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## Ethical and Psychological Considerations in Fertility Preservation Counseling

Hyacinth Browne, MD\*, Sahadat Nurudeen, MD†, Alicia Armstrong, MD, MHSCR\*, and Alan DeCherney, MD\*

\*Program in Reproductive and Adult Endocrinology, NICHD, NIH, Bethesda, Maryland

†Department of Obstetrics and Gynecology, Georgetown University Hospital, Washington, DC

The retrospective analysis by Jennings et al of their 5-year clinical experience with fertility preservation therapies and the ethical considerations associated with these therapies is timely and relevant. Over the past 25 years, the 5-year relative survival rate for all cancers combined improved from 56% to 64% in women.<sup>1</sup> Furthermore, cure rates for 2% of all malignant diseases occurring during childhood and adolescence can exceed 90%.<sup>2–4</sup> By 2010, 1 of 250 adults will be childhood cancer survivors.<sup>4–6</sup> As the life expectancy of cancer survivors improves, the effect of cancer treatment on fertility has become paramount. With increasing survival rates, physicians should be encouraged to discuss fertility preservation options with their patients at the earliest opportunity.<sup>7</sup>

The ethical considerations and dilemmas associated with fertility preservation therapies must be addressed as this field continues to evolve. The use of fertility preservation therapies should take into consideration the age and marital status of the patient, religious or ethical objections to embryo freezing, the type of malignancy and treatment, the risk-to-benefit ratio of delaying treatment, and the patient's prognosis after treatment.<sup>1,7</sup> Furthermore, greater awareness about the psychosocial and psychosexual morbidity associated with cancer-related infertility and cancer patients' attitudes, emotions, and choices with regard to having children is needed.<sup>8</sup> The loss of fertility not only equates to an inability to bear children, but can also affect one's sexuality, identity and role expectations, and the pursuit of intimacy and marriage.<sup>9</sup>

Currently, the choices for preserving fertility in chemotherapy and radiation patients are limited. Down-regulation of the hypothalamic-pituitary-ovarian axis with hormonal agents, such as GnRH analogues, has been used in reproductive- aged patients receiving chemotherapy. In vitro fertilization with embryo cryopreservation, ovarian transposition, and techniques for gamete preservation such as sperm cryopreservation, oocyte, and ovarian tissue cryopreservation are all surgical techniques to preserve fertility though with limited success. Sperm and embryo cryopreservation are the only clinically well-established procedures that have been shown to be effective fertility preservation therapies.

Sperm cryopreservation should be offered to all men undergoing cancer treatment, whereas embryo cryopreservation should be considered first-line therapy for fertility preservation in women who have a partner and enough time to undergo at least one in vitro fertilization cycle.<sup>1</sup> Although these techniques are not feasible for prepubertal girls, women without a partner, and men with low sperm counts, they are associated with higher pregnancy rates compared with oocyte and ovarian tissue cryopreservation. These latter techniques are still investigational and all have demonstrated variable success. They should only be performed as experimental procedures under IRB approved protocols and at centers with the necessary expertise.<sup>1,7,10</sup>

Despite the advances that have been made in this field, patient counseling about fertility preservation is limited. In the present study by Jennings et al, they showed that only 2% of patients in their study, who were at risk for developing premature ovarian failure, were referred to their center to undergo fertility preservation therapy. This is despite the fact that more women in the Netherlands, according to the Dutch Cancer Registry, were reported to have an eightfold risk of developing premature ovarian failure.

Underuse of these techniques may be due to a lack of timely discussions<sup>7</sup> between physicians and patients about treatment-induced infertility.<sup>11,12</sup> Prior studies<sup>13-17</sup> have shown that health care professionals are inconsistent with their discussions involving decisions about fertility preservation despite being aware of the adverse affects of cancer treatment on fertility. This may be attributed to decreased knowledge about the safety, efficacy, and experimental advances in assisted reproductive technology.<sup>13,15</sup> Practitioners have also expressed difficulty in finding facilities and reproductive specialists who perform these procedures.<sup>13,15</sup>

Schover et al,<sup>12</sup> in a recent survey, showed that young male cancer survivors who desired future children lacked timely information about sperm cryopreservation. They reported this to be the most common reason for not banking sperm. Only 60% of these cancer survivors recalled a health provider having discussed fertility before cancer treatment began, and even fewer recalled being given the option of banking sperm (51%). A pilot study by the same group<sup>18</sup> revealed that only 57% of reproductive-aged men and women who survived cancer received information from their health care providers about infertility after cancer, and reported that they had received insufficient information about reproductive issues. Ginsberg et al<sup>19</sup> also showed that young, male cancer patients and their parents wanted to be offered information about fertility preservation early on in treatment, and did not regret their decision to bank sperm even when the semen analyses were abnormal.

