Fertility Preservation After the Diagnosis of Cancer

Desire of Future Parenthood is Significant
- Over 70% express a desire for future offspring
- Over 70% are concerned about the possibility of becoming infertile
- Almost 1/3 report that infertility concerns influenced their treatment decisions

Partridge et al, J Clin Oncol. 2004

Preview
- Fertility preservation – benefits as a survivor
- Treatment effects – previously underestimated
- Options for preserving fertility - considerations
- Survivors - options

Counseling Benefits Survivors
- Questions:
  - Counseled About Risk by Oncology Team?
  - Visited Fertility Specialist?
  - Preserved Fertility?

Letourneau, 2012
Counseling Benefits Survivors

- Measures:
  - Regret
  - QOL
  - SWLS

Letourneau, 2012

Less Regret with Counseling

<table>
<thead>
<tr>
<th></th>
<th>Mean DRS Score</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Counseled About Risk by</td>
<td>10.8 (+/- 5.0)</td>
<td>12.6 (+/- 5.4)</td>
</tr>
<tr>
<td>Oncology Team?</td>
<td>(n=499)</td>
<td>(n=278)</td>
</tr>
<tr>
<td>Visited Fertility</td>
<td>8.5 (+/- 5.2)</td>
<td>11.6 (+/- 4.5)</td>
</tr>
<tr>
<td>Specialist?</td>
<td>(n=42)</td>
<td>(n=726)</td>
</tr>
<tr>
<td>Preserved Fertility?</td>
<td>6.5 (+/- 3.1)</td>
<td>11.6 (+/- 4.2)</td>
</tr>
<tr>
<td>(n=31)</td>
<td>(n=736)</td>
<td></td>
</tr>
</tbody>
</table>

Less Regret with Counseling

Letourneau, 2011 Cancer

CCR/UCSF Study on Psychosocial Outcomes

- Measures:
  - Regret score
  - QOL
  - SWLS

Letourneau, 2012
Risk of Infertility after Cancer Treatment

Age

Type of cancer

Ovarian reserve

Genetics

Reproductive Impairment - Chemotherapy only

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Acute Ovarian Failure</th>
<th>Infertile but Menstruating</th>
<th>Early Menopause</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukemia</td>
<td>3%</td>
<td>30%</td>
<td>9%</td>
</tr>
<tr>
<td>HD</td>
<td>8%</td>
<td>33%</td>
<td>9%</td>
</tr>
<tr>
<td>NHL</td>
<td>10%</td>
<td>26%</td>
<td>20%</td>
</tr>
<tr>
<td>Breast</td>
<td>13%</td>
<td>61%</td>
<td>28%</td>
</tr>
<tr>
<td>GI</td>
<td>7%</td>
<td>53%</td>
<td>13%</td>
</tr>
</tbody>
</table>

Letourneau et al., 2011 Cancer

Reproductive Impairment - Chemotherapy only

Letourneau et al., Cancer 2011
• 26 yo G0
  – Breast cancer
  – HR-
  – Stage 1 disease
  – Oncotype-26
  – ACT
  – Ovarian failure

26 yo G0
  – Breast cancer
  – HR-
  – Stage 1 disease
  – Oncotype-26
  – ACT
  – 2 children post therapy

Assessment of Ovarian reserve: AFC

Ovarian Reserve and Reproductive Impairment

Risks of infertility after Treatment?

Anticipate fertility window will be reduced in all patients receiving cytotoxic therapy

Letourneau et al., Nature Oncology 2010

Anderson, 2011
## Options for Fertility Preservation

### Options for Women

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Timeframe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryo &amp; Egg Freezing</td>
<td>Before &amp; After</td>
</tr>
<tr>
<td>Ovarian Tissue Freezing</td>
<td>Before, During &amp; After</td>
</tr>
<tr>
<td>In Vitro Maturation</td>
<td>Before &amp; After</td>
</tr>
<tr>
<td>Ovarian Transposition</td>
<td>Before</td>
</tr>
<tr>
<td>GnRH Analog/Antagonist Treatments</td>
<td>Before</td>
</tr>
<tr>
<td>Radical Trachelectomy (Cervical Cancer)</td>
<td>During</td>
</tr>
<tr>
<td>Natural Conception</td>
<td>After</td>
</tr>
<tr>
<td>In Vitro Fertilization</td>
<td>After</td>
</tr>
<tr>
<td>Donor eggs or embryos</td>
<td>After</td>
</tr>
<tr>
<td>Adoption (domestic, international, public, private)</td>
<td>After</td>
</tr>
<tr>
<td>Surrogacy</td>
<td>After</td>
</tr>
</tbody>
</table>

### Embryo/Egg Cryopreservation

- Established treatment
- Takes 2-6 weeks**
  - Ovarian stimulation, egg retrieval

