# Synopsis of published literatures on health effects of Endosulfan

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## 1) NERVOUS SYSTEM

| 1.1 | Title: Developmental exposure to pesticides zineb and/or endosulfan renders the nigrostriatal dopamine system more susceptible to these environmental chemicals later in life  
Authors and their affiliations:  
Zhenquan Jia a, Hara P. Misra a,b,*  
a Department of Biomedical Sciences and Pathobiology, College of Veterinary Medicine, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA  
b Edward Via Virginia College of Osteopathic Medicine, Virginia Tech Corporate Research Center, 2265 Kraft Drive, Blacksburg, VA 24060, USA  
Published in: NeuroToxicology 28 (2007) 727–735  
| Major Findings:  
The study was to test the hypothesis that exposure to pesticides such as endosulfan and/or zineb during critical periods of postnatal development could result in neuronal dysfunction and enhance the impact of these pesticides during exposure as adults.  
The findings support our hypothesis that exposure to pesticides such as endosulfan and zineb during critical periods of postnatal development contributes to neurotransmitter changes upon re-challenge in adulthood.  
<p>|</p>
<table>
<thead>
<tr>
<th><strong>Endosulfan Poisoning and Chronic Brain Syndrome</strong></th>
<th>This report describes a case of chronic brain syndrome following poisoning by endosulfan; it is believed to be the first recorded case of such a complication due to that compound.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors and their affiliations:</strong></td>
<td><strong>Published in:</strong></td>
</tr>
<tr>
<td>Dov R. Aleksandrowicz</td>
<td>Arch. Toxicol. 43, 65-68 (1979)</td>
</tr>
<tr>
<td>Shalvata Psychiatric Center</td>
<td><strong>1.3</strong></td>
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<tr>
<td>Hod Hasharon, Israel</td>
<td><strong>Title:</strong></td>
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<tr>
<td></td>
<td>Effects of in utero and lactational exposure to endosulfan in prefrontal cortex of male rats</td>
</tr>
<tr>
<td><strong>Authors and their affiliations:</strong></td>
<td><strong>Major Findings:</strong></td>
</tr>
<tr>
<td>Teresa Cabaleiro, Ana Caride, Alejandro Romero, Anunciación Lafuente *</td>
<td>The possible neurotoxic effects of the organochlorine pesticide endosulfan have been evaluated on male offspring rats exposed in utero and during lactation.</td>
</tr>
<tr>
<td>Laboratorio de Toxicología, Facultad de Ciencias, Universidad de Vigo, Campus de Ourense, Las Lagunas, 32004 Ourense, Spain</td>
<td>The developing nervous system is proposed to be a potentially sensitive target for pesticide exposure (Tilson, 1998, 2000; Nakai and Satoh, 2002; Shafer and Meyer, 2005)</td>
</tr>
<tr>
<td><strong>Published in:</strong></td>
<td><strong>Summarizing,</strong> in utero and lactational treatment to endosulfan induces several alterations in content and metabolism of amino acids and biogenic amines in prefrontal cortex in male rats during the development. These variations are age- and dose-</td>
</tr>
</tbody>
</table>
| Toxicology Letters 176 (2008) 58–67 | }
| 1.4 | **Title:** Effects of endosulfan on brain acetylcholinesterase activity in juvenile bluegill sunfish  
**Authors and Affiliations:** Hiran M. Dutta and Dane A. Arends  
Department of Biological Sciences, Kent State University, Kent, OH 44242, USA  
**Published in:** Environmental Research 91 (2003) 157–162 | **Major Points:**  
The effects of endosulfan upon brain acetylcholinesterase (AChE) activity were measured in juvenile bluegill sunfish (Lepomis macrochirus).  
The duration of exposure was related to the reduction in the AChE activities which reflected the biotoxicity of endosulfan.  
The changes in the AChE activities will certainly affect the normal behavior of the juvenile bluegill which is detrimental to their very existence in the natural habitat. |
| 1.5 | **Title:** Selective involvement of basal ganglia and occipital cortex in a patient with acute endosulfan poisoning  
**Authors and Affiliations:** Department of Neurology, Sunjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India  
Department of Radiology, Sunjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India | **Major Points:**  
We report a teenage girl with acute endosulfan poisoning who developed psychosis, generalized tonic-clonic seizures, myoclonic jerks, cortical blindness and limb rigidity. Serial magnetic resonance imaging (MRI) showed bilateral reversible lesions localized to caudate nucleus, putamen and occipital cortex; internal capsule and thalamus were spared. This selective involvement may have a bearing on mechanisms underlying endosulfan toxicity. |
2) REPRODUCTIVE SYSTEM

2.1 Title:
A method to determine residue levels of persistent organochlorine pesticides in human milk from Indonesian women

Authors and their affiliations:
Emma R. Burke a, Alexis J. Holden a*, Ian C. Shaw b

a Department of Environmental Management, University of Central Lancashire, Preston PR1 2HE, UK
b Environmental Science & Research Institute, 27 Creyke Rd, Christchurch, New Zealand

Published in:
2002 Elsevier Science Ltd

Major Findings:
A method has been developed for the analysis of organochlorine pesticides in human milk using solvent extraction, Florisil_ solid phase extraction clean-up and analysis by gas chromatography with an electron capture detector.

There was no significant difference (at the 95% confidence level) in levels of pesticides between urban and rural areas

2.2 Title:
Endosulfan sulphate interferes with reproduction, embryonic

Major Findings:
The aim of this study was to evaluate the
<table>
<thead>
<tr>
<th>development and sex differentiation in Daphnia magna</th>
<th>possible effects promoted by endosulfan sulphate in changes on the life cycle, embryo development and sex differentiation of Daphnia magna.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors and their affiliations:</strong> P. Palma a, c, V.L. Palma a, R.M. Fernandes a, A.M.V.M. Soares b, I.R. Barbosa a Departamento de Cieˆncias do Ambiente, Escola Superior Agra’ria de Beja, Beja 7800-295, Portugal b CESAM &amp; Departamento de Biologia da Universidade de Aveiro, Aveiro 3810-193, Portugal c Centro de Estudos Farmaceˆuticos, Faculdade de Farmaˆcia, Universidade de Coimbra, Rua do Norte, Coimbra 3000-295, Portugal</td>
<td></td>
</tr>
<tr>
<td><strong>Published in:</strong> Ecotoxicology and Environmental Safety 72 (2009) 344–350</td>
<td><strong>Endosulfan sulphate promoted a significant decrease of the offspring number in all concentrations.</strong> Results showed a reduction of the size of females, together with a decrease in moulting frequency. <strong>Furthermore, an increase in embryo deformities was observed at all concentrations tested.</strong> Above a concentration of 91.7 mgL_1 there was an increased production of males. The results suggest that endosulfan sulphate interferes with the life cycle and sex determination of the crustacean D. magna.</td>
</tr>
<tr>
<td><strong>2.3 Title:</strong> Persistent Pesticides in Human Breast Milk and Cryptorchidism</td>
<td><strong>Major Findings:</strong> Eight organochlorine pesticides (including Endosulfan) were measured in all samples (medians; nanograms per gram lipid) for cases/controls. Statistical analysis showed that pesticide</td>
</tr>
</tbody>
</table>
| Shen,3 Karl-Werner Schramm,3 Jørgen H. Petersen,1,4 Tina K. Jensen,1 Katharina M. Main | levels in breast milk were significantly higher in boys with cryptorchidism (p = 0.032).

