Webinar Series:
Early Environmental Exposures to Hazardous Pollutants/Chemicals and their Associations with Chronic Disease

Webinar 3:
Policy Implications
March 6, 2013

Kathleen Cooper, Senior Researcher
Canadian Environmental Law Association
Report Co-Authors

Kathleen Cooper
Canadian Environmental Law Association

Dr. Lynn Marshall
Environmental Health Institute of Canada

Franca Ursitti
Peel Region Public Health

Dr. Loren Vanderlinden
Toronto Public Health and Dalla Lana School of Public Health, University of Toronto
Webinar 1: Introduction to the Scoping Review
Webinar 2: Focus on Endocrine Disruption, Obesogens and Diabetogens

Webinar 3: Policy Implications

• Challenges in Evaluating Evidence
• Re-cap – Endocrine Disrupting Chemicals
  – Science Demands a Paradigm Shift
• Responses - a “progress report”
Scoping Review: Main Findings

- Increasing evidence of associations
- Early exposures, despite uncertainty, should be seen as chronic disease risk factors
- Developmental origins (DOHaD) concept – very solid evidence and rapidly expanding to include early life exposures
- 3+ decades of complex and inter-related changes to consider
- Continuum of shared, well-known risk factors across multiple chronic diseases
  - Primacy of social determinants of health
  - Environmental risk factors likely also shared
- Wide range of chemicals and pollutants implicated
Evaluating the Evidence in Environmental Cases

Complex and uncertain science about early life env’l risks for many reasons

- Complex biochemical influences on multiple, inter-related developing systems
- Considering the entire life course
- Low level, chronic exposure to multiple substances, through diverse media, changing over time and location

Causal webs vs linear systems

- Can have many-to-many relationships between variables or complex inter-relationships where “confounders” (e.g., social circumstances) can actually be co-causal factors.

Impossible and unethical to run controlled experiments to fully understand environmental risks

Randomized Controlled Trials? No human population is now unexposed to low levels of endocrine disrupting chemicals
Type II Errors Frequent in Environmental Case Studies

Type I – concluding associations exist when not the case (false positive)

Type II – missing causal associations (false negative)

Lead – six flaws in study design contributing to Type II errors (Needleman and Bellinger, 1991)

Review of multiple env’l health studies – systematic bias towards Type II errors (Grandjean, 2005)

European Environment Agency, 2001 and 2013 – multiple examples of Type II errors in environmental case studies (Late Lessons from Early Warnings reports)
Public Health Definition of a Risk Factor

- Scoping Review: chronic disease evidence via discussion of multiple risk factors and evidence type and strength
- Traditional public health definition of a risk factor:

  an aspect of personal behavior or lifestyle, an environmental exposure, or an inborn or inherited characteristic, that, on the basis of epidemiologic evidence, is known to be associated with health-related condition(s) considered important to prevent (emphasis added).

  (Govt of Canada, Chronic Disease Risk Factor Atlas)

- Doesn’t sufficiently recognize primary influence of SDOH
- Epidemiological evidence for environmental problems – very difficult; once obtained, can be far too late to achieve prevention or even clean-up in some cases
“We should keep in mind that a positive finding in an epidemiology or clinical study is, in reality, a failure of preventive medicine policy.”

Dr. George Lucier, September 2007 to Domestic Policy Subcommittee Oversight and Government Reform Committee “Will NIEHS’ new direction protect public health?”
Webinar 1: Introduction to the Scoping Review
Webinar 2: Focus on Endocrine Disruption, Obesogens and Diabetogens

**Webinar 3: Policy Implications**

- Challenges in Evaluating Evidence

- **Re-Cap: Endocrine Disrupting Chemicals**
  
  — Science Demands a Paradigm Shift

- Responses - a “progress report”
Endocrine-Disrupting Chemicals

• Diverse mechanisms and pathways that are highly conserved across species

• Shared properties of EDCs with endocrine receptors and enzymes – likely that no endocrine system is immune from EDCs