Based on the above studies, well-informed cancer patients are more likely to undergo fertility preservation therapies when they discuss their options in a timely manner. Another survey<sup>20</sup> investigated the reasons given by 30 female cancer patients who chose to undergo ovarian cryopreservation and their experiences with this technique. The main reason that these women gave to cryopreserve their ovarian tissue was a desire for children, and that they wanted to have a sense of control over their fertility preferences. In addition, all participants reported that they were well informed about the experimental nature of this

technique, although some patients criticized their physician's lack of knowledge on preserving fertility.

Interest in fertility preservation therapies up to this point has focused on techniques to improve these procedures and pregnancy outcomes. The psychologic aspects of these therapies and the consequence of infertility for cancer survivors have not been adequately addressed. The onset of menopause with its associated symptoms and infertility as a result of treatment has been associated with significant psychosocial distress.

Knobf<sup>21</sup> showed that female cancer patients experienced distress initially after treatment. Their distress was mainly due to the early timing of menopause, but also to the realization that menopause was more than just the loss of their menses. These women felt older and more isolated from their peers. Knobf also showed that younger cancer survivors who were more likely not to have completed their childbearing experienced more quality of life-related issues. These included more psychologic distress, increased anxiety, more unmet needs, and increased worry about finances, work, and self image.

Connell et al<sup>22</sup> also explored the quality of life issues surrounding fertility in women diagnosed with breast cancer at 40 years of age and younger over a 12- to 18-month period. In addition to the uncertainty about current fertility status and anxiety about future reproductive abilities, these women were concerned about the risks of pregnancy to themselves and their unborn infants. They expressed concern of recurrence or progression of their disease during a possible future gestation, passing cancer genes on to their offspring, congenital abnormalities secondary to cancer treatment, and the ability to properly care for a child. These patients conveyed feelings of guilt, selfishness, and anxiety with the notion of actually achieving a pregnancy after completing cancer treatment. These same concerns have also been expressed by male cancer survivors. Even when male cancer patients had cryo-preserved sperm, they were concerned about being unable to father children or the long-term detrimental effects of chemotherapy on their children.<sup>11</sup>

For those individuals who made the decision to forego any future childbearing, another level of unease came with fears of unplanned pregnancies and choices of contraception. Some considered permanent sterilization for themselves but not their partner, because they did not want to limit their partners' abilities to reproduce in the future if they did not survive their cancer. There was even less interest in using hormonal options because of the fear of disease recurrence or progression.<sup>22</sup>

When faced with a loss or impairment of their fertility, a cancer survivor's view of the importance of their fertility can change. Connell et al<sup>22</sup> showed that fertility concerns remained constant over time in cancer patients undergoing treatment except in individuals who initially had no fertility interests. These individuals later experienced regret over not using fertility preservation techniques.

Finally, the psychosocial impact of a successful pregnancy or the option to use fertility preservation therapies can have positive psychologic effects on cancer survivors. Studies<sup>21,23</sup> have shown that patients shared feelings of gratitude, happiness, sense of normalcy, and improved quality of life once they became parents. Saito et al<sup>11</sup> showed that

sperm cryopreservation helped male cancer survivors with their battle against cancer. The knowledge that their fertility potential was secured, by banking sperm, helped them cope with their disease. These patients even went on to recommend sperm cryopreservation to other patients with cancer.

Optimal treatment of infertility in cancer patients, according to Jenninga et al, requires both effective fertility preservation therapies and fulfillment of patients' psychologic needs. Their proposal for an individual approach to discuss and perform these techniques is warranted since the psychologic impact of treatment-induced infertility differs among patients. Individual risk profiles would aid in counseling patients about the most suitable fertility-sparing treatment options available to them.

While the authors effectively inform the reader about the scope of the problem and the failure to offer fertility preservation counseling and fertility preservation therapy, there are limitations of the study. As the authors note, the investigation is limited by its retrospective design, lack of a precise definition of chemotherapy-induced amenorrhea and small numbers. Another important variable, partner data, is not available. As the article states, resumption of menses is not an accurate predictor of ovarian reserve and there is a need for prospective trials with additional hormonal studies such as AMH and inhibin B. Despite these limitations, this article provides additional evidence for fertility counseling and treatment in this population.

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