Persistent Organic Pollutants: Metabolic Effects and Interventions to Reduce Body Burdens

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Aims

1. Overview of metabolic disturbances associated with POPs exposures

2. Overview of existing interventions aimed at enhancing the excretion of POPs

Discussion

Continuation of POPs biomonitoring

Beyond regulation: Public health messages to reduce body burdens of POPs
Persistent Organic Pollutants (POPs)

Organochlorine pesticides
PBDEs (flame retardants)
PCBs

Chemicals resistant to environmental degradation

Half-lives in human tissues
- PCB-52: 2.6y
- PCB-153: 14.4y
- PCB-170: 15.5y
POPs and Diabetes

POPs are endocrine disruptors associated with Type 2 diabetes, hypertension, cardiovascular disease, thyroid hormone alterations

Catalunya, Spain
N=866

Outcome: Diabetes

Outcome: Insulin Resistance

NHANES

Lee, 2010

Gasul, Env Sci & Tech 2012

Ref
PIVUS study: 70-year-olds in Sweden. 5-year follow-up, n=725

- Participants with the highest levels of POPs at 70y (upper 60th percentile) had 7-8x the risk of developing diabetes by 75y
- PCBs and organochlorine pesticides:
  - Positive associations with
    - Total cholesterol
    - LDL-c
  - Weak or no associations with HDL-c

Sources: Lee, Diabetes Care 2011
Penell, Environmental Research 2014
Nested Case-Control study within the CARDIA study

Participant ages: 18-30 years of age in 1985–1986 (year 0) - 50% black, 50% white
Locations: Minneapolis, Oakland, Chicago, Birmingham (USA)

90 CASES: diabetic by Year 20
   Type-2 diabetes: glucose lowering medication use or fasting glucose ≥126mg/dl at ≥2 exams

90 CONTROLS: non-diabetics at Year 20
   Fasting glucose <100mg/dl during all follow-up exams
   Frequency matched to controls on BMI at Y0

Follow-up years: 2, 5, 7, 10, 15, 20 and 25
Exposure and outcome measures

Exposure: POPs in serum obtained in 1987-88 (CARDIA Year 2)
- 55 POPs measured: 9 organochlorine pesticides, 35 PCBs, 10 PBDEs, and 1 PBB
  (Measured at the CDC Laboratories using GC/MS)
- Included in study: POPs with >75% detectability (32 POPs)
  8 organochlorine pesticides, 23 PCBs, and 1 PBB
- Concentrations of POPs in CARDIA (1987-88) were 3-5x higher than similar aged people in NHANES (2003-04)

Outcomes: Glucose and lipid metabolism markers (years 2, 7, 10, 15, 20, 25)
POPs and glucose regulation

23-year follow-up
32 POP Summary and Fasting Glucose (mg/dl)

Summary score: \( \Sigma \left( \frac{\log POP_{\text{individual}}}{\log POP \text{ std. deviation}_{\text{group}}} \right) \)

**No Diabetes**

\( \beta = 0.21, p=0.001 \)

\( \beta = 0.05, p=0.05 \)

**Diabetes**

\( \beta = -0.21, \beta^2 = 0.0005, p_{\text{quadratic}} = 0.04 \)

Age Interaction: \( p = 0.001 \)

Age Interaction: \( p = 0.004 \)

Same participants at different ages

Adjustments: race, sex, exam center, exam period and concurrent BMI

Suarez-Lopez JR, *Environmental Research* 2015
PCBs and hemoglobin A1c%

Suarez-Lopez JR, Environmental Research 2015
PCBs and β-cell function

Suarez-Lopez JR, Environmental Research 2015
POPs in young adulthood

Associated with alterations in glucose metabolism when participants reached the 5th decade of life

- Positive associations: fasting glucose, HbA1c% levels
- Inverse associations: β-cell function and insulin sensitivity (HOMA-2)
- No associations with BMI
POPs and blood lipids

23-year follow-up
**Figure.** Longitudinal associations of PCB summary scores (year 2) and blood lipids (years 2 - 25). Excludes participants using lipid-lowering medication at blood draw.

Adjusted for age, race, gender, concurrent BMI, exam center, exam year, diabetes and smoking status.

*Suarez-Lopez JR, Environmental Toxicology and Pharmacology, 2019*
**Figure.** Longitudinal associations of PCB summary scores (year 2) and blood lipids (years 2 - 25). Excludes participants using lipid-lowering medication at blood draw.

No interaction by age at blood draw or diabetes status

Adjusted for age, race, gender, concurrent BMI, exam center, exam year, diabetes and smoking status.

