The Maternal-Infant Research on Environmental Chemicals (MIREC): A Canadian biomonitoring birth cohort research platform
The Exposome

- The cumulative measure of environmental influences and associated biological responses throughout the lifespan, including exposures from the environment, diet, behavior, and endogenous processes

The MIREC Study Cohort
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MIREC Study Objectives

• To obtain national-level data on maternal and newborn exposure to priority environmental chemicals

• To obtain contemporary levels of priority environmental chemicals, selected nutrients and relevant immunoprotective endpoints in mature human milk

• To investigate potential associations between early life exposure to environmental chemicals and adverse effects on health of pregnant women and their infants
MIREC Study Design

- A national-level pregnancy cohort study
- 2001 participants from 10 cities across Canada
- Interdisciplinary framework and team:
  - Epidemiology, toxicology, psychology, obstetrics, pediatrics, chemistry, nutrition, endocrinology, biostatistics, etc.
Description of the Cohort: Comparison with Canadian Birth Statistics (2009) or Canadian Health Measures Survey (CHMS) Women

- Parity – similar (44% had no previous live births)
- Preterm births somewhat higher (8.8 vs 7.7%)
- Birth weight tended to be higher (3420 vs 3391 g)
- Somewhat fewer multiple births (2.4 vs 3.3%)
- Slightly higher M:F infant ratios (52.5 vs 51.3% male)
- More educated (62 vs 42% in CHMS with university degree)
Description of the Cohort: Comparison with Canadian Birth Statistics or CHMS Women

- Maternal age – tended to be slightly older (32 vs 29 years)
- More likely to be married or living as married (95 vs 60%)
- Less likely to be current smoker (6 vs 21% in CHMS)
- Less likely to be obese (15 vs 21% in CHMS)
- Higher household income (38 vs 21% > $100,000 in CHMS)
- Women more likely to be born in Canada (81 vs 73%)
Selection of Chemicals for Biomonitoring

- Sub-set of chemicals from Canadian Health Measures Survey
- Potential for reproductive toxicity and/or endocrine modulation
- Feasibility – valid biomarker of exposure
- Metals, phenols, phthalates, brominated flame retardants, organophosphate pesticides, perfluoroalkyl acids, cotinine, PCBs and other POPs
Data Collection

Prenatal Visit 1 (6-13 wks)
- Maternal Blood
  - PFAAs, cotinine, metals, PCBs, PBDEs, OC Pesticides, selenium, glutathione peroxidase, Vit D, PTH, lipids, endothelins, oxidative stress markers, SNPs
- Maternal Urine
  - Biobank
  - phthalates, arsenic speciation, bisphenol-A, OP pesticides, specific gravity, telopeptide bone resorption, pyridinium, creatinine, oxidative stress markers

Prenatal Visit 2 (16-21 wks)
- Maternal Blood
  - Biobank
  - cotinine, metals, selenium, glutathione peroxidase, Vit D, PTH, endothelins, oxidative stress markers
- Maternal Urine
  - Biobank
  - pyridinium, creatinine, oxidative stress, telopeptide bone resorption

Prenatal Visit 3 (32-34 wks)
- Maternal Blood
  - cotinine, selenium, glutathione peroxidase, Vit D, PTH, endothelins, oxidative stress markers
- Maternal Urine
  - pyridinium, creatinine, oxidative stress, telopeptide bone resorption

Delivery
- Maternal Blood
  - cotinine, selenium, glutathione peroxidase, Vit D, PTH, endothelins, oxidative stress markers
- Maternal Urine
  - pyridinium, creatinine, oxidative stress, telopeptide bone resorption

Postpartum Day 1 or 2
- Meconium
  - metals, tobacco metabolites

Post delivery (2-10 wks)
- Breast Milk
  - total mercury (for mothers who will breast feed)
  - metals, ochratoxin A, PBDEs, OCs, PCBs, PFCs, bisphenol A, phthalates, perchlorate, Ca, Mg, P, K, Na, Al, Ba, Be, Cr, Cu, Fe, Li, Mo, Ti, U, vanadium, Zn, secretory IgA, lactoferrin, lysozyme, prolactin, cytokine IL-6, vitamin D, E, carotenoids, total folate, folic acid, fatty acids profile, antioxidant enzymes, MCPD esters

Biobank: 83/126 aliquots
Labs: 43/126 aliquots
Findings: Maternal exposure to environmental chemicals in 1st trimester

- **Bisphenol A (BPA):**
  - Almost 88% of the women had detectable urinary levels of BPA.
  - The GM urinary BPA levels: (1) decreased with increasing maternal age, (2) were higher in current smokers or women who quit during pregnancy compared to never smokers, and (3) tended to be higher in women who provided a fasting urine sample and who were born in Canada, and had lower incomes and education.

- **Phthalate metabolites (n = 11)**
  - MCHP, MMP, MiNP, MOP rarely detected
  - Highest measured levels were MEP (GM: 32.02 μg/L) and MnBP (GM: 11.59 μg/L).

