

Sperm banking and patients with cancer

Issues concerning patients and healthcare professionals

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In 1994, ~52,000 new cancers will have occurred in patients ≤34 years of age. Reported survival rates for tumors common to males in this age group are promising and are expected to improve. Chemotherapy treatment may produce infertility, and without appropriate intervention, the aspiration of producing offspring may never be realized. Semen cryopreservation (sperm banking) may be offered to male patients with cancer as an intervention to circumvent loss of procreation ability resulting from chemotherapy-induced infertility. Oncology nurses can discuss infertility and sperm banking with patients at the most opportune time, before initiation of chemotherapy. Considerable debate exists among health-care professionals regarding the practicality and usage of sperm banking for young adult male patients with cancer being treated with chemotherapy. In addition, health-care professionals may be uncomfortable discussing issues of a sexual nature with patients. Staff nurses administering

chemotherapy to young adult males need to work toward improving their knowledge about the effects of cancer and cancer treatment on reproduction. Improved knowledge will reinforce the importance of offering sperm banking to circumvent treatment-induced infertility.

Key Words: Semen preservation—Frozen semen—Chemotherapy—Male infertility.

In 1994, ~52,000 new cancers will have occurred in patients ≤34 years of age (1). A diagnosis of cancer during young adulthood forces individuals to seek immediate treatment aimed at cure. Thus, issues such as chemotherapy-induced infertility and its potential impact on the development of one's own family may never be realized unless appropriate intervention is taken. Semen cryopreservation (sperm banking) may be offered to male patients with cancer as an intervention to circumvent loss of procreation ability resulting from chemotherapy-induced infertility.

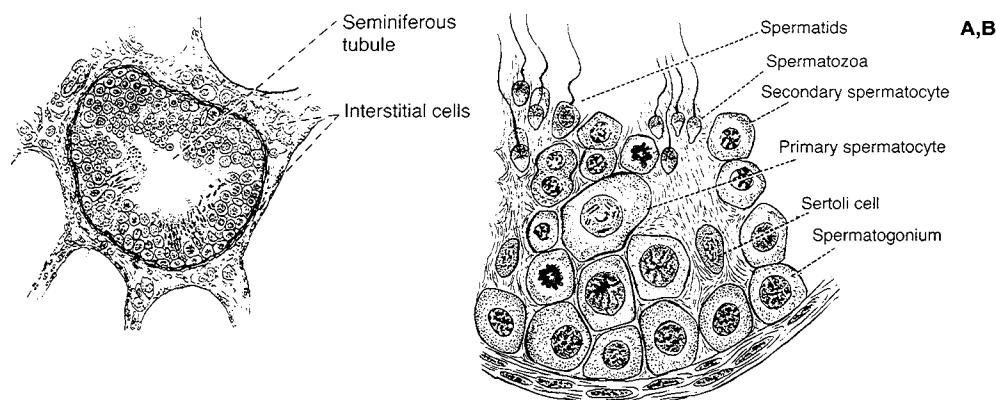
Common tumors affecting young men include testicular cancer, Hodgkin's disease, osteogenic sarcoma, and the leukemias (2–5). Their combined incidence accounts for ~5% of all cancer diagnoses

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FIG. 1. A: Cross sectional view of seminiferous tubule. **B:** Cross sectional view of spermatogenesis within seminiferous tubule. Reproduced with permission (15).



(3–6). Reported survival rates are promising and are expected to improve in the future (2,7).

Men diagnosed with testicular cancer or Hodgkin's disease have at least an 80% chance of achieving 5-year disease-free survival after completion of chemotherapy treatment (3,4). Survival rates for the leukemias are not as encouraging, with ~20–35% of patients achieving a 2-year complete remission after induction and consolidation chemotherapy treatment (6). Bone marrow transplantation offers potential long-term survival, and with improved methods of managing the immunocompromised patient and graft-versus-host disease, long-term survival rates are expected to increase (8).

Osteosarcoma is mainly treated by surgery. Ten to twenty percent of osteosarcoma patients treated either with surgery alone or in combination with chemotherapy achieve 5-year disease-free survival (5).

Although many lives are saved with combination chemotherapy, survivors must deal with quality of life issues such as infertility. Oncology nurses often care for patients during the most opportune time to discuss infertility and sperm banking, that is, before initiation of chemotherapy.

