Women at Risk?
Endocrine Disrupters in the Plastics Industry

James Brophy and Margaret Keith
September 12, 2012
• Carcinogens and/or EDCs
• Few improvements
• Exposures to mixtures
• Regulatory inadequacies
• Health problems
• Who knows?
• Who cares?
Hormones image from Skeptic
Atrazine
“Really?”

Yes...

desPLEX
to prevent ABORTION, MISCARRIAGE and
PREMATURE LABOR

recommended for routine use in ALL pregnancies...

96% per cent live delivery with desPLEX
in one series of 1200 patients—
—bigger and stronger babies, too."

No gastric or other side effects with desPLEX
—in either high or low dosages.
p-Nonyl-phenol: an estrogenic xenobiotic released from "modified" polystyrene.

A M Soto, H Justicia, J W Wray, and C Sonnenschein

Abstract

Alkylphenols are widely used as plastic additives and surfactants. We report the identification of an alkylphenol, nonylphenol, as an estrogenic substance released from plastic centrifuge tubes. This compound was extracted with methanol, purified by flash chromatography and reverse-phase high performance liquid chromatography, and identified by gas chromatography-mass spectrometry. Nonylphenol induced both cell proliferation and progesterone receptor in human estrogen-sensitive MCF7 breast tumor cells. Nonylphenol also triggered mitotic activity in rat endometrium; this result confirms the reliability of the MCF7 cell proliferation bioassay. The estrogenic properties of alkylphenols, specifically nonylphenols, indicate that the use of plasticware containing these chemicals in experimental and diagnostic tests may lead to spurious results, and these compounds as well as alkylphenol polyethoxylates may also be potentially harmful to exposed humans and the environment at large.
Estrogen-Induced Stimulation of Cell Proliferation

High estrogen concentration → Breast or uterine cell → Cell proliferation
Hormone Blocking

receptors

nucleus

DNA
Emerging science on the impacts of endocrine disruptors on people.

*Our Stolen Future* reviews scientific studies of the impacts of endocrine disruptors on human health through 1995 (hardback) and 1996 (paperback). The most detailed information available was from studies of the daughters and sons of women who took diethylstilbestrol (DES) during pregnancy. The impacts were devastating and included severe reproductive tract deformities, declines in sperm count, alterations in behavior and a greatly elevated risk of a rare cancer. Several industrial accidents involving relatively high exposures also provided concrete examples of human harm by endocrine disruptors, with the most dramatic effects seen in children exposed in the womb. Ongoing studies of human impacts at environmental levels (exposures experienced by a significant portion of the US population) were consistent with significant impacts (especially neurological) but were insufficient to prove, with scientific certainty, that harm had occurred.
Hormones and Endocrine-Disrupting Chemicals: Low-Dose Effects and Nonmonotonic Dose Responses

Laura N. Vandenberg, Theo Colborn, Tyrone B. Hayes, Jerrold J. Heindel, David R. Jacobs Jr., Duk-Hee Lee, Toshi Shioda, Ana M. Soto, Frederick S. vom Saal, Wade V. Welshons, R. Thomas Zoeller and John Peterson Myers

Center for Regenerative and Developmental Biology and Department of Biology (L.N.V.), Tufts University, Medford, Massachusetts 02155; The Endocrine Disruption Exchange (T.C.), Paonia, Colorado 81428; Laboratory for Integrative Studies in Amphibian Biology (T.B.H.), Molecular Toxicology, Group in Endocrinology, Energy and Resources Group, Museum of Vertebrate Zoology, and Department of Integrative Biology, University of California, Berkeley, California 94720; Division of Extramural Research and Training (J.J.H.), National Institute of Environmental Health Sciences, National Institutes of Health, U.S. Department of Health and Human Services.
Breast Lobule Maturation During First Pregnancy

- After puberty
- Before pregnancy
- End of 1st Trimester
- End of 3rd Trimester
- After weaning

Image from Breast Cancer Prevention Institute
“a mix of smoke and smells from heated plastics”
Acute symptoms
Health Hazards in the Plastics Products Industry

prepared by:

Occupational Health Clinics for Ontario Workers (OHCOW) - Windsor
&
Windsor Occupational Health Information Service (WOHIS)

January, 1996
All Departments

Sometimes or Often

- nosebleeds (26%)
- dizziness (49%)
- nausea or vomiting (34%)
- unusual tiredness (54%)
- 11 cases of cancer
- 39 women with reproductive problems
Occupational and Environmental Risk Factors for Breast Cancer

James T. Brophy, PhD & Margaret M. Keith, PhD
Co-Principal Researchers
Lifetime Histories
BREAST CANCER
Research Study

Towards a better understanding of the causes of BREAST CANCER

If you have recently been diagnosed with breast cancer, you can help with a one-time interview.
Postmenopausal breast cancer and occupational exposures

France Labrèche,1,2 Mark S Goldberg,3,4 Marie-France Valois,3 Louise Nadon5

ABSTRACT

Objective To determine whether exposures in the workplace to organic solvents and to other agents, such as polycyclic aromatic hydrocarbons, are associated with increased risks of developing postmenopausal breast cancer.

