Your environment: Your fertility

Strong Fertility Center Education Series
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Has fertility declined?

The answer depends on the definition of fertility
Demographers’ definition of fertility:
- Average number of children per woman
- By this measure *fertility has declined dramatically* worldwide since 1965
If you are not fertile are you infertile?

- Not necessarily
  - You may have chosen
    - Not to have a child
    - To delay childbearing

- So, what defines infertility?
Impaired fecundity

• A woman has "impaired fecundity" if:
  – It is difficult or physically impossible for her to conceive and bring a child to term or
  – Impossible for her husband to conceive a child or
  – She was continuously married or cohabiting and had not used contraception without conceiving for the prior 3 years.

By this measure, infertility is increasing
But, by another definition…

A woman has **12-month infertility** if she did not conceive (with or without treatment) **during the preceding 12 months**, and was:

- 15-44 and married
- Sexually active
- Not sterilized
- Not using any contraceptives

**By this measure, infertility is declining**
Two measures of infertility: Two answers

Time to Pregnancy (TTP)

TTP: number of months (cycles) of unprotected intercourse until conception

Strengths of TTP compared to other measures:

• More precisely defined
• More consistently used
• Most suitable for cross-study comparisons

(Joffe, 1996)
Planning or “wantedness” of pregnancy

- TTP Most useful for couples planning pregnancy
- TTP poorly defined for unplanned pregnancies
- But 49% of pregnancies in the US (not ending in miscarriage) in 1994 were unplanned (Henshaw 1998)

All these factors make TTP very variable
Distribution of Percent Subfertile
\((TTP\geq=12 \text{ months})\)

Range: 2.8% to 31.8%
Mean 12.8% (median 11.7%)
# Prospective studies of pregnancy planners

<table>
<thead>
<tr>
<th>Study Area</th>
<th>UNITED STATES</th>
<th>EUROPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample Size</td>
<td>611</td>
<td>430</td>
</tr>
<tr>
<td>Study Years</td>
<td>1963-68</td>
<td>1992-95</td>
</tr>
<tr>
<td>Study Years</td>
<td>1983-85</td>
<td></td>
</tr>
<tr>
<td>Study Area</td>
<td>United States</td>
<td>North Carolina</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rate of clinically-recognized pregnancy after:</th>
<th>UNITED STATES</th>
<th>EUROPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 cycles</td>
<td>.60</td>
<td>.40</td>
</tr>
<tr>
<td>6 cycles</td>
<td>.76</td>
<td>.70</td>
</tr>
<tr>
<td>9 cycles</td>
<td>.83</td>
<td>.78</td>
</tr>
</tbody>
</table>
Infertility

• Inability to become pregnant after 12 months of unprotected intercourse
  – Ovulation disorders 27%
  – Semen abnormality 25%
  – Tubal defect 22%
  – Unexplained 17%
  – Endometriosis 5%
  – Other 4%

Barbieri. In: Yen and Jaffe’s Reproductive Endocrinology 2004
Infertility

• 10 to 15% of couples trying meet definition
  – Over 7 million in the United States

• Frequency may increase with delayed childbearing
  – Mean age at 1st and 2nd pregnancy has increased by about 4 years over the past 3 decades.

• Few modifiable risk factors for infertility known
Possible environmental factors

- Environmental = non-genetic
- Includes:
  - Lifestyle factors (smoking, drinking, stress)
  - Diet, nutrition and exercise
  - Chemicals in our food, water air
    - At home, work and elsewhere
Nonchemical agents
BMI and ovulatory infertility

Fatty acid intake

-7
-14
-25
9
73
79
131

Percent Change in Risk of Ovulatory infertility

Protein intake


- All protein for carbs, 5% of energy: 22%
- Animal protein for carbs, 5% of energy: 19%
- Vegetable protein for carbs, 5% of energy: -43%
- Vegetable for animal protein, 5% of energy: -58%

