Links Between Cancer and Early Life Exposures to Environmental Pollutants

A Webinar on the Latest Science, and its Implications for Health Professionals

December 8, 2016
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EXPLORING THE ENVIRONMENTAL CONTRIBUTION to CHILDHOOD CANCER

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December 8, 2016
Childhood Cancer in the US
An Overview

• Beyond infancy, cancer is the leading cause of death by disease among children in the United States. Only injuries kill more children.

• In 2014, an estimated 15,780 children and adolescents ages 0 to 19 years in the US were diagnosed with cancer.

• In 2014, an estimated 1,960 American children died of cancer.
First Recognition of Environmental Cancer - 1776

Scrotal Skin Cancer in London Chimney Sweeps
Sir Percival Pott
Childhood Cancer (Age 0-19)
Age-Adjusted Incidence and Death Rates
United States, 1975-1996

Source: Pediatric Monograph 1999, Surveillance, Epidemiology, and End Results Program
Division of Cancer Control and Population Sciences, National Cancer Institute.
American Cancer Society, Surveillance Research
Incidence of Childhood Leukemia 1975–2004

Source: National Cancer Institute
Increasing Incidence of Childhood Leukemia, USA, 1992-2011

Incidence of Childhood Brain Cancer 1975–2004

Source: National Cancer Institute
Increasing Incidence of Testicular Cancer, USA, 1973-2003

![Graph showing increasing incidence of testicular cancer by race and gender from 1973 to 1995.](image)

*Incidence rate per 100,000*

- **White males**
- **All races, males**
- **Black males**

**Year of diagnosis**

*Age-adjusted to the 1970 U.S. standard population.*

Increasing Incidence of Hypospadias/Cryptorchidism, 1968-95
Possible Causes of Increasing Incidence of Childhood Cancer

• Genetics – too rapid

• Diagnostic artefact – would have explained a one-time “bump”, but not a consistent rise of several different cancers over several decades

• Environmental exposures
Children’s Exposures to Chemicals in the Environment

- 85,000 + chemicals in commerce today
- 3,000 synthetic chemicals are produced in quantities of 1 million pounds or more per year – High Production Volume chemicals
- Widespread exposure – documented in CDC national surveys
- No basic toxicity information is available for fewer than half of HPV chemicals
- Information on developmental toxicity is available for fewer than 20% of HPV chemicals
- Almost nothing is known about synergistic effects of simultaneous exposures to multiple chemicals
Children are Uniquely Vulnerable to Toxic Chemicals

- Greater exposure Kg-per-Kg
- Diminished ability to detoxify and excrete many chemical toxins
- Heightened biological vulnerability
- More years of future life

“Children are not Little Adults”
Infants and Children are Exquisitely Sensitive to Toxic Chemicals in the Environment

Examples:

• Phocomelia in infants exposed *in utero* to thalidomide.

• Epidemic of neurobehavioral disease in Minamata Japan caused by *in utero* exposure to methylmercury

• Adenocarcinoma of the vagina in girls exposed in the womb to di-ethylstilbestrol (DES)
Phocomelia following *in utero* Exposure to Thalidomide
A Child Massively Exposed to Mercury
Minamata, Japan, 1960

No visible damage to the mother
Growing Evidence for Environmental Causation of Childhood Cancer

- Radiation – post Hiroshima and Nagasaki and Alice Stewart’s studies
- DES and adenocarcinoma of vagina
- Solvents, especially benzene – and parental employment in industries that use solvents – painting and printing
- Pesticide exposure, especially prenatally
- Air pollution
- Aspartame – experimental evidence
- Protective effects of folic acid and breast feeding
Key Elements of a Research Strategy to Discover the Environmental Causes of Childhood Cancer

- **Toxicology.** Independent, publicly funded testing of chemicals to discover developmental carcinogens

- **Epidemiology.** Independent, publicly funded epidemiologic studies of children – especially large, multi-year prospective birth cohort studies that incorporate careful measures of chemical exposures and of genetic susceptibility

- **Research translation.** Translation of research findings into evidence-based prevention
The Good News: Progress is Possible

Examples of evidence-based prevention:

- Removal of lead from gasoline
- Reduction in use of X-rays during pregnancy
- Decline in exports of toxic pesticides
- Global control of asbestos
Challenges Remain

- Rising global levels of air pollution
- Increasing use of carcinogenic pesticides, e.g., glyphosate
- Migration of polluting industries to the world’s least developed countries
- Persistent global trade in asbestos – 2 million tons of new asbestos enter global trade each year
A Final Thought for Those Who Provide Clinical Care for Children