There is a great deal of confusion among health-care professionals regarding the practicality and usage of sperm banking for male patients with cancer being treated with chemotherapy. Many physicians are reluctant to recommend sperm banking because the malignant process itself renders male patients with cancer with poor quality semen (1,9,10). In addition, the required freezing process causes further damage to the semen quality (11,12). Physicians are also concerned about delaying initiation of antitumor treatment to accommodate semen collection (7,9,10).

Lastly, health-care professionals are uncomfortable discussing issues of a sexual nature with patients and avoid consideration of these issues as a part of

their routine care of patients (13,14). The purposes of this article are to present information regarding successful use of semen cryopreservation for the oncology patient and to discuss issues related to care of the patient who might be a candidate for semen cryopreservation.

SPERMATOGENESIS AND CHEMOTHERAPY

A brief overview of spermatogenesis and a brief discussion of the reproductive side effects related to chemotherapy will serve as a guide to understand the vulnerability of sperm production to chemotherapy agents. "Spermatogenesis occurs in the seminiferous tubules during active sexual life, beginning approximately at age thirteen" (15). Figure 1A illustrates a cross-sectional view of a seminiferous tubule. In these seminiferous tubules are large numbers of germinal epithelial cells called spermatogonia. "They continually proliferate to replenish themselves and a portion of them differentiate to form sperm" (Fig. 1B) (15). Most of the stages of germinal cell division, as well as the final conversion of the spermatocytes into sperm, occur within the Sertoli cells. Sertoli cells have specific functions in nurturing and controlling the spermatogenesis process. The sperm mature and gain motility in the epididymis, which takes 18–24 h (15). "The entire period of spermatogenesis from germinal cell to sperm takes about seventy four days. A normal sperm ejaculate at coitus in a healthy male is approximately 3.5 ml., and in each milliliter there is an average of approximately one hundred and twenty million sperm. When the number of sperm in each milliliter falls below approximately twenty million, the person is likely to be infertile" (15).

Two important hormones, luteinizing hormone and follicle-stimulating hormone (FSH) secreted by the anterior pituitary gland, are essential for the

successful formation of sperm. The Leydig cells (Fig. 1A), which lie in the interstices between the seminiferous tubules, produce testosterone when they are stimulated by luteinizing hormone. Testosterone is essential for one or more steps in the division of the germinal cells to form sperm (15). FSH stimulates the Sertoli cells that provide nutrition for the developing spermatozoa. The Sertoli cells release inhibin, sending a negative feedback signal to the anterior pituitary gland to inhibit the production of FSH. Thus, spermatogenesis by the testes inhibits the secretion of FSH (15). Elevated FSH levels have been documented in azoospermic men treated with polychemotherapy regimens (1).

Chemotherapy directly damages the germinal epithelium, the functional unit of the male reproductive tract. The Leydig cells that lie in the interstices of the seminiferous tubules are not harmed (2). Thus, libido and potency are preserved (7). The most harmful chemotherapeutic agents affecting fertility status are the alkylating agents (nitrogen mustard, cyclophosphamide). They are often part of treatment protocols for many of the cancers that commonly affect males during young adulthood (1). Infertility also has been noted to occur after treatment with cisplatin-based chemotherapy regimens for testicular cancer (16).

SPERM BANKING

The goal of semen cryopreservation in the patient with cancer is to store sperm for future use. Before semen collection, the client is instructed to refrain from having sexual intercourse for at least 3 days. The collection is accomplished by masturbation of the ejaculate into a bottle. A split ejaculate is used. The client is advised to catch only the first 1.5–2 ml in the sterile bottle and discard the rest. "The initial portion of the ejaculate contains the highest concentration of sperm, the remainder comprises a higher volume but consists largely of prostatic and seminal vesicle fluid" (2). At this point analysis of the ejaculate is performed to determine suitability for storage and later insemination. The guidelines for a suitable sample were established by the American Fertility Society (17), and are defined as (a) a volume >1 ml, (b) ≥ 50 million motile sperm per milliliter, (c) >60% of sperm moving actively in a purposeful direction, (d) normal sperm morphology, and (e) $\geq 50\%$ of sperm with initial motility after cryopreservation.

"The sperm are mixed with a sodium bicarbonate and formaldehyde solution to immobilize

them for counting. Motility is graded from 0 (no motility) to 4 (vigorously progressive motility). Grade 2 (sluggish) is considered a minimum rating for possible fertility" (2).

