Abstract
Most adolescents and young adults (AYAs) with cancer will survive their disease, and fertility issues are a major concern for this population. The ASCO and new NCCN Clinical Practice Guidelines in Oncology for Adolescent and Young Adult Oncology recommend that oncologists offer the option of fertility preservation to all postpubertal AYAs before the start of potentially gonadotoxic chemotherapy or radiotherapy, providing that the patient does not require emergent start of therapy. Despite the published practice guidelines, many AYAs diagnosed with cancer are still not offered fertility preservation, with oncologists citing lack of time, lack of knowledge, and discomfort in discussing fertility and sexuality with AYAs as reasons. Developing a systematic and coordinated multidisciplinary strategy for fertility preservation referrals within a practice site may streamline the referral process, off-loading some tasks from the oncologist and potentially increasing patient satisfaction, provider satisfaction, and compliance with the guidelines. (JNCCN 2013;11:71–77)

Each year in the United States, approximately 70,000 adolescents and young adults (AYAs) between ages 15 and 39 years are diagnosed with cancer, and most will become long-term survivors. With improving cancer survival rates in the United States over the past several decades, survivorship issues are an increasing priority in cancer care for all age groups. Fertility is an issue of critical importance to AYA survivors, and AYAs who become infertile after cancer therapy are at risk for long-term psychological distress.

ASCO, the American Society for Reproductive Medicine, and the American Academy of Pediatrics have issued guidelines and position statements recommending that oncologists inform patients of the risks that cancer treatments pose to fertility, and that they refer interested patients for appropriate fertility preservation. All patients of reproductive age who will receive therapy that is potentially gonadotoxic are considered candidates for fertility preservation. According to the guidelines, this referral should occur before the start of cancer treatment. The recently published NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines) for AYA Oncology identify fertility preservation as an essential element in the management of AYAs with cancer. However, research shows that as many as 54% of oncologists are still not routinely discussing fertility with AYAs, particularly female patients. In a recent survey of AYA patients, 80% of males but only 48% of females recalled being offered information about fertility risks, and 68% of males and only 14% of females recalled being offered referral to fertility preservation services. Oncologists’ reasons for not addressing fertility preservation with AYAs include constraints in time, difficulty accessing fertility preservation resources, concerns over treatment delays, and concerns that the conversation will distress the patient. Providers’ conversations with adolescents may be further complicated by the sensitive nature of discussions about sexuality and fertility with young patients, and by the added complexity of including parents in decision-making. Oncologists may be particularly challenged if their practice group does not have a relationship with reproductive services or if these services are not conveniently located in their region. This article provides guidance for oncologists wishing to establish best practices to address this important survivorship issue in AYAs. The approach described here was used at Seattle Children’s Hospital.
and resulted in an 8-fold increase in AYA males who elected to bank sperm before undergoing treatment for cancer, and a 90% referral rate of AYA males to fertility preservation services. A similar program in an adult medical oncology clinic increased the rate of fertility preservation consultation in 18- and 40-year-old males 2.4-fold, from 23% to 43% (P<.05). This approach could be applied in any oncology care setting.

Creating Institutional Practices That Support Fertility Preservation for AYAs

Creating standard processes and role expectations is key to successfully meeting the ASCO recommendation to offer fertility preservation to all newly diagnosed AYAs before starting gonadotoxic cancer therapy. Accomplishing this objective begins with education of the multidisciplinary oncology health care team, including oncologists, nurse practitioners, social workers, and nurses. Topics that must be mastered by team members include an understanding of the gonadotoxocities of chemotherapy and radiation therapy, awareness of the currently available fertility preservation methods, knowledge of the highly time-sensitive nature of this intervention, and understanding of the developmental issues that may impact decision-making in AYAs. Table 1 briefly summarizes the potential treatment effects of cancer therapy. In addition to the published literature on fertility risks in AYAs, many online resources are available that may be valuable to both patients and clinicians. Some of these are included in Table 2. With a sound knowledge base, an oncology team can move forward with creating reliable institutional practices to support fertility preservation for AYAs.

Standard Expectations and Roles

Fertility preservation is best approached as a multidisciplinary endeavor. One way to structure the approach used would be to make it the oncologist’s responsibility to review fertility risks and briefly initiate the discussion of fertility preservation, followed by a more prolonged discussion with a designated team member (nurse or social worker) for the purpose of in-depth patient education and subsequent referral to a reproductive specialist.

