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Fertility preservation

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Abstract

Many women of childbearing age who have been diagnosed with cancer think that preserving their fertility is important and want information about their options. However Women may later regret not considering fertility issues prior to starting cancer treatment. Understanding that there are fertility preservation options available and referring at-risk patients to specialists can improve patients' emotional outlook and future quality of life. Even women with a poor prognosis may want to consider fertility preservation.

Keywords: Cancer, fertility, cryopreservation, chemotherapy, azoospermia, radiotherapy, Oophorectomy, embryo, *in vitro* fertilization, adoption

Introduction

Cancer treatment can have a major impact on fertility. Fertility Preservation is typically used by patients concerned about their future fertility. Fertility can be affected by a number of different factors, including disease, lifestyle, career, or age. The ability to preserve reproductive tissues is a great option and often recommended by doctors for cancer patients, military personnel, high impact athletes, and transgender clients. Regardless of the causes of infertility, cryopreservation and cryostorage are advances in the medical field that allow patients another attempt at having a family—an option that is priceless to many who have practically given up on raising children.

If you're looking for proof of success in long-term fertility preservation, then we have the perfect story for you...

In 1971, a Japanese American man, who was the last hope in maintaining his family's bloodline, was also informed that he and his wife were unable to have children together. He decided that sperm banking was his only option. He spent years trying to find a surrogate to have his child, but to no avail. Finally, 40 plus years later, his sperm was used in an *in vitro* fertilization procedure that was a success—and a set of twin girls were born. The surrogate couple was eager to parent the twins and allow the man's bloodline to carry on.

Increased Survival and Reduced Fertility

Improvements in treating cancer have enabled many younger persons with cancer to survive. Five-year survival rates with testicular cancer, hematologic malignancies, breast cancer, and other cancers that strike young people may be in the 90% to 95% range. However, treatment of these cancers is often highly detrimental to both male and female reproductive function.

The testis is highly susceptible to the toxic effects of radiation and chemotherapy at all stages of life. Cytotoxic chemotherapy and radiotherapy may produce long-lasting or persistent damage to primordial sperm cells, leading to oligo- or azoospermia. The most common strategy to preserve fertility is cryopreservation of sperm before treatment for later use. Cryopreservation of testicular tissue from prepubescent males remains experimental. Female fertility also may be impaired following surgery, chemotherapy, or radiotherapy treatment for cancer. Ovarian damage is drug- and dose-dependent and is related to age at the time of treatment, with progressively smaller doses producing ovarian failure as the patient's age increases. Total body, abdominal, or pelvic irradiation may cause ovarian and uterine damage, depending on radiation dose, fractionation schedule, and age at time of treatment. An elevated serum follicle-stimulating hormone (FSH) level is the most commonly used biochemical indicator of ovarian damage and failure. However, antimüllerian hormone (AMH) and antral follicle count (AFC) are emerging as other

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markers of ovarian aging Preservation of fertility in females is more complicated than in males. Conservative fertility-sparing treatment such as radical trachelectomy in cervical cancer, hormonal treatment of early endometrial cancer, and conservative surgical management of early-stage epithelial ovarian cancer may be possible for certain women with early invasive disease. Reducing the radiation dose to the ovary by shielding or surgically removing the ovaries from the field of radiation (i.e., oophorectomy) may preserve ovarian function. Suppression of folliculogenesis with GnRHs for fertility preservation has long been controversial. Several small randomized studies

Fertility—a woman’s ability to get pregnant or maintain a pregnancy—can be damaged by some cancer treatments. Many young women facing a cancer diagnosis want to have children in future. Some may not know they have options to protect their fertility. The best time to preserve your fertility is before cancer treatment starts.

For women

The standard fertility preservation methods include:

- Embryo cryopreservation: The process of collecting a woman’s eggs followed by *in vitro* fertilization and freezing of the embryos
- Oocyte cryopreservation: The collection and freezing of unfertilized eggs
- Oophorectomy or ovarian transposition: This procedure involves surgically moving the ovaries to another place in your body, away from where radiation therapy will be directed.
- Specific methods of performing surgery and giving radiation therapy can help protect a woman’s fertility.

Methods of fertility preservation still being researched include

- Ovarian tissue cryopreservation: The freezing of ovarian tissue that can be placed back in the body after cancer treatment
- Ovarian suppression: The use of specific hormones to stop the ovaries from working. Current research suggests that this does not work well for protecting

fertility during cancer treatment, but clinical trials are ongoing.

For men

- Sperm cryopreservation (also called sperm banking) is an effective method for fertility preservation. It involves the freezing and storing of sperm. This is best done before treatment begins, as there is a higher risk of genetic damage in the sperm collected once treatment has started.
- Other methods, such as testicular tissue cryopreservation and reimplantation, are still being studied. This is the removal, freezing, and storage of testicular tissue that can be placed back in the body after cancer treatment.
- Hormonal therapy is not effective for preserving fertility in men.