If the sample is suitable, it is stored in a preservative through a two-step freezing process for later use by the client. Liquid nitrogen is the most common method of cryopreserving semen. First, the semen is diluted with a cryoprotective medium and frozen in the vapors of the liquid nitrogen. Then, the sample is totally immersed in the liquid nitrogen itself (18). The sample is stored in liquid nitrogen until used by the donor.

Before 1990 semen did not have to be frozen and many couples used fresh semen samples for attempts at achieving pregnancy through in vitro fertilization. In an effort to prevent transmission of sexually transmitted diseases, all couples who currently wish to undergo artificial insemination must have the donor semen frozen and quarantined before use. After 180 days, the donor is tested for human immunodeficiency virus and must be found seronegative before the semen is released (19). The mandatory semen-freezing guidelines have led to increased awareness among health-care professionals regarding the damaging effects of cryopreservation on semen viability and motility. Currently researchers are investigating different types of freezing methods and using different types of preservatives to help decrease the damage caused by the freezing process (11,18). This research will lead to improved semen cryopreservation techniques in the future that will ultimately benefit patients with cancer.

SPERM BANKING ISSUES INVOLVING PATIENTS WITH CANCER

Issues involving sperm banking in patients with cancer are related both to clients and to health-care personnel. Those issues that directly involve the client are the success of sperm banking and delay in initiation of antitumor treatment to bank sperm. Issues that concern health professionals include (a) willingness to discuss issues involving sexuality with patients; (b) viewing quality of life as important while attending to the patients present and future needs; (c) adequate knowledge regarding semen cryopreservation and patients with cancer; and (d) availability of the service and arrangements with an institution for timely collection. Extensive professional debate exists regarding whether or not to advocate sperm banking for patients with cancer. This controversy has led to a sense of

apathy toward potential infertility in men receiving chemotherapy treatment.

Patient-related Issues

Success of Sperm Banking

One issue of debate is the futility of advocating sperm banking for many patients with cancer who at diagnosis present with low sperm counts or poorly motile sperm (20). Additionally, the cryopreservation process will further compromise the semen. Damage that may be caused by the cryopreservation process includes histologic and chemical changes, diminished postthaw survival, diminished life span, and altered functional capacity (12). Paz et al. (18) demonstrated that freezing of semen caused a 14% reduction in sperm vitality and an 8% reduction in motility. As a result, many professionals believe that attempting pregnancy at some later time with pretreatment cryopreserved semen would be unsuccessful.

Despite these problems, researchers have demonstrated successful achievement of pregnancy after using semen that was cryopreserved before chemotherapy treatment. Milligan et al. (7) used retrospective analysis to investigate pregnancy rates of patients with cancer that cryopreserved their semen before receiving chemotherapy. They found that artificial insemination of cryopreserved semen in 133 couples resulted in 27 pregnancies. Six miscarriages and 21 normal deliveries were reported. The mean postthaw sperm count was 55 million per milliliter, and the mean sperm motility was 39%. Most importantly, the lowest sperm count that achieved successful pregnancy was 10 million per milliliter, and the lowest motility rate was 20%. Tournaye et al. (21) found that five patients with Hodgkin's disease who cryopreserved their semen before treatment with chemotherapy achieved successful pregnancy via in vitro fertilization with embryonic transfer or through zygote intrafallopian transfer. Seven healthy infants were born, including one set of twins. The semen analysis findings were similar to those of the Milligan study. The postthaw semen analyses showed low sperm densities (average 26.5 ± 15.9 million per milliliter) and poor initial progressive motility (average $15.9 \pm 9.1\%$).

Sanger et al. (22) reported normal births occurring after artificial insemination using semen that had been frozen for up to 10 years. The patients in the aforementioned studies presented with semen parameters below the criteria established by the American Fertility Society and published scholars. Their success in achieving paternity provides evidence that offering

sperm banking to male patients with cancer is worthwhile and can lead to successful pregnancy after treatment.

