Oncology nurses should play an active role in teaching patients about how cancer and its treatment affect fertility. Join ONS Clinical Award winner Joanne Kelvin, RN, MSN, AOCN®, for an empowering presentation on what you need to know. You’ll learn about the biologic effects of treatment on reproductive health, options for preserving fertility before treatment and building a family afterward, and resources for educating patients, including when to refer someone to a reproductive specialist. You’ll come away with new oncology nursing strategies and an increased awareness of the updated American Society of Clinical Oncology guidelines about fertility preservation.

**Content Area:** Clinical Practice

**Content Level:** Intermediate

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**Full Disclosure:**
Nothing to Disclose

**Objectives:**
At the end of this session, participants will be able to:
1. Explain effects of cancer treatment on reproductive health.
2. Discuss options for patients to preserve fertility before treatment and build a family after treatment.
3. Describe strategies to communicate with patients about fertility and family building.

**Content Outline:**
I. Effects of treatment on reproductive health
   A. Males (impaired sperm production, impaired sperm transport, pituitary gland dysfunction)
   B. Females (depletion of ovarian follicles, uterine damage, pituitary gland dysfunction)
II. Fertility preservation before treatment
   A. Options for males (sperm banking, electroejaculation, testicular sperm extraction, and gonadal shielding)
   B. Options for females (embryo/oocyte cryopreservation, ovarian tissue cryopreservation, ovarian transposition, ovarian suppression, alternative treatment)
C. Options for children (ovarian/testicular tissue cryopreservation)
III. Family building after treatment
   A. Options for men to have a biologic child (natural conception, frozen sperm, testicular sperm extraction)
   B. Options for women to have a biologic child (natural conception, frozen embryos/oocytes, ovarian stimulation with in vitro fertilization)
   C. Alternative options (donor sperm/oocytes/embryos, surrogacy/gestational carrier, adoption)
IV. Strategies for discussing fertility with patients
   A. Introducing the topic
   B. Explaining risks and options
   C. Making referrals
   D. Recognizing associated social, cultural, religious, and ethical issues
   E. Supporting patients around decision-making

**Bibliography:**

**Guidelines**


**Males**


**Females**


**MALES**

Basics of Reproductive Biology  
Effects of Cancer Treatment  
Fertility Preservation before Treatment

**Fertility Effects of Treatment**

**Impaired sperm production**  
- Depletion of stem cells and developing sperm  
  Recovery – Oligospermia – Azoospermia

**Impaired sperm transport**  
- Injury to pelvic ducts/blood vessels/nerves  
  → erectile/ejaculatory dysfunction

**Pituitary gland dysfunction**  
- Disruption of hypothalamic-pituitary-gonadal axis

Howell & Shallet 2005; Meistrich 2009

**Fertility Preservation Options**

**Cryopreservation**  
- Post-Pubertal  
  - Sperm banking  
  - Electroejaculation  
  - Testicular sperm extraction

- Pre-Pubertal  
  - Testicular tissue

**Reduction of Toxicity**  

**Gonadal shielding**

**Sperm Cryopreservation (Banking)**

Semen collected, analyzed, placed in vials, frozen, and stored for possible future use

- **Sperm Bank Collection**  
  Manual stimulation  
  3 collections  
  Abstain 2-5 days

- **Electroejaculation (EEJ)**  
  If patient is unable to collect manually

- **Testicular Sperm Extraction (TESE)**  
  If patient is azoospermic

Katz et al 2013; Trost & Brannigan 2012

**Testicular Tissue Cryopreservation**

Investigational  
- Pre-pubertal boys  
Tissue biopsied, frozen, and stored for potential future use  
- Tissue reimplantation – no live births to date  
  Concern about re-implanting cancer cells  
- In vitro maturation – no live births to date  

*Available only at select centers*

Katz et al 2013; Trost & Brannigan 2012

**Gonadal Shielding**

During pelvic/inguinal field radiation  
- With IMRT to minimize testicular dose  
- Recommend sperm banking before treatment

Katz et al 2013; Trost & Brannigan 2012
FEMALES

Basics of Reproductive Biology
Effects of Cancer Treatment
Fertility Preservation before Treatment

