The purview of pediatrics includes the growth, development, and health of the child and therefore begins in the period before birth when conception is apparent. It continues through childhood and adolescence when the growth and developmental processes are generally completed. The responsibility of pediatrics therefore may begin during pregnancy and usually terminates by 21 years of age.

Describe and review the special needs of Adolescents and Young Adults as it pertains to Oncology.

Discuss specific needs related to fertility in the oncology population.

Review data obtained with regard to current pediatric oncology practices.

Discuss a proposal for early intervention to preserve fertility in the AYA population.

Adolescents (ages 10 – 19) and young adults (ages 20 – 24) together compose about 21% of the population of the United States.

70,000 new cases of AYA cancers annually
- 32.1 cancer diagnoses per 100,000 children ages 0 to 14 years
- 138.6 cancer diagnoses per 100,000 adolescents and young adults ages 15 to 39 years
- 2,053.8 cancer diagnoses per 100,000 people aged 40 years or older
Still the leading cause of death

Cancer is the #1 cause of disease-related death for children

![Graph showing cancer as the leading cause of death for children](image)

Survival in Children

![Graph showing survival rates for children with cancer](image)

The AYA “Hole”

![Graph showing improvement in 5-Year Relative Survival for AYA patients](image)

Is it Biology or Culture?

![Graph comparing survival rates for acute lymphoblastic leukemia](image)

Global Experience

<table>
<thead>
<tr>
<th>Country</th>
<th>Region</th>
<th>Age Range</th>
<th>Patient group</th>
<th>Adult group</th>
<th>Complete N</th>
<th>Complete N*</th>
<th>Event-free survival</th>
<th>Event-free survival*</th>
</tr>
</thead>
<tbody>
<tr>
<td>France</td>
<td>Europe</td>
<td>1-5 years</td>
<td>FRLLA22</td>
<td>LALA-9902</td>
<td>624</td>
<td>352</td>
<td>57.0%</td>
<td>52.0%</td>
</tr>
<tr>
<td>UK</td>
<td>Europe</td>
<td>1-5 years</td>
<td>ALL9413/15</td>
<td>MRC-UK1577</td>
<td>262</td>
<td>146</td>
<td>62.4%</td>
<td>58.2%</td>
</tr>
<tr>
<td>Netherlands</td>
<td>Europe</td>
<td>1-5 years</td>
<td>ALL9413/15</td>
<td>MRC-UK1577</td>
<td>262</td>
<td>146</td>
<td>62.4%</td>
<td>58.2%</td>
</tr>
<tr>
<td>Italy</td>
<td>Europe</td>
<td>1-5 years</td>
<td>ALL9413/15</td>
<td>MRC-UK1577</td>
<td>262</td>
<td>146</td>
<td>62.4%</td>
<td>58.2%</td>
</tr>
<tr>
<td>North America</td>
<td>USA</td>
<td>1-5 years</td>
<td>ALL9413/15</td>
<td>MRC-UK1577</td>
<td>262</td>
<td>146</td>
<td>62.4%</td>
<td>58.2%</td>
</tr>
<tr>
<td>Australia</td>
<td>Oceania</td>
<td>1-5 years</td>
<td>ALL9413/15</td>
<td>MRC-UK1577</td>
<td>262</td>
<td>146</td>
<td>62.4%</td>
<td>58.2%</td>
</tr>
<tr>
<td>Brazil</td>
<td>South America</td>
<td>1-5 years</td>
<td>ALL9413/15</td>
<td>MRC-UK1577</td>
<td>262</td>
<td>146</td>
<td>62.4%</td>
<td>58.2%</td>
</tr>
</tbody>
</table>

Global Experience:

- **France:** LALA-9902
- **UK:** ALL9413/15
- **Netherlands:** ALL9413/15
- **Italy:** ALL9413/15
- **North America:** USA
- **Australia:** Oceania
- **Brazil:** South America

Age Specific Care

- **Medical:** Need for age-specific care
  - 1. Provision of medical care tailored to the age group
  - 2. Provision of psychological support
  - 3. Psychosocial support

- **Psychological:** Need for age-specific care
  - 1. Psychological support tailored to the age group
  - 2. Psychosocial support

- **Social:** Need for age-specific care
  - 1. Social support tailored to the age group
  - 2. Financial support

- **System:** Need for age-specific care
  - 1. Systematic approach tailored to the age group
  - 2. Holistic care

![Diagram showing components of age-specific care](image)
Cancer Survival

Late Effects of Therapy

Morbidity of Late Effects

Multiple Management Concerns

Affected Ovarian Reserve

*Image source for Cancer Survival and Multiple Management Concerns: Nature Reviews | Cancer*
Fertility preservation for adults and children with cancer is an important part of patient care.