• Cancers of environmental origin in children have no distinctive clinical features.
• Therefore a careful history of environmental exposure is in most cases the way to diagnose environmental causation.
• A careful history is also the only way to discover new environmental causes of cancer.
• Pioneering pediatrician and cancer epidemiologist Robert W. Miller spoke of “The Critical Importance of the Alert Clinician.”
Thank You
Childhood cancer and environmental exposures – a focus on air pollutants

Richard W. Clapp, D.Sc., MPH
B.U. School of Public Health and U. of Mass.- Lowell
Outline

- Additional information on environmental risk factors for childhood cancer
  - Two recent meta-analyses of air pollution and leukemia
- Cancer in teenagers
- Conclusions and recommendations
Additional information on environmental risk factors

- Evidence of “windows of vulnerability” for breast cancer following early life exposure

Two examples:

- Cohn, et al., 2007 found risk of breast cancer before age 50 was significantly higher in those exposed to DDT before age 14.

- Cohn, et al., 2015 found increased risk of breast cancer in young women whose mothers had elevated maternal DDT levels.
Environmental risks (cont.)

- Multiple air pollution and childhood leukemia studies published between 1989 and 2014.
- Recent meta-analyses suggest associations between traffic density, specific air pollutants and childhood leukemia, especially acute myelogenous leukemia.
  - Boothe, et al., 2014 found 50% excess childhood leukemia with post-natal exposure to residential traffic in seven studies.
Studies of Air Pollution and Childhood Leukemia

Bottom line: 53% elevated risk of childhood leukemia based on post-natal exposure to traffic-related pollutants
Filippini, et al., 2015 included review of studies published through 2014.

- Results suggest modest increase in leukemia risk associated with traffic density in multiple studies.
- Four studies which estimated benzene exposure found 64% increased risk of leukemia; two studies found greater than two-fold risk of acute myelogenous leukemia.
- Authors discuss benzene leukemogenic mechanisms and suggest motorized traffic increases risk.
Childhood (0-19) Cancer – Allegheny Co.

Childhood (0-19) Leukemia – Allegheny Co.

Pennsylvania Department of Public Health’s Epidemiologic Query and Mapping System (EpiQMS) [cancer incidence: https://apps.health.pa.gov/EpiQMS/asp/ChooseDataset.asp.]
Trends in teenage cancer incidence

- Most common cancers in teenagers age 15-19 are Hodgkin lymphoma (15%), thyroid cancer (11%), brain and central nervous system (10%), testicular germ cell cancer (8%)
- There were an estimated 5,330 cases in 2014 in the U.S.
- Source: American Cancer Society, 2014
FIGURE 1
Childhood cancer incidence in the United States. Surveillance, Epidemiology, and End Results data for all cancer sites combined, both sexes, in 3 age groups, 1975–2012.
Cancer in teenagers

- Overall incidence rates are similar to those in children under age 5, and are increasing over time.
- Fastest rising cancer types are non-Hodgkin lymphoma, thyroid cancer, acute myeloid leukemia and testicular cancer.
- Increased screening and medical radiation does not explain entire pattern.

Conclusions and recommendations

- Childhood cancer incidence is steadily increasing, as are numbers of early adult survivors of childhood cancer.
- One in 285 children will be diagnosed with cancer before age 20.
  - One in 530 adults age 20 to 39 are childhood cancer survivors.
- Source: American Cancer Society, 2014
Conclusions and Recommendations

○ Reduction of carcinogenic exposures to parents, the developing fetus, newborns and young children will prevent some childhood and teen cancers.
  ○ Green chemistry and alternatives assessment provide a way forward for many companies.
  ○ Health care providers can join efforts to reduce childhood cancer incidence.
References

• Cohn B, et al. DDT Exposure in Utero and Breast Cancer. J Clin Endocrinol Metab. Doi: 10.1210/jc.2015-1841
Exposure to air toxics from mobile and point sources in Southwest PA

Jim Fabisiak, Ph.D.
Dept. of Environmental & Occupational Health
University of Pittsburgh
What are air toxics?

- The Clean Air Act amendments of 1990 listed 188 hazardous air pollutants (HAPs) known or highly suspected to cause cancer or other serious non-cancer health effects (usually respiratory, neurological, or reproductive/development effects).

- Contrast to NAAQS criteria pollutants (PM, O₃, NOₓ, SO₂, CO, Pb)

Not all hazardous air pollutants are created equal, and they can produce differing health effects from varying chemical properties. Some produce cancer in regions of the body; others are respiratory irritants, while others may affect the nervous system, reproduction, or neurological development.
About 50% of HAPs have been classified as “known”, “probable”, or “possible” human carcinogens. Each has a unique estimate of its potency to induce cancer.

**URE** = risk of cancer per million people / (µg/m³ in air).

EPA uses a threshold of “one-in-a-million” probability of lifetime (70 yrs) cancer risk above which is unacceptable or cause for concern.