In conclusion, our study suggests an association between congenital cryptorchidism and persistent organochlorine pesticides present in mothers’ breast milk. Prenatal exposure to persistent organochlorine pesticides may adversely affect testicular descent in boys. |

| 1University Department of Growth and Reproduction, Copenhagen, Denmark; 2Departments of Physiology and Pediatrics, University of Turku, Turku, Finland; 3GSF-National Research Center for Environmental and Health, Institute for Ecological Chemistry, euherberg, Germany; 4Department of Biostatistics, University of Copenhagen, Denmark |


| 2.4 Title: Organochlorine pesticide residue levels and oxidative stress in preterm delivery cases |

| Authors and their affiliations: Rahul Pathak1, Sanvidhan G. Suke1, Tanzeel Ahmed1, Rafat S. Ahmed1, AK Tripathi1, Kiran Guleria2, CS Sharma3, SD Makhipani3 and BD Banerjee1 |

| Major Findings: The aim of the present study was to analyze the OCP residues in maternal and cord blood of women and assess the levels of different non-enzymatic oxidative stress markers as well as to establish correlation with OCP levels, if any. Levels of OCPs like Hexachlorocyclohexane (HCH), endosulfan, and DDT were analyzed by gas chromatography. Non-enzymatic oxidative stress was measured. In conclusion, our results suggest that |
2.5 Title: Endosulfan and its metabolites in fertile women, placenta, cord blood, and human milk

Authors and their affiliations:
Isabel Cerrilloa, Alicia Granadada, Mari’a-Jose’ Lo’pez-Espinosaa, Begon’ a Olmosa, Margarita Jimenez, Africa Can’ ob, Nicolas Olea, Mari’a Fa’ tima Olea-Serranoca
La Laboratory of Medical Investigations, Department of Radiology, School of Medicine, Hospital Clinico, University of Granada, 18071 Granada, Spain bGynecology & Obstetric Service, University College of Medical Sciences & G.T.B. Hospital (University of Delhi), Delhi, India

Published in:
Human and Experimental Toxicology 29(5) 351–358

Major Findings:
The present study investigated the presence of endosulfan I, endosulfan II, and endosulfan metabolites in fatty and non-fatty tissues and fluids from women of reproductive age and children in Southern Spain.

The highest concentration of commercial endosulfan I and endosulfan II was found in adipose tissue, with a mean value (I+II) of 17.72 ng/g lipid, followed by human milk, with a mean value (I+II) of 11.38 ng/mL milk.

This study suggests that exposure from mother to child is a common event, both
2.6 Title: Effect of Endosulfan on Male Reproductive Development

Authors and Affiliations:
Habibullah Saiyed, 1 Aruna Dewan, 1 Vijay Bhatnagar, 1 Udyavar Shenoy, 2 Rathika Shenoy, 2 Hirehall Rajmohan, 3 Kumud Patel, 1 Rekha Kashyap, 1 Pradip Kulkarni, 1 Bagalur Rajan, 3 and Bhadabhai Lakkad 1

1 National Institute of Occupational Health (Indian Council of Medical Research), Meghani Nagar, Ahmedabad, India;

2 Department of Pediatrics, Kasturba Medical College, Mangalore, India; 3 Regional Occupational Health Research Centre, Bangalore, India

Published in: VOLUME 111 | NUMBER 16 | December 2003 • Environmental Health Perspectives

Major Points:
A study to examine the relationship between environmental endosulfan exposure and reproductive development in male children and adolescents.
The study population was composed of 117 male schoolchildren (10–19 years of age) of a village situated at the foothills of cashew plantations.
The study parameters included recording of clinical history, physical examination, sexual maturity rating (SMR) according to Tanner stages, and estimation of serum levels of testosterone, luteinizing hormone (LH), follicle-stimulating hormone, and endosulfan residues.
Our study results suggest that endosulfan exposure in male children may delay sexual maturity and interfere with sex hormone synthesis.

in utero and via breastfeeding, due to the high frequency of exposure of women of reproductive age.
### 3) ENDOCRINE SYSTEM

#### 3.1 Title:
Effect of pesticides on estrogen receptor transactivation in vitro: A comparison of stable transfected MVLN and transient transfected MCF-7 cells

**Authors and their affiliations:**
Eva C. Bonefeld-Jorgensen *, Heidi T. Grünfeld, Irene M. Gjermandsen

Unit of Environmental Biotechnology, Department of Environmental and Occupational Medicine, University of Aarhus, Venneyst Boulevard 6, DK-8000 Aarhus, Denmark

**Published in:**
Molecular and Cellular Endocrinology 244 (2005) 20–30

**Major Findings:**
The estrogenic potential of four pesticides (endosulfan, prochloraz, toclhlofos-methyl and propamocarb) was compared in parallel with 17β-estradiol (E2) by reporter constructs in transient transfected MCF-7BUS and in stable transfected MVLN cells.

In MVLN cells, endosulfan, prochloraz, toclhlofos-methyl and propamocarb caused cytotoxic responses at concentrations higher than 10, 25, 25 and 100 μM, respectively.

#### 3.2 Title:
Xenoestrogen-Induced ERK-1 and ERK-2 Activation via Multiple Membrane-Initiated Signaling Pathways

**Authors and their affiliations:**
Bulayeva, Nataliya N; Watson, Cheryl S

Department of Human Biological Chemistry and genetics, University of Texas Medical Branch, Galveston,

**Major Findings:**
The objective of the study was to investigate the ability of some of the estrogen mimetics (belonging to major classes of environmental estrogens) to produce rapid activation of ERKs via various signaling pathways in the GH3/B6/F10 prolactinoma cell lines.

Endosulfan was able to produce phosphorylation at almost all tested concentrations.