Suarez-Lopez JR, Environmental Toxicology and Pharmacology, 2019
• PCBs were positively associated with alterations in blood lipids up to 23 years later, using both wet-weight and lipid-standardized concentrations
  • *total cholesterol, triglycerides, LDLs, oxidized LDLs and cholesterol-HDL ratio*

• Associations stronger among participants with higher BMI

• Associations did not vary as participants aged

• Organochlorine pesticides (OCPs) probably not associated with lipid changes
  • *Associations were only observed using the wet-weight score*
Interventions to Reduce Body Burdens of POPs

Currently there is no standard regime to eliminate POPs from the body
Pilot studies: Bile acid resins and POPs

- Cholestyramine treatment for 48-72hrs
  - Increase fecal excretion of chlordecone (organochlorine pesticide) by 7x
  - Output of chlordecone was 10-20x greater in bile than in feces
    - Suggests that chlordecone is reabsorbed in intestine

Source: Cohn, NEJM 1978
Before and after 6m treatment with colestimide on serum Dioxins and PCBs

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Blood level of dioxins before and after the treatment in nine subjects</th>
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<td>Dioxins (pg-TEQ/g-fat)</td>
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<table>
<thead>
<tr>
<th>Table 2</th>
<th>Blood level of PCBs before and after the treatment in nine subjects</th>
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<td>mean</td>
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<tr>
<td>SD</td>
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</tbody>
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Mochida, Fukuoka Acta Med., 2007 (review)
Sakurai, Internal Medicine 2004 and 2006
Total PCB reduction between Standard Pringles vs Olestra Pringles for 1 year

- Location: Anniston, AL - PCB manufacturing for 40 years
- Mean age: 60y
- 62% female
- BMI: 33
- Anniston, AL: >50\textsuperscript{th} \%tile of PCBs of NHANES 2005-2007

- **Intervention**
  - 15g of Olestra: (≈12 pringles) x 1 year

Source: Jandacek, J Nutr Biochem 2014
Serum PCB reduction between Standard Pringles vs Olestra Pringles for 1 year

**Results:** Olestra (vs standard) resulted in:
- 2x the decrease in PCBs
  - 8% vs 4% decrease
- 3x the decrease in DDE
  - 16% vs 5% decrease

Source: Jandacek, J Nutr Biochem 2014
Breastfeeding can reduce body burdens of POPs (POPs go to the child!)

Higher DDT Contamination Levels in Breast Milk of Mothers Nursing Their First Child, Veracruz, Mexico (1994–1995)

Source: NECC
Nuts and Olestra for Persistent Organic Pollutant Reduction Trial

Research Team

- **Jose Ricardo Suarez, MD, PhD**, Principal Investigator
- **Cheryl Rock, PhD**
- **Andrea LaCroix, PhD**
- **Elizabeth Quintana, MS RDN**, Research Coordinator and Dietitian
- **Eunha Hoh, PhD**, POPs measurement
- **Bilge Pakis, EdD**, Project Manager

Students:

- Brianna Thrift
- Anita Dev
- Susan Saleh
- Jia Li Chen
- Dana Datuin

Funding: JPB Foundation: JPB Environmental Health Program, Harvard University
Objectives: Randomized controlled trial

- To assess if daily supplementation with A) nuts or B) olestra vs Placebo
  - Increases the fecal excretion of POPs
    - Measured at baseline and 4-5 days after treatment start
  - Decreases the levels of POPs in plasma
    - Measured at baseline and after 6 months

- Participants: 46 Healthy adults (50-70y) in San Diego, CA
Mechanism of action

Chlordecone levels in bile are 10-20x greater in bile than feces

Cohn, NEJM 1978
Specimens
- Plasma
- Serum
- Whole blood
- Stool

Measures
- Height/Weight
- HbA1c
- Serum Lipids (HDL, LDL, Triglycerides, Total Cholesterol)
- DEXA – Body Fat%

**POPs Measurement**
Hoh Laboratory at San Diego State U.
- 6 Organochlorine pesticides
- 4 PCB congeners
- 5 PBDEs
Conclusions/Discussion

- Experimental and epidemiological evidence indicate that POPs can alter glucose and lipid metabolism in adults
  - Strong associations with diabetes and pre-diabetes

- There is still rationale for biomonitoring for POPs
  - Present in food webs (fish, meat, dairy primarily)
  - Concentrations in people are declining (NHANES)
    - Higher concentrations in older populations

- Important to continue regulation of persistent compounds

- Expand research on identifying methods to enhance the excretion of persistent pollutants
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  Dr. David Jacobs Jr., University of Minnesota

  Dr. Duk-Hee Lee, Kyungpook National University
Acronyms

- BMI: Body mass index
- CARDIA: Coronary Artery Risk Development in Young Adults
- DEXA: Dual-energy X-ray absorptiometry
- HbA1c%: Hemoglobin A1c %
- HDL: High-density lipoprotein cholesterol
- HOMA-2: Homeostasis model assessment-2
- LDL: Low-density lipoprotein cholesterol
- NHANES: National Health and Nutrition Examination Survey
- OCPs: Organochlorine pesticides
- PBB: Polybrominated biphenyl
- PBDEs: Polybrominated diphenyl ethers
- PCBs: Polychlorinated biphenyls
- PIVUS: Prospective Investigation of the Vasculature in Uppsala Seniors
- POPs: Persistent organic pollutants
- WW: Wet weight