Researchers currently are investigating new methods in which to achieve ovum fertilization other than in vitro fertilization in cases of severe male factor infertility. Sperm microinjection is one such method. In this technique, "sperm are injected into the perivitelline space of a mature human oocyte (subzonal sperm microinjection)" (23). This method of attempting ovum fertilization is beneficial for men with poor semen parameters because very few sperm (10–25) are necessary for fertilization and the sperm do not have to navigate through the zona pellucida (23,24). A successful microinjection pregnancy was reported in a case study from a couple in which the male had semen parameters of one million sperm per milliliter, 40% normal forms, and <25% motility. A healthy normal girl weighing 3.83 kg was born after 9 months' gestation (24).

Delaying Treatment

A second issue relates to the delay in initiation of antitumor treatment to allow a patient to bank an adequate amount of semen. Delay in initiation of antitumor treatment is a significant barrier to implementation of sperm banking for patients with cancer. Delaying chemotherapy treatment allows time for continued tumor growth and progression. A large tumor burden can lead to serious life-threatening complications when chemotherapy is initiated. The serious complications include tumor lysis syndrome and disseminated intravascular coagulation (25). A period of 2–3 days is recommended between semen collections, and abstinence from sexual intercourse during semen collection is suggested (2). Sanger et al. (22) recommend approximately three to eight semen specimens, depending primarily on the volume, density, and postthaw semen qualities. This could delay initiation of antitumor treatment for at least 6 to a maximum of 18 days.

Although most researchers advocate semen collection before initiation of chemotherapy, one group of researchers collected semen samples from a 40-year-old man undergoing combination cyclophosphamide-vincristine-prednisone therapy for diffuse large cell lymphoma. They collected samples worthy of cryopreservation for up to 39 days after the start of chemotherapy, after which time oligospermia ensued. As a result of their studies, they found no objective basis for proscribing semen collection during chemotherapy and concluded that fertile specimens are

obtainable during initial chemotherapy treatment (26). Pregnancy had not been attempted with semen cryopreserved by this subject. Therefore, fetal safety issues regarding semen collection during chemotherapy treatment remain unanswered.

The currently preferred practice for patients with cancer is to collect semen before initiation of chemotherapy; therefore, careful consideration of each individual's case must be the rule when determining how long therapy can be delayed without jeopardizing the patient's health. In most cases the patient is not critically ill at diagnosis and has a substantial period of time during diagnostic workup for collection of adequate amounts of semen. The plan of care must be individualized for each patient regarding their status at diagnosis and the time available to collect the optimum amount of samples.

There is a considerable need for research investigating delays in initiating chemotherapy treatment to allow for semen cryopreservation. Investigation is needed to determine how many samples are sufficient to achieve successful pregnancy "most of the time" in patients with cancer. In addition, genetic semen analyses of individuals undergoing chemotherapy treatment would be beneficial in determining chemotherapy's effect on semen before the development of azoospermia. This information could help determine the usefulness of collecting semen samples during initial chemotherapy treatment. Retrospective analyses must be performed on patients who have delayed initiation of treatment for cancer to sperm bank. Nurses need to investigate how long treatment was delayed and how successful the treatment after an initial delay to allow for sperm banking. The answers to such questions are necessary to further validate the importance, safety, and practicality of offering sperm banking to male patients with cancer in an effort to improve quality of life after cancer.

Issues for Professionals

Professional's discomfort discussing sexuality

Health-care professionals need to incorporate sexuality into the plan of care when discussing side effects related to chemotherapy administration with patients, specifically reproductive system damage. Assessing patient's sexuality is an issue that must be addressed early, during the initial client assessment. Oncology nurses should assess the patient's feelings regarding their desire to start a family or their desire to add to an already established family. This assessment should take place during a discussion of the

side effects of chemotherapy, specifically reproductive side effects. Once the nurse finds that the patient is interested in future paternity, he or she may then initiate a discussion regarding semen cryopreservation.

In this author's experience, matters concerning sexuality are rarely discussed with clients. There are many reasons why health-care professionals avoid addressing sexuality issues with patients. Discomfort related to discussing issues of a sexual nature seems to be a major problem. Wilson and Williams (14) surveyed the attitudes and practices of 937 oncology nurses regarding sexuality in patients with cancer. They found that nurses' attitudes regarding sexuality determined whether or not they integrated nursing interventions concerning alterations in sexuality into the plan of care. The authors found that many nurses in their sample did not offer general sexual counselling and failed to initiate referrals for problems related to altered sexuality in patients with cancer.