The oncologist’s role is to provide patients with information about the risks regarding fertility that are associated with the planned cancer treatment, recognizing that, in many cases, adequate data to predict individual outcome are not available, and with an individualized assessment of the risk associated with delaying treatment for fertility preservation to occur. Discussion of the risks of various treatment regimens may be informed by recent articles on fertility risks associated with cancer treatment in AYAs, or by resources such as the risk calculators published by Fertile Hope on their Web site.

Within an oncology practice, a knowledgeable nurse or social worker can assume the role of point person for educating patients about their options and navigating the logistical challenges of pursuing fertility preservation. This point person can provide information about the location of services, the costs of fertility preservation, and the availability of financial assistance programs, and can facilitate first contact between patients and fertility clinics or sperm banks. Male patients who wish to bank sperm may need to do so during initial hospitalization. This task may require careful coordination with an outside sperm bank or fertility clinic. The designated point person for fertility preservation is in an ideal position to facilitate inpatient banking. Other nurses and social workers who interact with newly diagnosed patients should also be educated about the risks and options, because they may have opportunities to advocate for AYA patients and assist in decision-making. Educating the entire treatment team will also ensure that AYAs receive uniform and accurate information about their options for fertility preservation.

Cultivating consultative partnerships with local or regional specialists in reproductive endocrinology and urology is a key element in developing a robust system for fertility preservation in any oncology practice. Fertility clinics partnering with oncology practices must understand the highly time-sensitive nature of fertility inquiries in patients with cancer, and should be prompt in arranging intake visits for those with newly diagnosed cancer. Many AYA patients will need access to services within days after receiving a cancer diagnosis. For males who are unable to bank sperm because of ejaculatory dysfunction, testicular sperm extraction or electroejaculation may be performed by a urologist working in tandem with a sperm bank. Partner services should also be willing to submit the costs of fertility preservation to the
patient’s insurance company for reimbursement. Reimbursement for fertility services is not guaranteed and patients may bear the costs themselves, but the attempt should be made because reimbursement patterns for fertility preservation in the context of cancer are changing.  

Standard Processes for AYA Fertility Preservation

The goal of any fertility preservation program should be to educate patients about the risks that cancer treatment has on fertility so that they are able to make informed decisions about fertility preservation. A simple standard approach used for all patients can greatly improve patient and provider satisfaction. Special sensitivity to the unique needs and developmental issues of AYAs is crucial for providers who care for this population.

Inform

There is no replacing an individualized conversation between oncologist and AYA patient/family regarding the potential risk to fertility by a proposed cancer treatment. Oncology clinics can reinforce the information presented by the physician by including statements about fertility risks in treatment consent documents. Clinicians should document the provision of fertility-related information in the medical record along with other treatment side effects and risks.

Educate

In-depth patient education should be provided by a designated team member who has the time to reinforce information provided by the oncologist, talk through the patient’s fertility preservation options, and answer questions raised by the AYA patient and family. (Tables 3 and 4 outline the fertility preservation options for males and females.) The information presented can be reinforced by written and online patient education materials on the topic of fertility preservation for AYAs. These documents should be succinct and written in lay terms, with simple explanations and emphasis on the importance of completing fertility preservation before the start of therapy.

Special Considerations for Adolescents

Adolescents are a developmentally distinct group in the AYA age spectrum, and require special consideration from the oncology care team. Patient education approaches for teens must be age-appropriate, with sensitivity to the potentially embarrassing nature of the topic for some patients. Adolescents vary widely in their knowledge and experience regarding sexuality and fertility, and are frequently accompanied to clinic visits by their parents. The comfort level of patients in this age group can be maximized by interaction with a provider who is comfortable and skillful in discussing sexuality and fertility, and by the assurance that conversations about fertility preservation are the norm for all newly diagnosed AYAs.
Adolescents should be offered the opportunity to speak one-on-one with the fertility point person from the oncology team. During the conversation, the provider should use simple, direct language and should assess the patient’s knowledge and comfort with fertility and sexuality. This approach allows adolescents the choice of avoiding an overt discussion of potentially stressful topics of sexuality, such as masturbation for sperm banking, in front of their parents. At the conclusion of the one-on-one interview, the provider can briefly summarize the outcome of the discussion in the presence of both the teen and parents, and proceed with further discussion of fertility preservation options. Adolescents, who may have given little thought to future parenting, often benefit from the encouragement of parents and health care providers as they consider their options for fertility preservation before cancer therapy.

