Anogenital distance: Linking the fetal hormonal environment and reproductive function

Shanna H. Swan
CHE Call
September 20, 2012
Anogenital distance (AGD)

• In rodents, twice as long in males as in females

• Prenatal anti-androgen exposure shortens male AGD

• Size of AGD reflects intrauterine position
AGD: Reflects fetal androgen exposure

In early fetal life:
• Anti-androgens *shorten male AGD*

• Androgens *lengthens female AGD*

*Seen in many mammalian species*
*We hypothesize also true in humans*
Antiandrogen-treated rats with reduced AGD at birth have reduced AGD as adults.
Hotchkiss et al. 2004
DEHP and AGD (Moore, 2001)
Together these comprise the “phthalate syndrome”
Gray and Foster 2003, Foster 2005

- Reduced AGD
- Malformations of Epididymis, Vas deferens, Seminal Vesicles, Prostate
- Hypospadias
- Undescended Testicles
- Nipple retention
Measured in boys

Mid-pregnancy urine sample for phthalate metabolites

- Measure penile width
- Measure AGD
- Measure scrotal size

Measure testicular descent
<table>
<thead>
<tr>
<th>Monoester Metabolite</th>
<th>25th</th>
<th>50th</th>
<th>75th</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEHHP</td>
<td>6.0</td>
<td>11.4</td>
<td>20.1</td>
</tr>
</tbody>
</table>

Likelihood of shorter AGD:
- 4.6x
- 13x
DEHP exposure was associated with multiple endpoints in boys but not girls.

- Decreased testicular descent
- Reduced penile width
- Reduced AGD
- Reduced scrotal size
Prenatal exposure to many EDCs reduce male AGD in rodents

- Vinclozilin
- PCB 126
- DDT
- TCDD
- Genistein
- Azole fungicides

- Flutamide
- PBDE 99
- P,p DDE
- BPA
- DES
- Procymidone
Does short male AGD matter?

• Boys with genital defects (hypospadias and cryptorchidism) have shorter AGD (Hsieh et al, 2008)

• In rodents, short AGD predicts low sperm count and problems with fertility

• Is AGD related to semen parameters and fertility in humans?
Figure 3. Partial regression plot (mean ± SE) of sperm concentration modeled as a function of (A) $AGD_{AS}$ and (B) $AGD_{AP}$.

Mendiola et al., 2011, Environ Health Perspect.
AGD in Childless Men vs Fathers

Eisenberg et al 2011