Basically two patterns of stimulations were seen: Compounds active in both
<table>
<thead>
<tr>
<th>Texas, USA</th>
<th>subpicomolar and nanomolar ranges (Endosulfan, nonylphenol and coumestrol) versus compounds active only in the nanomolecular range (DDE and dieldrin).</th>
</tr>
</thead>
</table>
| **Published in:** Environmental Health Perspectives; Nov 2004; 112, 15; ProQuest pg. 1481 | 3.3 **Title:** Effects of Currently Used Pesticides in Assays for Estrogenicity, Androgenicity, and Aromatase Activity in Vitro

**Authors and their affiliations:**
Helle Raun Andersen,*, Anne Marie Vinggaard,† Thomas Høj Rasmussen,*, Irene Marianne Gjermandsen,‡ and Eva Cecilie Bonefeld-Jørgensen‡

*Environmental Medicine, Institute of Public Health, University of Southern Denmark, Odense, Winsløwparken 17, DK-5000 Odense C, Denmark;
†Institute of Food Safety and Toxicology, Division of Biochemical and Molecular Toxicology, Danish Veterinary and Food Administration, Mørkhoj Bygade 19, DK-2860 Søborg, Denmark; and
‡Department of Environmental and Occupational Medicine, Unit of Environmental Biotechnology, University of Aarhus, Building 260, Vennelyst Boulevard 6, DK-8000 Aarhus C, Denmark

**Major Findings:**

Twenty-four pesticides were tested for interactions with the estrogen receptor (ER) and the androgen receptor (AR) in transactivation assays.

The two organochlor insecticides dieldrin and Endosulfan increased cell proliferation and ER transactivation gene response in MCF-7 cells significantly at 5 and 1 M, respectively. Both compounds induced maximum response at 25 M, whereas higher concentrations resulted in a decreased response due to cytotoxicity. **In both assays, the response induced by endosulfan was higher than the response induced by dieldrin.** Endosulfan potentiated the 17-estradiol-induced proliferation when it was tested together with a concentration of 17-estradiol causing a submaximum response. Dieldrin did not enhance the 17-estradiol-induced response in any of the assays.
| 3.4 | **Title:**  
Endosulfan effects on pituitary hormone and both nitrosative and oxidative stress in pubertal male rats  

**Authors and Affiliations:**  
A. Caride, A. Lafuente*, T. Cabaleiro Laboratorio de Toxicologia, Facultad de Ciencias, Universidad de Vigo, Campus de Orense, Las Lagunas, 32004 Orense, Spain  

**Published in:**  
Toxicology Letters 197 (2010) 106–112  

**Major Points:**  
The study was undertaken to investigate in pubertal male rats possible effects of endosulfan administered throughout lactation and gestation on: (a) pituitary gene expression of prolactin, luteinizing hormone (LH), growth hormone (GH) and thyroid stimulating hormone (TSH); and (b) circulating levels of these hormones.  

In pubertal male rat, prenatal and lactational exposure to endosulfan modifies expression and release of prolactin, LH, GH and TSH, and pituitary NOS1 and NOS2 mRNA levels, suggesting that nitrosative stress can be implicated in the endocrine toxicity of endosulfan at pituitary level. |
| 3.5 | **Title:**  
Screening of some anti-progestin endocrine disruptors using a recombinant yeast based in vitro bioassay  

**Authors and Affiliations:**  
Shamba Chatterjee a,1, Vikas Kumar a,1, Chandrajeet B. Majumder b, Partha Roy a,*  
a Molecular Endocrinology Laboratory, Department of Biotechnology, Indian Institute of Technology Roorkee, Roorkee 247 667, Uttarakhand, India  
b Fluid Particle Research Laboratory, Department of  

**Major Points:**  
About 7 different chemicals (mostly pesticides or their metabolites) like DDT and its metabolites, nonylphenol, endosulfan were screened in this assay system for their role in transactivation and they were all found to be anti-progestative. |
3.6 Title:
Circulating thyroid hormone levels and iodothyronine deiodinase activities in Nile tilapia (Oreochromis niloticus) following dietary exposure to Endosulfan and Aroclor 1254

Authors and Affiliations:
Ana Maria Coimbra, a,b,*, Maria Armanda Reis-Henriques, b, Veerle M. Darrasc
a) ICBAS-Instituto de Ciências Biomeédicas de Abel Salazar, Laboratório de Fisiologia Aplicada, Largo do Prof. Abel Salazar 2, 4099-003, Porto, Portugal
b) CIIMAR-Centro Interdisciplinar de Investigação e Ambiente, Laboratório de Fisiologia Ambiental, Rua dos Bragas 289, 4050-123, Porto, Portugal
c) Laboratory of Comparative Endocrinology, Zoological Institute K.U. Leuven, Naamsestraat 61, B-3000 Leuven, Belgium

Published in:
Comparative Biochemistry and Physiology, Part C 141 (2005) 8 – 14

Major Points:
We evaluated the effects of two organochlorinated environmental contaminants, Endosulfan and Aroclor 1254 on peripheral thyroid hormone metabolism and thyroid hormone plasma levels in Nile tilapia (Oreochromis niloticus).

It is concluded that dietary exposure of tilapia to Endosulfan or Aroclor 1254 can lead to changes in circulating thyroid hormone levels and/or in peripheral thyroid hormone metabolism. The changes in hormone metabolism differ between tissues, eventually reflecting tissue-specific differences in adaptation.
| 3.7 | Title: Human Exposure to Endocrine-Disrupting Chemicals and Prenatal Risk Factors for Cryptorchidism and Hypospadias: A Nested Case-Control Study  
Authors and Affiliations: Mariana F. Fernandez, 1 Begoña Olmos, 1 Alicia Granada, 1 Maria José López-Espinosa, 1 José-Manuel Molina-Molina, 1 Juan Manuel Fernandez, 2 Milagros Cruz, 3 Fátima Olea-Serrano, 4 and Nicolás Olea-1  
1 Laboratory of Medical Investigations, 2 Department of Pediatrics, and 3 Department of Gynecology and Obstetrics, San Cecilio University Hospital, Granada, Spain; 4 Department of Nutrition, University of Granada, Granada, Spain  
Published in: VOLUME 115 | SUPPLEMENT 1 | December 2007 • Environmental Health Perspectives | Major Points: In this study we aimed to determine whether the combined effect of environmental estrogens measured as total effective xenoestrogen burden (TEXB) is a risk factor for male urogenital malformations. We found an increased risk for male urogenital malformations related to the combined effect of environmental estrogens in placenta. |
|---|---|---|---|
| 3.8 | Title: Endocrine disrupters and human puberty  
Authors and Affiliations: E. Den Hond and G. Schoeters  
Department of Toxicology, VITO (Flemish Institute for Technological Research), Mol, Belgium  
Published in: International Journal of Andrology 29 (2006) 264–271 | Major Points: Epidemiological research studying the effect of endocrine disrupters on the onset of puberty is summarized. In girls, earlier age at menarche was reported after exposure to polychlorinated biphenyls (PCBs), polybrominated biphenyls (PBBs), persistent pesticides (DDT, endosulfan) and phthalate esters. In boys, exposure to PCBs, PCDFs or the pesticide endosulfan was associated with delayed puberty or decreased penile length. |
| 3.9 | **Title:** Oxidative stress and loss of cortisol secretion in adrenocortical cells of rainbow trout (Oncorhynchus) exposed in vitro to endosulfan, an organochlorine pesticide  
**Authors and Affiliations:** J. Dorval, V.S. Leblond, A. Hontela *  
De’partement des Sciences Biologiques, Universite’ du Que’bec a’ Montre’al, TOXEN Research Centre, C.P. 8888, succ. Centre-ville, Montre’al, Que’, Canada H3C 3P8  
**Published in:** Aquatic Toxicology 63 (2003) 229–241 | **Major Points:**  
The effects of endosulfan on cortisol secretion, cell viability, antioxidants and lipid peroxidation were investigated.  
The in vitro study identified endosulfan as a chemical inducing a loss of secretory responses in teleost adrenocortical steroidogenic cells and alterations in the activity of enzymes known to be involved in oxidative stress pathways.  
Moreover, the significant increase in lipid hydroperoxides levels provided further evidence for endosulfan-induced oxidative stress. |
| 3.10 | **Title:** Effect of in vitro estrogenic pesticides on human oestrogen receptor _α_ and _β_ mRNA levels  
**Authors and Affiliations:** H.T. Grünfeld, E.C. Bonefeld-Jorgensen*  
Unit of Environmental Biotechnology, Department of Environmental and Occupational Medicine, University of Aarhus,  
Vennelyst Boulevard 6, DK-8000 Aarhus, Denmark  
**Published in:** Toxicology Letters 151 (2004) 467–480 | **Major Points:**  
Nine widely distributed pesticides were recently demonstrated to possess potential estrogenic properties in oestrogen receptor (ER) transactivation and/or E-screen assays.  
This study demonstrated that organochlor and organo-phosphorous pesticides possess the ability to interfere with the ER _α_ and ER _β_ mRNA steady state levels. |
### 4) IMMUNE SYSTEM

