Comprehensive Fertility Care and Preservation for Male Cancer Survivors

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Disclosure Statement

• We do not have any conflict of interest, nor will we be discussing any off-label product use.

• This class has no commercial support or sponsorship, nor is it co-sponsored
Survivorship and Fertility

In a survey questioning the importance of fertility preservation in women of childbearing age recently diagnosed with cancer.

77.6% (66 of 85) reported that the possibility of preserving their fertility was instrumental to coping before and after treatment.
Testicular tissue serves a role in both hormone production and reproduction

Ovary

- **Reproduction**
  - Females born with lifetime oocytes
- **Hormones**
  - Progesterone
  - Estrogen (estradiol, estrone, and estriol)

Testes

- **Reproduction**
  - Ongoing production of sperm after puberty
- **Hormone**
  - Testosterone
Spermatogenesis

Breuss et al. Trends in Genetics (2021)
Risk Quantification and Gonadal Failure
Gonadotoxic Therapy

- **RADIATION**
- **ALKYLATING CHEMOTHERAPY**
  - Chlorambucil
  - Melphelan
  - Nitromin
  - Cyclophosphamide
- **CISPLATIN & CARBOPLATIN**
- **SURGERY**
Male Risk Stratification

<table>
<thead>
<tr>
<th></th>
<th>Minimally Increased Risk</th>
<th>Significantly Increased Risk</th>
<th>High level of Increased risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alkylators CED* gm/m2</td>
<td>CED &lt; 4</td>
<td></td>
<td>CED ≥ 4</td>
</tr>
<tr>
<td>Hematopoietic Stem Cell Transplant</td>
<td></td>
<td></td>
<td>Alkylator +/- Total body irradiation Myeloablative and Reduced intensity regimens</td>
</tr>
<tr>
<td>Heavy Metal mg/m2</td>
<td>Cisplatin Carboplatin</td>
<td>Cisplatin &gt; 500</td>
<td></td>
</tr>
<tr>
<td>Radiation Exposure Testicular</td>
<td>0.2-0.6Gy</td>
<td>0.7-3.9 Gy</td>
<td>≥ 4.0 Gy</td>
</tr>
<tr>
<td></td>
<td>Hypothalamus 26-29.99</td>
<td>&gt; 30-39.9 Gy</td>
<td>&gt; 40 Gy</td>
</tr>
<tr>
<td>Surgery</td>
<td>RPLND^</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Meacham et al. Journal AYA. 2020
### Cyclophosphamide Equivalent Dose Calculator

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg/m²)</th>
<th>Multiplier</th>
<th>Equivalent dose (mg/m²)</th>
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</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>1</td>
<td>0.244</td>
<td>0</td>
</tr>
<tr>
<td>Ifosfamide</td>
<td>0.857</td>
<td>0.244</td>
<td>0</td>
</tr>
<tr>
<td>Procarbazine</td>
<td>0.857</td>
<td>0.244</td>
<td>0</td>
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<tr>
<td>Chlorambucil</td>
<td>14.286</td>
<td>0.244</td>
<td>0</td>
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<tr>
<td>BCNU</td>
<td>15</td>
<td>0.244</td>
<td>0</td>
</tr>
<tr>
<td>CCNU</td>
<td>16</td>
<td>0.244</td>
<td>0</td>
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<tr>
<td>Melphalan</td>
<td>40</td>
<td>0.244</td>
<td>0</td>
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<tr>
<td>Thio-TEPA</td>
<td>50</td>
<td>0.244</td>
<td>0</td>
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<tr>
<td>Nitrogen Mustard</td>
<td>100</td>
<td>0.244</td>
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<tr>
<td>Busulfan</td>
<td>8.823</td>
<td>0.244</td>
<td>0</td>
</tr>
</tbody>
</table>

**Total CED** 0

Male Infertility Risk: Principles

- Long term outcomes: mostly binary (fertile vs not fertile)
- Risks do not vary greatly with age
- Temporary azoospermia is of variable length.
### Options for Males

#### Before Treatment Options

<table>
<thead>
<tr>
<th>Potential Use</th>
<th>Dis-advantages</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>IUI, IVF</td>
<td>Limited Sperm</td>
<td>Standard</td>
</tr>
<tr>
<td>IUI, IVF</td>
<td>Few sperm Surgery</td>
<td>Experimental</td>
</tr>
</tbody>
</table>

#### After Treatment Options

<table>
<thead>
<tr>
<th>Fresh Sperm</th>
<th>Frozen Sperm</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>✔</td>
<td>✔</td>
<td>Standard</td>
</tr>
<tr>
<td>✔</td>
<td>✔</td>
<td>Standard</td>
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<td>✔</td>
<td>Standard</td>
</tr>
</tbody>
</table>

- **Sperm Freezing (Semen/Testis)**
- **Prepub Testicular Tissue Freezing**
- **Diagnostic Semen Analysis**
- **Natural Conception**
- **IntraUterine Insemination**
- **In Vitro Fertilization**
- **Donor sperm**
- **Adoption**
Sperm cryopreservation

- Must be Tanner Stage 3
- Masturbated previously
- No lubricants or saliva
- Sperm must be collected prior to any chemotherapy

Raya et al. Invitra (2019)
Testicular Tissue Cryopreservation

Offered by experimental protocol only
No human live births to date.

Comprehensive Fertility Preservation at Seattle Children's Hospital

MALE

Prepubertal
  • Testicular Tissue Cryopreservation
    (Experimental - Protocol at SCH)

Pubertal
  • Sperm Cryopreservation
  • Testicular Sperm Extraction/Aspiration
    (TESE/TESA)
  • Testicular Tissue Cryopreservation
    (Experimental - Protocol at SCH)

Comprehensive evaluation and evaluation of all patients facilitated by Oncofertility team including oncology, general surgery, urology, and reproductive endocrinology.
Resources

Seattle Children’s Fertility Preservation Team
   FertilityPreservationRN@seattlechildrens.org
   Kristin.gard@seattlechildrens.org

UW Male Fertility Lab
   www.malefertilitylab.com

Seattle Reproductive Medicine
   www.seattlefertility.com