Fertility Effects of Treatment

Depletion of ovarian follicle pool (oocytes)
- Premature ovarian failure → infertility, menopause
  Narrowed window of reproductive opportunity

Uterine damage
- Vascular changes, endometrial injury → inability to support embryo implantation
- Myometrial fibrosis → inability to accommodate a growing fetus

Pituitary gland dysfunction
- Disruption of hypothalamic-pituitary-gonadal axis

Ben-Aharon & Shalgi 2012; Gracia et al 2012; Meirow et al 2010; Morgan et al 2012; Wo & Viswanathan 2009

Fertility Preservation Options

Cryopreservation
- Post-Pubertal
  - Embryos
  - Oocytes
  - Ovarian tissue

Pre-Pubertal
  - Ovarian tissue

Reduction of Toxicity
- Ovarian transposition
- Ovarian suppression
- Alternative treatment

ASRM 2013; Rodriguez-Wallberg & Oktay 2012; Westphal & Massie 2012

Embryo Cryopreservation

Ovarian stimulation
→ Oocyte retrieval
→ In vitro fertilization
→ Cryopreservation

ASRM 2013; Rodriguez-Wallberg & Oktay 2012; Westphal & Massie 2012

Oocyte Cryopreservation

Ovarian stimulation
→ Oocyte retrieval
→ In vitro fertilization
→ Cryopreservation

ASRM 2013; Rodriguez-Wallberg & Oktay 2012; Westphal & Massie 2012
### Embryo/Oocyte Cryopreservation

**Medical Concerns**
- Delay in treatment
- ↑ Estrogen
- Specific medical risks

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### Ovarian Tissue Cryopreservation

**Investigational**
- Post-pubertal, can not delay treatment
- Pre-pubertal girls
- Ovary resected, cortex dissected, frozen, and stored for potential future use
- Tissue reimplantation – ~30 live births to date
- Concern about re-implanting cancer cells
- In vitro maturation – no live births to date

*Available at selected centers*

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### Ovarian Transposition

Prior to pelvic/inguinal field radiation
- With IMRT to minimize ovarian & uterine dose
- Also consider embryo/oocyte cryopreservation
- If IVF needed in the future patient will need transabdominal retrieval
- Does not protect the uterus

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### Ovarian Suppression

GnRH agonist (leuprolide)
- To prevent recruitment of follicles, potentially protecting them from effects of chemotherapy
- Initiated 2-4 weeks before starting chemotherapy, continued monthly throughout treatment
- Investigational - studied primarily in breast cancer and lymphoma with conflicting results

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### Alternative Treatment For Select Patients

- Early stage cervical cancer
  - Radical Trachelectomy
- Rectal cancer
  - No pelvic radiation
- Non-gonadotoxic chemotherapy regimen

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### BUILDING A FAMILY AFTER TREATMENT

Evaluation of Fertility
Family Building Options
Evaluation of Fertility

- It is impossible to predict with certainty who will be affected permanently.
- Timing of evaluation is a consideration:
  - Men can recover sperm production years later.
  - Females may initially be fertile but lose fertility at a young age.
- Schedule evaluation 12 months or longer after completion of treatment.

Evaluation of Male Fertility

<table>
<thead>
<tr>
<th>Semen analysis (WHO criteria, 2010)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Volume</td>
</tr>
<tr>
<td>Sperm count</td>
</tr>
<tr>
<td>Sperm concentration</td>
</tr>
<tr>
<td>Progressive motility</td>
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<tr>
<td>Vitality</td>
</tr>
</tbody>
</table>

Hormonal analysis:
- FSH, LH, Testosterone

Samplaski & Sabanegh 2013

Evaluation of Female Fertility

- Reproductive Endocrinologist
- Transvaginal ultrasound:
  - Ovarian antral follicle count
- Hormonal analysis:
  - Anti-Mullerian Hormone (AMH)
  - Follicle Stimulating Hormone (FSH)
  - Estradiol

Fertility Preservation After Treatment

An option to consider for:
- Adolescent and young adult females
- Did not undergo egg freezing before treatment
- Menstruating regularly, but are at risk for premature ovarian failure
- Not yet ready to start a family