Strong evidence:

• Adverse reproductive effects (infertility, cancers, malformations)

Mounting evidence:

• Effects on thyroid, neuroendocrine, and metabolic systems as well as on insulin and glucose homeostasis

WHO-UNEP: EDCs have the capacity to interfere with tissue and organ development and function, and therefore they may alter susceptibility to different types of disease throughout life. This is a global threat that needs to be resolved.
Chemicals Suspected as Obesogens/Diabetogens

Most are POPs:
- Persistent Organic Pollutants (POPs) including polybrominated diphenyl ethers (PBDEs), organochlorine pesticides, PCBs, dioxins, polyfluoroalkyl compounds

Many more that aren’t POPs but widespread use means “quasi-persistence”:
- Bisphenol A (BPA)
- Phthalates
- Tributyltin
- Organophosphate pesticides

~ 800 chemicals known or suspected as EDCs. 10s of 1000s are untested for endocrine disruption potential. Vast uncertainty remains.

Many endocrine-related diseases and disorders on the rise

Metabolic changes from obesogens are superimposed on current trends in other obesity risk factors
Paradigm Shift in Toxicology: demanded by endocrine disruption science

- New mechanisms of action and measuring different pathways and endpoints (molecular mechanisms and signalling pathways vs. whole animal effects)
- Timing of exposure is crucial, esp. fetal
- Development looks normal but functional changes (at gene and cell level) persist... after exposure gone... and lead to increased sensitivity to disease later in life
- Latent effects are permanent, irreversible and some are intergenerational
- Effects at very low doses, non-linear dose response curves, and likely no safe level of exposure
EDCs: Scientific Evidence Creates Fundamental Challenge to Regulatory Approaches

Assumptions and challenges in regulatory toxicology:

- Treat mutagenic carcinogens differently than other chemicals (carcinogens have no threshold)
- Chemicals have toxicity thresholds and a linear dose-response
- Assess chemicals one at a time, one disease at a time, seeking one dose (animal models, humans, and wildlife)
- Very limited assessment of mixtures
EDCs: Scientific Evidence Creates Fundamental Challenge to Regulatory Approaches cont’d

Assumptions and challenges in regulatory toxicology, cont’d:

• EDCs – narrow focus on halogenated chemicals
• EDCs – narrow focus on estrogenic, androgenic and thyroid pathways
• Lack of agreement on how to evaluate strength of evidence
• Need for improvements in risk assessment approaches
Four Areas of Reform Needed in Risk Assessment to Protect Human Health


- Phthalates and Cumulative Risk Assessment: The Tasks Ahead
- Science and Decisions: Advancing Risk Assessment

Most recommendations yet to be implemented

Selected Recommendations - Relevant to Chronic Disease Risk Factors and Endocrine Disrupting Chemicals

After Janssen et al, 2012

- Consider multiple stressors (chemical and non-chemical), how they interact, and apply population-focused assessment (including variability among sub-populations)
  - would address social determinants and circumstances of greater exposure (nutrition, housing condition and location, etc)
- Give special attention to hormonally active compounds
- Address highly problematic default assumptions, such as:
  - No data = no effect (common re endocrine disruption)
  - Chemicals without epi or animal bioassay data pose no risk
- Conduct cumulative risk assessment on chemicals that share a common adverse health outcome (i.e., not limited to those with common biological pathway)
- Assume all exposures, even low level, are associated with some level of risk and remove “scientifically unjustified” distinction between cancer and non-cancer outcomes
Scientific and Medical Organizations Call for Regulatory Action to Decrease the Public’s Exposure to Endocrine Disrupting Chemicals

8 mainstream scientific societies:

“Although chemical testing and risk assessment have long been in the domain of toxicologists, it is clear that the development of improved testing guidelines and better methods of assessing risks posed by common chemicals to which all Americans are exposed requires the expertise of a broad range of scientific and clinical disciplines.”

