A Pilot Study of Endocrine Disrupting Chemicals in Iowa Public Drinking Water

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Challenges to Providing Safe Drinking Water in the Midwest
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NITRATE

- MCL for nitrate-nitrogen (NO₃-N), 10 mg/L
  - Methemoglobinemia
- IARC Group 2A: N-nitroso compounds (NOCs) formed after nitrate/nitrite ingestion are probable human carcinogens

ATRAZINE

- MCL, 3 ppb
- Cardiovascular and reproductive effects
- IARC Group 3: not classifiable as to human carcinogenicity
Nitrate and cancer

- Two cohorts: drinking water source data, residence histories
  - Iowa Women’s Health Study (IWHS) -- public water
  - Agricultural Health Study -- public water, private well estimates (Wheeler et al. STOTEN, 2015)

- Nitrate associated with risk of several cancers that have suspected hormonal etiology
  - Ovary, thyroid, bladder

- Is it nitrate? Something else?
EDC in drinking water

- Many known EDC; few are regulated in drinking water
- Conventional water treatment may not remove all EDC
- Traditional single chemical assays cannot capture a wide range of known and emerging EDC in drinking water
- New methods that broadly assess EDC activity in a complex mixture are needed for epidemiologic studies
- Are people exposed to EDC in treated drinking water?
Objective: Characterize global endocrine disruption activity in samples from public water utilities in Iowa

No study has evaluated holistic exposure to EDC in drinking water and cancer risk

Secondary aim: Evaluate feasibility for developing an exposure model that relates EDC activity to known water characteristics
Mammalian cell-based assays to detect global EDC activity

- Bioassay developed by the NCI Center for Cancer Research
- Capture total endocrine disruption as a global index of EDC activity, rather than a single hormone
- Steroid receptors reside in the cytoplasm bound to GFP, translocate to the cell nucleus upon hormone binding
- Translocation quantified expressed as ratio of nuclear vs. cytoplasmic intensity normalized to a DMSO-treated control
Mammalian cell-based assays to detect global EDC activity

- Estrogen
- Aryl hydrocarbon
- Androgen
- Glucocorticoid
- Thyroid β

Stavreva et al., *Sci Rep*, 2012
Stavreva et al, *Toxicology*, 2016
GFP-tagged translocation of known concentrations of hormones

![Bar chart showing translocation of GFP-GR in response to different concentrations of hydrocortisone, dexamethasone, and corticosterone.](image)

- **GFP-GR**
- **Concentration (nM)**: 0, 1, 3, 5, 10, 15, 20
- **Translocation**
  - **Hydrocortisone**
  - **Dexamethasone**
  - **Corticosterone**

* indicate statistical significance.
Pilot study: selection of utilities for water sample collection

- N=473 in IWHS
- Identified key predictive characteristics for EDC from the literature
  - e.g., NO₃-N, TTHMs, CAFOs
- Selected utilities that covered both population and diversity across these characteristics
## Characteristics of 10 utilities in pilot study

<table>
<thead>
<tr>
<th>Utility</th>
<th>Water Source</th>
<th>Tertiary treatment*</th>
<th>Atrazine (ppb)</th>
<th>NO$_3$-N (mg/L)</th>
<th>TTHM* (ppb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Shallow alluvial groundwater</td>
<td>Activated carbon (AC)</td>
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<td>2.98</td>
<td>41.1</td>
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<td>2</td>
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<td>5</td>
<td>Deep groundwater</td>
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<td>-</td>
<td>53.1</td>
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<tr>
<td>6</td>
<td>Surface water</td>
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<td>0.93</td>
<td>4.65</td>
<td>58.4</td>
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<tr>
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<td>Surface water</td>
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<td>5.59</td>
<td>5.3</td>
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<tr>
<td>9</td>
<td>Deep groundwater</td>
<td>No AC</td>
<td>-</td>
<td>-</td>
<td>3.4</td>
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<tr>
<td>10</td>
<td>Deep groundwater</td>
<td>No AC</td>
<td>-</td>
<td>0</td>
<td>40.0</td>
</tr>
</tbody>
</table>
Water sample collection & processing
-- May & November 2016

- Collection on approximately the same day
- Extracted according to USGS protocol & concentrated
- 31 raw & 31 finished each season (N=62)
1) Detection of biologic activity in each sample compared to a negative control

2) Prevalence of activity for each global EDC class

3) Contrast EDC detections by:
   - Ground vs. surface supplies
   - Season
   - Raw vs. finished samples
   - Levels of nitrate, TTHMs
Preliminary results: summary

- At 200x, both raw and finished water samples screened positive for AhR and androgen activity

- Seasonal differences, greater detections in surface source waters and in raw water samples

- At 100x, screens weakly positive or null
Discussion: Epidemiology

- Scalability to large population
  - How to use to assess “exposure”
  - Historical extrapolation difficult

- Possible interference with estrogen assay

- The biological relevance of positive screens is unclear
Discussion: Iowa water quality

- Source water contamination unique
- Low/no estrogen, thyroid, glucocorticoid receptor activity
- Next steps
  - Higher potential prevalence (EPA UCMR database)
  - Private well samples
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**Participating utilities**

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- Iowa City
- Cedar Rapids
- Dubuque
- Ottumwa
- Waterloo
- Sioux City
- Mason City
- Council Bluffs
- Keokuk