Exposures to Persistent Organic Pollutants and Metabolic Health Consequences

Qi Sun
Assistant Professor of Medicine
Brigham and Women’s Hospital and Harvard Medical School
Department of Nutrition, HSPH
Mariana Trench

Species and depth

<table>
<thead>
<tr>
<th>Species and depth</th>
<th>Dry weight</th>
<th>Lipid weight</th>
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<tbody>
<tr>
<td>H. gigas (7,841 m)</td>
<td>750</td>
<td>1,000</td>
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<tr>
<td>H. gigas (7,912 m)</td>
<td>250</td>
<td>1,250</td>
</tr>
<tr>
<td>H. gigas (8,028 m)</td>
<td>500</td>
<td>1,500</td>
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<tr>
<td>H. gigas (8,847 m)</td>
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<tr>
<td>H. gigas (8,942 m)</td>
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<tr>
<td>H. gigas (10,250 m)</td>
<td>750</td>
<td>2,000</td>
</tr>
</tbody>
</table>

Jamieson et al. nature ECOLOGY & EVOLUTION, (2017)
Persistent Organic Pollutants (POPs) are synthetic chemical substances that persist in the environment, bioaccumulate through the food web, and pose a risk of causing adverse effects to human health and the environment.

----United Nations Industrial Development Organization
The Dirty Dozen

- Pesticides
  - DDT
  - Aldrin
  - Chlordane
  - Endrin
  - Heptachlor
  - Mirex
  - Mirex
  - Toxaphene
The Dirty Dozen (cont)

- Industrial chemicals
- Unintended byproducts

- PCBs

- Dibenzodioxins

- HCB

- Dibenzofurans
Human exposure

PHOTO BY GEORGE KONIG/KEYSTONE FEATURES/GETTY IMAGES
Emission time trend

National emissions reported to the Convention on Long-range Transboundary Air Pollution (LRTAP Convention) provided by United Nations Economic Commission for Europe (Environment and Human Settlements Division, UNECE)
Human biomonitoring data

Nost et al. EHP 2013
Persistence + Continuous Background exposure = highly stable in human body

<table>
<thead>
<tr>
<th>Pollutants</th>
<th>Spearman r</th>
<th>ICC</th>
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<tbody>
<tr>
<td>PFOA</td>
<td>0.87</td>
<td>0.90</td>
</tr>
<tr>
<td>PFHxS</td>
<td>0.91</td>
<td>0.94</td>
</tr>
<tr>
<td>PFNA</td>
<td>0.91</td>
<td>0.87</td>
</tr>
<tr>
<td>PFDA</td>
<td>0.81</td>
<td>0.82</td>
</tr>
<tr>
<td>PFOS</td>
<td>0.86</td>
<td>0.91</td>
</tr>
<tr>
<td>HCB</td>
<td>0.65</td>
<td>0.60</td>
</tr>
<tr>
<td>DDE</td>
<td>0.91</td>
<td>0.85</td>
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<td>PCB118</td>
<td>0.75</td>
<td>0.81</td>
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<td>PCB138</td>
<td>0.72</td>
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<td>PCB153</td>
<td>0.73</td>
<td>0.71</td>
</tr>
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<td>PCB180</td>
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<td>0.58</td>
</tr>
<tr>
<td>PCB99</td>
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</table>
Persistent Organic Pollutants and Cardiometabolic Disorders in NHANES and NHSII

Geng Zong, PhD
Post-doctoral Research Fellow
Harvard T.H. Chan School of Public Health
Transportation and Metabolism of POPs

**Lifetime exposure determinants**

- Age, occupation, geographic region, smoking, etc

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**1 Release**

Dioxins and Furans

- Chlorinated POPs (lipophilic) and body fat distribution
- Chlorinated POPs/PFAS, lactation, and diabetes

Pesticides

- Preliminary results regarding diet
- Chlorinated POPs, lifetime exposure determinants, and T2D
- PCBs
- Chlorinated POPs, lifetime exposure determinants, and T2D