#### 4.1

<table>
<thead>
<tr>
<th><strong>Title:</strong></th>
<th>Determination of the immunotoxic potential of pesticides on functional activity of sheep leukocytes in vitro</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Authors and Affiliations:</strong></td>
<td>Juraj Pisl *, Natašia Kovalkovic’ova’, Vanda Holovska’, Jaroslav Lega’th, Ivan Mikula</td>
</tr>
<tr>
<td><strong>Published in:</strong></td>
<td>Toxicology 188 (2003) 73-81</td>
</tr>
<tr>
<td><strong>Major Points:</strong></td>
<td>The effect of eight pesticides with different chemical structure (atrazine, bentazon, chloride-zone, dichlofluanid, endosulfan, MCPA, simazine, triallate) on sheep peripheral blood phagocytes and lymphocytes was examined. Three of the pesticides tested suppressed both, the metabolic activity of phagocytes and mitogenic activation of lymphocytes (dichlofluanid, endosulfan and simazine).</td>
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#### 4.2

<table>
<thead>
<tr>
<th><strong>Title:</strong></th>
<th>Toxic effects of endosulfan on blood lymphocyte subsets in adult rats</th>
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<tbody>
<tr>
<td><strong>Authors and Affiliations:</strong></td>
<td>A. Lafuente, T. Cabaleiro, A. Caride, A. Romero Laboratorio de Toxicolog’ia, Facultad de Ciencias, Universidad de Vigo, Campus de Orense, Las Lagunas s/n, 32004-Orense, Spain</td>
</tr>
<tr>
<td><strong>Published in:</strong></td>
<td>Toxicology Letters 164S (2006) S1–S324</td>
</tr>
<tr>
<td><strong>Major Points:</strong></td>
<td>The objective was to evaluate possible immune alterations induced by endosulfan exposure during pregnancy and lactation in both male and female adult rats. The results suggest that endosulfan exposure during pregnancy and lactation could modify humoral immunity in offspring adulthood, and that females are more susceptible to this pesticide because their cellular immunity was also altered.</td>
</tr>
</tbody>
</table>
### 5) GENOTOXICITY, CYTOTOXICITY AND TERATOGENICITY

| 5.1 | Title:  
Comet assay in phytoplankton as biomarker of genotoxic effects of environmental pollution  
Authors and their affiliations:  
Akcha a,*, G. Arzul a, S. Rousseau a, M. Bardouil b  
aIFREMER, Laboratoire d’Ecotoxicologie, Rue de l’Ile d’Yeu, 44311 Nantes Cedex 03, France  
b IFREMER, Laboratoire Phycotoxines, Rue de l’Ile d’Yeu, 44311 Nantes Cedex 03, France  
Published in:  
journal homepage: www.elsevier.com/locate/marenrev  
- 2008 Elsevier Ltd. | Major Findings:  
Genotoxicity was observed from 1 lg/L of endosulfan and was not concentration dependent.  
Endosulfan exposure resulted in DNA strand breaks from the concentration of 1 lg/L (p < 0.05), but effect did not appear to be concentration dependent |

| 5.2 | Title:  
Endosulfan Decreases Cell Growth and Apoptosis in Human HaCaT Keratinocytes: Partial ROS-Dependent ERK1/2 Mechanism  
Authors and their affiliations:  
SEBASTIEN ANThERIEU,1* NATHALIE LEDIRAC,1 ANNE-PASCALE LUZY,2 PHILIPPE LENORMAND,3 JEAN-CLAUDE CARON,2 | Major Findings:  
This study was designed to assess the mitogenic, apoptogenic, and genotoxic effects of endosulfan on the HaCaT cell line.  
**Endosulfan** has been shown to generate transient reactive oxygen species (ROS), and blocking this oxidative stress by
AND ROGER RAHMANI1*

1 INRA, UMR 1112 “Réponses des Organismes aux Stress Environnementaux”, Equipe de Toxicologie Cellulaire, Moleculaire et Génomique, Sophia-Antipolis, France

2 Galderma R&D, Les Templiers, Biot, France

3 Institute of Signaling, Developmental Biology and Cancer Research, CNRS-UMR 6543, Centre Antoine Lacassagne, Nice, France

Published in:

N-acetyl cysteine (NAC) strongly prevented both persistent nuclear ERK1/2 phosphorylation and cell growth decrease. Additional experiments demonstrated that unchanged endosulfan rather than its metabolites has mutagenic effects and increased DNA strand breaks in human keratinocytes.

In conclusion, the results show that human keratinocytes are more affected by a chronic than an acute exposure to endosulfan.

On the whole, our findings demonstrate that endosulfan disrupts epidermal homeostasis by two concomitant independent mechanisms: a ROS-dependent mechanism responsible for DNA damage and decrease in cell proliferation, and a ROS-independent inhibition of apoptosis that could contribute to mutant cell survival and therefore have possible carcinogenic effects.

