7th INTERNATIONAL SYMPOSIUM ON CHILDREN'S ENVIRONMENTAL HEALTH

MINISTRY OF ENVIRONMENTOF J APAN

14 to 16 December 2008
Tokyo, Japan

BIRTH COHORT STUDIES IN DEVELOPING COUNTRIES

GLOBAL AND LOCAL CHALLENGES

Dr. Jenny Pronczuk
Public Health and Environment
World Health Organization
The children of today live in environments that are vastly different than those of a few generations ago.

*This is telescoped in low and middle-income countries.*
The children of today are exposed to:

- Transition from agrarian to urbanized industrial societies
- Increasing production and use of chemicals
- Movement of hazardous wastes across national borders
- Global climate change
- Emerging and re-emerging risks: EDCs, nanoparticles, atmospheric brown clouds, ....
The children of today are exposed to:

- Transition from agrarian to urbanized industrial societies
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- Global climate change
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Risks are enhanced in countries undergoing industrial transition – is there locally relevant data?.

Is the "epidemiological transition" detected?
HOW DO SPECIFIC DISEASES AND INJURIES RELATE TO ENVIRONMENTAL RISK FACTORS?

WHICH REGIONS AND POPULATIONS ARE THE MOST VULNERABLE

Burden of disease attributable to environmental factors

- 24% of global disease burden (healthy life years lost)
- 23% of all deaths (premature mortality)
  - 25% in developing countries
  - 17% in developed regions
- 36% of deaths in children 0-14 years
Environmentally-related diseases in children

On average, children in developing countries lose 8-times more healthy life years per capita than children in developed countries.

In very poor regions of the world, the disparity is greater: number of healthy life years lost due to lower respiratory infection is 800 times greater per capita.

Mental retardation caused by lead in gasoline is 30 times higher in areas where it is used, if compared with areas where it was banned.
Cooking and heating with solid fuels over an open fire in Latin America. Many women and children in developing countries are thus exposed to very high concentrations of indoor air pollution, a major risk factor for respiratory infections.

Credit: Nigel Bruce/University of Liverpool

A child directly exposed to tailpipe emissions from an automobile, which may heighten environmental exposure to lead in countries where leaded gasoline has not yet been phased out.

Credit: Harmut Schwarzbach/Still Pictures

A schoolgirl with a face mask for protection from smokestack pollution emissions of factories in her neighbourhood in the eastern Mediterranean region.

Credit: Munir NASA/UNEP/Still Pictures
Country profiles of Environmental Burden of Disease

Japan

Population 128.1 mio
GNI/capita 31,410 US$
% urbanization 66%
% people living in cities greater than 100,000 inhabitants 64%
Population below the poverty line (national) NA
Population below the poverty line (international, <$1/day) NA

Under age 5 mortality rate 4/1000 live births
Life expectancy 82 years

Environmental burden of disease for selected risk factors, per year

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Exposure</th>
<th>Deaths/year</th>
<th>DALYs/1000 cap/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water, sanitation and hygiene</td>
<td>Improved water: 100%</td>
<td>-</td>
<td>0.2</td>
</tr>
<tr>
<td>(diarrhoea only)</td>
<td>Improved sanitation: 100%</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>Indoor air</td>
<td>SFU% households: &lt;5%</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Outdoor air</td>
<td>Mean urban PM10: 33 ug/m3</td>
<td>23,800</td>
<td>0.9</td>
</tr>
<tr>
<td>Main malaria vectors</td>
<td>No transmission</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main other vectors</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## COUNTRY PROFILE – ENVIRONMENTAL BURDEN OF DISEASE - JAPAN

