1995-2009: What Have We Learned About Effluent Biotreatment in Relation to Environmental Protection?
Author(s): Kovacs T, Martel P, Gibbons S, et al.
Conference Information: 7th International Conference on Fata and Effects of Pulp and Paper Mill Effluents Returned to Canada/9th International-Water-Assocation Symposium on Forest Industry Wastewaters, 2009 Fredericton, CANADA
Source: WATER QUALITY RESEARCH JOURNAL OF CANADA Volume: 45 Issue: 2 Pages: 251-262

Title: Bisphenol A content in fish caught in two different sites of the Tyrrhenian Sea (Italy)
Author(s): Mita L, Bianco M, Viggiano E, et al.
Source: CHEMOSPHERE Volume: 82 Issue: 3 Pages: 405-410

Title: Comparison of Cytotoxicity Induced by 17 alpha-Ethynylestradiol and Diethylstilbestrol in Fish CCO and Mammalian CHO-K1 Cell Lines
Author(s): Radosevic K, Tonkovic T, Slivac I, et al.
Source: BULLETIN OF ENVIRONMENTAL CONTAMINATION AND TOXICOLOGY Volume: 86 Issue: 3 Pages: 252-257

Title: Science based guidance for the assessment of endocrine disrupting properties of chemicals
Author(s): Bars R, Broeckaert F, Fegert I, et al.
Source: REGULATORY TOXICOLOGY AND PHARMACOLOGY Volume: 59 Issue: 1 Pages: 37-46

Title: Endocrine disruption and altered biochemical indices in male Oncorhynchus mykiss in response to dimethoate
Author(s): Dogan D, Can C
Source: PESTICIDE BIOCHEMISTRY AND PHYSIOLOGY Volume: 99 Issue: 2 Pages: 157-161

Title: Adverse outcome pathways and ecological risk assessment bridging to population-level effects
Author(s): Kramer VJ, Etterson MA, Hecker M, et al.
Conference Information: SLTAC Pellston Workshop, APR 18-23, 2009 Forest Grove, OR
Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 1 Pages: 64-76

Title: Response of white sucker (catostomus commersoni) to pulp and paper mill effluent in the Androscoggin River, Maine, USA
Author(s): Mower BF, Munkittrick KR, McMaster ME, et al.
Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 1 Pages: 142-153

Title: Predicting National Exposure to a Point Source Chemical: Japan and Endocrine Disruption as an Example
Author(s): Johnson AC, Yoshitani J, Tanaka H, et al.
Source: ENVIRONMENTAL SCIENCE & TECHNOLOGY Volume: 45 Issue: 3 Pages: 1028-1033

Title: The unpredictable effects of mixtures of androgenic and estrogenic chemicals on fish early life
Author(s): Sarria MP, Santos MM, Reis-Henriques MA, et al.
Source: ENVIRONMENT INTERNATIONAL Volume: 37 Issue: 2 Pages: 418-424

Title: Stress hormone masculinizes female morphology and behaviour
Author(s): Knapp R, Marsh-Matthews E, Vo L, et al.
Source: BIOLOGY LETTERS Volume: 7 Issue: 1 Pages: 150-152

Title: Early expression of zona pellucida proteins under octylphenol exposure in Cichlasoma dimerus (Perciformes, Cichlidae)
Author(s): Genovese G, Da Cuna R, Towle DW, et al.
Source: AQUATIC TOXICOLOGY Volume: 101 Issue: 1 Pages: 175-185

Title: Environmental cues influence EDC-mediated endocrine disruption effects in different developmental stages of Japanese medaka (Oryzias latipes)
Author(s): Jin YX, Shu LJ, Huang FY, et al.
Source: AQUATIC TOXICOLOGY Volume: 101 Issue: 1 Pages: 254-260

Title: Molecular characterization of estrogen receptor genes in Gobiocypris rarus and their expression upon endocrine disrupting chemicals exposure in juveniles
Author(s): Wang HP, Wang JJ, Wu TT, et al.
Source: AQUATIC TOXICOLOGY Volume: 101 Issue: 1 Pages: 276-287