European Society for Paediatric Endocrinology and Pediatric Endocrine Society:

“..., urge members to be alert to the possible significance of EDCs when assessing both clinical problems and research data about endocrine problems when endocrine disease etiologies are lacking.”

Science 331: 1136. 2011

Examine EDCs in the Context of Endocrinology
Non-linear dose-response; high dose cannot predict low dose

Endocrine Disrupting Chemicals and Public Health: Endocrine Society Statement of Principles

- Standard dose tests on range of ~50-fold (below toxic/lethal effect) → low dose hormone potency range can be 10,000-fold
- Threshold doses derived from standard toxicology always very high by endocrine standards → based on sub-lethal dose vs. mechanistic information about biochemical or molecular actions of EDCs observable at doses more than a million times lower than the assumed threshold dose

Webinar 1: Introduction to the Scoping Review
Webinar 2: Focus on Endocrine Disruption, Obesogens and Diabetogens

Webinar 3: Policy Implications
• Challenges in Evaluating Evidence
• Re-Cap: Endocrine Disrupting Chemicals
  – Science Demands a Paradigm Shift

• Responses - a “progress report”
Monitoring, Research, New Testing Protocols

Worldwide, collective and often collaborative efforts among academic and government scientists:

• Human biomonitoring and diverse environmental exposure and surveillance studies (including indoors)
• Toxicity and toxicogenomic studies of individual chemicals or groups of chemicals
• Development of test methods and models for in vivo, in vitro, and in silico applications
• Examples of above in Canadian work
  • in vitro model of adipocyte development to screen for obesogens
  • Expertise to OECD groups developing test methods

Creating Lists of EDCs - Europe

European Commission

Starting from a “working list” (564 chemicals)

• Category 1 - evidence of endocrine disrupting activity in at least one species using intact animals (66 chemicals);
• Category 2 - at least some in vitro evidence of biological activity related to endocrine disruption (52 chemicals);
• Category 3 - no evidence of endocrine disrupting activity or no data available.
Creating Lists of EDCs - United States

US Endocrine Disruptor Screening Program

• Tier 1 lists for further screening
  – 1\textsuperscript{st} list: 67 chemicals (pesticides, HPV inerts or industrial chemicals)
  – 2\textsuperscript{nd} list: 133 chemicals (pesticides, PFCs, drugs, industrial, plasticizers, personal care products, etc.)
  – Revised approach as of 2011- creation of “universe of chemicals” list. 10,000 chemicals $\rightarrow$ HTP testing

• Tier 2: detailed testing of prioritized substances

Overtaken by Toxicity Forecaster (ToxCast) program

• Advancing high throughput, in vitro testing
High Throughput Testing - Pros and Cons


**Key Benefits:**
- Speed
- Human relevance
- Multiple cell types and, potentially, multiple life stages
- Exposure relevance
- Assessing mixtures
- Crisis situations
- Green chemistry

**Key Challenges**
- *In vivo versus in vitro*
- Coverage of the full biological response landscape
- Accounting for chemical metabolism
- Ability to account for diversity in the population
- Accounting for multiple exposures and different timing of exposures
- Accounting for different patterns of exposure
- Determining a significant and adverse level of perturbation
- Insufficient accounting for epigenetic effects
- False negatives/False positives

Precaution and Prevention

Parallel Policy Issues

Measures to Address the Social Determinants of Health

• Poverty Reduction Plan (e.g., Bill C-233)
• National Housing Strategy (e.g., Bill C-400)
• Jobs Strategy
• Ensuring comprehensive health, pharma and dental coverage for all income groups

Land use planning and the built environment

Local food production

Measures to address childhood obesity

European Environment Agency: learn the lessons of early warnings and apply science, precaution and innovation
Report Co-Authors

Kathleen Cooper
Canadian Environmental Law Association

Franca Ursitti
Peel Region Public Health

Dr. Lynn Marshall
Environmental Health Institute of Canada

Dr. Loren Vanderlinden
Toronto Public Health and Dalla Lana School of Public Health, University of Toronto
When is Precaution Considered?