### Environmental burden by disease category [DALYs/1000 capita], per year

<table>
<thead>
<tr>
<th>Disease group</th>
<th>World's lowest country rate</th>
<th>Country rate</th>
<th>World's highest country rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diarrhoea</td>
<td>0.2</td>
<td>0.3</td>
<td>114</td>
</tr>
<tr>
<td>Respiratory infections</td>
<td>0.1</td>
<td>0.5</td>
<td>56</td>
</tr>
<tr>
<td>Malaria</td>
<td>0.0</td>
<td>0.0</td>
<td>32</td>
</tr>
<tr>
<td>Other vector-borne diseases</td>
<td>0.0</td>
<td>0.0</td>
<td>4.2</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>0.0</td>
<td>0.8</td>
<td>2.5</td>
</tr>
<tr>
<td>Other cancers</td>
<td>0.5</td>
<td>2.6</td>
<td>4.1</td>
</tr>
<tr>
<td>Neuropsychiatric disorders</td>
<td>1.4</td>
<td>1.6</td>
<td>4.4</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>1.3</td>
<td>2.8</td>
<td>13</td>
</tr>
<tr>
<td>COPD</td>
<td>0.0</td>
<td>0.3</td>
<td>4.7</td>
</tr>
<tr>
<td>Asthma</td>
<td>0.3</td>
<td>1.0</td>
<td>2.4</td>
</tr>
<tr>
<td>Musculoskeletal diseases</td>
<td>0.5</td>
<td>1.0</td>
<td>1.5</td>
</tr>
<tr>
<td>Road traffic injuries</td>
<td>0.3</td>
<td>0.3</td>
<td>10</td>
</tr>
<tr>
<td>Other unintentional injuries</td>
<td>0.9</td>
<td>1.3</td>
<td>19</td>
</tr>
<tr>
<td>Intentional injuries</td>
<td>0.1</td>
<td>0.8</td>
<td>7</td>
</tr>
</tbody>
</table>

### Other Indicators
- Use of leaded gasoline (2004): No
- Overcrowding: NA
- Malnutrition (% stunting): NA
Every year more than 3,000,000 children under 5 die due to diseases linked to the environment

- Diarrhoeal disease 1,800,000
- Respiratory diseases 1,000,000
- Malaria/vector-borne disease 1,000,000
- Poisonings/Injuries 300,000
Every year more than 3,000,000 children under 5 die due to diseases linked to the environment.

- Diarrhoeal disease: 1,800,000
- Respiratory diseases: 1,000,000
- Malaria/vector-borne disease: 1,000,000
- Poisonings/Injuries: 300,000

What happens with those who survive?
MAIN GLOBAL ENVIRONMENTAL HEALTH RISKS

Climate - Global change

 Ambient Air pollution

Chemical hazards

Unsafe water

Poor hygiene and sanitation

Indoor Air pollution

Disease vectors

Injuries and accidents

Radiations
World’s annual urban growth rate at 1.8% vs. rural growth rate of 0.1%

World’s urban population will go from 2.86 billion (in 2000) to 4.98 billion by 2030

High-income countries will account for only 28 million out of the 2.12 billion increase

2004-5 UN-HABITAT
State of the world’s cities’
Urbanization trends - as cities grow anarchically,

- Slums emerge near industrial sites, power stations, garbage dumps, busy roads without services, degrading the natural environment.
- Housing is unsafe, no ventilation, no natural light, prone to fire
- In areas with dust, smoke, noise pollution, disease vectors
- Chemicals unsafely stored and dumped
- Pollutants released by factories and vehicle exhaust fumes
- Slum children are especially vulnerable
- Child labor develops...

*Urbanization and its consequences on children*
*P. Mehta, ICCW News Bull. 1992*
GLOBAL ENVIRONMENTAL CHANGE