US EPA periodically conducts the National Air Toxics Assessment (NATA) that tries to characterize cancer and non-cancer risk based on estimations HAP concentrations at the census tract level throughout the U.S.

We conducted an analysis of NATA (2005) specifically within the 10 county region of Southwest PA in a form relateable to the non-technical community.

**Risk ≠ Rate**

Total lifetime cancer risk from all HAPs Southwest PA ten county area as predicted by NATA (2005)

1. Median cancer risk across entire 10-county area > 120 per million.

2. Residents of Allegheny County are at least twice as much risk as rural areas.

3. Allegheny County ranks 63rd out of 3,225 U.S. counties ranking it in the top 2% nationally.

4. Some areas reach risk levels in excess of 1,000 per million by proximity to various point sources.
Comparison of cancer risk estimates for various environmental exposures

Overall risk of Cancer
Smokers
Non-smokers radon (4 pCi/L)
Non-smokers exposed to tobacco
Risk from AT in highest tract
Median risk from AT in SW PA
EPA Baseline

Lifetime Cancer Risk Estimate (per million people)
Top HAP Drivers of Cancer Risk in the Southwest PA 10 County Area

<table>
<thead>
<tr>
<th>Rank within PRETA</th>
<th>Air Toxic Name</th>
<th>Cancer Risk (lifetime risk, in a million)$^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>DIESEL PARTICULATE MATTER</td>
<td>93.43</td>
</tr>
<tr>
<td>2</td>
<td>FORMALDEHYDE</td>
<td>16.37</td>
</tr>
<tr>
<td>3</td>
<td>BENZENE (INCLUDING BENZENE FROM GASOLINE)</td>
<td>7.49</td>
</tr>
<tr>
<td>4</td>
<td>COKE OVEN EMISSIONS</td>
<td>7.05</td>
</tr>
<tr>
<td>5</td>
<td>CARBON TETRACHLORIDE</td>
<td>2.86</td>
</tr>
<tr>
<td>6</td>
<td>ACETALDEHYDE</td>
<td>2.75</td>
</tr>
<tr>
<td>7</td>
<td>ARSENIC COMPOUNDS(INORGANIC INCLUDING ARSINE)</td>
<td>2.71</td>
</tr>
<tr>
<td>8</td>
<td>CHROMIUM COMPOUNDS</td>
<td>2.13</td>
</tr>
<tr>
<td>9</td>
<td>1,3-BUTADIENE</td>
<td>1.99</td>
</tr>
<tr>
<td>10</td>
<td>NAPHTHALENE</td>
<td>1.44</td>
</tr>
<tr>
<td>11</td>
<td>POLYCYCLIC AROMATIC HYDROCARBONS</td>
<td>1.30</td>
</tr>
<tr>
<td>Median</td>
<td>All HAPs</td>
<td>122</td>
</tr>
</tbody>
</table>
Cancer-driving HAPs from mobile sources

Diesel Particulate Matter

Formaldehyde
Cancer-driving HAPs from stationary sources

Coke Oven Emissions

Chromium
Five out of the 10 census tracts with the highest cancer risk (excluding DPM) in PA, MD, OH, WV are in Allegheny county

<table>
<thead>
<tr>
<th>Rank</th>
<th>State</th>
<th>County</th>
<th>Tract Number</th>
<th>Total Cancer per Million</th>
<th>Major Contributing Source Type</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PA</td>
<td>Allegheny</td>
<td>4927</td>
<td>289</td>
<td>Point</td>
<td>Clairton</td>
</tr>
<tr>
<td>2</td>
<td>WV</td>
<td>Brooke</td>
<td>0312</td>
<td>243</td>
<td>Point</td>
<td>Follansbee (Weirton-Steubenville)</td>
</tr>
<tr>
<td>3</td>
<td>OH</td>
<td>Hamilton</td>
<td>0007</td>
<td>199</td>
<td>Non-point</td>
<td>Cincinnati (Central Business Dist.)</td>
</tr>
<tr>
<td>4</td>
<td>PA</td>
<td>Allegheny</td>
<td>4928</td>
<td>184</td>
<td>Point</td>
<td>Clairton</td>
</tr>
<tr>
<td>5</td>
<td>PA</td>
<td>Allegheny</td>
<td>4970</td>
<td>156</td>
<td>Point</td>
<td>Lincoln</td>
</tr>
<tr>
<td>6</td>
<td>PA</td>
<td>Allegheny</td>
<td>4980</td>
<td>143</td>
<td>Point</td>
<td>Liberty</td>
</tr>
<tr>
<td>7</td>
<td>PA</td>
<td>Allegheny</td>
<td>4994</td>
<td>142</td>
<td>Point</td>
<td>Glassport</td>
</tr>
<tr>
<td>8</td>
<td>OH</td>
<td>Cuyahoga</td>
<td>1024.1</td>
<td>142</td>
<td>Point</td>
<td>West Boulevard (Cleveland)</td>
</tr>
<tr>
<td>9</td>
<td>OH</td>
<td>Cuyahoga</td>
<td>1132</td>
<td>128</td>
<td>Non-point</td>
<td>Fairfax (Cleveland)</td>
</tr>
<tr>
<td>10</td>
<td>OH</td>
<td>Hamilton</td>
<td>0006</td>
<td>125</td>
<td>On-road</td>
<td>Cincinnati (Central Business Dist.)</td>
</tr>
</tbody>
</table>
Sources of HAPs (excluding DPM)

