Environmental Risk Factors for Breast Cancer

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University of California Office of the President
February 21, 2019
Outline

- Regional variations in breast cancer
- Environmental risk factors
- Challenges for research
- Current initiatives
Breast cancer incidence rates in the San Francisco Bay Area have been reported to be among the highest in the world.
Breast Cancer Incidence, Females 1987

Cancer Incidence in Five Continents (IARC)

Per 100,000

- US, SF Bay Area N-H White
- US, Hawaii N-H White
- US, Seattle N-H White
- US, Detroit N-H White
- US, Connecticut N-H White
- US, LA N-H White
- US, Iowa N-H White
- Israel-born Jews
- Netherlands
- Italy
- Sweden
- Australia
- Philippines
- Brazil
- China
- Kuwait

Years born: 1910 to 1939
Breast Cancer Incidence, Females, 1997

Cancer Incidence in Five Continents (IARC)

Age-standardized incidence rates, per 100,000

US, LA NH-white
US, SF Bay Area NH-white
US, CT N-H White
US, N-H white
Israel, Jews
US, Utah N-H white
US Hawaii, Japanese
Finland
US, Central Louisiana
Japanese
Costa Rica
Isreal, Non-Jews
Algeria
India
Korea
Regional Variations in Breast Cancer Incidence in California

Funded by NCI Grant #U01CA81789 and BCRP Grant #6JB-0111
Study Comparison Areas

- Rest of California
- San Francisco Bay Area
- South Coast Area

Map showing areas:
- San Francisco
- Pacific Ocean
- Los Angeles
Breast Cancer Rate Ratios, by Region

Adjusted for Age and Race/Ethnicity

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<th>Region</th>
<th>Statewide</th>
<th>CTS Cohort</th>
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Why Might Rates Differ?

- Differences in:
  - Race/Ethnicity
  - Urbanization
  - Socioeconomic status
  - Personal risk factors
  - Something else?
    - Environmental contaminants?
CTS Personal Risk Factor Covariates

- Family history of breast cancer
- Age at menarche
- Parity
- Age at first full term pregnancy
- Physical activity (last three years)
- Body mass index
- Menopausal status
- Body mass*menopausal interaction
- Alcohol consumption
- Hormone replacement therapy
- Breastfeeding history
CTS Cohort Breast Cancer Hazard Ratios, by Region
Adjusted for Age, Race/Ethnicity, Socioeconomic Status, Urbanization and Personal Risk Factors

Reynolds, et al. Epidemiology, 2004
Established Environmental Risk Factor for Breast Cancer

- Ionizing radiation
  - High doses
  - In adolescence
Exposures from the Physical Environment

- Environmental Tobacco Smoke/Secondhand Smoke
- Combustion byproducts
- Persistent organic pollutants
- Pesticides
- Solvents and industrial chemicals
- Water contaminants
- Hormones in food
- Metals
- Flame retardants - PBDEs
- Plastics
- Bisphenol A
- Compounds in Personal Care Products
- Pharmaceuticals
- Radiation (medical and non-medical)
- Electric and Magnetic Fields
- Light-at-night
- Vitamin D/sunlight
Environmental Chemicals/Pollutants

- The U.S. EPA has registered approximately 85,000 synthetic chemicals for use.
- More than 200 chemicals have been shown in animal studies to increase mammary tumors.
- Timing of exposure is critical for some compounds.

BUT WE DO NOT KNOW …

- The potential health effects of about 90% of the synthetic chemicals registered by U.S. EPA overall or at critical periods.
- Much about human exposure or health effects of chronic, low-level exposure to mixtures.
Chemicals of Concern

Solvents & industrial chemicals: PCBs
- Higher breast cancer risk from PCB exposure associated with a **genetic variant** in a recent study.

Flame Retardants: PBDEs
- Measurable quantities of these persistent chemicals found in almost every human. Limited data indicate the potential for carcinogenic and endocrine disrupting effects.

Combustion By-Products: PAHs
- From active/passive smoking, diet and air; current research is focused on **genetic susceptibility** affecting DNA repair.
Virtually everyone has low-levels of BPA in their body, primarily due to canned foods and plastic beverage containers.

There is strong evidence of estrogenic effects of BPA, and of a link between low-level exposure and breast cancer in animal studies.

BUT WE DO NOT KNOW. . .

