Environmental Effects on Women’s Health

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Currently on sabbatical from USEPA
85,000 synthetic chemicals registered for use in the US.

Human health is affected by:

- multiple chemical exposures
- simultaneous, overlapping/non-overlapping exposures
- low level vs. high level exposures
- duration of exposure
- exposure in utero vs. adult
- genetic context

Giudice et al., 2004
Where do we get our information?

Wildlife  Laboratory  Humans
How Much Do We Know?

3000 high volume chemicals lack data
MIXTURES ARE THE RULE

Biomonitoring

210 chemicals sampled:

- Baltz: 106
- Brody: 85
- Hardin: 77
- Lerner: 101
- Martin: 95
- Moyers: 84
- Patton: 105
- Rome: 86
- Waletzky: 78
Mixtures Are the Rule

Yet all regulatory standards to protect people are based on considering one chemical at a time.

By themselves, these contaminants appear to have no effect.
Mixtures

The impact of mixtures can be dramatically greater than the effects of chemicals one by one.

Together these 11 contaminants double the effect of estrogen alone.
The absence of human data is not proof of safety.

It is proof of the lack of data.
Critical Windows

Buck Louis et al., 2005
INFERTILITY

- Tubal and pelvic pathology (35%)
- Male factor (35%)
- Ovulatory dysfunction (25%)
- Unexplained (15%)
- Unusual (1%)
- Premature ovarian failure
- Recurrent miscarriage

From 2002 to 2002:
- 12%
- 10%
- 8%
- 8%
Environmental Contaminant Effects on Reproductive Health and Fertility

*Some of the culprits*

- Heavy metals - lead, mercury, cadmium, arsenic
- Solvents
- Pesticides, herbicides, fungicides
- Dioxins
- PCBs (electrical transformers)
- PBDEs (flame retardants, computers, furniture, clothes, carpets).
- PVCs and plastics
  - Phthalates - plasticizers to soften plastics (shower curtains, vinyl floor coverings, plastic wraps, makeup, lotions, shampoos, nail polish, adhesives, IV bags, building materials, gelatin pill capsules).
  - Bisphenol A - plastic monomer in hard polycarbonates: sports bottles, baby bottles, dental sealants, food and milk carton lining, CD covers, glasses, lenses.
  - PFCs in Teflon
EDCs & Human Health

• Modulate hormonal function
• Environmental Estrogens: Examples
  – Pesticides
    • DDT, methoxychlor (HPTE), dimethoate, chlordecone, lindane
  – PCBs and their metabolites
  – Alkyphenols (detergents)
  – Bisphenol A (polycarbonate plastics, epoxy resins)
Background exposure to Bisphenol A

adapted from Schönfelder et al.
Target Tissue Effects of Ovarian Hormones in Women

Target Tissues

- Brain
- Skeleton
- Bone marrow
- Heart and arteries
- External genitalia
- Ovaries
- Breasts
- Muscle
- Skin and hair
- Liver
- Kidneys

Sarrel PM. 1996.
Endocrine Disrupting Chemicals

- Puberty
- Menstruation
- Endometriosis
- Time-to-pregnancy
- Pregnancy loss
- Reproductive Cancers

Toft et al., 2004
Human Studies

*Environmental Exposures: Women*

- Infertile women are 27 times more likely to have mixed or used herbicides within 2 yrs of attempting conception (Greenlee 2003).

- Women born 30 yrs ago with high DDT metabolites in their cord blood (thus in utero exposure) have longer times to pregnancy later in life (Cohn 2003).

- Women in the Air Force exposed to aromatic hydrocarbons in fuels and solvents show altered menstrual cycles and significantly lower LH levels (Reutman, 2004).

- Wives of Great Lakes sport fishermen who consume PCB-laden fish have longer time to pregnancy (Buck et al, 2002).
Environmental Exposures during Pregnancy

• A woman’s risk of fetal loss, still birth and bds increases, the closer she lives to an area of agricultural spraying with pesticides (Bell, et al, 2004)

• Pthalates in women linked to preterm birth and precocious puberty (Shearle and Franks 2004).

• PCBs, other organochlorines, and fine particulate matter are linked to LBW and prematurity (Bobak 2000)

• Bisphenol A associated to pregnancy loss in animals and small human study
Prenatal Exposure to DES


- Considered safe and effective

- Estimated 2-8 million births effected

- Adverse effects in children;
  - Vaginal cancer in female offspring (<.1%).
  - Reproductive tract dysfunction in male & female offspring (>90%).