**Delay treatment**

### Ovarian Physiology

- Antral follicle
- Ovulation
- 1 Cycle Days
- 14 Cycle Days
- 28 Cycle Days
Ovarian Physiology

Single wave of follicles

Antral follicle

Preovulatory follicles

Ovulation

atresia

Cycle Days 1 14 28

Antral follicle

Preovulatory follicles

Ovulation

atresia

Cycle Days 1 14 28

Ovarian Physiology

FSH

ovulation

estrogen

progesterone

Antral follicle

Preovulatory follicles

atresia

Cycle Days 1 14 28

Ovarian Stimulation

1. Conventional
**Ovarian Stimulation**

1. Conventional
2. Random stimulation

**Random Start = Conventional**

<table>
<thead>
<tr>
<th></th>
<th>Conventional Start (n=88; 903 cycles)</th>
<th>Late Follicular Phase Start (n=12; 12 cycles)</th>
<th>Luteal Phase Start (n=21; 21 cycles)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td>33.8 ± 5.3</td>
<td>33.3 ± 3.9</td>
<td>34.5 ± 5.1</td>
<td>NS</td>
</tr>
<tr>
<td>Antral follicle count (AFC)</td>
<td>13 (9-19)</td>
<td>11 (5.5-21)</td>
<td>13 (7-18.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Days of ovarian stimulation</td>
<td>8 (6-10)</td>
<td>11 (10-11.5)</td>
<td>11 (10-12)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total dose of gonadotropins (IU)</td>
<td>3405 ± 1127</td>
<td>3837 ± 1074</td>
<td>4208 ± 1462</td>
<td>0.014</td>
</tr>
<tr>
<td>Gonadotropin dose/day</td>
<td>361 ± 94</td>
<td>366 ± 88</td>
<td>369 ± 87</td>
<td>NS</td>
</tr>
<tr>
<td>Follicles ≥ 13 mm</td>
<td>12 (6-17)</td>
<td>11.5 (7.5-18.5)</td>
<td>13 (9-19.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Oocytes retrieved</td>
<td>15 (9-23)</td>
<td>14 (6.5-27)</td>
<td>16 (10-25)</td>
<td>NS</td>
</tr>
<tr>
<td>Mature oocytes (MII) retrieved</td>
<td>11 (6-16)</td>
<td>10.5 (5-16.5)</td>
<td>11 (6-16)</td>
<td>NS</td>
</tr>
<tr>
<td>MII oocyte / total oocytes ratio</td>
<td>0.71 (0.60-0.82)</td>
<td>0.74 (0.59-0.80)</td>
<td>0.69 (0.56-0.84)</td>
<td>NS</td>
</tr>
<tr>
<td>Oocyte / AFC ratio</td>
<td>1.14 (0.75-1.71)</td>
<td>1.27 (0.92-2.73)</td>
<td>1.20 (0.92-1.67)</td>
<td>NS</td>
</tr>
<tr>
<td>Mature oocyte / AFC ratio</td>
<td>1.83 (0.66-1.12)</td>
<td>1.84 (0.96-1.3)</td>
<td>1.83 (0.96-2.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Fert. rate after ICSI (2PN/MII)</td>
<td>0.83 (0.69-0.91)</td>
<td>0.78 (0.75-0.91)</td>
<td>0.96 (0.77-1.0)</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Calmaak, 2013*

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**Other considerations....**

- **Hormone receptors**
  - Modifications (i.e. aromatase inhibitors)
- **Ovarian reserve, desires**
  - Multiple cycles
  - Hormone treatment- delays in building a family
- **Genetic Risks (i.e BRCA)**
  - PGD for prevention of vertical transmission

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**The PROMISE trial**

**randomized trial: Triptorelin vs. Placebo**

The primary outcome: Immediate menopause

Results:
- Chemotherapy alone: 25.9%
- Chemotherapy + triptorelin-8.9%
- Difference: 17%
  - (95%CI 7.9 vs 26% P<0.001)

Not assessed:
- Fertility
- Early Menopause (after recovery)

*Del Mastro, 2011*
Ovarian Tissue freezing

- 20-30 live births
  - (All Orthotopic transplant)
- Challenges/Limitations
  - Risk for recurrences
  - Short life (3-5 yrs)
    - ischemia
  - General anesthesia

Post- Treatment Options

- Fertility preservation
- Infertility therapy
- Donor Eggs & Embryos
- Surrogacy
- Adoption

Conclusion

- Fertility preservation – **benefits** as a survivor
- Treatment effects – previously **underestimated**
- Options for preserving fertility- considerations
- Survivors- options

“**Parenting** is unlike anything else I have ever experienced. It is the most profoundly life-affirming thing I have ever done.

I am grateful that -- through all the uncertainty and fear surrounding my cancer diagnosis and treatment -- we held on to that dream of becoming parents and made it a reality.”