Semen Preservation in Male Adolescents and Young Adults With Cancer: One Institution’s Experience

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Semen preservation is a feasible procedure for male adolescents and young adults who may become infertile as a result of cancer therapy. Treatment for several pediatric malignancies puts adolescents and young adults at a significant risk for fertility dysfunction. Eligible male adolescents and young adults (N = 32) treated from January 2004 to June 2005 at Cook Children’s Medical Center were offered semen preservation at the time of diagnosis or presentation to the center for treatment. Fifteen (47%) young men were successful in semen preservation. Two (6%) adolescents did not participate because of parental refusal. Seven (22%) were too ill, and eight (25%) failed to produce an adequate sample. Several patients were not successful because of time constraints, lack of counseling, and parental anxiety. Efforts for success in semen preservation should include private discussions between nurses and adolescents. In addition, information on infertility needs to be given to families early in the diagnostic phase to provide them with an opportunity to ask questions.

At a Glance

✦ Cancer therapy may result in infertility for male adolescents and young adults.
✦ Early discussions with young men and their families are vital to successful semen preservation.
✦ Ethical dilemmas may exist when attempting to discuss semen preservation with male adolescents.

Aproximately 77% of children diagnosed with cancer will become long-term survivors of the disease (Mertens et al., 2001; Ries et al., 2005). Many children may experience late effects of cancer and cancer treatment because of significant advances in treatment, including combination chemotherapy and radiation, which have led to increased survival rates. The effects of treatment often depend on the type and dose of chemotherapy, radiation fields, and dose of radiation.

Endocrine dysfunction comprises almost 40% of the total late complications of cancer therapy (Sklar, 1999). The testes are highly sensitive to effects of cancer therapy (Thomson, Critchley, Kelnar, & Wallace, 2002). As a result, semen cryopreservation is an option to preserve fertility in male patients with cancer who would otherwise not be able to father biologic children (Oktay, 2005; Pfeifer & Coutifaris, 1999; Wallace, Anderson, & Irvine, 2005). Efforts are being implemented in several pediatric institutions to preserve semen in male adolescents diagnosed with cancer. The purpose of this article is to briefly describe the treatments for childhood cancer that may result in infertility and the experience of one institution in semen cryopreservation for a 15-month period.

Literature Review

The effects of chemotherapy on male fertility depend on the chemotherapy agent, dose, length of exposure, and age of patients (Thomson, Wallace, & Sklar, 2004). Multiple chemotherapy agents often are used in treating pediatric cancers, which makes determining the gonadotoxic effects of drugs more difficult (Thomson et al., 2002). Chemotherapy administered to men affects testicular function by damaging somatic (i.e., Sertoli and Leydig cells) and germ cells, resulting in reduced sperm production (i.e., spermatogenesis) (Wallace et al., 2005). Combination chemotherapy commonly is used in treating childhood cancers and results in gonadotoxic effects in male patients (see Figure 1). Alkylating agents (i.e., busulfan, cyclophosphamide, ifosfamide, and melphalan) destroy rapidly dividing cells, including hair, digestive tract cells, and cells in the testes. Cyclophosphamide is used to treat malignancies, as well as nephrotic syndrome (Saha & Singh, 2006). Mechlorethamine and procarbazine,
which currently have limited use in pediatrics, have been found to cause sterility in male patients treated for Hodgkin disease (Puscheck, Philip, & Jeyendran, 2004).

The total dose of chemotherapy also affects male fertility. Men receiving more than 7.5 g/m² total dose of cyclophosphamide for sarcomas usually are permanently sterile; individual fertility results may vary with the drug (Kenney, Lauer, Grant, Grier, & Diller, 2001). In addition, the dosages of ifosfamide and cisplatinum may have predictive value of fertility in men after treatment. In several studies (Petersen, Hansen, Giwercman, Rorth, & Skakkebæk, 1994; Pont & Albrecht, 1997), men treated with more than 600 mg/m² total dose of cisplatin had severe oligospermia or azoospermia, indicating sterility. Predicting which patients will be infertile as a result of specific chemotherapy agents is difficult because of individual variability in fertility outcomes among male adolescents treated for cancer. Therefore, pubertal male patients should be offered sperm preservation prior to cancer treatment as a method to preserve fertility (Wallace et al., 2005).