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**2 Transportation**

- NHANES
  - Chlorinated POPs, lifetime exposure determinants, and T2D

- NHSII
  - Chlorinated POPs/PFAS, lactation, and diabetes

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**3 Accumulation**

Foods, processing, storage

- Adipose tissue

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**4 Storage**

- Adipogenesis

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**5 Adipogenesis**

- Weight loss, breastfeeding

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**6 Excretion & EDR**

- Lifetime exposure determinants
- Chlorinated POPs, lifetime exposure determinants, and T2D

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**7 Elimination**

- PFAS, lifetime exposure determinants, and T2D
POPs and Body Fat Distribution

Fat in the trunk region is more detrimental

Upper body fat:

- Higher lipogenesis and lipolysis
- More sufficient exchange with blood flow

=> Strong effects of trunk fat on POP Pharmacokinetics

- More steroid receptors in visceral fat

=> Strong effects of POPs on trunk fat accumulation

Study population: **NHANES**

POP measurements:

- 20 chlorinated chemicals

Body fat measurement:

- Dual-energy X-ray absorptiometry (DXA)
### Stronger correlations for trunk fat

<table>
<thead>
<tr>
<th>Pollutants</th>
<th>Total FM%</th>
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<tbody>
<tr>
<td>Chlordane</td>
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<tr>
<td>Oxychlordane</td>
<td>-0.06</td>
</tr>
<tr>
<td>Trans-nonachlor Chlordane</td>
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<tr>
<td>p,p'-DDE</td>
<td>-0.04</td>
</tr>
<tr>
<td>β-HCH</td>
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<tr>
<td>PCDDs and PCDFs</td>
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</tr>
<tr>
<td>1,2,3,6,7,8-HxCDD</td>
<td>-0.01</td>
</tr>
<tr>
<td>1,2,3,4,6,7,8-HpCDD</td>
<td>0.08*</td>
</tr>
<tr>
<td>1,2,3,4,6,7,8,9-OCDD</td>
<td>0.05</td>
</tr>
<tr>
<td>1,2,3,4,6,7,8-HpCDF</td>
<td>-0.06</td>
</tr>
<tr>
<td>PCBs</td>
<td></td>
</tr>
<tr>
<td>PCBs with ≤5 Chlorines</td>
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<tr>
<td>PCB074</td>
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<td>PCB126</td>
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<tr>
<td>PCB138</td>
<td>-0.08*</td>
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<tr>
<td>PCB153</td>
<td>-0.17*</td>
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<tr>
<td>PCB169</td>
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<tr>
<td>PCBs with 7 Chlorines</td>
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<tr>
<td>PCB170</td>
<td>-0.24*</td>
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<td>PCB180</td>
<td>-0.28*</td>
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<td>PCB187</td>
<td>-0.19*</td>
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<td>PCBs with 8 Chlorines</td>
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<tr>
<td>PCB194</td>
<td>-0.27*</td>
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<tr>
<td>PCB196</td>
<td>-0.24*</td>
</tr>
<tr>
<td>PCB199</td>
<td>-0.29*</td>
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</tbody>
</table>

*Zong, et al. Obesity, 2015*
Study Population: **NHANES**

**POP included:**
- 20 chlorinated chemicals
- 4 polyfluoroalkyl substances

**Breastfeeding history:**
- *Number of children breastfed for one month or longer*

17/24 POPs were lower among women breastfed more kids
No significant changes in ORs of diabetes risk after further adjusting for POPs

Previous studies

- **N=6 prospective studies**
- **Small sample size**
- **Residual confounding**

Nurses’ Health Study II

Study design:

- **Nested case-control**

Sample size: **793 pairs**

Time of sample collection: **1995-2000**

Pollutants measured:

- **23 Chlorinated POPs**
- **6 PFASs**

Aims:

- **Diet**
- **Demographic and lifestyle determinant**
- **Body weight**
- **T2D risk**

Wu et al, EHP 2013
Summary

**Diet**
- Main sources

**Demographic/lifestyle factors**
- Early life exposure (eg, age)
- Elimination (eg, age, breastfeeding, smoking)
- Current exposure (eg, residence)

**Blood**

**Adipose tissue**

**Body POP Burden**

**T2D**

**Future directions**
- POP prediction model
- POP release after weight reduction and health
- Integrating multi-omic data to understand potential mechanism
Chemicals of Dietary Origin, Weight Change, and Diabetes Risk

Gang Liu, PhD
Research Fellow
Department of Nutrition
Harvard T.H. Chan School of Public Health

February 27, 2017
Background — PFASs

- Elimination half-lives: 3-8 years
- Exposure routes: diet, drinking water, food packaging...

Drinking water supplies for **6 million** U.S. residents exceed US EPA's lifetime health advisory (70 ng/L) for PFOA and PFOS

Background — PFASs in Animal Studies

Adverse Health Effects

- Carcinogenicity
- Immunotoxicity
- Reproduction toxicity
- Developmental toxicity
- Thyroid hormones
- Energy homeostasis

6 Years After “The Biggest Loser” Competition

60 kg

-60 kg

30 weeks

6 years

40 kg

Body Weight Change (kg)

p=0.0002

Metabolic Rate

E Fothergill et al, Obesity, 2016
Background — Weight Loss and Regain

Persistence of **Hormonal Adaptations** to Weight Loss

Adapted from P Sumithran et al, N Engl J Med, 2011
The POUNDS LOST trial

- 2-year randomized clinical dietary intervention trial
- 4 energy-reduced diets with different macronutrient compositions
- 811 overweight and obese participants (30-70 years)

Adapted from FM Sacks et al, N Engl J Med, 2009
Conclusion

- In this diet-induced weight-loss setting, higher baseline PFASs predict more weight regain, especially in women, possibly explained by the suppressed RMR levels associated with higher PFASs levels.

- A novel role of PFASs in weight regulation may help identify individuals more responsive to weight-loss diets.
Cooking Methods, Chemicals, and Diabetes Risk
Background – Chemicals from high-temperature cooking

PAHs: polycyclic aromatic hydrocarbons
HAAs: heterocyclic aromatic amines

- Carcinogenicity
- Oxidative stress
- Inflammation
- Insulin resistance
- Diabetes
- Other diseases

Knize et al., Food Chem Toxicol, 1994

Barbeque, Broil, Roast, Pan-fry, Boil/Stew
Study Design: A prospective cohort study with 26-year follow up

Study Population: NHS (59,033 women ≥2 servings/week red meat)

Exposure: broil, barbeque, roast, pan-fry, and boil/stew red meat
Results

Broiling, Barbequing & Roasting Red Meat → Weight Gain

*Multivariate adjustment including baseline weight and total red meat intake

G Liu et al, Under revision
Results

Pan-frying, Stewing/Boling Red Meat & Weight Gain

*Multivariate adjustment including baseline weight and total red meat intake

G Liu et al, Under revision
Results

Broiling, Barbequing & Roasting Red Meat ↑ T2D Risk*

* Multivariate adjustment including total intake of red meats

G Liu et al, Under revision
Conclusion

Our results suggest that, independent of total red meat consumption, open-flame and/or high-temperature cooking methods, especially broiling and barbequing, may further increase diabetes risk.
Our results suggest that, independent of meat consumption, open-flame and/or high-temperature cooking and high doneness level, especially for red meat, may further increase diabetes risk.
Conclusions

• POPs and PFASs are long-lasting pollutants and threats to human health.
• The inter-relationship between POPs, body adiposity, and diabetes risk is complicated.
• The role of environmental pollutants shall be considered in future precision medicine research.
• Cook a healthy meal in a healthy way.
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• Frank Hu
• Walter Willett

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