<table>
<thead>
<tr>
<th>5.3</th>
<th>Title : Analysis of Endosulfan and Its Metabolites in Human Serum Using Gas Chromatography–Tandem Mass Spectrometry</th>
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</thead>
<tbody>
<tr>
<td>Major Findings: A new analytical method combining solid-phase extraction and gas chromatography–tandem mass spectrometry used to determine the insecticide endosulfan as well as its</td>
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<td>Authors and their affiliations:</td>
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<tr>
<td>F.J. Arrebola1, J.L. Martínez Vidal1,*, and A. Fernández-Gutiérrez2</td>
<td></td>
</tr>
<tr>
<td>1 Department of Analytical Chemistry, University of Almeria, 04071 Almeria, Spain</td>
<td></td>
</tr>
<tr>
<td>2 Department of Analytical Chemistry, University of Granada, 18071 Granada, Spain</td>
<td></td>
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</tbody>
</table>

Published in:


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<table>
<thead>
<tr>
<th>5.4</th>
<th>Title:</th>
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<tbody>
<tr>
<td>Oxidative stress responses in different organs of Jenynsia multidentata exposed to Endosulfan</td>
<td></td>
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</tbody>
</table>

Authors and their affiliations:

M.L. Ballestrosa, D.A.Wunderlinb, M.A.Bistonia, a Universida Nacionalde Co’rdoba, Facultad de Ciencias Exacta sfíísacy

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<table>
<thead>
<tr>
<th>Major Findings:</th>
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<tbody>
<tr>
<td>Our present results demonstrate that exposure to a sublethal concentration of Endosulfan results in oxidative stress in several organs of J. multidentata.</td>
</tr>
<tr>
<td>The brain was the most sensitive organ to oxidative damage.</td>
</tr>
</tbody>
</table>
### 5.5

**Title:**
DNA Damage and Mutagenicity Induced by Endosulfan and Its Metabolites

**Authors and their affiliations:**
MahimaBajpayee,1 AlokKumar Pandey,1 SabinaZaidi,2 JavedMusarrat,2 Devendra Parmar,1 NeerajMathur,3 PrahladKishore Seth,1 and AlokDhawan1*

1) Developmental Toxicology Division, Industrial Toxicology Research Centre, Lucknow-226001, India
2) Department of Microbiology, Faculty of Agricultural Sciences, Aligarh Muslim University, Aligarh-202002, India
3) Epidemiology Section, Industrial Toxicology Research Centre, Lucknow-226001, India

**Published in:**

### Major Findings:
Endosulfan and metabolites may interact with DNA directly or through the production of ROS.

In conclusion, the present study is the first to compare endosulfan with its isomers and metabolites for their ability to induce mutations in a conventional bacterial test system and to induce DNA damage in mammalian cells. Endosulfan, its isomers, and metabolites were positive in both the bacterial and mammalian cell systems.
### 5.6 Title:
Selective induction of the CYP3A family by endosulfan and DNA-adduct formation in different hepatic and hepatoma cells

**Authors and their affiliations:**
M. Dubois a, A. Pfohl-Leszkowicz, I. De Waziers, P. Kremers S

a Université de Litge. Laboratoire de Chimie Médicale, Institut de Pathologique, B35, Centre Hospitalier Universitaire. B-4000 Surf Tilman, Belgium

h E.N.S.A.T. Laboratoire de Toxicologie et SCurité Alimentaire. 145 Al. de Muret. 31076 Toulouse. France

’ Unité de Recherche de Biochirurgie Pharmacologique et MPtabolique (INSERM U751. CHU Necker-Enfants Malades. 156 rue de Vougard. 75730 Paris Cedex 15. France

**Published in:**
Environmental Toxicology and Pharmacology 1 (1996) 249-256

**Major Findings:**
This report clearly shows the genotoxicity of endosulfan. This chlorinated insecticide induces the formation of abundant DNA adducts in both fetal rat hepatocytes and Hep G2 cells.

Endosulfan strongly correlated to the high induction of CYP3A gene expression.

Endosulfan has a major impact on the human liver via induction of CYP3A4 and CYP3A7.

### 5.7 Title:
Exposure to mixtures of endosulfan and zineb induces apoptotic and necrotic cell death in SH-SY5Y neuroblastoma cells, in vitro

**Authors and their affiliations:**
Zhenquan Jia1 and Hara P. Misra1,2,*

1 Department of Biomedical Sciences and Pathobiology, College of Veterinary

**Major Findings:**
A number of epidemiological studies have demonstrated a strong association between the incidence of Parkinson’s disease and pesticide exposure.

In conclusion, our results help to better characterize pesticide-induced neuroblastoma cell death. Both zineb and
endosulfan were found to induce cytotoxicity in SH-SY5Y cells via both apoptotic and necrotic pathways.

Together, with evidence provided in this study, it appears likely that endosulfan and zineb alone or in combination play a role in the cell death in an in vitro model system that may, at least in part, be involved in the degeneration of dopaminergic neurons and may be relevant for the pathogenesis of some of these neurodegenerative diseases.

<table>
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<tr>
<th>5.8</th>
<th>Title: Advantages of Human Hepatocyte-Derived Transformants Expressing a Series of Human Cytochrome P450 Isoforms for Genotoxicity Examination</th>
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<tbody>
<tr>
<td>Authors and their affiliations: Tsuneo Hashizume,* Sumie Yoshitomi,† Satoru Asahi,* Rieko Uematsu,* Shigeo Matsumura,* Fumio Chatani,* and Hiroaki Oda‡,1 *Development Research Center and †Discovery Research Center, Pharmaceutical Research Division, Takeda Pharmaceutical Company Limited, 17-85</td>
<td></td>
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<tr>
<td>Major Findings: Endosulfan was found to induce MN through the CYP3A4-mediated pathway Endosulfan sulfate was the genotoxic metabolite to induce MN; this metabolite was considered to be produced in the HepG2 transformant expressing human CYP3A4 by the treatment with b-endosulfan.</td>
<td></td>
</tr>
</tbody>
</table>
Jusohonmachi 2-chome, Yodogawa-ku, Osaka 532-8686, Japan; and ‡Laboratory of Nutritional Biochemistry, Nagoya University Graduate School of Bioagricultural Sciences, Furo-cho, Chikusa-ku, Nagoya 464-8601, Japan

Published in:

5.9

Title:
Citrinin and endosulfan induced teratogenic effects in Wistar rats

Authors and their affiliations:
Nittin D. Singh,† Anil K. Sharma,‡ Prabhaker Dwivedi, Rajendra D. Patil and Manoj Kumar
Division of Pathology, Indian Veterinary Research Institute, Izatnagar-243122, India

Published in:
JOURNAL OF APPLIED TOXICOLOGY
J. Appl. Toxicol. 2007; 27: 143–151
Published online 22 December 2006 in Wiley InterScience (www.interscience.wiley.com) DOI: 10.1002/jat.1185

2006 John Wiley & Sons, Ltd

Major Findings:
The present investigation was conducted to evaluate the teratogenic potential of citrinin (CIT) and endosulfan either alone or in combination in pregnant rats during gestational days 6–20.

In the present study, endosulfan treatment induced fetal gross anomalies The internal hydrocephalus, cerebellar hypoplasia, microphthalmia, contracted and notched kidneys, multilobulated liver, dilated renal pelvis, incomplete ossification of skull bones, rib anomalies and sacral and caudal vertebrae agenesis were the important fetal malformations.