In counseling male adolescents about sperm banking, providers are advised to point out in advance that a proportion of sperm banking attempts may not be successful; 12% of males with cancer, particularly Hodgkin lymphoma and testicular cancer, are azoospermic at diagnosis. Others, particularly inpatients and younger adolescents, may be too distracted or upset by their circumstances to produce an adequate semen sample.

In discussions with female adolescents about oocyte cryopreservation, providers are advised to note that the process requires transvaginal ultrasounds and harvesting of the eggs through the vagina. Although these procedures may be upsetting or mildly painful for some virginal adolescents, oocyte cryopreservation should still be offered as an option for younger AYAs. Oocyte cryopreservation may also be preferred when a female does not have an intimate partner at diagnosis and the use of donor sperm is undesirable.

**Refer**

AYAs are often overwhelmed with the life changes that accompany a new cancer diagnosis, including changes in school, employment, and family dynamics, and the internalization of a significant amount of new information about their disease and treatment. These challenges, on top of the emotional burden of cancer, may leave patients and their families with little capacity to arrange fertility preservation. AYAs who are interested in fertility preservation may need help identifying fertility services, and making first contact for them can be very helpful.

The fertility preservation point person must be knowledgeable about the local and regional fertility services and the length of time required for various types of fertility preservation. Table 5 lists directories of fertility services by location. Males who are able to bank sperm may be willing to travel a distance to a sperm bank, but the time required for actual sperm banking should not pose a barrier to patients or providers. Hospitalization should not be a barrier to sperm banking. Inpatient semen collection can be coordinated with a local sperm bank or fertility clinic. A method of transporting the collection is needed and often a family member can assume this role. Males who live in remote locations or who lack the time or finances to travel to a sperm bank can

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**Table 2 Resources for Oncology Providers, Patients, and Adolescents**

<table>
<thead>
<tr>
<th>Oncology Providers</th>
<th>Patients</th>
<th>Adolescents</th>
</tr>
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<tbody>
<tr>
<td>NCCN Clinical Practice Guidelines in Oncology for Adolescent and Young Adult Oncology: NCCN.org</td>
<td>SaveMyFertility: <a href="http://www.savemyfertility.org">www.savemyfertility.org</a></td>
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be offered the option of mail-in banking from home using collection kits such as those provided to patients by Fertile Hope or Reprotech, but because of the lower yield of mail-in kits, banking at a clinic remains the standard of care when feasible.

Females may also strongly desire to delay treatment and travel a distance so that they may preserve embryos or oocytes. Ovarian stimulation requires a 10- to 14-day delay in the start of treatment and may be costly. The potential risks of delaying treatment must be openly discussed, and ultimately the AYA and her family should be allowed to make this decision if the physician feels it is medically safe.

**Posttreatment Options for AYAs**

AYA patients who are unable to or choose not to undergo fertility preservation before treatment should be made aware of the options for fertility preservation after therapy. Females who are unable to freeze embryos or oocytes before treatment may be able to do so after treatment if their ovarian reserve is deemed sufficient by a reproductive endocrinologist. Many women continue menses through cancer therapy or resume menses after cancer therapy but remain at risk for premature ovarian failure, so this may be a very good option if biological children are desired in the future. Male sperm counts are lowest 6 months after the end of therapy and may remain transiently depressed for up to 2 years after the end of therapy. Some males develop permanent azoospermia after cancer treatment. Recent data from a series of 73 patients show that microdissection testicular sperm extraction (TESE) can be used to retrieve sperm for in vitro fertilization in 37% of azoospermic males.