About the levels and impacts of human exposures and body burdens over time.
Chemicals of Concern
Pesticides

Chemicals used to control insects, weeds, fungus, etc. are found in measurable levels in everybody due to exposure through food, air and water.

- **DDT/DDE** – Still found in human tissues. Evidence has not support increased incidence, but a new study suggests that exposure in childhood increases risk.

- **Other Organochlorines** – Dieldrin and 13 other OC have been linked to risk, but evidence is inconsistent and mostly negative.

- **Atrazine** – Linked to hormonal changes in wildlife, this herbicide induces mammary gland tumors in some rats.

BUT WE DO NOT KNOW. . .

- How long-term, lower level exposure from an early age is affecting breast cancer risk.
Chemicals of Concern
Compounds in Personal Care Products

- There is reason for concern about the compounds in personal care products, as they are:
  - Widely used;
  - Applied directly to and able to enter the body;
  - Composed of thousands of ingredients about which little is known;
  - Made from compounds linked to breast cancer and hormonal disruption; and
  - Minimally regulated.

BUT WE DO NOT KNOW . . .

- The nature and extent of the impact of compounds in personal care products and breast cancer.

Hair products that contain placenta and estrogen are heavily marketed to African American women and girls.

Has 5 ingredients posing potential breast cancer risks.
Source: Environmental Work Group
Institute of Medicine Report
December 7, 2011

BREAST CANCER AND THE ENVIRONMENT
A LIFE COURSE APPROACH

INSTITUTE OF MEDICINE
OF THE NATIONAL ACADEMIES
Susan G. Komen for the Cure® and its Scientific Advisory Board requested that the Institute of Medicine (IOM)

1. Review evidentiary standards for identifying and measuring cancer risk factors;
2. Review and assess the strength of science base on relationship between breast cancer and the environment;
3. Consider potential interaction between genetic and environmental risk factors;
4. Consider potential evidence-based actions that women could take to reduce their risk;
5. Review methodological challenges in research on breast cancer and the environment; and
6. Develop recommendations for future research.
Defining Environment

- Defined broadly: all factors not directly inherited through DNA
- Environmental exposures may act on multiple levels to influence breast cancer
Life Course Approach

- Substantial changes in the breast through the life course, especially in response to hormonal signals

- Timing of environmental exposures may be important in increasing or reducing breast cancer risks or influencing developmental events
Associations with Breast Cancer Risk

- Among the factors reviewed, consistent associations with increased risk in epidemiologic studies:
  - use of combination estrogen-progestin products
  - current use of oral contraceptives
  - exposure to ionizing radiation
  - overweight and obesity among postmenopausal women
  - alcohol consumption

- Decreased risk:
  - greater physical activity

- No indication of association:
  - personal use of hair dyes
  - non-ionizing radiation
Why don’t we know more?
Complexity of Origins of Breast Cancer

- Biology of breast development and origins and progression of breast cancer not fully understood
- Past focus on exposures during adulthood may have missed critical exposure windows during early life
- Exposure to a complex and changing mix of environmental agents over the course of a lifetime
- Many agents never studied in ways relevant to breast cancer
Challenges in Studying Breast Cancer and the Environment

Assessing human exposure
- Limitations in establishing timing and amount of exposure

Designing and analyzing epidemiologic studies
- Experiments rarely possible
- Likely long latency between exposure and diagnosis
- Widespread, low-level exposures limit contrasts

Identifying genetic influences
- Large studies needed to detect robust associations
- Limited environmental exposure data in genomic datasets

Interpreting animal and in vitro data
- Inconsistencies in results among species and strains
- Exposures not always comparable to human experience
Opportunities for Evidence-Based Actions

Examples of actions that may reduce breast cancer risks related to environmental exposures:

- avoid inappropriate medical radiation exposure throughout life
- avoid use of estrogen–progestin menopausal hormone therapy
- avoid or end active and passive smoking
- limit alcohol consumption
- maintain or increase physical activity
- minimize overweight and weight gain to reduce risk of postmenopausal breast cancer
- limit exposure to agents biologically plausible as contributors to breast cancer
Why not more opportunities for individual action?
Incomplete Evidence Base

Scientific community’s understanding is still incomplete regarding:

- which exposures might best be avoided and when
- whether interventions that modify exposures have long-term benefit in reducing breast cancer risk
- potential for unintended consequences of interventions
Report can be viewed and downloaded free at www.iom.edu/BreastCancerEnvironment
Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC)