**Radiation**

Radiation doses as low as 1.2 Gy may result in impaired spermatogenesis, and radiation more than 4 Gy will result in complete sterility (Centola, Keller, Henzlér, & Rubin, 1994). Recovery of spermatogenesis, however, may be possible at age 5 or older (Rowley, Leach, Warner, & Heller, 1974). The effects also may depend on age and pubertal status. A single dose of radiation in the amount of 6–8 Gy could result in irreversible azoospermia in healthy males (Rowley et al.). Children undergoing bone marrow transplantation or who receive radiation directly to the testes for recurrence or initial presentation of cancer most often are sterile. Doses of radiation to the testes usually are more than 20 Gy and result in permanent sterility (Petersen, Daugaard, Rorth, & Skakkebæk, 2003).

Treatments for testicular cancer, bone sarcomas, Hodgkin disease, and bone marrow transplantation (used frequently for disease recurrence or high-risk disease) may result in irreversible azoospermia in adolescents. In a study conducted by Ishikawa, Kamidono, and Fujisawa (2004), 50% of male patients who were treated for testicular cancer were azoospermic more than six months following the completion of therapy. Elevations in serum alphafetoprotein observed in germ cell tumors also may affect spermatogenesis in patients with cancer of the testes (Turek, Lowther, & Carroll, 1998).

Male adolescents treated for osteogenic sarcoma have significant risk for fertility dysfunction (Longhi, Macchiagodena, Vitali, & Bacci, 2003). Typically, patients with osteogenic sarcoma receive higher doses of ifosfamide, which may result in oligospermia or azoospermia. Therapy for Hodgkin disease historically has been gonadotoxic in males (Green et al., 1981; Kogel & Sweetenham, 2003; Mackie, Radford, & Shalet, 1996; Rueffer et al., 2001). Bone marrow transplantation requires the use of myeloablative doses of chemotherapy and, in some cases, total body irradiation. Recovery of spermatogenesis in young men may be impaired when using nonmyeloablative and myeloablative doses of chemotherapy or total body irradiation (Anserini et al., 2002; Kyriacou et al., 2003).

**Background**

Semen preservation in young adults and, specifically, adolescents is a new phenomenon that has been offered infrequently when compared to adults (Bahadur & Ralph, 1999). Semen preservation may be an option for pubertal adolescents based on data that suggest the presence of spermatozoon in the urine of pubertal males. Most males exhibit pubertal changes from ages 12–13, when spermatozoon is noted in urine and testicular volume is at least 5 ml (Bahadur, Whelan, Ralph, & Hindmarsh, 2001). Progression in puberty to Tanner stage II is observed when males develop scant pubic hair, with penile and testes enlargement to 4 ml in volume (Behrman, Kliegman, Jenson, 2004; Marshall & Tanner, 1970).

Semen preservation will be most effective prior to the initiation of cancer therapy because of the effects of cancer therapy on semen production. Multiple barriers prevent adolescents from semen preservation at the time of diagnosis, such as lack of time, a physician’s failure to discuss risks to fertility, and cost (Leonard, Hammelef, & Smith, 2004). Male adolescents and their families need accurate information on how semen is collected. When discussing semen preservation, education should be provided about the potential risk of infertility (Bahadur et al., 2001).