Percent Change in Risk of Ovulatory infertility
## Frequency of multivitamin use

<table>
<thead>
<tr>
<th>Multivitamin Use</th>
<th>Cases / Non-cases</th>
<th>Age-Adjusted RR (95% CI)</th>
<th>Multivariate-Adjusted RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non Users</td>
<td>224 / 10,926</td>
<td>1.00 (referent)</td>
<td>1.00 (referent)</td>
</tr>
<tr>
<td>Users</td>
<td>214 / 15,607</td>
<td>0.67 (0.55, 0.80)</td>
<td>0.65 (0.53, 0.80)</td>
</tr>
<tr>
<td>Frequency of use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non Users</td>
<td>224 / 10,926</td>
<td>1.00 (referent)</td>
<td>1.00 (referent)</td>
</tr>
<tr>
<td>≤ 2 tablets/wk</td>
<td>32 / 1,808</td>
<td>0.84 (0.58, 1.23)</td>
<td>0.88 (0.60, 1.28)</td>
</tr>
<tr>
<td>3 – 5 tablets/ wk</td>
<td>52 / 3,796</td>
<td>0.66 (0.49, 0.90)</td>
<td>0.69 (0.51, 0.95)</td>
</tr>
<tr>
<td>≥ 6 tablets/ wk</td>
<td>127 / 9,783</td>
<td>0.63 (0.51, 0.79)</td>
<td>0.59 (0.46, 0.75)</td>
</tr>
<tr>
<td>P trend</td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Chavarro et al. Fertil Steril 2007*
Low-fat dairy foods

Relative Risk (95% CI)

Chavarro et al. Hum Reprod 2007
High-fat dairy foods

Chavarro et al. Hum Reprod 2007
Lowest risk exposure levels

1. Vigorous physical activity: > 30 min/day
2. Body mass index: 20 – 24.9
3. Animal protein: < 10% of energy
4. Vegetable protein: >7% of energy
5. Blood sugar: bottom 10% of distribution
6. Iron: > 40 mg/day
7. Low fat dairy: < 1 serving/week
8. High fat dairy: ≥ 1 serving/day
9. Multivitamins: ≥ 6 tablets/week

Chavarro et al.
### How much can be prevented

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>%</th>
<th>RR (95% CI)</th>
<th>PAR% (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical activity &gt; 30 min/day</td>
<td>14</td>
<td>0.78 (0.58 – 1.05)</td>
<td>21 (0 – 40)</td>
</tr>
<tr>
<td>BMI 20 – 24.9</td>
<td>54</td>
<td>0.64 (0.53 – 0.78)</td>
<td>21 (12 – 29)</td>
</tr>
<tr>
<td>Diet score Q5</td>
<td>19</td>
<td>0.48 (0.35 – 0.67)</td>
<td>46 (29 – 60)</td>
</tr>
<tr>
<td>4+ factors</td>
<td>14</td>
<td>0.40 (0.27 – 0.59)</td>
<td>55 (36 – 70)</td>
</tr>
<tr>
<td>5+ factors</td>
<td>4</td>
<td>0.31 (0.14 – 0.70)</td>
<td>66 (29 – 86)</td>
</tr>
</tbody>
</table>

Chavarro et al. Obstet Gynecol 2007
## BMI and reproductive potential

<table>
<thead>
<tr>
<th>BMI</th>
<th>Testis Size (mL)</th>
<th>Semen Volume (mL)</th>
<th>Sperm concentration (%)</th>
<th>Sperm count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>-2.0 *</td>
<td>-0.24 *</td>
<td>-28.1 *</td>
<td>-36.4 *</td>
</tr>
<tr>
<td>20–24.9</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>≥ 25</td>
<td>0.1</td>
<td>-0.003</td>
<td>-21.6 *</td>
<td>-23.9 *</td>
</tr>
</tbody>
</table>

*Jensen et al. Fertil Steril 2004*
Guess Your Sperm Count

Win
Chemicals in the Environment
Carlsen et. al. 1992

- Meta-analysis of 61 studies published 1938-1991 (included 14,947 men)
- Found a significant decrease in sperm density:
  - 1940: $113 \times 10^6$/mL
  - 1990: $66 \times 10^6$/mL
- Average decline: 1%/yr ($-0.93 \times 10^6$/mL)
Carlsen et al. 1992

Circles proportional to log sample size
Chemicals in the environment

US Chemical Production 1947–2007

Production Index (100=year 2002)

Year

Swan et al. 2000

- New literature search: 1934-1996
- Analysis included 101 studies
- North America: 44
- Europe: 34
- Other: 23

Average decline: 1%/yr (-0.94 x 10⁶/mL)
Swan et al. 2000
• **Overall** sperm density appears to have declined.
• Not explained by *obvious confounders*.
• **Rate of decline varies** geographically.
• **Mean density varies** geographically.
• Though significant, decline was not convincing.