In 2009, a physician survey demonstrated that less than half of US physicians routinely refer patients of childbearing age to a reproductive endocrinologist.

Data suggests that oncologists desire more information regarding fertility preservation, yet 23% had never consulted any fertility preservation guidelines.

The American Society of Clinical Oncology (ASCO) has recently released new clinical practice guidelines for fertility preservation.

The new guidelines include embryo and oocyte cryopreservation as established fertility preservation methods.

Ovarian suppression, with a gonadotropin-releasing hormone analog (GnRH-a), is considered investigational for preservation of fertility.

"As part of education and informed consent before cancer therapy, health care providers… should address the possibility of infertility, with patients treated during their reproductive years… and be prepared to discuss fertility preservation options and/or to refer all potential patients to appropriate reproductive specialists."

A cross-sectional study was performed from May 26, 2014 to August 26, 2014.

Online survey was created and emailed once a month to members of the Children’s Oncology Group (COG).

**Primary outcome**: frequency of physician discussions with patients regarding fertility preservation.

**Secondary outcome**: the prescribing and counseling patterns in comparison to the new ASCO guidelines.
Pediatric Fertility Preservation Counseling is being Performed

Conclusions

The majority of pediatric hematology-oncology providers mention fertility preservation to their patients prior to treatment.

Education of providers should be promoted as only a third of the providers have read the new ASCO guidelines.

Despite still being considered experimental, 37% of providers are prescribing a gonadotropin-releasing hormone analog.

The majority of current practice patterns include providing ASCO endorsed options for fertility preservation.

References

**Fertility Preservation in the Cancer Patient**

Jennifer Finudison, MD, FACOG
Fellow, Reproductive Endocrinology and Infertility
Clinical Instructor, Obstetrics and Gynecology
UCSF/SA

**Female Options**
- **Established**
  - Embryo Cryopreservation
  - Oocyte Cryopreservation
  - Ovarian Transposition for pelvic radiation
- **Experimental**
  - Ovarian Suppression
  - Ovarian tissue cryopreservation

**In the Media... Baby after Cancer**
- Bill and Giuliana Rancic (E! news reporter and breast cancer survivor)
- Giuliana diagnosed breast cancer—underwent emergency IVF with

  **Provided by Oncofertility Consortium Blog**

**In Vitro Fertilization**
- In vitro fertilization (IVF) with embryo cryopreservation
- Well established, good success rate: live birth rate ~40%
  - **Limitations**
    - Requires delaying cancer treatment for 2 to 4 weeks
    - Partner or donor sperm
    - Supraphysiologic estradiol levels
    - Expensive
- Oocyte "Fan" Donor: Good option for patients with
  - Lack of male partner, time constraints
  - SART 2005 success rate 52%
  - Disclosure
  - High cost of treatment
  - Legal, ethical, emotional issues

**Embryo Cryopreservation**
- **Desires Future Fertility**
- Chemotherapy or Radiation treatment that may affect ovaries
  - Pelvic radiation
  - Alkylating agents
- Oncologist approval

- **Established**
  - Embryo Cryopreservation
  - Oocyte Cryopreservation
  - Ovarian Transposition for pelvic radiation

- **Experimental**
  - Ovarian Suppression
  - Ovarian tissue cryopreservation

- Bill and Giuliana Rancic (E! news reporter and breast cancer survivor)
- Giuliana diagnosed breast cancer—underwent emergency IVF with

  **Provided by Oncofertility Consortium Blog**

- In vitro fertilization (IVF) with embryo cryopreservation
- Well established, good success rate: live birth rate ~40%
  - **Limitations**
    - Requires delaying cancer treatment for 2 to 4 weeks
    - Partner or donor sperm
    - Supraphysiologic estradiol levels
    - Expensive
- Oocyte "Fan" Donor: Good option for patients with
  - Lack of male partner, time constraints
  - SART 2005 success rate 52%
  - Disclosure
  - High cost of treatment
  - Legal, ethical, emotional issues
**Oocyte “Egg” Cryopreservation**