Natural Conception

- Wait at least 1-2 years
- Time allows for:
  - Clearance of damaged gametes
  - Recovery from treatment
  - Pass time of greatest risk for recurrence/relapse


Pregnancy Considerations

- Ability to carry a pregnancy:
  - Hysterectomy
  - High dose pelvic RT
- Safety of carrying a pregnancy:
  - Late effects of treatment
  - Risk of recurrence
  - Patients with metastatic disease
- Consider referral to a Maternal Fetal Medicine Specialist or Cardiologist
Family Building Options for Men

Biologic Child
- Thawed Sperm
- TESE
- IUI or IVF +/- ICSI

Natural Conception
Embryo Transfer

Family Building Options for Women

Biologic Child
- Thawed Embryos
- Thawed Eggs
- Retrieval of Fresh Eggs
- IVF +/- ICSI

Natural Conception
Embryo Transfer

Surrogacy

For women who cannot carry a pregnancy

Traditional Surrogate
- Insemination of surrogate to create the embryo
  - Surrogate is birth mother AND biologic mother
  - Significant legal risks

Gestational Carrier
- IVF to create embryo transferred into carrier's uterus
  - Carrier is birth mother but NOT biologic mother
  - Favored approach

Alternative Family Building Options

Not Able to Have a Biologic Child
- Donor Sperm/Eggs/Embryos
- Adoption/Foster Parenting
- Child-Free Living

Donor Gametes and Embryos

- Finding gametes and embryos
  - Sperm – sperm banks
  - Eggs – fertility center or egg donor agency
  - Embryos – embryo donor agency
- Few government requirements for testing/screening
- No oversight to ensure compliance with standards
- Consider recommendations from fertility center or reproductive attorney

Adoption

- Domestic versus international
- Attorney versus agency (private or public)
- Issues for patients who have had cancer
  - Cancer-free for a period of time
  - May require medical letter
  - International adoptions generally more restrictive; regulations vary widely and change frequently
COMMUNICATING ABOUT FERTILITY

Parenthood After Cancer Treatment

Prepare
- Reflect on
  - Your patient population
  - How fertility is currently addressed
  - Your personal assumptions or biases

Prepare
- Identify reproductive specialists in your area
  - Males
    - Sperm banks: state licensure/FDA registration
    - Society for Male Reproduction and Urology
  - Females
    - American Society for Reproductive Medicine
    - Society for Assisted Reproductive Technology

Prepare
- Identify resources for patients
  - Informational brochures and/or web sites
    Cancer.net, SaveMyFertility, MyOncofertility
  - Financial
    LiveSTRONG/Fertility, HeartBeat

Prepare
- Collaborate with physician colleagues on how to integrate fertility discussion into practice
  - Clarify impact of frequently used treatments
  - Discuss safety of fertility preservation based on various patient situations
  - Establish the optimal timing for the discussion
  - Define roles and responsibilities

Assess
- Relationship status
- Prior children
- Desire for children in the future
- Awareness of treatment-related fertility risks
- Awareness of fertility preservation options
### Consider
- Factors related to planned treatment
  - Risk of impaired fertility
  - Consider future treatment as well
- Factors related to disease
  - Safety of delaying treatment
  - Safety of undergoing fertility preservation
- Factors that may influence decision-making

### Teach
- Discuss early enough that patient has time to act on the information
- Integrate into teaching about other treatment side effects
- Be direct, honest, and matter of fact
- Keep intent in mind
- Be respectful and nonjudgmental
- Consider the unique needs of adolescents

### Teach
- Explain risks
- Explain fertility preservation options

**Keep it simple**
ASCO guidelines - key discussion points listed in section on communication

### Refer
- For patients who are interested in learning more or who already know they want to pursue fertility preservation
- Facilitate scheduling the appointment
- Consider coordination needs of complex patients
- Clarify timing to plan start of treatment

### Summary
- It is our responsibility to ensure patients are informed of their treatment-related fertility risks and of their options to preserve fertility before cancer treatment. Interested patients should be referred to appropriate reproductive specialists.
- A systematic approach to communicating about fertility can help nurses better address these issues.