The dose of endosulfan (1 mg kg−1 body weight) employed in the present study
| Title: | Human health risk assessment of endosulfan. I: Toxicology and hazard identification |
| Authors and their affiliations: | Marilyn H. Silva *, Sheryl L. Beauvais Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA 95812, USA |
| Published in: | Regulatory Toxicology and Pharmacology 56 (2010) 4–17 0273-2300/$ - see front matter Published by Elsevier Inc. doi:10.1016/j.yrtph.2009.08.013 |
| Major Findings: | A primary risk assessment concern for endosulfan is that effects resulting from exposure during critical developmental stages (in utero, or to infants and children) will result in endocrine disruption and subsequent neurotoxicity, developmental or reproductive adverse effects that are irreversible. |

is lower than the dose established by the World Health Organization (WHO) for reproductive toxicity assessment in rats (WHO, 1984).

Because of widespread use or contamination of CIT and endosulfan in the environment and its occurrence in the animal and human food (Anderson, 1995) and the presence of residues in the blood and milk samples of females (Sancewicz-Pach et al., 1997; Sanghi et al., 2003), these might pose a potential risk to developing fetuses during pre-natal and post-natal life.
| 5.11 | **Title:**  
Genotoxicity evaluation of the insecticide endosulfan in the wetland macrophyte Bidens laevis L  

**Authors and their affiliations:**  
De’bora J. Pe’rez a,b,c, Mirta L. Menone b,c,* Elsa L. Camadro a,c, Víctor J. Moreno b  

a) Laboratorio de Gene´tica, Estacio´n Experimental Agropecuaria Balcarce INTA e Facultad de Ciencias Agrarias e UNMdP,CC 276, 7620 Balcarce, Argentina  

b) Laboratorio de Ecotoxicologí´a, Departamento de Ciencias Marinas, Facultad de Ciencias Exactas y Naturales UNMdP, Funes 3350 (7600) Mar del Plata, Argentina  

c) Consejo Nacional de Investigaciones Cientí´ficas y Te´cnicas (CONICET), Rivadavia 1917, 1033, Buenos Aires, Argentina  

**Published in:**  
Environmental Pollution 153 (2008) 695e698  
_ 2007 Elsevier Ltd. All rights reserved.  

**Major Findings:**  
The higher proportion of laggards and vagrard chromosomes observed at 5 mg/L would indicate that endosulfan interacts with the spindle interrupting normal chromosome migration.  

Endosulfan resulted genotoxic to B. laevis, a species of potential value for bioassays and in situ monitoring of environmental contamination by pesticides.
| 5.12 | **Title:**  
Genotoxicity evaluation of acute doses of endosulfan to freshwater teleost Channa punctatus (Bloch) by alkaline single-cell gel electrophoresis  

**Authors and their affiliations:**  
Sanjay Pandey, N.S. Nagpure, Ravindra Kumar, Shilpi Sharma, Satish K. Srivastava, Mahendra S. Verma  
National Bureau of Fish Genetics Resources, Indian Council of Agriculture Research, Lucknow 226002, Uttar Pradesh, India  

**Published in:**  
Ecotoxicology and Environmental Safety 65 (2006) 56–61  
2005 Elsevier Inc.  

**Major Findings:**  
The Indian freshwater air-breathing teleost fish Channa punctatus (Bloch) was exposed to acute concentrations of the organochlorine pesticide **Endosulfan.**  
The presence of **DNA strand breakage** in exposed specimens indicated the **genotoxic potential** of endosulfan. |
| 5.13 | **Title:**  
Genotoxic Effects of a-Endosulfan and f3-Endosulfan on Human HepG2 Cells  

**Authors and their affiliations:**  
Yuquan Lu, Kanehisa Morimoto, Tatsuya Takeshita, Toru Takeuchi, and Takeshi Saito  

**Major Findings:**  
In this study, we examined the **genotoxicity** of endosulfan in vitro with a HepG2 cell line.  
After treating HepG2 cells with a- or 13-endosulfan for 1 hr, **DNA strand breaks** were **significantly induced** by a-endosulfan at
1Department of Social and Environmental Medicine, Osaka University Graduate School of Medicine, Suita, Osaka, Japan;

2Laboratory of Environmental Biology, Department of Preventive Medicine, Hokkaido University School of Medicine, Sapporo, Japan

Published in:
Environmental Health Perspectives *
VOLUME 108 1 NUMBER 6 1 June 2000

<table>
<thead>
<tr>
<th>5.14 Title:</th>
<th>Major Findings:</th>
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<tbody>
<tr>
<td>Micronucleus induction in erythrocytes of the Hyla pulchella tadpoles (Amphibia: Hylidae) exposed to insecticide endosulfan</td>
<td>Results obtained here showed a genotoxic effect of the endosulfan on erythrocytes of H. pulchella.</td>
</tr>
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</table>

Authors and their affiliations:
Rafael C. Lajmanovich a,*, Mariana Cabagna b, Paola M. Peltzer a, Gabriela A. Stringhini c, Andrés M. Attademo c

a National Council for Scientific and Technical Research (CONICET), Faculty of Biochemistry and Biological Sciences, FBCB-UNL, Pje. El Pozo s/n (3000), Santa Fe, Argentina

b Cathedra of Normal Morphology, Faculty of Biochemistry and Biological Sciences, FBCB-UNL,

c It important noticed that commercial formulations of endosulfan utilized, contains many ‘inert’ ingredients that can increase the toxicity of the product when compared to the technical-grade material. Furthermore, ‘inert’ ingredients used in formulated pesticide
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<tr>
<td>Effects of endosulfan on B cells of Langerhans islets in rat pancreas</td>
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<th>Authors and their affiliations:</th>
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<tr>
<td>Yusuf Kalender a,*, Suna Kalender b, Meltem Uzunhisarcıklı a, Ayşe Ogutcu a, Fatma Açıkgöz a, Dilek Durak c</td>
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<tr>
<th>a</th>
<th>Biology Department, Faculty of Arts and Science, Gazi University, 06500 Ankara, Turkey</th>
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<tr>
<td>b</td>
<td>Biology Department, Faculty of Education, Gazi University, 06500 Ankara, Turkey</td>
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<tr>
<td>c</td>
<td>Biology Department, Yozgat Faculty of Arts and Science, Erciyes University, Yozgat, Turkey</td>
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</table>

**Major Findings:**

Chronic endosulfan administration for 2 months led to degenerative changes of various degrees of the pancreatic islets as well as the exocrine acini.

Insufficiency of insulin hormone causes the increase of blood glucose level at the end of the 5th and 6th weeks, blood glucose level significantly increased. This shows that B cells couldn’t secrete adequate insulin.

Biochemical studies show that endosulfan affects integral proteins and receptors of cell membrane.
In this study endosulfan caused vacuoles and swelling of mitochondria. Blood glucose levels and ultrastructural changes in this study show that endosulfan affects B cells of pancreas in rats even if it is under the LD50 dose level. Endosulfan not only has toxic effects on mammalian and other animals but it causes pollution as well. Therefore, microbial insecticides which are effective on target organisms and don’t cause pollution should be used instead of endosulfan.

