ENVIRONMENTAL CONTRIBUTORS TO BREAST CANCER

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Clues to Environmental Causes of Breast Cancer

Estimated Breast Cancer Incidence 2012

Incidence changes with ‘westernization’ of lifestyle, and with migration.
Bray et. al., Breast Cancer Research, August 2004

Source: GLOBOCAN 2012, IARC
Why the environment?

• Genetics explains ~ 5-27% of breast cancers
  – Inherited gene mutations
  – Physical traits that raise risk (e.g., breast density)

• Leaves the majority to:
  – Environment (chemicals in food, air, water, consumer products, workplaces)
  – Reproductive factors (puberty, childbearing, breastfeeding, menopause)
  – Lifestyle (physical activity, smoking, alcohol)

• Of the established breast cancer risk factors, a majority appear to have a mechanism that involves hormonal factors or exposure to a carcinogen
Known Breast Cancer Risk Factors

- Family history – 1st degree relative
- High risk genes – BRCA1 / BRCA2
- Ionizing radiation
- Combined hormone replacement therapy
- Tobacco smoke
- Alcohol
- Overweight (after menopause)
- Lack of physical exercise
- Reproductive history (age at menarche and menopause, number and timing of births)
- Shiftwork with circadian disruption (IARC 2A)
Impact of hormone replacement therapy

- Breast cancer rates dropped nationwide for women > 45 after studies showed risk of HRT outweighed benefits
  
  - Primarily seen in ER+ tumors from white women in higher SES counties
  
  - Studies prevented:
    - 126,000 breast cancers
    - 76,000 cardiovascular disease cases
    - $34 billion expenditures

1. Glass et al. 2007
3. Roth et al. 2014
Could Chemicals in the environment act similarly?

Chemicals linked to breast cancer:
• Benzene and 1,3, butadiene (gasoline and vehicle exhaust)
• Perfluorinated compounds (non-stick and stain-repellant coatings)
• Halogenated flame retardants (furniture foam, electronics)
• Organic solvents (paint strippers and dry cleaning)
• PAHs (vehicle exhaust)
• Heterocyclic amines (charred meat)

Possible links following early developmental exposure:
• DDT (insecticide)
• Dioxin
• Bisphenol-A (and related polymers)
• Atrazine (organochlorine herbicide)
Three paths to breast cancer

1. DNA damage

- Single strand break
- Link between adjacent bases
- Crosslink between DNA strands
- Double-strand break
- Hydroxylated base
- Missing base
- DNA adduct

Key:
- G
- C
- A
- T

2. Promoting tumor growth

- Estrogen stimulation
- Normal breast cell
- Mistake in DNA duplication
- Increased proliferation

3. Disrupting mammary gland development

Silent Spring Institute
1. DNA damage (direct or indirect)
2. Promoting tumor growth
3. Altering mammary gland development

Fenton et al., 2002 Tox Sci
Developmental exposures: delayed effects and delayed detection

Prescribed to pregnant women in 1940s-60s

Diethylstilbestrol (DES)
Cumulative risks of breast cancer by DES-exposure group, in the presence or absence of vaginal epithelial changes (VEC)

- DES was prescribed to women in the 1940s-1960s
- 60+ years to develop human evidence of breast cancer link

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Hoover et al. NEJM 2011
### Timing matters

<table>
<thead>
<tr>
<th>Gestation</th>
<th>Early life</th>
<th>Puberty</th>
<th>Pregnancy/lactation</th>
<th>Adulthood</th>
</tr>
</thead>
</table>
| Normal MG (rat) | • Fat pad and bud form
• Epithelium forms ductal tree | • Isometric epithelial growth
• Branching ducts and budding
• TEBs develop | • Exponential epithelial growth
• TEBs differentiate | • Epithelium is predominant
• Lobulo-alveolar development |

<table>
<thead>
<tr>
<th>MG after early EDC exposure</th>
<th>Altered growth and development; altered carcinogen susceptibility</th>
<th>Lactational impairment</th>
<th>Breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>Altered hormone/growth factor levels and responsiveness; effects may be systemic or localized to MG</td>
<td>Exposure during MG development</td>
<td>Rudel et al. EHP 2011</td>
<td></td>
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</tbody>
</table>
What you can do (individually)

Reduce exposure to some breast carcinogens:

• *Limit your exposure to gas fumes and exhaust*

• *Choose furniture and carpets without stain-resistant treatments*

• *Buy furniture without chemical flame retardants; replace polyurethane foam couch cushions; look for label TB117-2013*

• *For kids, use cotton rather than fleece pajamas*

• *Look for “wet cleaning” in place of dry cleaning with solvents*
What you can do (individually)

Reduce chemical exposures in general:

- *Eat low on the food chain and as much organically grown food as possible*
- *Avoid fragrances, including perfume, air fresheners, and scented personal care products or household cleaners*
- *Avoid antimicrobial soaps, or toys and clothing advertised as antimicrobial*
- *Choose food in glass jars or “tetra paks” in place of canned foods*
- *Leave shoes outside*
- *Vacuum with a HEPA filter, clean with a damp rag*
- *Wash hands frequently, especially before meals*
Synthetic Chemicals are Ubiquitous

72 billion lbs/day

Some undergo long range transport
Some persist and/or bioaccumulate
Many are in consumer products
False sense of security: If it’s sold it must be safe
All are new to human biology:

  Human evolution (14 million y)
  vs. modern chemical production (60 y.)

What you can do collectively

• Advocate for better chemical testing and chemical policy reform
  – http://saferchemicals.org

• Promote environmental justice movements
  – https://www.akaction.org
  – http://greenlining.org

• Support union health and safety organizing
  – https://www.bluegreenalliance.org

• Reward progressive companies
  – https://www.bizngo.org