Optimizing Fertility and Wellness After Cancer

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Optimism in Numbers

- 5-year survival rate for all childhood cancers: 78%
- >200,000 survivors of childhood cancers in the US
- 1 in 1000 adults is a survivor of childhood cancer
Our Responsibility Beyond Cancer

- Maintain a welcoming forum for comfortable discussion
- Be accessible
- Optimize reproductive health
- Build a family
The Importance of Fertility

- 75% discuss fertility with their physicians
  — Only 50% satisfied with addressed concerns

- Subgroups at highest risk of reproductive stress
  — Had 1 child prior, incomplete family
  — No children, but had strong desires for children pre-cancer treatment
Oncology Services:
- Oncologists
- NP, RN
- Social workers
- Psychiatrists

Reproductive Services:
- REI
- Urology
- Andrology

Research:
- Oncofertility
Diseases Requiring Gamete Cryopreservation

**Childhood**
- Lymphoma
- Leukemia
- Malignant bone tumors
- Soft-tissue sarcoma
- Brain
- Gynecologic cancers
  - Uterus
  - Cervix
  - Ovary
- Testicular cancer

**Adult**
- Similar to childhood cancers
- Breast cancer
- Gynecologic cancers
  - Uterus
  - Cervix
  - Ovary
- Testicular cancer
- Prostate cancer

**Non-Oncologic Diseases**
- Lupus
- Rheumatoid arthritis
Congenital Anomalies in Offspring of Cancer Survivors

- 2-3% incidence of congenital anomalies in general population
- Similar rates in offspring of cancer survivors
- No risk of de novo cancer in offspring
- No risk of genetic abnormalities in offspring

Healthy offspring can be expected

Li et al. JCI, 1979.
Green et al. JCO, 2009.
Pregnancy Outcomes in Childhood Cancer Survivors

- Compared to siblings, less likely to have livebirths
- No ↑ risk of miscarriage, except RT to the head and/or spine
- More likely to have terminations of pregnancy ✯

Healthy offspring can be expected

Green et al. JCO, 2009.
Pregnancy Outcomes in Childhood Cancer Survivors-2

- Pelvic RT ↑ risk of offspring with
  Preterm delivery <37 weeks gestation
  Low birth weight
  Small for gestational age
- Pelvic RT ↑ risk of postpartum hemorrhage
- No ↑ risk in other treated groups

Healthy offspring can be expected

Green et al. JCO, 2009.
Lie Fong et al. JCO, 2010.
Pregnancy After Breast Cancer

- A single retrospective cohort study
- 383 patients, younger than 35 at time of chemotherapy
- 13% achieved at least 1 pregnancy
  — Younger, earlier-stage disease, ER negative
- Not associated with increased recurrence
  — 23% vs. 54%
  — Wait 2 yrs before pregnancy

Human Eggs Are Finite and Do Not Regenerate
Gonadotoxicity of Chemotherapy

Irreversible Damage to Gonads

- Alkylating agents common in childhood and breast cancer chemotherapy regimens
  - Cyclophosphamide
  - Busulfan
  - Procarbazine

- Cross-link DNA and single-stranded DNA breaks

- “Good cells are destroyed along with bad cells.”
Gonadotoxicity of Radiotherapy

- **Ovaries**
  - Radiation dose threshold of 2000 cGy
  - 50% primordial pool of oocytes destroyed
  - Premature ovarian failure

- **Uterus**
  - Scarring of muscle, endometrium and vasculature
  - Promote by sex steroids in survivors after TBI
  - Uterine volume 17 vs. 42 cc (normal)
  - Thinner endometrium 5.9 vs 8.7 mm
  - Preterm delivery
  - Postpartum hemorrhage

Factors Affecting Ovarian Function

- **Age:** The older the patient at time of exposure to chemotherapy, the higher the risk of amenorrhea
  
  Hodgkins’ disease

<table>
<thead>
<tr>
<th>Age at Rx</th>
<th>Ov Dysfunction</th>
</tr>
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<tbody>
<tr>
<td>&lt;15</td>
<td>13%</td>
</tr>
<tr>
<td>&lt;30</td>
<td>2/3</td>
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<tr>
<td>&gt;30</td>
<td>All</td>
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- **Type of chemo:** alkylating agents & procarbazine

- **Radiation:** Exposure of ovaries to high-dose radiation

Green et al. JCO. 2009
Lie Fong et al. JCO. 2010
“So you’re having trouble conceiving. Have you tried sex?”
Ovarian Reserve Testing: What does it mean?

- Predicts response to **fertility treatments**
  
  How many eggs will I get when the ovaries are stimulated with hormones? How likely will I get pregnant?

- Does not predict natural fertility

- No data yet in cancer survivors

  Does decreased ovarian reserve in a 25 year-old female mean that her chance of getting pregnant with fertility treatments is poor, as would be expected of a 37 year-old?
Fertility Options Depend on Ovarian Function

- Assess ovarian function on cycle day 3
  - FSH, estradiol
  - Ultrasound for antral follicle count
  - AMH (*not cycle-dependent*)

- If diminished ovarian reserve, trial of fertility treatment or donor egg

- Younger age = greater success
Fertility Options: What’s available?

Get expert information!
Fertility Options: What’s available?

REI Consultation is Critical

- Determine reasonable time-frame for unassisted conception
- Optimize natural conception
  - Timed intercourse
  - Basal body temperature
  - Ovulation induction
  - Cervical mucus scores
  - PreSeed lubrication
Fertility Options: What’s available?
REI Consultation is Critical

- Choose best fertility treatment: low-tech vs. high-tech
- Ovulation induction with intrauterine inseminations
- In vitro fertilization (IVF)
- IVF with intracytoplasmic sperm injection (ICSI)
follicles

blastocysts

cleavage embryos

eggs

2:PN embryos
University Reproductive Care

- Affordability
- Fast-tracked, personalized care
- Financial counseling
- Partnering with Northwest Center for Reproductive Sciences (Kirkland)
- Focus on outreach and education

- Kat Lin, MD MSCE
- Brenda Houmard, MD PhD
- Paul Zarutskie, MD
Optimizing Reproductive Health

- Protective sexual practices / “safe sex”
  - Prevents tubal infertility

- Think ahead
  - Know your status to know your options

- Seek expert help
  - Reproductive Endocrinology & Infertility
Benefits of combination hormones

- **Contraception**
  - Prevents unplanned pregnancies

- **Replace necessary sex hormones**
  - Protects from endometrial cancer
  - Maintain bone health
  - Maintain vaginal & reproductive health
  - Improve sexual function
  - Normalize menstrual cycles