Global warming
Ozone depletion

WHO
svs.gsfc.nasa.gov

Ozone Hole
**Why and how are children vulnerable to climate change?**

<table>
<thead>
<tr>
<th>Modality</th>
<th>Mechanism</th>
<th>Increased Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Metabolic</strong></td>
<td>• &gt; Respiratory rate&lt;br&gt;• &gt; Metabolic rate&lt;br&gt;• &gt; Water demand per unit body mass</td>
<td>• Air pollution, allergens&lt;br&gt;• Malnutrition, thermal extremes&lt;br&gt;• Gastrointestinal Diseases, dehydration</td>
</tr>
<tr>
<td><strong>Behavioral</strong></td>
<td>• &gt; Outdoor time&lt;br&gt;• &gt; Vigorous activity&lt;br&gt;• &lt; Ability to avoid unhealthy situations&lt;br&gt;• &lt; Swimming capacity</td>
<td>• Infectious diseases, air pollution, UV radiation, thermal extremes, allergens&lt;br&gt;• Weather extremes, UV radiation, thermal extremes&lt;br&gt;• Drowning</td>
</tr>
<tr>
<td><strong>Physiology</strong></td>
<td>• &gt; Surface area: volume&lt;br&gt;• &lt; Detoxifying capacity&lt;br&gt;• &lt; Skin development&lt;br&gt;• &lt; Immunity</td>
<td>• Infectious diseases, UV radiation&lt;br&gt;• Air pollution, infectious diseases, thermal extremes&lt;br&gt;• UV radiation&lt;br&gt;• Infectious diseases, allergens/mycotoxins</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td>• &gt; Latency for genetic/long-term effect&lt;br&gt;• &gt; Lifetime exposure time</td>
<td>• UV radiation, malnutrition, allergens</td>
</tr>
<tr>
<td><strong>Development</strong></td>
<td>• Undergoing development</td>
<td>• Malnutrition, stunting, psychosocial trauma&lt;br&gt;• Morbidity and quality of life</td>
</tr>
</tbody>
</table>

(> indicates greater, < indicates less)

*Figure 3. Modalities and mechanisms by which children may be more susceptible to climate change than adults.*
Global warming – potential health impacts

Direct Effects:

- Respiratory problems
- Weather disasters: death, injuries, trauma, disease
- Dehydration and diarrhoeal disease
- Thermal extremes: heat stroke

Indirect Effects:

- Food scarcity: malnutrition, growth retardation, developmental delay
- Malaria, dengue fever, and other vector-borne diseases
- Increased aeroallergens: asthma, allergies
Future climate change and malaria

1.1 million death/year – most of them children!

Climate change is likely to change transmission – *but* to what extent?

(Tanser et al, Lancet, 2003)
Future climate change and dengue

Increase in the proportion of global population exposed to dengue from 35% to 50-60% by 2085.

Hales et al, Lancet 2002
GLOBAL ENVIRONMENTAL CHANGE AND CHILD HEALTH

- **Ozone Depletion**
  - Melanoma, Non-Melanoma Skin Cancer,
  - Immune Damage, Cataracts

- **Global Warming**
  - Increased heat related deaths
  - Increased air pollution related illness
  - Injury, death from extreme weather events
  - Increased waterborne diseases
  - Changes in vector/rodent-borne illness

- **Globalization of travel and food**
  - Infectious disease increase

- **Chemicals**
  - Effects of long-term, low dose exposure
Promotion of international collaborative research

*NIEHS-WHO Grant for the promotion of collaborative international research enables to promote cooperation and networking -*

- Asthma and respiratory diseases (Australia & India)
- *Carbon particles in macrophages* (UK and 10 countries)
- Arsenic in pregnant women (Thailand & USA)
- Biomarkers of PAH exposure (Thailand, Czech Republic)
- POPs in breast milk (Mexico & Canada)
- Long-term cohort studies (15 countries)
Longitudinal cohort studies on CEH

WHO Informal Consultations *(co-sponsors: NIH, USEPA, CDC)*

**Are LTS feasible in developing countries?**
Oct 2003 (Glion, Switzerland)

**What are the key issues for harmonized international work?**
July 2004 (PAHO, USA 2004)

**Need for "core" hypotheses**
Nov 2004 (Cuernavaca, Mexico)

**Set of measurements required and a "matrix"**
Aug 2005 (Bangkok, Thailand)
Longitudinal cohort studies on CEH

Core hypothesis on:

1. RESPIRATORY EFFECTS
2. PREGNANCY OUTCOME
3. NEURODEVELOPMENT
4. GROWTH AND DEVELOPMENT
5. INJURIES
6. BIRTH DEFECTS
7. CHILDHOOD CANCER
### Longitudinal cohort studies on CEH

#### SPECIMENS FOR COLLECTION
- Blood (maternal, paternal, child, cord)
- Amniotic fluid
- Placenta
- Meconium
- Urine (maternal, child)
- Semen
- Hair
- Nails
- Bucal swabs
- Vaginal/cervical swabs
- Saliva
- Tooth
- Stools
- Other