Title: 17 beta-Oestradiol may prolong reproduction in seasonally breeding freshwater gastropod molluscs
Author(s): Benstead RS, Baynes A, Casey D, et al.
Source: AQUATIC TOXICOLOGY Volume: 101 Issue: 2 Pages: 326-334

Title: Estrogenic effects of leachates from industrial waste landfills measured by a recombinant yeast assay and transcriptional analysis in Japanese medaka
Author(s): Kamata R, Shiraishi F, Nakajima D, et al.
Source: AQUATIC TOXICOLOGY Volume: 101 Issue: 2 Pages: 430-437

Title: Gene expression profiling of the androgen receptor antagonists flutamide and vinclozolin in zebrafish (Danio rerio) gonads
Author(s): Martinovic-Weigelt D, Wang RL, Villeneuve DL, et al.
Source: AQUATIC TOXICOLOGY Volume: 101 Issue: 2 Pages: 447-458

Title: Estrogen receptors in medaka (Oryzias latipes) and estrogenic environmental contaminants: An in vitro-in vivo correlation
Author(s): Chakraborty T, Katsu Y, Zhou LY, et al.
Source: JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY Volume: 123 Issue: 3-5 Pages: 115-121

Title: Uptake and elimination, and effect of estrogen-like contaminants in estuarine copepods: an experimental study
Author(s): Cailleaud K, Budzinski H, Lardy S, et al.
Source: ENVIRONMENTAL SCIENCE AND POLLUTION RESEARCH Volume: 18 Issue: 2 Pages: 226-236

Title: Tributyltin and the obesogen metabolic syndrome in a salmonid
Author(s): Meador JP, Sommers FC, Cooper KA, et al.
Source: ENVIRONMENTAL RESEARCH Volume: 111 Issue: 1 Pages: 50-56

Title: The effects of estrogenic and androgenic endocrine disruptors on the immune system of fish: a review
Author(s): Milla S, Depiereux S, Kestemont P
Source: ECOTOXICOLOGY Volume: 20 Issue: 2 Pages: 305-319

Title: Expression Profiles of Reproduction- and Thyroid Hormone-Related Transcripts in the Brains of Chemically-Induced Intersex Frogs
Author(s): Langlois VS, Duarte-Guterman P, Trudeau VL
Source: SEXUAL DEVELOPMENT Volume: 5 Issue: 1 Pages: 26-32

Title: Short-term exposure to the environmentally relevant estrogenic mycotoxin zearalenone impairs reproduction in fish

Author(s): Schwartz P, Thorpe KL, Bucheli TD, et al.
Source: SCIENCE OF THE TOTAL ENVIRONMENT Volume: 409 Issue: 2 Pages: 326-333

Title: Effects of metolachlor on transcription of thyroid system-related genes in juvenile and adult Japanese medaka (Oryzias latipes)
Author(s): Jin YX, Chen RJ, Wang LG, et al.
Source: GENERAL AND COMPARATIVE ENDOCRINOLOGY Volume: 170 Issue: 3 Pages: 487-493

Title: Gene expression changes in female zebrafish (Danio rerio) brain in response to acute exposure to methylmercury
Author(s): Richter CA, Garcia-Reyero N, Martyniuk C, et al.
Conference Information: 30th Annual Meeting of SETAC, NOV 19-23, 2009 New Orleans, LA
Source: ENVIRONMENTAL TOXICOLOGY AND CHEMISTRY Volume: 30 Issue: 2 Pages: 301-308

Title: Development of an enzyme-linked immunosorbent assay for quantifying vitellogenin in Pacific salmon and assessment of field exposure to environmental estrogens
Author(s): Peck KA, Lomax DP, Olson OP, et al.
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Author(s): Pottinger TG, Cook A, Jurgens MD, et al.
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Author(s): Webb MAH, Doroshov SI
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Author(s): Rhee JS, Kim RO, Chang HH, et al.
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Author(s): Langlois VS, Duarte-Guterman P, Trudeau VL
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Author(s): Yamashita R, Oshima A, Hasegawa-Baba Y, et al.
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Author(s): Van den Steen E, Eens M, Geens A, et al.
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Author(s): Yigit F, Daglioglu S
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Author(s): Zhou J, Zhu XS, Cai ZH
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Author(s): Dahms HU, Hagiwara A, Lee JS
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