For parents or guardians of children and teens with cancer

- The standard ways to preserve fertility for teens who have gone through puberty include semen cryopreservation for boys and oocyte cryopreservation for girls.

Methods of fertility preservation for children who have not been through puberty are still being studied and include testicular cryopreservation for boys and ovarian cryopreservation for girls.

Options for Fertility Preservation

The following table gives a brief description of options available to women who wish to preserve their fertility. The American Society of Clinical Oncology and American Society for Reproductive Medicine recommend that, when possible, at-risk patients be referred to a fertility preservation specialist prior to starting cancer treatment. Several resources are listed on the back cover that can help you and your patients locate a fertility preservation specialist.

Fertility preservation options for women diagnosed with cancer

Option	Definition	Timing	Time Requirement	Other Considerations
Embryo Banking	Harvesting eggs, IVF, and freezing of embryos for later implantation	Before or after treatment	10–14 days from menses; outpatient surgical procedure	Need partner or donor sperm
Egg Banking (Experimental)	Harvesting and freezing of unfertilized eggs for IVF and implantation after cancer treatment	Before or after treatment	10–14 days from menses; outpatient surgical procedure	May be attractive to single women or those opposed to embryo creation
Ovarian Tissue Banking (Experimental)	Freezing of ovarian tissue and reimplantation of tissue or <i>in vitro</i> maturation of follicles and fertilization of eggs after cancer treatment	Before or after treatment	Outpatient surgical procedure	Tissue not suitable for transplant if high risk of ovarian metastases; no live births to date from <i>in vitro</i> maturation
Radiation Shielding	Use of shielding to reduce scatter radiation to the ovaries	During treatment	In conjunction with radiation treatments	Does not protect against effects of chemotherapy
Ovarian Transposition	Surgical repositioning of ovaries away from the radiation field	Before treatment	Outpatient procedure or in conjunction with gynecologic cancer surgery	
Radical Trachelectomy	Surgical removal of the cervix with preservation of	During treatment	Inpatient surgical procedure	Limited to early stage cervical

	the uterus			cancer
Ovarian Suppression (Experimental)	GnRH analogs or antagonists used to suppress ovaries	During treatment	In conjunction with chemotherapy	Does not protect from radiation effects
Donor Embryos	Embryos donated by a couple	After treatment	Varies; is done in conjunction with IVF	Donor embryo available through IVF clinics or private agencies
Donor Eggs	Eggs donated by a woman	After treatment	Varies; is done in conjunction with IVF	Patient can choose donor based on various characteristics
Gestational Surrogacy	Woman carries a pregnancy for another woman or couple	After treatment	Varies; time is required to find surrogate and implant embryos	Legal status varies by state
Adoption	Process that creates a legal parent-child relationship	After treatment	Varies depending on type of adoption	After puberty; medical history may be a factor

Table adapted from 2006 American Society of Clinical Oncology recommendations on fertility preservation in cancer patients; and Fertile Hope. Cancer and Fertility: Fast Facts for Reproductive Professionals. IVF=*in vitro* fertilization • GnRH=gonadotropin-releasing hormone

The Role of Oncologists and Other Medical Specialists in Preserving Fertility

Physicians treating younger patients for cancer and noncancerous conditions should be aware of the adverse effects of treatment on fertility and of ways to minimize those effects. Issues to be considered in choosing a treatment plan include the risk of gonadal failure and/or uterine damage with the proposed treatment program, the overall prognosis for the patient, the potential risks of delaying treatment, the impact of any future pregnancy upon the risk of tumor recurrence, and the impact of any required hormonal manipulation on the cancer itself. If gonadal toxicity is unavoidable, physicians also should be knowledgeable about options for fertility preservation and offer patients a referral to a fertility specialist.

While many physicians treating cancer in younger patients are sensitive to these issues, oncologists traditionally have focused on providing the most effective treatments available to help prolong life. With the growing number of cancer survivors, much attention is now focused on their quality of life and the physical, psychological, social, and spiritual issues that they confront. A high quality of life for younger survivors may include the ability to have and raise a family. With such great improvements in survival rates for younger patients, oncologists also must pay attention to the impact of treatment on fertility and ways to preserve it.