#### ENVIRONMENTAL

#### TIMING OF SAMPLE COLLECTION
- Enrolment, 2nd and 3rd trimester
- Birth, 3-6-12 months, yearly
- Other

#### TECHNIQUES (standard and "omics")

#### STORAGE

*Biomarkers of exposure, outcome and susceptibility*
# A matrix for sampling and data collection

<table>
<thead>
<tr>
<th>Time point</th>
<th>Antenatal</th>
<th>Birth</th>
<th>Week 6</th>
<th>Month 6-9</th>
<th>Year 1</th>
<th>Year 2</th>
<th>Year 3</th>
<th>Year 4</th>
<th>Year 5</th>
</tr>
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<tbody>
<tr>
<td>Visit</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>

**Clinical Assessments and Questionnaires:**
- **X = Essential**
- **X = Optional**

- Inclusion/exclusion criteria, PIC, repeat consent for biological samples: X X X X X X X X X
- Contact Details: X
- Demographic Data: X
- Family and Lifestyle Questionnaire: X X X X X X X X X
- Maternal Medical History: X
- Paternal Medical History: X
- Maternal Physical Examination: X X X X X X X X X
- Maternal Physical and Mental Health: X X X X X X X X X
- Pregnancy, Delivery and Neonatal Record: X
- Maternal Food Frequency & Diet Questionnaire (while breastfeeding): X X X X X X
- Child Food frequency & Diet: X X X X X X X X X
- Developmental Assessment: X X X X X X X X X
- Child medical history: X X X X X X X X X
- Child Physical Examinations: X X X X X X X X X
- Record Of Vaccination: X X X X X X X X X
# A matrix for sampling and data collection

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<td>8</td>
<td>9</td>
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</table>

**Biological Samples**  
- **X** = Essential  
- **X** = Optional

- Cord blood (or cord slice)  
  - Antenatal: X
  - Birth: X
  - Week 6-9: X
  - Year 1-5: 

- Placenta  
  - Antenatal: X
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

- Meconium  
  - Antenatal: X
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

- Breast Milk  
  - Antenatal: 
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

- Maternal Blood Sample  
  - Antenatal: X
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

- Child Blood Sample  
  - Antenatal: 
  - Birth: X
  - Week 6-9: X
  - Year 1-5: X

- Child Faecal Sample  
  - Antenatal: 
  - Birth: X
  - Week 6-9: X
  - Year 1-5: X

- Maternal Urine  
  - Antenatal: 
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

- Child Urine  
  - Antenatal: 
  - Birth: X
  - Week 6-9: X
  - Year 1-5: X

- Hair  
  - Antenatal: 
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

- Teeth  
  - Antenatal: 
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

**Environmental Questionnaires & Measures**

- Environmental Questionnaire  
  - Antenatal: X
  - Birth: X
  - Week 6-9: X
  - Year 1-5: X

- Outdoor Air Quality  
  - Antenatal: X
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

- Water Quality  
  - Antenatal: X
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

- Indoor Air Quality  
  - Antenatal: X
  - Birth: X
  - Week 6-9: 
  - Year 1-5: 

Longitudinal cohort studies on CEH

Other need/issues identified

• Terminology/definitions
• Environmental "history"
• Informatics' support
• Capacity building
• Biostatistics
• Funding: seed, bilateral and main
• Ethical aspects
• Community involvement/incentives

