Family planning after a diagnosis of cancer ... What’s the next step?

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Director, Oncoreproduction Clinic, Seattle Cancer Care Alliance
Better Treatment = Better Survival
LIVING AFTER CANCER—NOT JUST SURVIVING
To be discussed..

• What determines the chance for a future pregnancy?
  • Basic fertility facts
  • Ovarian reserve
  • Cancer diagnosis

• Which treatments modify the chance for pregnancy?

• Which family planning options exist for women with a history of cancer?
  • Spontaneous pregnancy
  • Assisted Reproduction
  • Third Party Reproduction
  • Adoption

• What are the risks for pregnancy risks after a diagnosis of cancer?
COMMUNICATION BETWEEN THE BRAIN-OVARY AND UTERUS IS CRITICAL FOR FERTILITY

Hypothalamus

Gn.R.H.

F.S.H.

L.H.

estradiol
estradiol

ovarian egg development

progesterone

UW Medicine
1. The women amass their greatest number of eggs before birth (6-7 million)
2. At birth, the ovaries house about 1 million eggs
3. By the 1st menses about 300-400,000 eggs remain

The average woman will release between 300-400 eggs over a lifetime

Broekmans et al., Endocrine Reviews 2009
Not all eggs are good=AGE matters

<table>
<thead>
<tr>
<th>Maternal Age at Delivery</th>
<th>Risk of Miscarriage</th>
<th>Abnormal oocyte</th>
<th>Abnormal embryos</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>12</td>
<td>&lt;40</td>
<td>&lt;55</td>
</tr>
<tr>
<td>35</td>
<td>16</td>
<td>40</td>
<td>56.4</td>
</tr>
<tr>
<td>38</td>
<td>22</td>
<td>49</td>
<td>71.4</td>
</tr>
<tr>
<td>40</td>
<td>33-40</td>
<td>59</td>
<td>74.5</td>
</tr>
<tr>
<td>45</td>
<td>60</td>
<td>70</td>
<td>80.9</td>
</tr>
</tbody>
</table>

Modifiers of pregnancy success in women with a history of cancer therapy
RISK OF OVARIAN FAILURE POST-CHEMOTHERAPY

Ovarian reserve

Toxicity risk*

- Pelvic Rx.
- Alkylating agents
- Platinum agents
- Taxanes
- Plant alkaloids
- Anthracyclines
- Anti-metabolites

Assessment of an individual patient sterilization risk

Primordial follicle population

Age (years)

Graph showing the decline in primordial follicle population with age, with arrows indicating the impact of previous chemotherapy and toxicity risk associated with different types of chemotherapy agents.
Does my history of cancer and cancer therapy affect my chance for pregnancy?
• Stensheim H et al, Inter J of Cancer 2011.
Figure 2. Cumulative probability of first pregnancy after cancer diagnosis (red) in all women with cancer compared to population controls (blue), and in women with breast, cervical, brain/CNS cancers, Hodgkin lymphoma and leukaemia. Tables under each panel indicate the number of women with cancer and controls at the time of diagnosis, and at subsequent time points up to 30 years.
CUMULATIVE PROBABILITY OF 1ST PREGNANCY AFTER CANCER DIAGNOSIS

Figure 3 Cumulative probability of first pregnancy after cancer diagnosis (red) in women with diagnoses other than those shown in Fig. 2 compared to population controls (blue). Tables under each panel indicate the number of women with cancer and controls at the time of diagnosis, and at subsequent time points up to 30 years.
What is my best path forward when I want to start a family?

BIG questions???

