Fertility preservation options for children and young adults

Dr Sheila Lane October 14th 2016
Childhood and Young Adult Cancer Survival Data
NICE Quality standard QS 55
Children and young people (aged 0–24 years) with cancer should be assessed for potential future fertility problems and advised about their options for fertility preservation before treatment is started.

February 2014
Female Fertility
Primordial follicles in the outer layer of the ovary ("ovarian cortex")
Ovarian Physiology

![Graph showing follicle number and age](image)

**Life History of Ovarian Follicles**

- Initial Recruitment
- Cyclic Recruitment
- Maturation
- Atresia
- Secondary
- Primary
- Primordial
- Ovulation
- Exhaustion of Follicles

*E.R. Te Velde et al., 1998*
Effect of Chemotherapy and Radiotherapy
# Treatment Related Risk of Infertility

<table>
<thead>
<tr>
<th>Low risk (&lt;20%)</th>
<th>Medium/High risk</th>
<th>Very High risk (&gt;80%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALL</td>
<td>AML</td>
<td>T Body Irradiation</td>
</tr>
<tr>
<td>Wilms’ tumour</td>
<td>Osteosarcoma</td>
<td>Pelvic/abdominal RT</td>
</tr>
<tr>
<td>Brain tumour</td>
<td>Ewing’s sarcoma</td>
<td>Chemo pre BMT</td>
</tr>
<tr>
<td>Sx, RT &lt; 24Gy</td>
<td>STS: stage II/III</td>
<td>Metastatic Ewing's</td>
</tr>
<tr>
<td>Soft tissue sarcoma (STS) stage 1</td>
<td>Neuroblastoma</td>
<td>HL (Pelvic RT/ relapse)</td>
</tr>
<tr>
<td>Hodgkin (Low stage)</td>
<td>Non-Hodgkin Lymphoma</td>
<td>STS – very high stage</td>
</tr>
<tr>
<td></td>
<td>Breast CA</td>
<td></td>
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<tr>
<td></td>
<td>Brain tumour with HD chemotherapy</td>
<td></td>
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<tr>
<td></td>
<td>Hodgkin (High Stage)</td>
<td></td>
</tr>
</tbody>
</table>
Shielding/Ovarian Transposition

Medical Management

Cryopreservation

- Post Pubertal
  - Hormone Stimulation
    - + Sperm
      - Embryos
  - Oocyte
    - Ovarian Tissue
- Pre-Pubertal
  - Ovarian Tissue
Post Pubertal Egg/Embryo Storage

- Post Pubertal
- Minimum 2 weeks stimulation – delays Rx
- Daily injections/regular scanning/transvaginal collection
- Exposure to High dose gonadotropins
- Risk of Hyperstimulation
Egg and Embryo Freezing for use in IVF Treatment

- **Egg Freezing** 15-20% success rate
- Ideally need at least 20 eggs - 2 cycles

- **Embryo Freezing** 30+% success rate
- Need a partner or donor sperm
Ovarian Tissue Cryopreservation
Laparoscopic Procedure 1
Ovarian Tissue Cryopreservation
Processing of Ovarian Tissue
Current options for use of stored tissue

Autotransplantation

Figure 2 Diagram illustrating the different steps of the cryopreserved ovarian tissue transplantation procedure in human by two-step laparoscopy.
Ovarian Function Post Auto Transplantation
Ovarian Tissue Cryopreservation

Historical perspective


• NICE Fertility clinical guideline 156 (2013), Quality standard 9

• In UK, Regulated by Human Tissue Authority (HTA) and Human Fertility and Embryology Authority (HFEA)
Children Born from Transplantation of Frozen Ovarian Tissue
(Andersen 2014 and others)

- Donnez et al 2013 Belgium, Denmark, Spain – 60 women – 20%
- Jensen et al, 2015, Copenhagen, Denmark - 32 women – 31%
- Meirow et al 2016 Israel - 20 women – 32% success rate
Future Use of Cryopreserved Ovarian Tissue
Development of the Oxford Service