- Exposure among this population of pregnant women was comparable to or even lower than that observed in a Canadian national population-based survey.
Median Maternal Urinary Concentrations of Total BPA
Median Maternal Urinary Concentrations of Phthalates

Median Urinary Concentration (µg/L)

- INMA SPAIN 1997-2002
- MT SINAI USA 1998-2001
- MIREC 2008-2011
- CHMS 2007-09 F 20-39
- CHMS 2009-11 F 20-39
- ODENSE DENMARK 2010-2012
- TIDES USA 2010-2012*

Phthalates:
- MBP
- MBzP
- MEHHP
- MEHP
- MEOHP
- MCPP
Findings: Maternal exposure to environmental chemicals in 1st trimester

- Free and Conjugated forms of BPA and Triclosan (TCS)
  - The glucuronides of BPA and TCS were the predominant forms measured (detected in 95% and 99% of samples, respectively),
  - The free forms were detected in 43% and 80% of samples, respectively.
  - Urinary TCS levels were significantly higher in women ≥ 25 years of age, never vs. current smokers, and women with high household income and high education.
  - These results suggest maternal characteristics predicting elevated urinary levels of BPA and TCS largely act in opposite directions.
# Metals in Maternal-Fetal Biospecimens

<table>
<thead>
<tr>
<th>Metal</th>
<th>Sample</th>
<th>N</th>
<th>LOD</th>
<th>%&lt;LOD</th>
<th>Median</th>
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</thead>
<tbody>
<tr>
<td>Cadmium (Cd)</td>
<td>1\textsuperscript{st} trimester</td>
<td>1938</td>
<td>0.0450</td>
<td>2.63</td>
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<td>Meconium \textsuperscript{a}</td>
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<td>0.004</td>
<td>97.36</td>
<td>ND</td>
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<td>Lead (Pb)</td>
<td>1\textsuperscript{st} trimester</td>
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<td>0</td>
<td>0.6009</td>
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<td>3\textsuperscript{rd} trimester</td>
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<td>0.1036</td>
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<td>Cord blood</td>
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<td>0.2072</td>
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<td>Manganese (Mn)</td>
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<td>1591</td>
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<td>Total Mercury (Hg)</td>
<td>1\textsuperscript{st} trimester</td>
<td>1938</td>
<td>0.1204</td>
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</tbody>
</table>

\textsuperscript{a} unit for levels of heavy metals in meconium is µg/g.

\textsuperscript{b} significantly higher than maternal median concentrations (p<0.0001)
Geometric Mean Maternal Blood Levels of Pb, Cd and Hg

- **Pb (µg/dL)**
- **Cd (µg/L)**
- **Hg (µg/L)**

**Data Sources**
- ALSPAC 1st T 1991-1992
- NHANES 2003-2010
- Pregnant
- Norway 2nd T 2007-2009
- MIREC 1st T 2008-2011
- MIREC 3rd T 2008-2011
- CHMS 2007-2009 F 20-39
- CHMS 2009-2011 F 20-39
- Baffin-Inuit late pregnancy
MIREC Follow-up Studies
## MIREC Research Platform Biospecimens in one glance

<table>
<thead>
<tr>
<th>1st Trimester</th>
<th>2nd Trimester</th>
<th>3rd Trimester</th>
<th>Delivery/early postpartum</th>
<th>2-10 weeks postpartum</th>
<th>6 months postpartum</th>
<th>15 months - 5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal urine</td>
<td>Maternal urine</td>
<td>Maternal urine</td>
<td>Cord blood</td>
<td>Meconium</td>
<td>Cord blood</td>
<td>Meconium</td>
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<tr>
<td>Maternal DNA</td>
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<td>Maternal DNA</td>
<td>Maternal DNA</td>
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<td>Maternal DNA</td>
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</tbody>
</table>

### MIREC: 2001 pregnant women in Vancouver, Edmonton, Winnipeg, Toronto, Hamilton, Sudbury, Kingston, Ottawa, Montreal and Halifax

- Infant blood spots
- Infant vaginal cells (birth)

### MIREC-ID: 525 MIREC babies

- Child blood
- Child urine

### MIREC-CD+: 803 MIREC kids
Analysis of Child Biospecimens (ages 2-5 years)

- **Urine**
  - Bisphenol A and triclosan
  - 22 phthalate metabolites
  - Pyrethroid pesticides

- **Blood**
  - Lead, Mercury, Cadmium,
  - Arsenic, Manganese, Silver,
  - Copper, Molybdenum,
  - Nickel, Selenium, Zinc
Selection of Publications to Date


MIREC Biobank
MIREC Biobank Access

- Important: *individual-level data* cannot leave Canada

- **3-step application process**
  1. Submit the 1-page preliminary application
     - MBMC assesses *feasibility, scientific value, contribution to MIREC*
     - If deemed suitable, MBMC provides preliminary cost estimate
  2. Submit the full application package
     - Project is a) refused or b) receives letter of provisional support confirming:
       - biospecimens and data are still available
       - the associated accessing costs
  3. Once funding is secured and ethics approvals obtained, MBMC conducts final review prior to releasing data and/or biospecimens
     - To ensure the biospecimens are still available, and
     - The proposed research questions are still scientifically relevant
MIREC Ancillary Studies using Biobank

- Diabetes, metabolic syndrome and obesity
- Fatty acid ethyl esters in meconium
- Time-dependent vulnerability to air pollution and multi-pollutant sector impacts on fetal growth
- Impact of prenatal exposure to multiple chemicals on newborn immune system development
- Exposure to free and conjugated forms of BPA and TCS during pregnancy
- Exposure to phthalates, phenols and pyrethroids in young children
Path Going Forward: MIREC- ENDO?

Primary objective:

- To determine whether prenatal or early life exposures to priority environmental chemicals are related to:
  - A modification of the onset of puberty
  - Adverse effects on child growth and metabolic function.
Summary

MIREC is a unique research platform by virtue of its:

- Large, geographically diverse and susceptible study population of mothers and infants/children
- Extensive assessment of prenatal risk factors, especially environmental chemicals
- Large biobank
- Multi-site design
- Established network of multi-disciplinary investigators
- Regulatory and policy development potential
- Measures of the early exposome
For more information:

- [http://www.mirec-canada.ca/](http://www.mirec-canada.ca/)
- Biobank access: mirec.project@recherche-ste-justine.qc.ca