Families of children with cancer may not be concerned with the risk of infertility, which makes discussing fertility preservation options difficult. In addition, parent anxiety often is significant at diagnosis (Allen, Newman, & Souhami, 1997; Boman, Lindahl, & Bjork, 2003), complicating the discussion further. Leonard et al. (2004) suggested that private conversations with adolescents may be useful and may allow adolescents to ask questions they might be uncomfortable asking in their parents’ presence. Furthermore, the presence of parents during semen collection may impact the success of obtaining semen for preservation. Bahadur et al. (2002) noted that adolescents who were accompanied by a parent during semen collection (8%) were less likely to be successful than patients who were unaccompanied (29.7%).

Men diagnosed with cancer are encouraged to cryopreserve semen if treatment is likely to result in infertility. Most often, semen is collected through masturbation prior to initiation of cancer therapy, processed carefully, and cryopreserved in subzero temperatures. More invasive methods of semen collection include epididymal sperm aspiration (Pfeifer & Coutifaris, 1999), penile vibration, and electroejaculation (Schmiegelow et al., 1998). Electroejaculation requires general anesthesia because of the pain induced by the procedure and should be used only if the family wishes to pursue more invasive means of semen preservation.
The University Health System in Ann Arbor, MI, under the coordination of an oncology nurse practitioner in collaboration with the assisted reproductive technologies director, developed the Fertility Counseling and Gamete Cryopreservation Program (FCGCP). FCGCP offers fertility counseling, education, and semen preservation to eligible men diagnosed with cancer (Leonard et al., 2004). Male adolescents as young as age 11 have been offered the potential fertility-preserving procedure, and oncology professionals have published on the success of semen preservation in male adolescents (Muller et al., 2000; Postovsky et al., 2005). In a study by Muller et al., 42% of male adolescents who presented to the center from 1995–1998 were successful in semen preservation. In another study, Postovsky et al. indicated that 64.5% of patients successfully preserved semen.

The Children’s Oncology Group (COG) nursing discipline completed an initiative to identify male adolescents at risk for infertility as a result of cancer treatment. The goal of the nursing initiative is to provide information to healthcare providers and patients to assist in decisions about fertility preservation. Another goal of the initiative is to optimize physicians’ use of reproductive services to preserve fertility in male adolescents at risk for reproductive problems as a result of treatment. A survey of Pediatric Oncology Group institutions conducted to determine how many centers provided semen preservation to children found that semen preservation had been offered in 93% of centers and 77% had established links with preservation services (Glaser, Wilkey, & Greenberg, 2000). Most centers offered semen preservation to male adolescents with lymphomas and bone sarcomas. No center indicated that guidelines were established regarding who should be offered semen preservation, indicating a potential gap in the number of adolescents and young adults offered the service.

**One Institution’s Experience**

From February 2004 to June 2005, 32 adolescents and young adults who presented for treatment to the Hematology and Oncology Center at Cook Children’s Medical Center met eligibility for cryopreservation (see Table 1). Through a generous grant from the Lance Armstrong Foundation, the center was able to provide semen analysis and preservation for participants for a period of 10 years. After 10 years, survivors will be responsible for continuing payment on the preserved semen.

Consent for semen collection and preservation was obtained from parents and young adults, and assent was obtained from minors prior to semen collection. As part of the process, minors, specifically, had to assent that they understood the process of semen preservation. Participants were asked to initial and sign in the presence of a notary that, in the event of their death, the semen would be destroyed because it is the property of the adolescent or young adult. The information contained in the consent was discussed with consenting individuals prior to signing and semen collection to verify their full understanding of the procedure.

Fifteen (47%) adolescents and young adults were successful in preserving semen (see Table 2). Successful participants procured the specimen by masturbation. Seven (22%) patients were too ill at the time of diagnosis to provide a sperm sample prior to treatment. Parents of two (6%) adolescents, ages 12 and 17, did not consent to their sons being approached to discuss semen preservation. The mother of a 12-year-old patient indicated that her decision was based on religious beliefs, which did not condone masturbation. The mother of a 17-year-old patient believed that masturbation was not a proper act for her son to perform. Eight (25%) patients failed to produce adequate semen samples, two of which were found to be azoospermic. Unfortunately, one of the azoospermic adolescents was unable to attempt semen preservation until after his first cycle of therapy. Another young adult who was unable to produce an adequate sample was diagnosed and given his first cycle of therapy prior to coming to the center; he was not offered sperm banking at the time of diagnosis.