<table>
<thead>
<tr>
<th>Source Type</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Point (stationary)</td>
<td>Large industrial stacks, power plants, incinerators, factories</td>
</tr>
<tr>
<td>Nonpoint (stationary)</td>
<td>Smaller facilities – dry cleaners, gas stations, minor manufacturing (less than 10 TPY of one HAP or &lt; 25 of total HAPs)</td>
</tr>
<tr>
<td>On-road (mobile)</td>
<td>Vehicles including cars and trucks that travel along roadways</td>
</tr>
<tr>
<td>Non-road (mobile)</td>
<td>Construction machinery, marine vessels, trains, etc.</td>
</tr>
<tr>
<td>Background</td>
<td>Anthropogenic and natural sources that persist in the environment or sources that are emitted from distances greater than 50 km</td>
</tr>
<tr>
<td>Secondary (formation)</td>
<td>Point-, non-point, and mobile-source types that emit compounds that are readily transformed in the atmosphere into HAP compounds</td>
</tr>
</tbody>
</table>
Similar analysis using 2011 NATA data for Allegheny County. (Excluding DPM)

John Graham
Boston, MA

- Allegheny county ranked 21st out of 3,200 US counties (top 1%) for cancer risk from HAPs (57 per million people).

- Only 0.2% of ≈78,000 census tracts in the US had HAP cancer risk > 100 per million people, but 12% of those were located in Allegheny county.

- Almost 40% of that risk was attributed to point source emissions, which is nearly 20X greater than that of urban counties in general.

- Amongst all US counties, Allegheny County ranks third in cancer risk from point source emissions.
PA has high rates of cancer

- PA ranked third highest in overall cancer rate in the US *(CDC, 2013)*.

- Rates of lung, laryngeal, bladder, and thyroid cancer in Allegheny County exceed national averages *(PA-DOH, 2009-2013)*

- Mortality from lung cancer, C-V and respiratory disease exceed national averages in 14 SWPA counties **after correcting for smoking**. Between 12 - 13,000 excess deaths during that time period. *(http://scienceblogs.com/thepumphandle/2010/12/15/the-pittsburgh-post-gazette-co/)*
What does the future hold?

- Multiple data sources examined over the last decade highlight:
  - Pervasive, geographic variability, and persistence.
  - Emerging and novel potential pollution sources.

- A changing and challenging political landscape.
Respondent

DR. MARSHA HALEY
Magee Women’s Hospital – University of Pittsburgh Medical Center
Respondent

DR. EDWARD KETYER
Pediatric Alliance
Respondent

DR. MATT MEHALIK
Air Quality Collaborative
Community Organizations Engaged in Improving Air Quality in Southwestern Pennsylvania

- Homewood Children’s Village: http://hcvpgh.org
- Women for a Healthy Environment: http://www.womenforahealthyenvironment.org
- Clean Water Action: http://www.cleanwateraction.org
- CREATE Lab: http://www.cmucreatelab.org
- Sustainable Pittsburgh: http://sustainablepittsburgh.org
- Go GBA: https://www.go-gba.org
- PennFuture: http://www.pennfuture.org
- GASP: http://gasp-pgh.org
- Clean Air Council: http://cleanair.org
- Southwest Pennsylvania Environmental Health Project: http://www.environmentalhealthproject.org
- ACCAN: http://www.facebook.com/AghCoCAN/
- PennEnvironment: http://www.pennenvironment.org
- Environmental Integrity Project: http://www.environmentalintegrity.org
- American Lung Association of the Mid-Atlantic: http://www.lung.org
Webinar Audio & Slides

The audio recording and slides shown during this presentation will be available by next week at:

https://www.uml.edu/Research/Lowell-Center/Cancer-Free-Economy/Preventing-Cancer/webinar.aspx
Thank you for attending!

Evaluation survey to follow by email

Questions? Contact: molly_jacobs@uml.edu