**Mature oocyte cryopreservation: a guideline**


---

**Ovarian Cryopreservation Auto-transplant potential sites**

- Auto transplant
- Orthotopic (original site)
- Heterotopic (alternative site)

---

**Ovarian Transposition**

- Standard of care for women undergoing pelvic radiation

---

**Uterine Transplant**

- First ever baby born from a transplanted womb is a healthy boy

---

**Ovarian Suppression**

- Medication administered prior to chemo
- “Medical menopause”
- Controversial
- More studies needed

---

**GnRH agonists**

- Cochrane Database Systemic Review 2011:
  - GnRH agonists should be considered in women of reproductive age receiving chemotherapy
  - GnRH analogues seem to be effective in protecting ovaries during chemo
  - No significant different in pregnancy rates
GnRH antagonists
- Do not have flare effect
- Previous studies (Sauer 2006, Whitehead 2011)
  - limited numbers
  - resumed spontaneous menses
- Elgindy 2013: GnRH antagonist/agonist combined protocol in breast cancer women to prevent chemotherapy induced amenorrhea
  - limited by small numbers
  - does not offer a significant protective effect

Elagolix
- Gonadotropin-Releasing Hormone (GnRH) Antagonist
- Oral
- Currently in Phase III trials for Treating Endometriosis

Adolescent Population and GnRH antagonist
- Mardesic et al 2004:
  - Example of GnRH antagonist suppressing flare effect
  - 6 post-pubertal young women with hematological malignancies
  - GnRH agonist and GnRH antagonist
  - Suppression of FSH and LH almost complete at 90 hours but complete by 96 hours - not influenced by menstrual cycle

Adolescents and Young Girls
- By 2010, 1 in every 250 people in adult population will be a childhood cancer survivor
- Not as many options due to:
  - Usually no partner
  - Not thinking about family at that time
  - Usually need to quick start chemo

Research Proposal
- 12-25yo menstruating adolescents and young women who are newly diagnosed with:
  - lymphoma (Hodgkin's or non-Hodgkin's)
  - acute myelogenous leukemia (AML)
  - neuroblastoma
  - soft tissue sarcoma
  - osteosarcoma
- Needing Chemotherapy
- Intervention:
  - GnRH antagonist/agonist co-treatment
- Randomized but no placebo will be administered

Proposal
- Primary outcome marker
  - Resumption of menses - standard to monitor for premature ovarian failure
- Power
  - Extrapolating from previous data, we hypothesize that 70% of patients treated with the GnRH combination will resume regular menses after completion of chemotherapy versus only 40% in the control group.
  - Using a power of 80%, a p-value of 0.05, 30% drop out rate:
    - 69 girls will be enrolled in each arm
    - Total of 138 patients
- Secondary outcomes
  - Anti-mullerian hormone, FSH, Estradiol, LH
Leukemia/Lymphomas

- Usually present after induction of chemotherapy
- Are candidates for cryopreservation but pregnancy outcomes using embryos created after recent exposure to chemo are not known
- Animal data suggest that there may be an increase risk of miscarriage and birth defects
- Good candidates for GnRH analogs in order to manage ovulation and menstrual bleeding during chemotherapy given that fertility options are limited

Risk of pregnancy and to children after cancer

- Data are limited, seems to be no increased risk of cancer recurrence from fertility preservation methods or pregnancy
- No evidence that history of cancer, cancer therapy or fertility interventions increases the risk of cancer or congenital abnormalities in the progeny aside from hereditary genetic syndromes

Male Options

- Sperm Cryopreservation (sperm banking)
  - Can be done quickly
  - Can repeat multiple times to collect desired number of samples
- Costs (approximate)
  - Semen analysis $125
  - Freezing $100
  - Storage (1 year) $500
  - Intrauterine insemination $450

Resources

- Livestrong
- Oncofertility Consortium
- Myoncofertility.com
- UT MARC Reproductive Endocrinology and Infertility Department
  - 450-9500
  - Counseling sessions, Full IVF lab and capabilities
  - LIVESTRONG Foundation Fertile Hope Program

Questions?

- Thank you for attending 😊