- Created by congressional mandate in 2008
- Charge: to identify a comprehensive strategy for research across the federal agencies in breast cancer and the environment
- Led by NIEHS and NCI
- Final Report – February 2013
IBCERCC Recommendations

- Prioritize prevention
- Transform how research is conducted
- Intensify the study of chemical and physical factors
- Plan strategically across Federal agencies
- Engage public stakeholders
- Train transdisciplinary researchers
- Translate and communicate science to society
Breast Cancer and the Environment
Prioritizing Prevention
Report of the Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC)

Available at http://www.niehs.nih.gov/ibcercc
Purpose

With the information and resources available on this website, we aim to:

- Raise awareness about the potential relationship between environmental exposures during certain vulnerable times in the life course, known as windows of susceptibility, and breast cancer risk.
- Explain why a precautionary approach is being taken to aid decision-making where the evidence of harm is stronger in animal than in human studies.
NIEHS Sister Study

"Woman by woman, sister by sister, we can make a difference."

A Study of the Environmental and Genetic Risk Factors for Breast Cancer.

https://sisterstudy.niehs.nih.gov
Women’s Work and the Environment

- Almost entirely neglected in the literature.
- “Canary in the coal mine” effect
  - Workplace chemical hazards typically higher than the general population.
  - Can help identify risk factors of concern.
Development of a Data Visualization Tool to Explore Occupational Chemical Exposures among California Working Women

Funded by CBCRP Grant #212B0901
Background – *Women’s Occupations and Risks from Chemicals (WORC)*

- Funded by California Breast Cancer Research Program (CBCRP, Grant#21ZB-0901; Co-PIs=Robert Harrison, Peggy Reynolds)

- Response to CBCRP’s California Breast Cancer Prevention Initiative (CBCPI) RFP on “*Occupational Chemical Exposures in California and Breast Cancer Risk*”

- 5-year project (2016-2020), 3 phases

- Overarching objective: advance our understanding of the degree to which workplace chemical exposures may increase breast cancer risk among California working women
Community Engagement: 
WORC Advisory Committee

Knowledge Gap
Connect to Workers
Community Voice in Research Process

Julia Liou, MPH
CA Healthy Nail Salon Collaborative/Asian Health Services (Shared Role)

Gail Bateson, MS
WorkSafe

Laura Stock, MPH
Labor Occupational Health Program (LOHP)

Janette Robinson Flint
Black Women for Wellness

Mila Thomas
SEIU Local 1021

Catherine Porter, JD
Two Phases to Date

- **Phase I:**
  - Identify where women are employed in California.
  - Identify workplace chemicals of concern (CoC) for breast cancer risk.
  - Identify the overlap between where women are employed in California and workplace exposures to groupings of CoC for breast cancer risk.

- **Phase II:**
  - Develop a visualization tool based on information from Phase I.
  - Identify data gaps.
California Women by Employment Status*, 2010-2014

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<th>Category</th>
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<td>All women (16+) in CA</td>
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<td>Working Women</td>
<td>7,774,697</td>
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<td>Non Working Women</td>
<td>7,405,301</td>
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<td>6,464,108</td>
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<td>Unemployed</td>
<td>941,193</td>
<td>6%</td>
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Chemical Data Sources

Lists identifying relevant chemicals

- *Carcinogens* – International Agency for Research on Cancer, Silent Spring Institute, EPA
- *Endocrine disruptors* - TEDX & IEH lists
- *Mammary gland toxicants* – Silent Spring Institute
Creation of WORC Database

- Created a list of 1,000+ chemicals-of-concern (CoC) for breast cancer
  - Includes indicators for mammary gland carcinogens, endocrine disruptors, mammary gland toxicants, and high production volume chemicals
  - Categorized in 27 groups based on chemical properties and/or usage
- Constructed dataset summarizing workplace sampling data (OSHA) for limited number of CoCs by industry
- Created Job Exposure Matrix (JEM) to identify overlap of occupations with exposures to CoCs for:
  - 145 occupations (representing ~ 85% of CA female workforce)
  - 9 broad occupational groups identified as likely to have high proportion of informal workers
- Provided data to data visualization vendor
Visualization Tool

Created an interactive online tool to:
- Provide information about the California female workforce
  - By occupation, race/ethnicity, age group
- Summarize groups of chemicals of concern
- Identify potential chemical exposures by occupation
- Be useful to multiple stakeholder groups

Now available on the CBCRP website:
http://www.cbcrp.org/research-topics/worker-exposure.html
Women in California are being exposed to risky chemicals at work.
## Working Women at Risk

161 occupations were reviewed for potential exposure to chemical groups linked to breast cancer.