Public concern

Issue arises

Some studies indicate health concern

State of science uncertain

Protective programs, policies and regulations limited or absent

Issue response?

What degree, if any, of precaution should be applied?
TPH has applied PP via programs/practice, policies, legislation, advocacy and education

Some examples include:
- Pesticides Bylaw
- WNV Management program
- CCA-wood play structures
- Fish Consumption info for women of childbearing age
- Environmental Reporting & Disclosure Bylaw (ChemTRAC program)
- AQHI - Air Quality Health Index
- Advice on food exposures for child care setting

Choose fresh/frozen food when possible
Follow recommendations in Canada’s Food Guide

Avoid heating fluids in plastic baby bottles

Equity considerations of telling public to avoid canned foods for their children.

Phthalates

BPA

Food Additives

PFCs
Creating Healthy Environments for KIDS

Toxic substances are common in our environment, both indoors and out. Harmful chemicals that stick to dust, fumes from cleaning and renovation products, chemicals in plastics, mercury in fish—all of these can have serious impacts on the health of children. The good news is that parents can take some simple steps—beyond what they already do—to reduce risks in the home.

Children are at greater risk than adults because their natural defences are not fully developed. Babies and toddlers also explore the world with their hands and mouths, which exposes them more to harmful substances. This guide will help parents protect their kids by offering tips for “environmental childproofing.”

CPCHE’s Outreach Approach - Top 5 tips

Strong evidence:

- Greater exposure and greater vulnerability
- Top five areas – distilling complexity and giving people actionable steps that address important areas of exposure.
Precautionary Principle in Clinical Practice

Purpose:

• To protect the most vulnerable
• To advise individuals expressing concern about exposure(s) for themselves or family members
• To improve quality of life for the sick

Considerations:

• Strength of scientific evidence for association of exposures(s) with adverse outcome(s)
• The severity and frequency of adverse outcome(s)
• Weighing with the person the benefits and costs of action, or lack of action, or partial action, as informed professionals
• Feasibility of reducing exposure and availability of resources
Examples of Application of PP in Clinical Practice

Science
• Literature review of health effects of pesticides (x 2), urban sprawl, climate change, Air Quality Health Index, nuclear energy industry, and promotion of findings on website, and at local, provincial, national and international conferences

Vulnerability
• Literature review of exposures of most concern to the most vulnerable ages-a. the unborn, infants & children up to age 5, and b. children & adolescents from 6-17
• Addition of exposure questions to the Rourke Baby Record (1 wk to 5 yrs) & Greig Health Record (6-17 yrs), commonly used by FPs in office visits, in order to flag exposure concerns (in progress)
Examples of Application of PP in Clinical Practice

Informing Professionals

• Publication of articles in peer-reviewed journals on taking an exposure history, environmental contaminants series, climate change & lead
• Developing/delivering to Ontario FPs several *Environment Health Days*, & accredited 4-module teaching program *Environment-linked Illnesses: Prevention, Diagnosis & Management from Preconception to Old Age*
• Linking with CFPC and WONCA

Resources

• Development/distribution of exposure history forms & OCFP pamphlets on website and in conferences
• Participation in development and distribution via website, courses and conferences of CPCHE pamphlets, fact sheets and video for use by FPs in clinical practice, to serve persons with varying languages and literacy levels
Selected References


Acknowledgements and Thanks

Thanks to:

• CELA and CPCHE Colleagues
• Adele Iannantuono, Chito Diorico, Suzanne Leppinen, Health Canada
• Linda Birnbaum and Jerrold Heindel, US NIEHS
• Laura Vandenberg, Tufts University
• David Gee, European Environment Agency
• Ted Schettler, Science and Environmental Health Network
• Richard Denison, Environmental Defence Fund

Kathleen Cooper, Senior Researcher
kcooper@cela.ca