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<th>5.16</th>
<th>Title:</th>
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<tr>
<td>Effect of pesticides on estrogen receptor transactivation in vitro: A comparison of stable transfected MVLN and transient transfected MCF-7 cells</td>
<td></td>
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</table>

Authors and their affiliations:

Eva C. Bonefeld-Jorgensen *, Heidi T. Gr’unfeld, Irene M. Gjermandsen

Unit of Environmental Biotechnology, Department of Environmental and Occupational Medicine, University of Aarhus, Vennelyst Boulevard 6, DK-8000 Aarhus, Denmark

Published in:

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<tr>
<th>5.16</th>
<th>Major Findings:</th>
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<tr>
<td>The estrogenic potential of four pesticides (endosulfan, prochloraz, tolchlofos-methyl and propamocarb) was compared in parallel with 17-estradiol (E2) by reporter constructs in transient transfected MCF-7BUS and in stable transfected MVLN cells.</td>
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In MVLN cells, endosulfan, prochloraz, tolchlofos-methyl and propamocarb caused cytotoxic responses at concentrations higher than 10,
5.17

**Title:**

Reactive oxygen species in in vitro pesticide-induced neuronal cell (SH-SY5Y) cytotoxicity: Role of NFκB and caspase-3

**Authors and their affiliations:**

(Sh-SY5Y) cytotoxicity: Role of NFκB and caspase-3
Zhenquan Jia, Hara P. Misra

Edward Via Virginia College of Osteopathic Medicine, Virginia Tech Corporate Research Center, 2265 Kraft Drive, Blacksburg, VA 24060, USA

**Published in:**


**Major Findings:**

Our laboratory has demonstrated that mice exposed to endosulfan (an organochlorine cyclodiene pesticide) and zineb (zinc ethylene bisdithiocarbamate (EBDC) fungicide) as juveniles and re-exposed at 8 months of age showed loss of dopamine (DA) in striatum. Mixtures of these pesticides also caused significantly increased levels of alphasynuclein, a major component of Lewy bodies and a hallmark of neurodegenerative diseases such as PD and Alzheimer's disease (AD).

In summary, the results of the present study demonstrate that neuronal cells (SH-SY5Y) exposed to endosulfan and zineb individually or in a mixture increase the production of
| 5.18 | **Title:**  
Organochlorine pesticide residue levels and oxidative stress in preterm delivery cases  
**Authors and their affiliations:**  
Rahul Pathak1, Sanvidhan G Suke1, Tanzeel Ahmed1, Rafat S Ahmed1, AK Tripathi1, Kiran Guleria2, CS Sharma3, SD Makhijani3 and BD Banerjee1  
1) Environmental Biochemistry and Immunology laboratory, Department of Biochemistry, University College of Medical Sciences & G.T.B. Hospital (University of Delhi), Delhi, India  
2) Department of Obstetrics and Gynecology, University College of Medical Sciences & G.T.B. Hospital (University of Delhi), Delhi, India  
3) Instrumentation and Bio-Labs, Central Pollution Control Board, Ministry of Environment, Forest and Climate Change, New Delhi, India | **Major Findings:**  
The aim of the present study was to analyze the OCP residues in maternal and cord blood of women and assess the levels of different non-enzymatic oxidative stress markers as well as to establish correlation with OCP levels, if any.  
Levels of OCPs like Hexachlorocyclohexane (HCH), endosulfan, and DDT were analyzed by gas chromatography. Non-enzymatic oxidative stress was measured.  
In conclusion, our results suggest that higher levels of some of the OCP (like Endosulfan) may be associated with preterm delivery and increased oxidative stress.  
hydrogen peroxide as well as superoxide anion, decrease SOD GPX, and CAT enzyme levels and increase lipid peroxide levels.  
This holds tremendous implication for the derivation of risk assessment guidelines for human exposure to pesticides. |
| Published in: | Environment and Forest, Delhi, India |
| Published in: | Human and Experimental Toxicology 29(5) 351–358 |
| 5.19 Title: | HUMAN RED BLOOD CELL MEMBRANE DAMAGE BY ENDOSULFAN |
| Authors and Affiliations: | CLIVE SUNIL DANIEL, SARITA AGARWAL and SHYAM S. AGARWAL |
| Published in: | Toxicology Letters, 32 (1986) 113-118 |
| Major Points: | Endosulfan’s in vitro toxicity on human red blood cell membrane was studied by staining with a fluorochrome dye, merocyanine-540 (MC-540) and Scanning Electron Microscopy (SEM). At a concentration of 0.001 pg/ml (1 ppb) endosulfan was found to damage human red cell membranes as demonstrated by fluorescence of 30-50% of red cells on staining with MC-540. At concentration of 1 pg/ml (1 ppm) the cells were markedly damaged. |
## 6) CARCINOGENCITY

### 6.1 Title:
Carcinogenic potential of endosulfan and its metabolites based on a quantum chemical model

**Authors and their affiliations:**
C.N.G. Bedor a, R.J.L. Morais a, L.S. Cavalcanti a, J.V. Ferreira b, A.C. Pavão

Universidade Federal do Vale do São Francisco, Av. José de Sá Maniçoba, S/N, Centro, 56304-205, Petrolina, PE, Brazil

b Instituto Federal de Alagoas, Rua Mizael Domingues, 75, Poço, 57020-600, Maceió, AL, Brazil

c Universidade Federal de Pernambuco, Av. Prof. Moraes Rego, 1235, Cidade Universitária, 50670-901, Recife, PE, Brazil

**Published in:**

2010 Elsevier B.V. All rights reserved.

**Major Findings:**
The aim of the present study was to investigate the carcinogenic potential of endosulfan and its metabolites through electronic parameters that characterize the action of carcinogens, the findings of the present study indicate that the use of this pesticide represents a risk to the health of the general population, especially rural workers.

The data from the present study indicate that endosulfan and all its metabolites have carcinogenic potential, based on the computational quantum chemical model. This places human health at risk, which is especially true for agriculture workers who are most exposed to this compound and therefore the most vulnerable.

### 6.2 Title:
Breast cancer risk and the combined effect of environmental estrogens

**Authors and their affiliations:**
Jesús M. Ibarluzea1, Mariana F. Fernández2, Loreto Santa-Marina1, Maria F. Olea-Serrano2, Ana M. Rivas2, Juan J.

