Chemicals and Children’s Health

The Early and Delayed Consequences of Early Exposures

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Children and the environment

1. Fetuses, infants and children are *exquisitely sensitive* to environmental exposure.
   a) Vulnerability is greatest in the fetal period.

2. Recent evidence confirms that children are *exposed more* than adults.

3. Evidence is mounting that *environmental exposures in early life can cause disease* in children - and also in adults.

4. Environmentally related disease is *costly*.

5. *Policy informed by scientific evidence can reduce exposure, improve health, and reduce costs.*
Fetuses, infants and children are uniquely vulnerable to environmental exposure.
The Barker Hypothesis

Proposed by Prof. David Barker, University of Southampton, UK

The early environment is a powerful determinant of health and disease across the entire human lifespan.

Original concept (fetal under-nutrition associated with increased adult risk of Coronary Heart Disease) can be broadened to include fetal exposure to environmental toxins.
The Barker Hypothesis and Toxic Chemicals

- Children are surrounded by a large and increasing number of chemicals.
  - Many *benefits* including improved food supplies (pesticides), prevention of disease (mosquitoes/Malaria and disinfectants), and treatment of disease (antibiotics)
  - But increasing evidence of *toxic effects* and causation of disease
- Dozens of chemicals are detectible at measurable levels in humans and in many cases at higher levels in children - *CDC surveys.*
- Evidence is mounting that children and the developing fetus are especially vulnerable to toxic chemicals.
Most chemicals to which children are exposed have not been tested for toxicity

- 80,000 + chemicals in commerce
- Approximately 3,000 produced in quantities of 1 million pounds or more per year (high production volume [HPV] chemicals)
- No basic toxicity information is publicly available for about half of HPV chemicals
- Information on developmental toxicity is publicly available for fewer than 20% of HPV chemicals

--EPA: Chemical Hazard Data Availability Study, 1998
Fetuses, infants and children are especially vulnerable to toxic chemical exposure.

- Greater exposure proportionate to body mass—7 times more water per Kg per day; Crawling on floor; Hand-to-mouth activity
- Reduced ability to break down and excrete many chemicals compared to adults
- Great vulnerability during windows of susceptibility in early development.
- More years of future life—i.e., many decades in which consequences of early exposures can become manifest

US National Academy of Sciences, 1993
Recent data demonstrate greater exposure in children.
Evidence for higher exposure and body burden in children

  - Biomonitoring exposure data for 148 environmental chemicals for the noninstitutionalized, civilian U.S. population over the 2-year period 2001 - 2002
  - Many chemicals are found in greater amounts in children than adults suggesting that children really are exposed to a greater degree
Chlorpyrifos exposure higher in Children

Table 277. 3,5,6-Trichloro-2-pyridinol (creatinine corrected)

Geometric mean and selected percentiles of urine concentrations (in µg/g of creatinine) for the U.S. population aged 6-59 years, National Health and Nutrition Examination Survey, 1999-2002.