Additional data describing nurses' current management of sexuality issues in hospitalized patients was obtained from a study of continuous quality improvement at the University of Kentucky Hospital. Kautz et al. (13) studied reasons why nurses do not meet established sexuality nursing care standards. They distributed a questionnaire to 555 full- and part-time registered nurses, of which 312 were returned. The main reported reasons why nurses did not discuss sexual/reproductive issues with clients were as follows: (a) the patients were perceived as being too ill and too anxious to discuss sexual concerns; (b) sexual concerns of patients were perceived as being minor problems of low priority; and (c) the nurses reported that they did not see other nurses addressing patients' sexual problems.

The results of this study were shared with the participants after data collection and analysis was complete. The participants agreed that the above findings were valid. They collectively discussed a need for written material that could be distributed to the clients. They felt that written material would help them to address and teach patients regarding sexual/reproductive concerns. A need for role models was also discussed as a method to help overcome anxiety regarding talking to patients about their sexual concerns.

Overcoming barriers to discussing sexually related issues with patients will need to be accomplished to manage male patients with cancer who are receiving chemotherapy. Nurses may understand the importance of offering semen cryopreservation to this patient population, but if they are uncomfortable, discussing

sexuality issues such as sperm banking may be overlooked if the patient does not initiate the discussion. Most patients are unable to think beyond immediate survival at diagnosis; therefore, the health-care team must think ahead for patients and offer them a chance at future paternity.

Quality of Life After Chemotherapy

Health-care professionals need to become more future oriented in terms of quality of life concepts. Nurses tend to focus on present quality of life issues during active treatment more than those that relate to the future. Hydzik (27) believes that health-care providers need to address the issues of quality of life for individuals who will likely survive active treatment. She claimed that little attention has been focused on the late effects of chemotherapy on gonadal function because it is not a life-threatening problem (27). Although the late effects of chemotherapy on gonadal function do not cause life-threatening complications, they can lead to serious complications regarding quality of life for an individual who has survived active treatment. Nurses who are caring for this population must look beyond the immediate active treatment phase and offer patients sperm banking in an effort to help improve their quality of life in the future.

Knowledge of Chemotherapeutic Effects on Reproduction and of Sperm Banking

Without adequate knowledge regarding chemotherapy and its effect on reproduction, the issue of semen cryopreservation and the patient with cancer will continue to be overlooked. Wilson and Williams (14) investigated nurses' behaviors related to sexuality of patients with cancer and found that oncology nurses lack the knowledge essential to manage reproductive/sexual side effects resulting from cancer treatment. Wilson and Williams further explained that this finding was disturbing in light of the fact that a majority of the nurses in their sample were baccalaureate-prepared nurses with 3–10 years of experience and were members of professional oncology nursing organizations.

No nursing studies regarding nurses' knowledge of reproductive side effects of chemotherapy treatment or nursing management of male infertility resulting from chemotherapy treatment could be located. Nursing research is necessary to help answer basic questions regarding nurses' current knowledge base regarding infertility related to chemotherapy and cur-

rent management of male infertility after chemotherapy treatment.

In addition to knowledge regarding chemotherapy and its effect on reproductive function, oncology nurses need to know the logistics of semen collection and preservation. Nurses need to know how to collect semen for cryopreservation and who to contact for appropriate analysis and handling once collection is complete. Some institutions where young men are treated with chemotherapy for cancer have no association with a cryobank for patients interested in preserving their own semen. Increasing nurses' awareness regarding the success and practicality of sperm banking for male patients with cancer who are receiving chemotherapy treatment may be the beginning step at improving their reproductive potential.

CONCLUSION

There is confusion and lack of support among health-care professionals for offering sperm banking to male patients with cancer. Professionals need to fully understand sperm banking for patients with cancer to form an educated opinion. It should not be assumed that all male patients are unable to produce viable sperm for collection and storage. Researchers have shown that patients with poor semen can successfully father children even with a diagnosis of cancer. Nurses need to work toward improving their knowledge about reproduction and the effects of cancer and cancer treatment on reproduction and should work toward increased acceptance of sperm banking for patients who desire such service. More efficient methods of referring patients for sperm banking need to be devised to ensure timely collection with minimal treatment delay.

During a time when more and more patients with cancer are expected to survive cancer, investigating methods that will help improve quality of life after cancer has become an important aspect of oncology nursing practice. Helping male patients with cancer maintain fertility after cancer is a demonstration of oncology nurses' commitment to improved quality of life for patients with cancer. □

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