Endocrine Disruption in Plastics

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What are endocrine disrupting chemicals?

“An exogenous chemical, or mixture of chemicals, that interferes with any aspect of hormone action.”

-The Endocrine Society
What do endocrine disrupting chemicals affect?

- Reproduction
- Sexual maturation
- Metabolism
- Brain function
- Thyroid function
- Immune function
- Cardiovascular function
- Development and growth

Image from Schug et al. 2013
$340 billion

Estimated US disease burden related to endocrine disrupting chemical exposure
How are we exposed to endocrine disruptors?

- Oral: Food and drink packaging
- Inhalation: Household dust and air pollution
- Dermal: Personal care product use
What is unique about endocrine disruptors?

- Effects
- Exposure

Endocrine Mediated Effects

Exposure

Toxic Effects
What is unique about endocrine disruptors?

• Effects
• Exposure
• Timing
What endocrine disruptors are in plastics?

- Bisphenols - polymer
- Phthalates – softeners
- Triclosan & triclocarban – antimicrobials
- PBDEs – flame retardants
- Benzophenones – UV stabilizers
Bisphenol A

• Monomer for polycarbonate plastic
• Detected in >90% of population
• Estrogenic and other endocrine activities
• Epidemiological data linking it to:
  • Obesity
  • ADHD
  • Asthma
  • Reproductive defects
## BPA structural & functional analogues

<table>
<thead>
<tr>
<th>Structure</th>
<th>Chemical</th>
<th>Structure</th>
<th>Chemical</th>
<th>Chemical</th>
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</thead>
<tbody>
<tr>
<td><img src="image" alt="Bisphenol F (4,4)" /></td>
<td>Bisphenol F (4,4)</td>
<td><img src="image" alt="Bisphenol P" /></td>
<td>Bisphenol P</td>
<td>D-90</td>
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<tr>
<td><img src="image" alt="Bisphenol AF" /></td>
<td>Bisphenol AF</td>
<td><img src="image" alt="Bisphenol S" /></td>
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<td>DD-70</td>
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<tr>
<td><img src="image" alt="Bisphenol B" /></td>
<td>Bisphenol B</td>
<td>2,4-BPS</td>
<td></td>
<td>BPA bis(diphenyl phosphate)</td>
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<tr>
<td><img src="image" alt="Bisphenol C" /></td>
<td>Bisphenol C</td>
<td>D8</td>
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<td>Bisphenol PH</td>
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<tr>
<td><img src="image" alt="Bisphenol E" /></td>
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<td>BPS-MAE</td>
<td>Bisphenol F (2,2)</td>
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<tr>
<td><img src="image" alt="Bisphenol Z" /></td>
<td>Bisphenol Z</td>
<td>BPS-MPE</td>
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<td>MBHA</td>
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<td><img src="image" alt="TMBPA" /></td>
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<td>TGSA</td>
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<td>Pergafast 201</td>
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<tr>
<td><img src="image" alt="Bisphenol AP" /></td>
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<td>BTUM</td>
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<td>Urea Urethane Compound</td>
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<tr>
<td><img src="image" alt="Bisphenol A" /></td>
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</tbody>
</table>

Pelch et al. 2017
What evidence is available for BPA analogues?

Evidence Stream
- Human
- Animal
- In Vitro

Number of Studies

Peich et al. 2017
Are BPA analogues estrogenic too?

Uterine Weight After 3 Day Exposure in Weanling Rats

Chemicals
- 2,2'-Bisphenol F
- 4,4'-Bisphenol F
- Bisphenol AF
- Bisphenol B
- Bisphenol S
- Bisphenol Z

% change from control vs. Dose (mg/kg-day)
What other activities do BPA analogues display?

**ToxPI Legend**

- ER agonism
- ER antagonism
- AR agonism
- AR antagonism
- Stress
- PPARγ antagonism
- PPARδ antagonism
- DNA damage
- TR antagonism
- RSP agonism
- FXR antagonism
- RORγ antagonism
- GR antagonism
- CAR antagonism
- CAR agonism
- AhR agonism

Pelch et al. 2017
Phthalates

- Make plastics softer and more flexible
- Make fragrances last longer
- Detected in >97% of population
- Primarily anti-androgenic
- Epidemiological data linking to:
  - Hypospadias
  - Incomplete testicular descent
  - Abdominal obesity
  - Insulin resistance
Phthalates are male reproductive toxicants

<table>
<thead>
<tr>
<th>Phthalate</th>
<th>Anogenital Distance</th>
<th>Fetal Testosterone Concentration</th>
<th>Hypospadias Incidence</th>
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</thead>
<tbody>
<tr>
<td>DEHP</td>
<td>Presumed human hazard</td>
<td>Presumed human hazard</td>
<td>Suspected human hazard</td>
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<td>Presumed human hazard</td>
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<tr>
<td>DBP</td>
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<td>Presumed human hazard</td>
<td>Presumed human hazard</td>
</tr>
<tr>
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<td>Not classifiable</td>
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<td>DIBP</td>
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</tr>
<tr>
<td>DPP</td>
<td>-</td>
<td>Presumed human hazard</td>
<td>-</td>
</tr>
</tbody>
</table>

Systematic reviews for each chemical considered rodent and human data. Meta-analyses were conducted when possible. “-” indicates systematic review not performed.
Triclosan & Triclocarban

- Antimicrobials
- Detected in 35% to >85% of population
- Concerns for associations with:
  - Increased allergen sensitivity
  - Advanced puberty in girls
  - Thyroid hormone disruption

Brief Communication

The Florence Statement on Triclosan and Triclocarban

Tricolsan decreases thyroxine

"Triclosan is possibly toxic to reproductive and developmental health"

Johnson et al. 2016
What are the take home messages?

- Adverse effects occur at levels considered safe by the EPA
- Infants and children are particularly susceptible
- Linked to numerous diseases and disorders
- Regrettable substitutions must be avoided