• Is it OK to get pregnant after being treated for cancer?
• Can I get pregnant on my own and with my own eggs?
• Do I have enough eggs remaining in my ovary to get pregnant?
• Is my uterus OK to carry a pregnancy after pelvic radiation?
• Am I at increased risk for miscarriage?
• Can I breast feed after receiving whole body or chest radiation?
• What do I do if I do not have my own eggs?
Is it OK for me to be pregnant?
## POTENTIAL RISKS TO PREGNANCY AFTER CANCER THERAPY

<table>
<thead>
<tr>
<th>Anatomical Region Affected</th>
<th>Cause/THERAPEUTIC Exposure</th>
<th>Potential Risk</th>
<th>Screening/Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiac Function</td>
<td>Chemotherapy • Anthracyclines Radiation • Mediastinal or chest • Scatter from abdominal</td>
<td>Restrictive or dilated cardiomyopathy and congestive heart failure • 1&lt;sup&gt;st&lt;/sup&gt; and 3&lt;sup&gt;rd&lt;/sup&gt; trimester of pregnancy and Postpartum</td>
<td>• Echocardiogram • ECG • Preconception consultation with MFM • Monitoring by MFM • Gestation carrier</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Radiation Pelvic and Abdominal</td>
<td>• Dysfunction labor</td>
<td>• Preconception consultation with MFM • Monitoring by MFM • Gestation carrier</td>
</tr>
</tbody>
</table>
POTENTIAL RISKS TO PREGNANCY AFTER CANCER THERAPY

<table>
<thead>
<tr>
<th>Anatomical Region Affected</th>
<th>Cause/Therapeutic Exposure</th>
<th>Potential Risk</th>
<th>Screening/Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary</td>
<td>Chemotherapy: • Bleomycin • Busulphan • BCNU and CCNU Radiation: • Whole lung • Mediastinal • Craniospinal • Total body</td>
<td>Restrictive Lung Disease</td>
<td>Pulmonary Function: MFM consult Anesthesia consult</td>
</tr>
<tr>
<td>Uterus</td>
<td>Radiation: • Pelvic • Total body • Scatter from abdominal</td>
<td>Reduced uterine blood flow and muscular hypofunction: • Miscarriage • Fetal growth restriction • Placental dysfunction</td>
<td>Preconception consultation: Monitoring by MFM Gestation carrier</td>
</tr>
</tbody>
</table>
Can I get pregnant on my own and with my own eggs?

Do I have enough eggs in my ovaries to get pregnant?
COMMUNICATION BETWEEN THE HPG AXIS IS CRITICAL FOR FERTILITY.
PATIENTS WITH A HISTORY OF PELVIC SURGERY SHOULD HAVE A HYSTEROSALPINGOGRAM
OVARIAN RESERVE TESTING

Ovarian Retirement Fund
ANTRAL FOLLICLES
### AMH NOMOGRAM

AMH nomogram from birth to menopause in 804 healthy females from Lie Fong et al.

<table>
<thead>
<tr>
<th>Interpretation</th>
<th>AMH Serum Level (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High (PCOS)</td>
<td>&gt; 4.0</td>
</tr>
<tr>
<td>Normal</td>
<td>1.6-4.0</td>
</tr>
<tr>
<td>Low Normal</td>
<td>1.1-1.5</td>
</tr>
<tr>
<td>Low</td>
<td>0.5-1.0</td>
</tr>
<tr>
<td>Very low</td>
<td>&lt;0.5</td>
</tr>
</tbody>
</table>
LIMITATIONS OVARIAN RESERVE MARKERS......

• Do not define egg quality
• Do not define absolute probability for pregnancy
• Suppressed by oral contraceptives
• Nutritional status matters (obesity and anorexia)
FERTILITY PROFILE OF THE TYPICAL COUPLE

- 20-25% chance of pregnancy in each cycle
- 60% achieve pregnancy within 3 months
- 70-80% conceive achieve pregnancy within 6 months
- 93% achieve pregnancy within 1 year
PATHWAYS TO PREGNANCY IN WOMEN DIAGNOSED WITH CANCER

Desires Pregnancy

Autologous

Sex
- Intrauterine insemination
- In Vitro Fertilization

Donor

Donor eggs

Donor embryos

In Vitro Fertilization
- Uterine transplant
How do I use my frozen eggs or embryos to achieve pregnancy?
Assisted Reproductive Technology

In Vitro Fertilization

Embryo Transfer
Is my uterus OK for pregnancy after pelvic radiation?
## Fertility Risks and Pelvic and Total Body Radiation