Outcomes:
- White paper (publication)
- Guidance paper
- Hypotheses
- Measurements
- Specialized WG
- Harmonized protocols
<table>
<thead>
<tr>
<th>Country</th>
<th>Objectives/Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thailand</td>
<td>Biological, psychosocial, and moral development in Thai children, from the perinatal period to adulthood</td>
</tr>
<tr>
<td>Cuba</td>
<td>Injuries and respiratory morbidity in children</td>
</tr>
<tr>
<td>Guatemala</td>
<td>Growth and development in children and cardiovascular risk factors and economic productivity in adults in relation to prenatal and childhood nutrition</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>Cooking with charcoal indoors and respiratory illnesses infants and young children</td>
</tr>
<tr>
<td>Chile</td>
<td>Ambient air pollution and respiratory disorders in children</td>
</tr>
<tr>
<td>Brazil</td>
<td>Social inequities and health outcomes in children</td>
</tr>
<tr>
<td>China</td>
<td>Folic acid supplements before an early in pregnancy and risk of neural tube defects</td>
</tr>
<tr>
<td>South Africa</td>
<td>Health and development of children born in a 7 week period in 1990 in the Greater City of Johannesburg</td>
</tr>
<tr>
<td>Peru, India, Ethiopia,</td>
<td>Causes and consequences of childhood poverty</td>
</tr>
<tr>
<td>Viet Nam</td>
<td></td>
</tr>
<tr>
<td>Multinational</td>
<td>Growth and nutrition</td>
</tr>
</tbody>
</table>
New studies

- Seoul, Korea (10,000)
- CHILD Canada (5,000)
- Paarl, South Africa (1000)
- Peel, Australia (1500)
- Barwon, Australia (1000)
- Athens, Greece (500)
- Other…
Guide to Undertaking a Birth Cohort Study

- Based on the outcome of the four consultations
- Plus input of academia, governmental and non-governmental organizations in different countries, with different backgrounds – and a shared concern about the environmental health of children and future adults.

- Prepared by ALSPAC
- Publication: March 2009

*Pediatric and Perinatal Epidemiology, 23 (Suppl 1), …2008*
Guide to Undertaking a Birth Cohort Study

I. WHY CARRY OUT A LONGITUDINAL SURVEY?
II. WHO SHOULD BE STUDIED AND WHEN IN A LONGITUDINAL BIRTH COHORT?
III. THE OVERALL PLACING AND MANAGEMENT STRUCTURE OF A LONGITUDINAL BIRTH COHORT
IV. IMPORTANCE OF BIOLOGICAL SAMPLES IN LONGITUDINAL BIRTH COHORT STUDIES
V. CHOICE OF TYPES OF SAMPLE TO COLLECT IN LONGITUDINAL BIRTH COHORT STUDIES
VI. IMPORTANCE OF A GENETIC COMPONENT
VII. NESTING SUB-STUDIES AND RANDOMISED CONTROLLED TRIALS WITHIN BIRTH COHORT STUDIES
VIII. ETHICS AND GOVERNANCE FOR A LONGITUDINAL BIRTH COHORT
IX. SOURCES OF DATA FOR A LONGITUDINAL BIRTH COHORT
X. HOW MANY SUBJECTS ARE NEEDED IN A LONGITUDINAL BIRTH COHORT?
XI. THE FUNDING OF COHORT STUDIES
Guide to Undertaking a Birth Cohort Study

X. INFORMATION TECHNOLOGY (IT)
XI. TAKING AND STORING BIOLOGICAL SAMPLES FOR LONGITUDINAL BIRTH COHORTS
XII. EXTRACTING, STORING AND DISTRIBUTING DNA FOR A BIRTH COHORT STUDY
XIII. CHOICE OF ENVIRONMENTAL COMPONENTS
XIV. ASSESSING DIET IN BIRTH COHORT STUDIES
XV. OUTCOME MEASURES
XVI. ENROLMENT AND RESPONSE RATES
XVII. PREPARATION, PILOTING AND VALIDATION PRIOR TO STARTING A BIRTH COHORT STUDY
XVIII. DATA ORGANISATION
XIX. THE IMPORTANCE OF A COLLABORATING CENTRE TO GUIDE COMPARATIVE DATA COLLECTION
International collaboration on LTCS is crucial – it enables:

• Identify critical environmental health issues
• Improve detection of environmental factors and emerging health threats (sentinel cases or events).
• Baseline information & characterization of patterns of children’s EH
• Comparability of data across countries
• Transfer of knowledge and study technologies
• Efficient use and sharing of resources
• A sufficiently large cohort on "rare" diseases
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PROMOTE SAFER ENVIRONMENTS FOR CHILDREN ...AND ALL