Methods Between 1996 and 1997 a case—control study was conducted in Montreal, Quebec. Cases comprised 556 women, aged 50—75 years, with incident malignant breast cancer, and their controls were 613 women with other cancers, frequency matched for age, date of diagnosis and hospital. An expert team of chemists and industrial hygienists translated their job histories into exposure to about 300 agents.

Results Odds ratios (ORs) were increased for the usual risk factors for breast cancer and, adjusting for these, risks increased with occupational exposure to several agents, and were highest for exposures occurring before age 36 years. Increased ORs were found for each 10-year increment in duration of exposure, before age 36 years (OR<36 = 7.69) and to nylon fibres (OR<36 = 1.99). For oestrogen-positive and progesterone-negative tumours, the OR doubled or more for each 10-year increase in exposure to monoaromatic hydrocarbons, and to acrylic and rayon fibres. The OR<36 also doubled for exposure to organic solvents that metabolise into reactive oxygen species, and to acrylic fibres. A threefold increase was found for oestrogen- and progesterone-negative tumours exposed to solvents that metabolise into reactive oxygen species.

What this paper adds

Main messages

- Occupational and environmental agents may be contributing factors in the aetiology of breast cancer.
- Occupational exposure to acrylic and nylon fibres, and to polycyclic aromatic hydrocarbons may increase the risk of developing postmenopausal breast cancer.
- For breast tumours with certain hormonal receptor subtypes, exposure to organic solvents that metabolise into reactive oxygen species and to monoaromatic hydrocarbons may also be associated with an increased risk.
- The risks appear to be higher when exposures occur at a younger age.

Policy implications

- Our findings are consistent with the hypothesis that breast tissue is more sensitive to adverse effects if exposure occurs when breast cells are still proliferating. Young female workers should be protected from exposure to such agents.
Breast Cancer Risk by Occupation and Industry: Analysis of the CECILE Study, a Population-Based Case-Control Study in France

Sara Villeneuve, MSC, Joëlle Févotte, Dipl.-Ing., Antoinette Anger, MSC, Thérèse Truong, PhD, Farida Lamkarkach, MSC, Oumar Gaye, MSC, Pierre Kerbrat, MD, Patrick Arveux, MD, Laurent Miglianico, MD, Ellen Imbernon, MD, and Pascal Guénel, MD, PhD

Background It has been suggested that certain occupational exposures may play a role in breast cancer etiology. The recognition of high-risk occupations may give clues about potential mammary carcinogens in the work place.

Methods We conducted a population-based case-control study in France including 1,230 breast cancer cases and 1,315 population controls with detailed information on lifetime work history. Odds ratios for women ever employed in an occupation or indu-
Exposure to Phthalates and Breast Cancer Risk in Northern Mexico

Lizbeth López-Carrillo¹, Raúl U. Hernández-Ramírez¹, Antonia M. Calafat², Luisa Torres-Sánchez¹, Marcia Galván-Portillo¹, Larry L. Needham², Rubén Ruiz-Ramos³, Mariano E. Cebrián³

1 National Institute of Public Health, Cuernavaca, Morelos, México, 2 Division of Laboratory Sciences, National Center for Environmental Health, Centers for Disease Control and Prevention, Atlanta, Georgia, USA, 3 Departamento de Toxicología, Centro de Investigación y de Estudios Avanzados del Instituto Politécnico Nacional, Mexico City, México

Abstract

Background: Phthalates, ubiquitous environmental pollutants that may disturb the endocrine system, are used primarily as plasticizers of polyvinyl chloride and as additives in consumer and personal care products.

Objectives: In this study, we examined the association between urinary concentrations of nine phthalate metabolites and breast cancer (BC) in Mexican women.
• acrylonitrile
• styrene
• phthalates
• brominated fire retardants
• bisphenol A
<table>
<thead>
<tr>
<th>Plastic</th>
<th>By-Products</th>
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<tbody>
<tr>
<td>ABS</td>
<td>Acrylonitrile, styrene, benzene,xylene,Trichloroethane, toluene, hydrogen cyanide</td>
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<tr>
<td>Polystyrene</td>
<td>Styrene, acrylonitrile, acrolein, toluene, benzene, PAHs, free radicals, aldehydes, ketones, alcohols, CO, CO₂</td>
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<td>Polyethylene</td>
<td>Acedaldehyde, formaldehyde, formic acid, ketones, free radicals, CO, CO₂</td>
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<tr>
<td>Polypropylene</td>
<td>Acetaldehyde, formaldehyde, acetone, acetic acid, methylacrolein, ketones, alcohols, CO, CO₂</td>
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<tr>
<td>Polyvinyl Chloride</td>
<td>HCL, phthalates, dichloromethane, xylene, aldehydes, methyl styrene, phthalic anhydride, azodicarbonamide, ketones, halogenated hydrocarbons, aliphatic hydrocarbons, CO, CO₂</td>
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<tr>
<td>Polytetrafluoroethylene</td>
<td>Hydrogen fluoride, tetrafluoromethane, carbonyl fluoride, tetrafluoroethylene, hexa fluoroethane, hexafluoropropene</td>
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<td>Nylon PA 6</td>
<td>Formaldehyde, e-caprolactam, methylmethacrylate, formic acid</td>
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<td>Polyurathane</td>
<td>Aldehydes, isocyanates, hydrogen cyanide</td>
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<td>Process</td>
<td>Job Task</td>
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<td>Resin Preparation</td>
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