<table>
<thead>
<tr>
<th>Survey years</th>
<th>Geometric mean (95% conf. interval)</th>
<th>Selected percentiles (95% confidence interval)</th>
<th>Sample size</th>
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<tbody>
<tr>
<td></td>
<td>Total, age 6 and older</td>
<td></td>
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</tr>
<tr>
<td>99-00</td>
<td>1.58 (1.35-1.85)</td>
<td>1.47 (1.24-1.74)</td>
<td>1994</td>
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<tr>
<td>01-02</td>
<td>1.73 (1.49-2.01)</td>
<td>1.88 (1.64-2.24)</td>
<td>2508</td>
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<tr>
<td></td>
<td>Age group</td>
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<tr>
<td>6-11 years</td>
<td>3.11 (2.31-4.19)</td>
<td>3.20 (2.05-4.80)</td>
<td>481</td>
</tr>
<tr>
<td>01-02</td>
<td>3.48 (2.80-4.32)</td>
<td>3.76 (3.17-4.36)</td>
<td>573</td>
</tr>
<tr>
<td>12-19 years</td>
<td>1.60 (1.34-1.91)</td>
<td>1.45 (1.21-1.81)</td>
<td>681</td>
</tr>
<tr>
<td>01-02</td>
<td>2.09 (1.72-2.56)</td>
<td>2.24 (1.92-2.66)</td>
<td>822</td>
</tr>
<tr>
<td>20-59 years</td>
<td>1.41 (1.23-1.62)</td>
<td>1.33 (1.11-1.56)</td>
<td>832</td>
</tr>
<tr>
<td>01-02</td>
<td>1.49 (1.30-1.71)</td>
<td>1.64 (1.39-1.88)</td>
<td>1113</td>
</tr>
<tr>
<td>Gender</td>
<td>Males</td>
<td></td>
<td></td>
</tr>
<tr>
<td>99-00</td>
<td>1.48 (1.27-1.72)</td>
<td>1.44 (1.19-1.68)</td>
<td>972</td>
</tr>
<tr>
<td>01-02</td>
<td>1.71 (1.47-2.00)</td>
<td>1.87 (1.57-2.22)</td>
<td>1183</td>
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<tr>
<td>Females</td>
<td>1.69 (1.42-2.01)</td>
<td>1.51 (1.25-1.85)</td>
<td>1022</td>
</tr>
<tr>
<td>01-02</td>
<td>1.75 (1.49-2.07)</td>
<td>1.93 (1.59-2.33)</td>
<td>1325</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td>Mexican Americans</td>
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<tr>
<td>99-00</td>
<td>1.46 (1.20-1.77)</td>
<td>1.44 (1.05-1.93)</td>
<td>697</td>
</tr>
<tr>
<td>01-02</td>
<td>1.86 (1.63-2.12)</td>
<td>2.06 (1.83-2.35)</td>
<td>660</td>
</tr>
<tr>
<td>Non-Hispanic blacks</td>
<td>1.47 (1.09-1.99)</td>
<td>1.33 (0.93-1.94)</td>
<td>521</td>
</tr>
<tr>
<td>01-02</td>
<td>1.56 (1.19-2.03)</td>
<td>1.92 (1.57-2.40)</td>
<td>700</td>
</tr>
<tr>
<td>Non-Hispanic whites</td>
<td>1.66 (1.45-1.90)</td>
<td>1.54 (1.31-1.83)</td>
<td>602</td>
</tr>
<tr>
<td></td>
<td>01-02</td>
<td>1.78 (1.49-2.14)</td>
<td>947</td>
</tr>
</tbody>
</table>

Third Report on Environmental Exposure to Chemicals - CDC 2005
Evidence of early and late health effects of early environmental exposures
First dramatic examples of disease in childhood and young adult life caused by early exposures to toxic chemicals

- Phocomelia in infants exposed in the womb to thalidomide.
- Cancer of the reproductive organs in girls exposed in the womb to di-ethyl stilbestrol (DES)
The spectrum of brain injury caused by toxic chemicals

Initial recognition was of obvious, massive damage caused by high-dose exposures.

But later studies with more sophisticated tools have shown in every case that the brain injury caused by toxic chemicals is not limited to obvious conditions.

It is now recognized that there exists an entire spectrum of diminished brain function in persons exposed to toxic chemicals, termed *subclinical toxicity*. 
Severe brain damage due to fetal mercury exposure – Minamata, Japan, 1960
Known Environmental Causes of Neurodevelopmental Disorders

- Lead
- Methyl Mercury
- Polychlorinated Biphenyls (PCBs)
- Certain Pesticides
Widespread Subclinical Neurotoxicity Can Affect the Health, Well-being, Intelligence and even the Security of Entire Societies

Lead provides an example
Societal impact of 5-point loss in IQ score

Fig. 3. Losses associated with five-point drop in IQ on a population of 100 million. Based on Weiss (1988) and modified by http://www.ourstolenfuture.org/NewScience/behavior/iqshift.htm.
Early exposure to toxic chemicals may increase risk of degenerative brain disease in later life.