Assent is the process of obtaining agreement from a minor to participate in research. Assent represents that an opportunity to discuss the procedure was offered to the minor. Adolescents wishing to preserve semen were asked to sign the consent with their parents, indicating an understanding of the procedure for semen preservation. Adolescents had to verbalize their understanding of what they were being asked to do and the consequences of undergoing semen preservation or not preserving sperm. The opportunity to discuss semen preservation with the two adolescents whose parents refused participation was lost, even though the staff perceived them to be mentally competent to fully understand the procedure and should have had the opportunity to assent to semen cryopreservation. Ethical issues exist as to whether parents, prior to making a final decision, have the right to refuse adolescents of at least hearing about semen preservation and consequences.

Discussing semen preservation with adolescents can be difficult, especially in the presence of parents. A private discussion about semen preservation with adolescents may be useful and should be conducted with tact and sensitivity (Robertson, 2005). As in the experience of Bahadur et al. (2002), reviewing semen preservation with adolescents alone may result in more successful sperm collections. Unfortunately, in several cases, staff at the center were not able to discuss the procedure privately with adolescents. Discussing options for fertility preservation with adolescents alone may encourage them to ask questions about the procedure and reduce the embarrassment of discussing semen collection. More formal fertility counseling during the diagnostic phase of therapy for several participants may have provided more credibility to the concept of semen preservation. The conversation about semen preservation might be more successful when physicians initiate and encourage it during the consenting phase of cancer therapy. Lack of time, personnel, and patient conditions all may contribute to unsuccessful semen preservation.

Unfortunately, some adolescents and young adults may not have had sufficient time to fully understand the process of semen

| **Table 1. Eligibility Criteria for Semen Preservation** |
|-----------------|-----------------|
| **CRITERIA**    | **REQUIREMENT** |
| Age             | ≥ 12 years      |
| Tanner stage    | Tanner II       |
| Disease         | Any malignancy  |
| Prognosis       | Any             |
| Cognition       | Able to understand procedure |
| Motor skills    | Able to perform masturbation |
| Competency      | Sign and initial for assent or consent |

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preservation. They are recommended to preserve samples for several days prior to the initiation of chemotherapy. Time is necessary to discuss the semen preservation process with patients and families, allow for questions about the process, and provide patients with the opportunity to collect at least two semen samples over a couple of days. Prognosis often depends on early initiation of cancer therapy; therefore, semen preservation may be delayed until cancer therapy has started.

Another important barrier is cost of semen preservation, which may not be covered by insurance companies. Patients with cancer and their families should investigate insurance coverage for fertility options. Prior to the initiation of the project at the center, costs of semen analysis and preservation were prohibitive for young men who chose sperm banking. Through the efforts of national organizations like the Lance Armstrong Foundation (www.laf.org), Fertile Hope (www.fertilehope.org), and Resolve (www.resolve.org), support for fertility preservation for men and women is being recognized as part of cancer treatment. Resolve has chapters throughout the United States that provide peer support and information about how to receive financial aid for fertility preservation.

Implications

Semen preservation is a relatively new phenomenon in pediatric oncology, but the benefits to the survivors’ long-term quality of life cannot be overstated. Efforts currently are under way through COG to make the procedure a standard process. Information about risks to fertility is available and should be offered to adolescents and their parents early in the diagnostic phase of cancer treatment. The American Society of Reproductive Medicine, FCGCP, Fertile Hope, and Resolve have information easily accessible online for professionals and patients. Families should be provided with fertility information early in the diagnostic phase of cancer treatment so they have time to review materials, ask questions, and make a decision.