**Table 3 Fertility Preservation Options for Females**

<table>
<thead>
<tr>
<th>Option</th>
<th>Description</th>
<th>Timing</th>
<th>Time Required</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryo banking</td>
<td>Ovarian stimulation, harvesting eggs, IVF, cryopreservation of embryos</td>
<td>Before or after treatment</td>
<td>10–14 days of ovarian stimulation; outpatient surgical procedure</td>
<td>Requires partner or donor sperm</td>
</tr>
<tr>
<td>Egg banking</td>
<td>Ovarian stimulation and harvesting and cryopreservation of unfertilized eggs</td>
<td>Before or after treatment</td>
<td>10–14 days of ovarian stimulation; outpatient surgical procedure</td>
<td>Widely offered but considered experimental</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>May be desired by single women who prefer not to use donor sperm</td>
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<tr>
<td>Intensity-modulated radiation</td>
<td>Shaping the field of pelvis radiation to minimize dose to ovaries</td>
<td>During treatment</td>
<td>In conjunction with radiation therapy</td>
<td>Provides no protection against effects of chemotherapy</td>
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<tr>
<td>therapy</td>
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<tr>
<td>Ovarian transposition</td>
<td>Surgical repositioning of ovaries away from field of radiation</td>
<td>Before treatment</td>
<td>Outpatient procedure or in conjunction with gynecologic surgery</td>
<td>Provides no protection against effects of chemotherapy</td>
</tr>
<tr>
<td>Ovarian tissue banking (prepubescent or menarchal females)</td>
<td>Removal and freezing of ovarian cortical tissue; reimplantation of tissue or in vitro maturation of follicles for IVF after cancer</td>
<td>Before or after treatment</td>
<td>Outpatient surgical procedure</td>
<td>Experimental</td>
</tr>
<tr>
<td>Ovarian suppression</td>
<td>GnRH analogs or antagonists use to suppress ovaries; thought to protect the ovaries</td>
<td>During treatment</td>
<td>Duration of treatment</td>
<td>Experimental</td>
</tr>
</tbody>
</table>

Abbreviations: GnRH, gonadotropin-releasing hormone; IVF, in vitro fertilization.

Data from Refs. 8,22–26
Although pretreatment sperm banking is recommended, microdissection TESE may be an option for AYA male survivors with long-term azoospermia after cancer treatment.

### Provider Challenges

Even after oncology groups adopt best practice strategies to support fertility preservation for AYAs, some internal roadblocks may continue to exist for providers. Certain patient populations of AYAs present special challenges. Health care providers must confront their personal assumptions and biases regarding the importance of fertility preservation in the context of AYAs with a poor prognosis. Some providers may be uncomfortable discussing fertility preservation with young teenagers or patients with developmental or emotional disabilities. Language, cultural, and religious beliefs may be perceived as barriers. Cost and lack of insurance coverage are significant challenges for many patients, but should not be barriers to educating patients about their fertility and fertility preservation options. Armed with good information, AYA patients and their families must make their own decisions.

### Conclusions

The risk of infertility related to a proposed cancer treatment and the potential options for fertility preservation before the start of therapy should be

<table>
<thead>
<tr>
<th>Table 4 Fertility Preservation Options for Males</th>
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<tbody>
<tr>
<td><strong>Option</strong></td>
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<tr>
<td>-----------------------------------------------</td>
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<tr>
<td>Sperm banking</td>
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<td></td>
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<tr>
<td>Testicular shielding</td>
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<tr>
<td>Electroejaculation</td>
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<tr>
<td>Testicular sperm extraction/aspiration</td>
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<tr>
<td>Testicular tissue banking (prepubescent males)</td>
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</tbody>
</table>

Data from Refs. 8,27,28

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<thead>
<tr>
<th>Table 5 Directories of Sperm Banks and Fertility Clinics</th>
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<tr>
<td>Sperm Center: <a href="http://www.spermcenter.com">www.spermcenter.com</a></td>
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addressed in the initial discussions between oncologists and AYA patients with newly diagnosed cancer. After this conversation, oncology groups may benefit from designating a nonphysician point person to shepherd AYA patients and families through the process of decision-making and then coordinate fertility clinic referrals. Establishing relationships with local fertility clinics, instituting standard practices for offering fertility preservation to eligible AYA patients, and educating all multidisciplinary care providers in the practice group about fertility preservation may off-load some tasks from the treating oncologist and streamline fertility preservation referrals. These steps will ensure that AYA patients interested in preserving their fertility before cancer treatment will have the opportunity to do so, maximizing patient satisfaction and meeting established practice guidelines for AYA cancer care.

References
19. Shnorhavorian M, Johnson R, Shear S, Wilford B. Responding to adolescents with cancer who refuse sperm banking: when “NO” should not be the last word. Journal of Adolescent and Young Adult Oncology 2011;11:114–117.