- Alzheimer’s disease – following exposure to lead
- Parkinson’s disease – following exposures in infancy to the herbicides maneb and paraquat
Recent evidence of early environmental exposure and health effects
Fetal DDT exposure associated with impaired mental development

- Study type: Prospective cohort of 360 pregnant Mexican immigrants in California
- Main Findings: Lower MDI (mental development index) on Bayley at 2 years old
- Well controlled for confounders:
  - Age, Income, Education, Gender, BF status, quality of home environment

(Eskanazi at al, Pediatrics 2006)
Proximity of pregnant mothers to toxic chemical facilities and releases associated with childhood cancer

- Study type: US case control study
- 382 cases of cancer in children <10 years from a registry in several eastern US states with matched community controls
- Main Findings: OR of 1.66 (CI 1.1-2.48) for case proximity (< 1 mile) to TRI sites and 1.72 (CI 1.05 - 2.82) to carcinogenic chemical releases
- Limited by crude proxy for exposure (proximity)
- Limited by complex multi-factorial etiology of cancer
- Confirms earlier finding of tumors associated with releases in NY state

TRI = “Toxic Release Inventory” (Choi at al, EHP 2006)
Fetal exposure to PAHs associated with decreased mental development

- Study type: Prospective cohort of 183 pregnant women in NYC
- Main Findings: Decreased MDI score (-5.69) on Bayley and increased OR of 2.89 (CI 1.3 - 6.25) of cognitive developmental delay (MDI score <85) at age 3 years in offspring with high prenatal PAH exposure.
- Exposure measured by personal air monitoring - provides good estimate of exposure

(Perera et al, EHP 2006)
Very low level childhood lead exposure associated with ADHD

Study Type: Cross sectional analysis using NHANES data

Exposures:
- ETS
- Concurrent Blood Lead

Outcome: ADHD
- Parent report of MD Dx. of ADHD and current use of stimulant medication

Main Finding:
- Association of elevated BLL (highest quintile (>2.0 μg/dL) vs. lowest quintile (<0.7 μg/dL)) had 4.5 (CI 1.3 - 15.3) times higher risk of ADHD

290,000 cases of ADHD attributable to BLL > 2.0 μg/dL

Braun et al, EHP Sept 2006
Mortality from bronchiectasis and lung cancer increased by fetal and early childhood exposure to Arsenic

- Study type: Historical Cohort in Region II of Chile where arsenic contaminated water was introduced into the municipal water supply as the population in Antofagasta grew.
- Main finding: Birth cohorts with fetal and early childhood exposure to Arsenic revealed dramatically increased SMRs (Standardized Mortality Ratios) for Lung Cancer (6.1) and Bronchiectasis (46.2) in adults age 30 - 49 years
- Remarkable natural experiment with very well defined exposure and standard health outcome

(Smith et al, EHP 2006)
The high cost of environmentally related disease
### Estimated total costs of pediatric disease of environmental origin

<table>
<thead>
<tr>
<th>Disease</th>
<th>Best Estimate</th>
<th>Low Estimate</th>
<th>High Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lead Poisoning</td>
<td>$43.4 billion</td>
<td>$43.4 billion*</td>
<td>$43.4 billion</td>
</tr>
<tr>
<td>Asthma</td>
<td>$2.0 billion</td>
<td>$0.7 billion</td>
<td>$2.3 billion</td>
</tr>
<tr>
<td>Cancer</td>
<td>$0.3 billion</td>
<td>$0.2 billion</td>
<td>$0.7 billion</td>
</tr>
<tr>
<td>Neurobehavioral Disorders</td>
<td>$9.2 billion</td>
<td>$4.6 billion</td>
<td>$18.4 billion</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>$54.9 billion</strong></td>
<td><strong>$48.8 billion</strong></td>
<td><strong>$64.8 billion</strong></td>
</tr>
</tbody>
</table>

* Major cost is lost IQ producing diminished productivity
The costs of methyl mercury exposure in the US