• 2007 Royal Colleges
• Oxford had Key Building Blocks
  – Professor Revel – Hadassah
  – Grade A Tissue Bank
  – Collaboration
• Protocol identical to Hadassah
• 2013 HTA/HFEA licence
• Clinical Service
• Website/Leaflets
• Research programme
Referral Criteria

- **Demographics**
  - 12 months – 35 years
  - Curative treatment
  - Cyropreservation will not delay treatment
  - Fit for surgery

- **Treatment Modality**
  - Abdo/pelvis DXT >15 Gy in prepubertal and 10 Gy in post pubertal
  - Cyclophosphamide >5 Gy/m²
  - Cisplatin >400 mg/m²
  - Ifosfamide >60 g/m²
  - Melphalan >140 mg/m²
  - Busulphan >8 mg/m²
  - Thiotepa 600 mg/m²
  - Procarbazine > 4 g/m²
Summary of Cases

• >136 referrals since Sep 2013
• 103 patients ovarian tissue cryopreserved
  ➢ 2013 – 4
  ➢ 2014 – 12
  ➢ 2015 – 30
  ➢ 2016 (forecast) – 70+
• 6 referrals did not fit criteria
• 9 patients/parents/consultants did not proceed
Referral Centres

<table>
<thead>
<tr>
<th>Centres</th>
<th>Children</th>
<th>Adult</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bristol</td>
<td>12</td>
<td>5</td>
</tr>
<tr>
<td>Oxford</td>
<td>21</td>
<td>13</td>
</tr>
<tr>
<td>Soton</td>
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<td>3</td>
</tr>
<tr>
<td>Bucks</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Wexham Park</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Swindon</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>St Georges</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>UCLH</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Marsden</td>
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<td>2</td>
</tr>
<tr>
<td>Birmingham</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Cardiff</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>St Marys</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Bath</td>
<td></td>
<td>2</td>
</tr>
</tbody>
</table>
Age profile - Ovarian Tissue donors (n = 95)

Age Range = 14 months - 39 yrs
Mean age = 15.75 yrs
age <18yrs  n= 61
100 Ovarian tissue patients 2013 - 2016

DIAGNOSIS

- Malignant (86%)
- Benign (14%)
Malignant diagnosis (n = 86,)

- Leukaemia (27%)
- Hodgkins lymphoma (17%)
- Non Hodgkins lymphoma (4%)
- Sarcoma (30%)
- Brain tumour (5%)
- Borderline ovarian tumour (5%)
- Colorectal (2%)
- Rhabdoid (1%)
- Nasopharyngeal (1%)
- Wilms (2%)
- Breast cancer (1%)
- Germ cell Tumour (2%)
- Neuroblastoma (1%)
Benign diagnosis (n = 14)

- ovarian dermoid cyst (8%)
- ovarian teratoma (8%)
- aplastic anaemia (8%)
- beta thalassemia (31%)
- sickle cell anaemia (31%)
- autosomal chronic disease (8%)
- BPEI syndrome (8%)
Male Infertility
Testicular Tissue patients

• Referrals to date 9

• Tissue stored
  o 2015 – 1 patient (Brain tumour pre high dose)
  o 2016 – 4 patients (AML/JMML/Diamond Blackfan)
In Conclusion

• Potential fertility problems and fertility preservation options should be discussed with ALL cancer patients before treatment starts wherever possible.

• About 1 in 10 patients will be at high risk of infertility following cancer treatment.

• There are options for all patients so seek advice.
Future Fertility Trust  www.futurefertilitytrustuk.org
• Jill Davies & Tissue Bank Team
• Stephen Kennedy
• Enda McVeigh
• Chandi Ratnatunga
• Christian Becker
• Muhammad Fatum
• Kokila Lakhoo
• Sanjiv Manek
• Clare Verrill
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• Suzannah Williams & research team
• Anne Goriely & research team