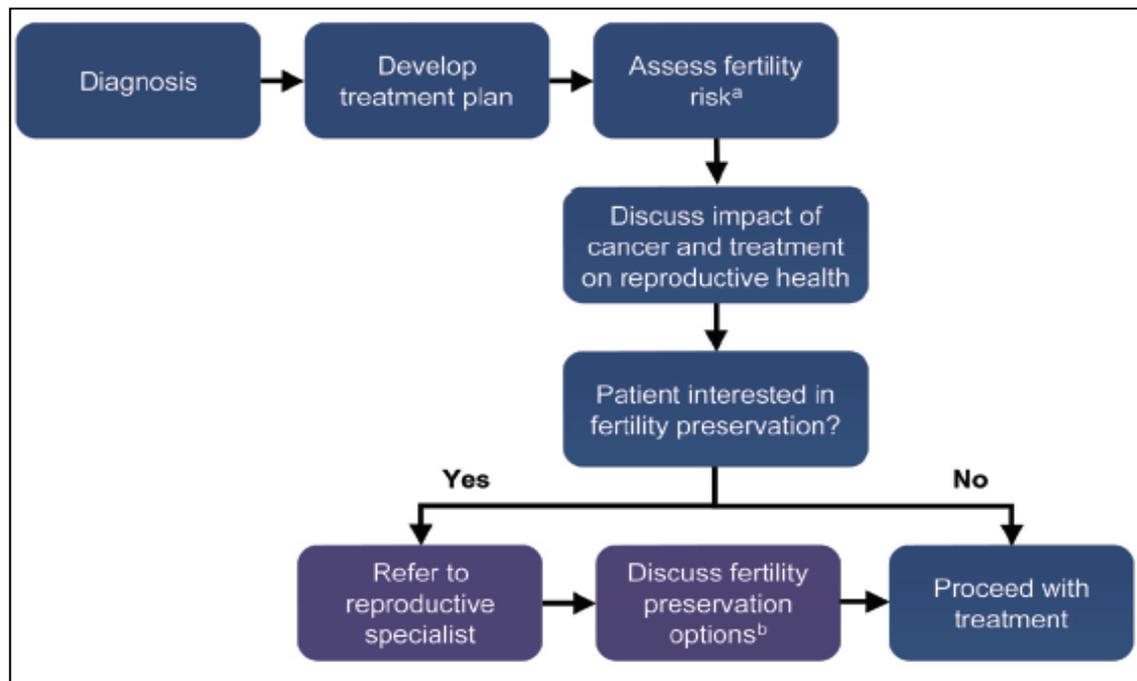
There is some evidence that not all oncologists are as attentive to issues of fertility as patients might wish them to be. If gonadal toxicity is likely, physicians might not always inform patients of options for gamete, embryo, or gonadal tissue storage. In surveys of male cancer patients, for example, 30% to 40% of patients report that physicians did not raise the issue of fertility or sperm preservation. A recent study showed that although 60% of oncologists reported an awareness of the American Society of Clinical Oncology's (ASCO's) guidelines for fertility preservation, less than 25% of the respondents said they follow them on a regular basis, distribute any type of educational materials, or refer patients for fertility-preservation discussions. In addition, some physicians raise the issue with adolescent patients in settings in which it may not be comfortable for the patient to discuss the matter (e.g., in the presence of parents). Oncologists may be unaware of the options available for women or to whom to refer patients for further advice.

We believe that a strong case exists for fertility preservation to be considered in cases of younger persons with treat-able cancers. This involves informing patients and/or their families of options, benefits, and risks, and referring them to fertility specialists, if appropriate. Unless patients are informed or properly referred before treatment, options for later reproduction may be lost. Fertility specialists and patient organizations should work with cancer specialists and cancer organizations to make certain that information is appropriately conveyed and options explained. Medical specialists who use gonadotoxic therapies to treat noncancerous conditions also should be aware of these fertility-preservation options and make appropriate resources available to their patients.

The Role of Fertility Specialists in Preserving Fertility

Reproductive physicians play important roles in helping to preserve the reproductive capacities of young cancer patients. First, they are involved in developing and using procedures to preserve gametes, embryos, and gonadal tissue before treatment. Second, fertility specialists will assist cancer survivors in using preserved gametes and tissue or in providing other assistance in reproduction. The fact that the patient has just been diagnosed with cancer or survived the acute or extended phase of coping with cancer distinguishes the cancer patient from other fertility patients. Variations in type of cancer, time available to onset of treatment, age, partner status, type and dosage of any chemotherapy and radiotherapy, and the risk of sterility with a given treatment regimen require that each case have its own treatment strategy. Consultation with the patient's oncologist is essential. A key issue at the time of treatment of the cancer is whether it is medically feasible to obtain gametes or gonadal tissue for storage and later use. Questions about the patient's health and prognosis also will arise when the patient is deciding later whether to reproduce. When a partner exists, he or she also should be included in the discussion.

Process of Fertility Preservation



Conclusion

Cancer detection and treatment follows international protocols and guidelines. This has enabled to increase survival and decrease adverse effects. Reduced fertility is a common long-term effect of cancer therapy. For young people and their parents, this is a major cause of concern when dealing with the diagnosis and future treatment of their disease. Assisted reproductive technology currently offers a variety of fertility preservation techniques. These possibilities are available in most countries. Although costly, these methods are increasingly in demand. We believe that discussing future fertility is part of the consultation of young female and male patients facing potentially gonadotoxic cancer therapy. Oncohematologists in pediatrics and young adults should recognize the various options available in their country. Cross-border reproductive tourism is however in demand, when options are not available in the patient's homeland. It is the role of reproductive specialists to create various options in their laboratory to preserve fertility potential of cancer patients.

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