- CDC national prevalence data (NHANES) used to estimate the number of newborns in a year born with Hg>5.8mcg/dL - level associated with intellectual impairment.
- Estimated decreased IQ from Faroes Islands cohort
- Correlated lost lifetime income with decreased IQ
- Used an environmentally attributable factor
- Lifetime lost income per birth cohort in US estimated at $8.7 billion (range 2.2 - 43.8) per year - $1.3 attributable to US power plant emissions

Trasande et al, EHP 2005
Impact of MeHg toxicity on IQ

Population

- Increased number of MR cases
- 3.2% (range .8-29.2%) of MR attributable to MeHg exposure from all anthropogenic emissions
- Health care, special education and other costs amounting to $2.0 billion (range $0.5-17.9) each year

Evidence based public policy can reduce exposure, improve health, and reduce costs
Case Study in Research: Rates of Heart Disease, Stroke and Lung Cancer Exploded after World War II

To find out why, US public health authorities launched the Framingham Heart Study, a prospective epidemiological investigation to identify risk factors.
The Framingham Heart Study

Identified the major risk factors for lung cancer and cardiovascular disease:

- Cigarette smoking
- High cholesterol
- Hypertension
- Sedentary life style
- Diabetes

The Result: Development of a blueprint for prevention that produced a massive (>50%) reduction in CVD incidence and mortality and parallel declines in cancer
Coronary Heart Disease
Age-Adjusted Death Rates: Actual and Expected
United States, 1950-2000

~ 815,000 Deaths Prevented in 2000
~ 1,329,000 Projected Deaths in 2000
~ 514,000 Actual Deaths in 2000
Prospective Cohorts and Environmental Health Toxicity

Important health outcomes:
- Neurodevelopmental disorders
- Cancer

These diseases have a complex, multi-factorial etiology. Estimating past exposures is exceedingly difficult in retrospective studies.

Prospective Cohorts:
- Address multiple simultaneous exposures and contributing factors
- Allow for accurate measurement of exposures from early in life over long durations
- Combined cohorts may even address rare outcomes like cancer

Prospective Cohorts would provide critical information unattainable from other study designs.
Selected International Prospective Epidemiologic Studies of Children

- US National Children’s Study
  - 100,000 children from prenatal life to 18 years old

- Norwegian Institute of Public Health
  - 100,000 pregnant women in study of environmental exposures and health outcomes

- Prospective Cohort Study of Thai Children
  - 4,200 subjects followed from 28 weeks gestation to 24 years old

- WHO has expressed interest in these studies
  - Meetings in Bangkok, Mar del Plata, Budapest
PBDEs and Breast Milk: Effectiveness of regulation

- In the United States, no federal regulatory action has been taken to ban or restrict PBDEs.
- In Sweden, PBDE phase-out began in 1990 and accelerated in the end of the decade.
The EPA Decision on Lead in Gasoline: Decline in Blood Lead Levels Greatly Exceeded Expectation
Economic Benefits of Reducing Population Blood lead Levels

- Between 1976 and 1999, the mean BLL of 1-5 y/o US children declined by 15.1 mcg/dl
- Each decline of 1 mcg/dl is associated with an increase of 0.18-0.3 IQ points
- Mean IQ of US children therefore increased between 2.2 and 4.7 points
- Each IQ point increases economic productivity by 1.76-2.38%
- The estimated economic benefit in each year’s birth cohort is $110-319 billion

Reducing Mercury exposure can have a similar effect
Conclusions

1. Fetuses, infants and children are *exquisitely sensitive* to environmental exposure.
2. Recent evidence confirms that children are *exposed more* than adults.
3. **Current** scientific evidence clearly demonstrates that *environmental exposures in early life cause disease* in children - and also in adults.
4. Environmentally attributable disease is *very costly to society.*
Conclusions

- Although there is much more to be learned, the existing scientific evidence cannot be ignored and demands international action.

- Global Public Health Policy informed by scientific evidence can reduce toxic environmental exposure, prevent disease, reduce costs, and save lives.

- The time to act is now.