There are more than 6.5 million women working in these occupations, according to the U.S. Census's American Community Survey. In addition, there are women who work in "informal" jobs. Informal jobs do not show up in official data sources and operate outside of established labor laws. The number of women working in informal jobs in California is not known. We can only estimate the number of women who work informally. Here, we examine what we do know about all women in the California workforce and the chemicals they are potentially exposed to.

### Viewing 161 occupations with 6,609,127 formal women workers:

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<th>Occupation</th>
<th>Ethnicity/Race</th>
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</table>
Working Women at Risk

161 occupations were reviewed for potential exposure to chemical groups linked to breast cancer.

There are more than 6.5 million women working in these occupations, according to the U.S. Census’s American Community Survey. In addition, there are women who work in "informal" jobs. Informal jobs do not show up in official data sources and operate outside of established labor laws. The number of women working in informal jobs in California is not known. We can only estimate the number of women who work informally. Here, we examine what we do know about all women in the California workforce and the chemicals they are potentially exposed to.

Viewing 161 occupations with 6,609,127 formal women workers:
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Viewing 161 occupations with 6,609,127 formal women workers:

- Secretaries and administrative assistants: 310,470 women
- Cashiers: 282,052 women
- Elementary and middle school teachers: 252,404 women
- Registered nurses: 243,053 women
- Retail salespersons: 229,713 women
- Personal care aides: 205,668 women
- Maids and housekeeping cleaners: 197,776 women
- Customer service representatives: 173,840 women

These women may be exposed to risky chemical groups at work.

EXPLORE
Working Women at Risk

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Viewing 161 occupations with 6,609,127 formal women workers:
Maids and housekeeping cleaners

Women may be exposed to harmful chemicals on the job. 24 categories of chemicals that include chemicals of concern for breast cancer are shown below. We investigated the potential exposure of women in this occupation group to these 24 categories of chemicals.

Being exposed to even **one** of the chemicals in these groups may be cause for concern.

Select a category to learn more about exposure, the chemicals, and the women who are exposed.

**Show:**
- 197,778 formal workers
- 76,600 informal workers

**Hispanic**
- 160,223 women | 81% of this occupation
Antimicrobials

32 Chemicals of Concern | 2,207,100+ formal women workers with possible or probable exposure
This category includes substances that suppress the growth of harmful microorganisms such as bacteria, viruses, or fungi on inanimate objects and surfaces. This category excludes crop and household pesticides (see Pesticides category).

Who Works with these Chemicals?

Formally employed women across 58 occupations:

Possible Exposure
1,514,500+ women

Who are the formal workers with probable or possible exposure?

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>20-29</th>
<th>30-39</th>
<th>40-49</th>
<th>50-59</th>
<th>60-64</th>
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<tbody>
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<td>White, non-Hispanic</td>
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</table>

Informally employed women across 19 occupations:
Data Gaps

- **Primary gap:** lack of systematically-collected quantitative chemical exposure data

- **Other gaps:**
  - Incomplete and inaccurate information on occupation and industry in cancer surveillance databases (e.g. CCR, SEER)
  - Dearth of simultaneously-collected information on cancer and occupation/industry in national and statewide population surveys
  - Limited biomonitoring data from nationally-representative workforces
  - Underrepresentation of informal workers in existing data sources
Recommendations for Future Research and Policy Directions

- Exploratory research that links:
  - existing cancer outcome data
  - occupation/industry data
  - sociodemographic data
  - national and statewide survey data
  - biomonitoring data

- Policy aimed at enhancing current data collection systems to fill data gaps and promote the initiation of new occupational health surveillance systems aimed at cancer outcomes
Phase III
Pilot Exposure Study, 2018-2020

Focus on domestic household cleaners and hotel housekeepers:
- Represent a large segment of the workforce
- Include a substantial number of informal workers
- 80% Latina
- Considerable opportunity for chemical exposures from cleaning products
- Understudied for breast cancer risks

Currently underway
Summary

- Relatively little is known about environmental risk factors and breast cancer
- Challenges for human health research
- Environmental risk factors are currently a high priority for:
  - Advocacy groups
  - CBCRP initiatives
  - New NIH initiatives
Thank you!