- Adverse effects in grandchildren;
  - Menstrual irregularities, ovarian cancer
  - Hypospadias (deformed penis)

From Newbold 2007 UCSF/CHE Summit
DES leads to concern for other chemicals

• Prenatal exposure to
  – Phthalates increases deformities of the penis and testicles in animals
  – Bisphenol A in animals increases risk of infertility in daughters
  – Perfluorinated chemicals in animals increases risk of premature mortality
Blood lead levels in the U.S.

We can do it!

Source: CDC. National Report on Human Exposure to Environmental Chemicals, March 2001
UCSF Program on Reproductive Health and the Environment

Vision
Advancing healthy conceptions, pregnancies, children and adults.

Mission
To advance scientific inquiry, professional training, citizen education, and health policies that reduce the impacts of environmental contaminants on reproductive and developmental health.

Department of Obstetrics, Gynecology and Reproductive Sciences/Center of Excellence in Women’s Health
Web Resources

www.CHEforHealth.org
www.ProtectingOurHealth.org
www.OurStolenFuture.org
www.EnvironmentalHealthNews.org
Figure 2: Major Pathways of Human Exposure to Environmental Contaminants

Source: Adapted from Health Canada, 1998.
Program Areas

• **Basic and epidemiologic research**
  – Expanding our knowledge

• **Policy and Healthcare**
  – Working toward improved health policy

• **Education**
  – Educating the current and next generation of environmental health professionals
UCSF – CHE Summit on Environmental Challenges to Reproductive Health and Fertility January 28-30, 2007 at UCSF

- Convey state of the science of environmental impacts on reproductive health
- Identify
  - What clinicians and other health care providers need to use the current science.
  - Key next steps in the research agenda and questions the research can answer.
  - Key next steps in policy that should be taken.
- Launch UCSF’s new Program on Reproductive Health and the Environment.
Can We Afford to Wait?

The health of our citizens is at stake: Men, women, and children. The future generation is most vulnerable and most at risk.

The time to act is now!
Endocrine disrupting chemicals can act wherever estrogens act.
Development Begins at Fertilization
Table 1: Reported responses to di-\textit{n}-butyl phthalate in the rat and human: a comparison of ‘phthalate syndrome’ and ‘testicular dysgenesis syndrome’

<table>
<thead>
<tr>
<th>Response</th>
<th>Rat</th>
<th>Human</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Components of testicular dysgenesis syndrome</strong>a</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypospadias</td>
<td>Identified</td>
<td>Inconclusive\textsuperscript{b}</td>
</tr>
<tr>
<td>Cryptorchidism</td>
<td>Identified</td>
<td>Inconclusive\textsuperscript{b}</td>
</tr>
<tr>
<td>Impaired spermatogenesis</td>
<td>Identified</td>
<td>Identified\textsuperscript{c}</td>
</tr>
<tr>
<td>Testicular Cancer</td>
<td>Identified: Leydig cell cancer</td>
<td>Inconclusive: Germ cell cancer\textsuperscript{b}</td>
</tr>
<tr>
<td><strong>Additional components of phthalate syndrome</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testicular dysgenesis\textsuperscript{d}</td>
<td>Identified</td>
<td>Identified</td>
</tr>
<tr>
<td>Reduced anogenital distance</td>
<td>Identified</td>
<td>Identified\textsuperscript{e}</td>
</tr>
<tr>
<td>Lowered testosterone or androgen activity</td>
<td>Identified</td>
<td>Identified\textsuperscript{e}</td>
</tr>
<tr>
<td>Retained thoracic nipples</td>
<td>Identified</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Delay in preputial separation</td>
<td>Identified</td>
<td>Not studied</td>
</tr>
</tbody>
</table>

\textsuperscript{a} As defined by Bay et al. (2006).
\textsuperscript{b} Nonspecific exposure metrics, such as job matrices, were used in available studies.
\textsuperscript{c} Response has been identified, but only a very small number of study or studies have done so.
\textsuperscript{d} This is typically expressed in tissues (cancerous and non-cancerous) among humans with germ cell cancer and is expressed in tissues among rats with Leydig cell cancer.

Data in table reported by (Bay et al. 2006; Fisher et al. 2003; Foster 2006; Hauser and Calafat 2005; Lottrup et al. 2006; Pan et al. 2006; Skakkebaek et al. 2001)

*From E. Wells et al. in process*
Next Steps

• RESEARCH
• POLICY
  – Improved testing for chemicals
  – Better policies for reducing harmful exposures
• EDUCATION
  – Postsecondary and professional
• COMMUNICATION
  – Public and policy makers