CHE Fertility call: Effects of BPA on in vitro Fertilization

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Study of metals & assisted reproductive technologies (SMART)

- In an effort to respond to the knowledge gap concerning environmental contaminants & periconceptual events, we initiated a prospective cohort of couples undergoing treatment at the Center for Reproductive Health at the University of California at San Francisco:

- The aim of this pilot study is to generate specific testable hypotheses concerning associations between background exposures to environmental toxicants suspected to interfere with human reproduction & proximal IVF endpoints.
Referral to IVF Clinic

Baseline evaluation

Baseline evaluation

Follicle stimulation

Oocyte collection

Semen donation

Fert.

Insemin

Transfers

Impl.

hCG

Preg.

US

Bloom et al., 2010
Approach

- Collection of biologic specimens for assessment of environmental exposures at the time of oocyte retrieval from female patients & their male partners:
  - Laboratory analysis for serum unconjugated BPA concentrations using HPLC with Coularray Detection
- Biomarkers of internal dose correlated with endpoints at the:
  - Follicle level
  - Oocyte level
  - Embryo level
- Analysis conducted using the person unit of measurement & using the oocyte/embryo unit of measurement

Bloom et al., 2010
No association between BPA in women & BPA in men, comprising 28 couples

- Linear correlation for BPA in women & men:
  - $0.15$ (95% CI $-0.24$, $0.49$)
  - No substantial change when adjusted for age, race/ethnicity, or cigarette smoking

- Fasting vs. non-fasting specimens?

Unpublished observations
Increased BPA is associated with decreased peak estradiol ($E_2$) in 42 women

- Doubling of BPA:
  - Reduction in peak $E_2$
    - $-11\%$ (95% CI $-89\%$, 27%)
  - Reduction in peak $E_2$ per mature-sized follicle
    - $-9\%$ (95% CI $-15\%$, -2%)
- Adjusted for AFC, cigarette smoking, & race/ethnicity
- BPA interferes with $E_2$ synthesis?

Bloom et al., in press
Increase in female BPA associated with decreased oocyte maturity in ICSI cases

- Doubling of BPA:
  - A reduction in probability for a mature oocyte among Asian women
    - 9% (95% CI -17%, 0%)
  - No effect on probability for mature oocyte among not-Asian women
    - 3% (95% CI -4%, 10%)

- Adjusted for age & cigarette smoking

- BPA interfere with 1st meiotic division?

Fujimoto et al., 2011
Increase in female BPA associated with decreased oocyte fertilization

<table>
<thead>
<tr>
<th>Predictor variable</th>
<th>aRR</th>
<th>Low 95% CL</th>
<th>High 95% CL</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BPA-female (ng/mL serum)</td>
<td>0.45</td>
<td>0.31</td>
<td>0.66</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>BPA-male (ng/mL serum)</td>
<td>0.96</td>
<td>0.88</td>
<td>1.04</td>
<td>.308</td>
</tr>
<tr>
<td>Age-female (y)</td>
<td>0.98</td>
<td>0.95</td>
<td>1.02</td>
<td>.261</td>
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<tr>
<td>Age-male (y)</td>
<td>0.96</td>
<td>0.94</td>
<td>0.99</td>
<td>.008</td>
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<tr>
<td>Race-female (not Asian/Asian)</td>
<td>1.17</td>
<td>0.70</td>
<td>1.97</td>
<td>.547</td>
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<tr>
<td>Race-male (not Asian/Asian)</td>
<td>1.25</td>
<td>0.75</td>
<td>2.08</td>
<td>.386</td>
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<tr>
<td>Smoking-female (never/ever)</td>
<td>1.15</td>
<td>1.03</td>
<td>1.28</td>
<td>.014</td>
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<tr>
<td>Smoking-male (never/ever)</td>
<td>0.82</td>
<td>0.69</td>
<td>0.98</td>
<td>.028</td>
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<tr>
<td>BPA-female x race-female</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>BPA-female x age-female</td>
<td>1.02</td>
<td>1.01</td>
<td>1.03</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>BPA-female x BPA-male</td>
<td>1.06</td>
<td>1.02</td>
<td>1.10</td>
<td>.001</td>
</tr>
<tr>
<td>BPA-male x race-male</td>
<td>0.88</td>
<td>0.79</td>
<td>0.98</td>
<td>.022</td>
</tr>
</tbody>
</table>

Doubling of BPA:
- Reduced probability for normal fertilization for women
  - 55% (95% CI -69%, 34%)
- Affected by age & race/ethnicity
- Reduced probability for normal fertilization for Asian men only
  - 12% (95% CI -21%, -2%)

Fujimoto et al., 2011
Increased male BPA associated with decreased embryo cleavage rate

- Doubling BPA:
  - No effect for women
    - 4% (95% CI -19%, 33%)
  - Reduced odds for men
    - -71% (95% CI -40%, 2%)
- Adjusted for partner BPA, age & race/ethnicity
- BPA in male partner interfere with early embryo cleavage?

Bloom et al., in press
Summary of BPA findings from the SMART Study

- Male BPA exposure may influence embryo quality in couples undergoing IVF.
- A doubling of female BPA exposure is associated with a 50% reduction in normally fertilized oocytes with IVF.
- There may be a race/ethnicity-specific association between female BPA exposure & reduction in mature oocytes retrieved during IVF.
- Increasing female BPA exposure alters the E₂ response during gonadotropin stimulation during IVF.
- Non-dietary sources of BPA exposure may be important.