**Major Findings:**
The estrogenicity of adipose tissue extracts due to bioaccumulated xenoestrogens was associated with a higher risk of breast cancer in the leaner women, especially in the
| Aurrekoetxea1, Jose² Expo² sito3, Miguel Lorenzo4, Pablo Torne² 5, Mercedes Villalobos6, Vicente Pedraza6, Annie J. Sasco7 & Nicolas Olea2,* | postmenopausal leaner group. Complex interactions between chemicals, endogenous or exogenous hormones and their natural ligands and receptors may alter the internal homeostasis of the estrogenic environment of mammary tissue, leading to malignant transformation and cancer. |
| 1Department of Health Guipuzkoa, San Sebastia´n, Basque Country, Spain; 2Laboratory of Medical Investigations, Hospital Clínico University of Granada, Granada, Spain; 3Department of Oncology, Virgen de las Nieves University Hospital, m Granada, Spain; 4Department of Surgery, Torreca´rdenas Hospital, Almer´ia, Spain; Published in: Cancer Causes and Control 15: 591–600, 2004. 591 _ 2004 Kluwer Academic Publishers. Printed in the Netherlands. |

<p>| 6.3 | Title: Modulation of aromatase activity and mRNA by various selected pesticides in the human choriocarcinoma JEG-3 cell line | Major Findings: Some pesticides may induce aromatase activity through transcriptional activation of the CYP19 gene. When considering the physiologic consequences of the modulating effects on aromatase by pesticides, it is important to relate the present findings to the levels of human exposure. |
| | Authors and their affiliations: Nathalie Laville a, Patrick Balaguer b, François Brion a, Nathalie Hinfray a, Claude Casellas c, Jean-Marc Porcher a, S´elim A¨t-A¨issa a,* a INERIS, Ecotoxicological Risk Assessment Unit, BP 2, F-60550 Verneuil- |
| en-Halatte, France | We found out new inducers of aromatase activity, namely aldrin, chlordane, cypermethrine, methylparathion, endosulfan, methoxychlor, oxadiazon and metolachlor. The present study strengthens the view that these chemicals may contribute to the occurrence of reproductive adverse effects in both human and aquatic organisms. |
| b INSERM, U540, Molecular and Cellular Endocrinology of Cancers, F-34090 Montpellier, France | |
| c CNRS UMR 5569, University of Montpellier 1, BP 14 491, F-34093 Montpellier Cedex 5, France | |
| Published in: Toxicology 228 (2006) 98–108 | © 2006 Elsevier Ireland Ltd. All rights reserved. |
| 6.4 Title: Relation of Prediagnostic Serum Estrogen and Androgen Levels to Breast Cancer Risk. | Major Findings: Results support the hypothesis that prediagnostic serum estrogens and androgens are related to the subsequent diagnosis of breast cancer in postmenopausal woman |
| Authors and their affiliations: CJoanne F. Dorgan,’ Christopher Longcope, Hugh E. Stephenson, Jr., Roni T. Falk, Rosetta Miller, Charlene Franz, Lisa Kahle, William S. Campbell, Joseph A. Tangrea, and Arthur Schatzkin Division of Cancer Prevention and Control, National Cancer Institute,Bethesda: Maryland 20892-7326 Departments of Obstetrics and Gynecology and Medicine, University of Massachusetts |</p>
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<th>Medical School, Worcester, Massachusetts 01655</th>
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<td>Cancer epidemiology biomarkers and prevention</td>
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<td>Cancer Epidemiol Biomarkers Prev 1996;5:533-539. Published online July 1, 1996.</td>
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**6.5**

**Title:**

The insecticide endosulfan and its two stereoisomers promote the growth of altered hepatic foci in rats

**Authors and their affiliations:**

Ronny Fransson-Steen1’2’3, Sten Flodstrdm1 and

Lars WMrngard1

1’Institute of Environmental Medicine, Karolinska Institutet, Box 60208, S-104 01 Stockholm and 2Department of Toxicology, Karolinska Institute*, Box 60400, S-104 01 Stockholm, Sweden

**Published in:**

Carcinogenesis vol.13 no. 12 pp.2299-2303, 1992

**Major Findings:**

Endosulfan was studied for its ability to act as a tumour promoter in a two-stage, altered hepatic foci bioassay in male Sprague-Dawley rats.

The results show that endosulfan and its two stereoisomers promote the development of altered hepatic foci, suggesting that endosulfan is a tumour-promoting agent acting by clonal expansion of initiated cells.

Our results show that the insecticide endosulfan is a potential liver tumour promoter in a similar manner to structurally-related chlorinated cyclodienes.

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<th>Effects of Pesticides on the Ratio of 160c/2- hydroxyestrone: A Biologic Marker of Breast Cancer Risk</th>
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<td>Authors and their affiliations:</td>
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<td><strong>Major Findings:</strong></td>
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<td>Xenobiotic estrogens are external compounds with estrogenic activity that may thereby affect the risk of breast cancer. <strong>This paper describes a mechanism by which</strong></td>
</tr>
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</table>
6.7 | Title:  
**Serum Sex Hormone Levels After Menopause and Subsequent Breast Cancer**  
Authors and their affiliations:  
F. Berrino, P. Muti, A. Micheli, V. Krogh, G. Secreto, Istituto Nazionale Tumori, Milan, Italy;  
G. Bolelli, Istituto di Clinica Ostetrica e Ginecologica “P Sfameni,” Universita di Bologna, Italy;  
P. Pisani, Unit of Descriptive Epidemiology, International Agency for Research on Cancer, Lyon, France;  

| Major Findings: | xenoestrogens may affect the development of breast cancer.  
These pesticides significantly increase the ratio of 16ct-OHE1/2-OHE, metabolites to values comparable to or greater than those observed after DMBA (the known rodent carcinogen 7,12-dimethylbenzyl anthracene (DMBA)). The ratio of 16a-OHE1/2-OHE1 may provide a marker for the risk of breast cancer. |
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<th>Title:</th>
<th>Major Findings:</th>
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<tr>
<td>Estrogen Receptor Activation via Activation Function 2 Predicts Agonism of Xenoestrogens in Normal and Neoplastic Cells of the Uterine Myometrium</td>
<td>This report describes an in vitro/in vivo system for identifying the effects of Estrogen receptor ligands in the myometrium and elucidating their mechanism of action. The results suggest that some exogenous Estrogens (like endosulfan) may mimic the effects of endogenous estrogens on uterine leiomyoma and may contribute to a complex hormonal milieu that impacts both normal and neoplastic myometrium.</td>
</tr>
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Authors and Affiliations:

Deborah S. Hunter, Leslie C. Hodges, Peter M. Vonier, Robin Fuchs-Young, Marco M. Gottardis, and Cheryl L. Walker2

The University of Texas M. D. Anderson Cancer Center, Science Park Research Division, Smithville, Texas 78957 [D. S. H., L. C. H., R. F-Y., C. L. W.];

The Tulane-Xavier Center for Bioenvironmental Research, Tulane University, New Orleans, Louisiana 70112 [P. M. V.]; and

Bristol Myers Squibb, Endocrine Oncology Pharmaceutical Research Institute,
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<th>Princeton, New Jersey 08543 [M. M. G.]</th>
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<td>Published in:</td>
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<td>CANCER RESEARCH 59, 3090–3099, July 1, 1999</td>
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