*A new approach was needed*
The Study for Future Families (SFF)

Designed to examine geographic variation in semen quality
Semen Quality by Center

Swan et al 2003

* P-Value for MO vs. all other centers < .001
MO – 57%  MN – 19%
Nested Case-Control Study in Missouri

- **Cases:** Poor semen quality
  - Mean concentration: $32.4 \times 10^6$/mL

- **Controls:** Normal semen quality
  - Mean concentration: $72.2 \times 10^6$/mL
Pesticides Detected More Often in Cases Than Controls

- Diazinon
- Metolachlor
- Alachlor
- Malathion
- Atrazine
- 2,4-D

Percent above LOD:

- Cases
- Controls
Chemicals and diet might act together
Xenoestrogens and sperm quality

- Maternal beef consumption
- Dairy foods
- Processed beef consumption

Diet: Another possible source of geographic variation in semen quality

- Hypothesis: Mother’s beef consumption during pregnancy can affect her son’s semen quality
Background

• Diethylstilbestrol present in US beef from 1954-1979.
• Six hormones (anabolic steroids) used in production of US beef:
  – Natural steroids: estradiol, testosterone and progesterone
  – Synthetic hormones, zeranol (an estrogen), trenbolone acetate (a steroid with androgen action) and melengestrol acetate (a progestin)
• Since 1988 no hormone-treated beef sold in the EU
We examined this hypothesis in our study

- We looked at semen parameters in SFF men in relation to amount of beef their mothers ate while pregnant.
- Mothers’ beef consumption was also analyzed in relation to her son’s history of previous subfertility.
- Regression analyses controlled for son’s age, abstinence time, and alcohol consumption.
- Definition:

  *Eating >1 beef meal a day = “High beef consumer”*
Results (1)

- *Sperm concentration* was inversely related to mothers’ beef meals per week (P = 0.041).
- Sons of “high beef consumers” vs. others:
  - Sperm concentration reduced 24.3% (P = 0.014)
  - 17% had sperm concentration < 20 x 10^6/ml compared to 5.7% of others (P = 0.002)

(Swan et al. 2007)
Results (2)

- History of previous subfertility twice as frequent among sons of high beef consumers frequency ($p = 0.016$).
- Sperm concentration was not significantly related to:
  - the mother’s consumption of other meat
  - the man’s consumption of any meat
Sperm Production Unlikely to be Effected in Isolation

• If sperm decline is real, we would expect trends in related parameters, such as steroid hormones.
• If geographic variability in semen quality is real, we would expect variability in other endpoints reflecting testicular development.
Total Testosterone: Declined 1.2% /yr (1980-2004)

Travison 2006
Conclusion (1)

• Sperm concentration shows significant declines in some areas of the world.
• Semen quality shows significant geographic variation.
• Environmental factors (such as pesticides and anabolic steroids) are suspect but not proven causes.
Conclusions (2)

Fertility can be influenced by a mixture of exposures at different developmental stages:

– *In utero exposures* including environmental endocrine disruptors (e.g. pesticides, hormones in beef)
– *Early postnatal development* (e.g. BPA in infant formula)
– *Adult exposure* (e.g. pesticides, phthalates)
Useful websites and groups to “Google”

- Shaping Our Legacy: Reproductive Health and the Environment (http://www.prhe.ucsf.edu/prhe/pubs/shapingourlegacy.html)
- Our Stolen Future (http://www.environmentalhealthnews.org)
- Environmental Health News
- Environmental Working Group
- National Geographic Green Guide
- National Resources Defense Council
Final Slide

Thank you