<table>
<thead>
<tr>
<th>Ovarian irradiation</th>
<th>Uterine irradiation</th>
<th>Head irradiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 20.3 Gy birth</td>
<td>• 20-30 Gy</td>
<td>• 45 Gy adult</td>
</tr>
<tr>
<td>• 18.4 Gy 10 yo</td>
<td>➢ Miscarriage</td>
<td>• 24-35 Gy children</td>
</tr>
<tr>
<td>• 16.5 Gy 20 yo</td>
<td>➢ Fetal growth restriction</td>
<td>➢ increased risk for pituitary function</td>
</tr>
<tr>
<td>• 14.3 Gy 30 yo</td>
<td>➢ High blood pressure during pregnancy</td>
<td>➢ Diabetes</td>
</tr>
<tr>
<td></td>
<td>➢ Preterm delivery</td>
<td>➢ Hypogonadism</td>
</tr>
<tr>
<td></td>
<td>➢ Dysfunctional labor</td>
<td>➢ Lactation difficulty</td>
</tr>
<tr>
<td></td>
<td>➢ Placental dysfunction</td>
<td>➢ Adrenal dysfunction</td>
</tr>
<tr>
<td>• immediate gonadal failure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Premature menopause</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Am I at increased risk for miscarriage?
### Table III  Outcomes of singleton first pregnancies among nulliparous women with cancer onset at age $\leq$39 years, Scotland, 1981–2012 and matched controls.

<table>
<thead>
<tr>
<th>Singleton first pregnancies following cancer onset/matching date to 31 December 2014</th>
<th>Nulliparous women with cancer</th>
<th>Control women</th>
<th>Difference</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number</td>
<td>%/rate*</td>
<td>Number</td>
<td>%/rate*</td>
</tr>
<tr>
<td>Total</td>
<td>2071</td>
<td>100</td>
<td>11772</td>
<td>100</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>203</td>
<td>9.8</td>
<td>1095</td>
<td>9.3</td>
</tr>
<tr>
<td>Termination</td>
<td>231</td>
<td>11.2</td>
<td>1725</td>
<td>14.7</td>
</tr>
<tr>
<td>Still birth</td>
<td>8</td>
<td>0.4</td>
<td>53</td>
<td>0.5</td>
</tr>
<tr>
<td>Live birth</td>
<td>1629</td>
<td>78.7</td>
<td>8899</td>
<td>75.6</td>
</tr>
<tr>
<td>Infant death</td>
<td>12</td>
<td>7.4</td>
<td>43</td>
<td>4.8</td>
</tr>
</tbody>
</table>

*% of all first singleton pregnancies apart from for infant deaths which is per 1000 live births.
Can I breast feed after chest radiation?
• Most women can breast feed
• Breast irradiation many be associated with reduced milk production
• Women who receive chest irradiation may be less successful than their siblings with breast feeding
• Studies are needed to determine if breast milk quality is adversely affected after chest radiation

• Int J Radiat Oncol Biol Phys. 1989;17:244.
What do I do if I did not freeze eggs or embryos before my cancer treatment?
DONOR CYCLES (POST-TREATMENT)

A. Eggs
- Directed
- Anonymous

B. Embryos
- Directed
- Anonymous

I. Advantage
- You do not need your own eggs
- You can use partner’s sperm
- You can experience pregnancy and birth
- High success rates

II. Challenges
- Cost
- Personal beliefs
- Ethnic/racial egg availability
- Surrogate may be needed
Pathways to travel.....
1. Gestation carrier / surrogate
2. Adoption
3. Foster Parenting to Adoption

Challenges.....
1. $$$
2. Parental rights
3. A reproductive lawyer is needed
1. Improved cancer treatment has resulted in more younger people living after a diagnosis of cancer.
2. Many cancer treatments are toxic to reproductive organs and have long term consequences.
3. Many young cancer patient survivors may have the opportunity for pregnancy with their own eggs.
PATIENTS EXPECT TO LIVE AFTER A CANCER DIAGNOSIS
QUESTIONS?

Thank You For Your Attention!

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Clinic Appointments (206-598-4225)