Table 2. Successful Semen Preservation

<table>
<thead>
<tr>
<th>PARTICIPANT</th>
<th>DIAGNOSIS</th>
<th>DISEASE STATUS</th>
<th>AGE (YEARS)</th>
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<tbody>
<tr>
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<td>14</td>
</tr>
<tr>
<td>2</td>
<td>ALL</td>
<td>Initial</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>ALL</td>
<td>Recurrence</td>
<td>14</td>
</tr>
<tr>
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<td>NHL</td>
<td>Initial</td>
<td>15</td>
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<tr>
<td>5</td>
<td>ALL</td>
<td>Recurrence</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td>ALL</td>
<td>Recurrence</td>
<td>16</td>
</tr>
<tr>
<td>7</td>
<td>GCT</td>
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</tr>
<tr>
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<td>17</td>
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</table>

ALL—acute lymphoblastic leukemia; GCT—germ cell tumor; NHL—non-Hodgkin lymphoma; OGS—osteogenic sarcoma; PNET—Primitive neuroectodermal tumor; RMS—rhabdomyosarcoma

Conclusion

The risk of losing the ability to biologically father children can be emotionally upsetting to survivors of cancer (Schover, 1997, 1999). In a study of cancer survivors, about 55% remember their physicians discussing fertility or mentioning something about it (Zebrack, Casillas, Nohr, Adams, & Zeltzer, 2004). In another study by Schover, Brey, Lich tin, Lipshultz, and Jeha (2002), 60% of male cancer survivors recalled a conversation about infertility and 51% of participants were offered semen preservation.

Childhood cancer survivors, despite doing well generally, do worry about their reproductive capacity (Gray et al., 1992; Lan geveld et al., 2003; Schover, 1999; Zebrack et al., 2004). Studies support the need for healthcare providers to discuss threats to reproductive health in male adolescents and young adults, specifically, at the time of diagnosis. At the center, the approach to semen preservation is viewed as part of the diagnostic process or at least considered when it is most clinically appropriate. The successes the center has experienced with adolescents and young adults are attributed to the discussion about semen preservation early in the diagnostic phase of cancer therapy.

For example, a 16-year-old patient who presented to the stem cell transplantation program after an immediate recurrence of leukemia was given a prompt referral for semen preservation, which allowed him and his family ample time to process information about the collection process and risk of infertility. Discussions with the adolescent privately and with his parents about semen preservation were conducted with instructions on how the collection of semen would proceed. Written materials about the probable risk of infertility because of intense radiotherapy also were provided to the patient and his family, as well as information on reproductive support techniques if necessary.

The preservation of semen in adolescents and young adults is a feasible procedure and should be offered to all men who are at risk for losing reproductive capabilities. The center continues to provide families with the necessary information for them to make informed decisions about the reproductive health of their children. The center strives to offer early fertility counseling and referrals for semen cryopreservation for adolescents and young adults. Opportunities for improvement in the semen preservation program include earlier referral to a nurse coordinator to provide greater ability in discussing semen preservation with adolescents privately and with parents. General education about fertility currently is provided for all adolescents diagnosed with cancer, including materials on the local reproductive center. Ideally, the information will prompt patients and parents to initiate discussions about the procedure.

Finally, nursing personnel not directly involved in the semen preservation program have opportunities to discuss fertility preservation with young men at the time of admission to the hospital. Staff nurses should be able to answer questions accurately and refer patients and their parents to appropriate personnel when necessary. Educational in-service programs for semen cryopreservation have been held, but ongoing opportunities to educate staff nurses are in development. Every male adolescent and young adult should be offered the chance for fertility preservation. Nursing personnel, specifically, are in a position to make the hope of parenthood for male patients a reality.
The author gratefully acknowledges Kathy Bean, PhD, at the University of Texas at Arlington for her patience and editorial comments during the writing of this article.

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References


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