María do Carmo Borges de Souza, Brazil
G&O Barra
Reprodução Humana
Rio de Janeiro, Brazil

She declares no potential conflict of interest.
Role of Life habits and environment on ovarian stimulation strategies

Pollutants

2003 - Multidisciplinary Research Programme on Reproductive Health

Physicians, Chemists, Anthropologists, Epidemiologists, Biologists, Psychologists, Nurses, Toxicologists, Attorneys, Education specialists
Ho Hypothesis

The plausability of environmental risk causing a negative impact on the reproductive capacity

Background

Deleterious findings in cancer and areas of chronic or accidental exposure

- Infertility disease* long latency, multiple factors

Environmental exposure x geographic regions x specific populations
(are global tendencies possible?)

Pollutants - the chemical nature, the concentration and the persistence
(biomagnification, bioaccumulation)
Who is the infertile population in Rio de Janeiro?
Is it urban?
What kind of exposure can we look for?
What kind of pollutants?

- Subfertility / infertility
- Congenital malformation / miscarriage
- Abnormal genitals
- Ovulation disturbs
- Abnormal folliculogenesis
- Oocytes anomalies
- Ovarian, uterus and breast cancer
- Deleterious effects on spermatogenesis

Possible adverse effects

Endocrine disruptors
- Organochlorines pesticides (OCPs)
- Polychlorinated biphenyls (PCBs)

Heavy metals
- Lead (Pb) and Cadmium (Cd)
Step 1 Identifying infertile population in Rio de Janeiro - Brazil
The risk perception

Costa et al, JBRA assist(2009)
Step 2 Life habits, residence, water and food supplies, occupational history, medical and reproductive history, emotional profile
adapted from Greenlee et al, 2003
Bastos et al, XIX cong Bras GO,2005

Step 3 Serum levels of Organochlorine Compounds and Female Fertility in the Metropolitan Population of Rio Janeiro State, Brazil
Bastos et al, submitted

Simplified questionnaire
Infertile and spontaneously pregnant women (in less than 12 months exposure)

Exclusion criteria
Infertile age >39  POF, tubal ligature, drugs within 3 months, male factor
Pregnant age>39, less than 3 months pregnancy, drugs, breast feeding less than 1 year

Case 100- 87- 27- 15  Controls 50- 27-21

Blood samples  P4, Prl, TSH (infertile group)
OCPs  HCB, pp' DDT, pp' DDD, pp' DDE
PCBs  28 52 101 138 153 180
TTP infertile 52.4 months x pregnant 2.7 months (p<0.0001)

Infertile
Less school time
Fewer partners (2.1)* p=0.023
Canned food 1x week 86.7% p=0.016
Insects repellents on body 20% p=0.032

Fertile
more partners (3.2)
47.6%
none

N.S menarche, BMI, budget, food intake, no fish both groups*, smoke and alcohol, Miscarriage*
pp’DDE Etiological diagnosis

Diagnosis etiological

Negative correlation to P4 intermediate levels

P=0.0001

P=0.019*
Step 4  Heavy metals  Lead (Pb) and Cadmium (Cd)

- Access to blood, follicular fluid (FF) and seminal fluid (SF) of couples in ART provides an ideal opportunity to observe in vitro the gametes and embryo quality, trying to identify potential adverse effects

25 Infertile couples on ART x 25 proven spontaneous fertile in less than 12 months of exposure not breastfeeding for a year, child < 5 years-old

Simplified questionnaire, Blood  Pb, Cd, Urine  Cd, Fluids  Pb-FF  Pb-SF  Cd-FF  Cd-SF

\[
\begin{align*}
PbS & \geq 10 \mu g dL^{-1} \\
CdS & e CdU \geq 1 \mu g L^{-1}
\end{align*}
\]

No references to FF and SF

Development of methodology

First results

N.S age, BMI, amount of gonadotropins, duration of stimulation, endometrial thickness

<table>
<thead>
<tr>
<th></th>
<th>pregnant</th>
<th>not pregnant</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MII oocytes (n)</td>
<td>7.50 ± 4.11</td>
<td>4.53 ± 3.53</td>
<td>0.07</td>
</tr>
<tr>
<td>Emb transf (n)</td>
<td>2.3 ± 0.67</td>
<td>1.71 ± 0.1</td>
<td>0.03*</td>
</tr>
<tr>
<td>8c G1/G2 transf (n)</td>
<td>1.8 ± 0.91</td>
<td>1.0 ± 0.2</td>
<td>0.04*</td>
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Triplicate determinations in all samples, no occupational exposure, 92% of detection

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<tr>
<td>Cadmium (women)</td>
<td>0.7830 ± 0.2150</td>
<td>0.8118 ± 0.1894</td>
<td>0.52</td>
</tr>
<tr>
<td>Follicular fluid</td>
<td>0.9566 ± 0.1651</td>
<td>0.8960 ± 0.2012</td>
<td>0.17</td>
</tr>
<tr>
<td>Urine women)</td>
<td>0.3925 ± 0.1794</td>
<td>0.2110 ± 0.1091</td>
<td>0.0001*</td>
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<tbody>
<tr>
<td>Lead (women)</td>
<td>2.2400 ± 1.046</td>
<td>2.3151 ± 1.1730</td>
<td>0.77</td>
</tr>
<tr>
<td>Follicular fluid</td>
<td>1.2220 ± 0.3177</td>
<td>1.0566 ± 0.2406</td>
<td>0.01*</td>
</tr>
<tr>
<td>Seminal fluid</td>
<td>0.7455 ± 0.2230</td>
<td>0.9976 ± 0.3223</td>
<td>0.004*</td>
</tr>
<tr>
<td>Serum (men)</td>
<td>2.6583 ± 0.7336</td>
<td>2.886 ± 1.0690</td>
<td>0.31</td>
</tr>
</tbody>
</table>
Open questions, prevention and outcomes

Long-term effects on offspring of exposure of oocytes and embryos to chemical and physical agents


Pb and Cd simultaneous effects on granulosa cells: ovarian toxicity, < binding to gonadotropins in mice

Gupta & Nampoothir Reprod Toxicol 21:2, 2006

Lead trace concentrations in ovarian follicles compromises pregnancy and may represent chronic exposure.

Silberstein et al, Fert Steril 91:5, 1771-74, 2009

Conclusion, Plausability possible

More research data

Informing population

Minimizing exposure risks

Environmental and exposure security

Sensitizing Public Authorities (Political decisions)

Access to ART
Multidisciplinary Research Programme on Reproductive Health

Maria do Carmo Borges de Souza
Carlos André Henriques
Roberto Azevedo Antunes
Haydée Castro Neves Santos
Ana Cristina Allemand Mancebo
Patricia Cristina Fernandes Areas
Ana Lucinda Sobral Rito Costa

Ana Marcia Xavier Bastos
Licinio Esmeraldo da Silva

Marilena Correa
Marisa Decat de Moura
Paulo Franco Taitson

Nanci dos Santos Barbi
Ronir Luiz
Tatiana Henriques
Tonia Costa
Whitaker Jean Jacques Silva

Danielle Grynszpan
Leonardo Luchetti Caetano da Silva
Maria de Fátima Ramos Moreira
Thomas Krauss