

Fertility preservation and reproduction in patients facing gonadotoxic therapies: an Ethics Committee opinion

Ethics Committee of the American Society for Reproductive Medicine

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Chemotherapy and radiation therapy often result in reduced fertility. Patients receiving gonadotoxic treatment should be informed of options for fertility preservation and future reproduction prior to such treatment. Reproduction in the context of cancer also raises a number of ethical issues related to the welfare of both patients and offspring. This document replaces the document titled, "Fertility preservation and reproduction in patients facing gonadotoxic therapies," last published in 2013. (*Fertil Steril*® 2018;110:380–6. ©2018 by American Society for Reproductive Medicine.)

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KEY POINTS

- Clinicians should inform patients receiving potentially gonadotoxic therapies about options for fertility preservation and future reproduction prior to the initiation of such treatment. A collaborative multidisciplinary team approach is encouraged.
- Established methods of fertility preservation include embryo cryopreservation for men and women, sperm cryopreservation in men, and oocyte cryopreservation in women.
- Due to technological advances made in the past decade, oocyte cryopreservation has become a viable option prior to gonadotoxic therapy. It may be appropriate for women whether single or partnered, for postpubertal girls, and for those who have objections to embryo cryopreservation. Data on long-term follow-up are still limited.
- Procedures such as cryopreservation of ovarian tissue in girls and women and testicular tissue in prepubescent males may be offered only in a research setting.
- Data on the use of gonadotropin-releasing hormone analogs (GnRHa) for ovarian suppression have been conflicting; until definitive proof of efficacy is established, other fertility preservation options should be offered in addition to considering GnRHa treatment.
- All available options should be offered and can be performed alone or in combination, often without causing significant delay to cancer treatment.
- Concerns about the welfare of resulting offspring are not sufficient reasons to deny patients facing gonadotoxic treatments assistance in reproducing.
- Parents may act to preserve the fertility of cancer patients who are minors and when the intervention is likely to provide potential benefits to the child. Assent of the child should be obtained if possible. Unless written instructions state otherwise, gametes should be discarded if the child does not survive to adulthood.
- Instructions should be specified about the disposition of stored gametes, embryos, or gonadal tissue in the event of the patient's death, unavailability, or other contingency.
- Preimplantation genetic testing (PGT) to avoid the birth of offspring with a high risk of inherited cancer is ethically acceptable.

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outcomes; however, long-term data on outcomes are still limited. Techniques for cryopreservation of testicular and ovarian tissue are still experimental.

The intersection of gonadotoxic therapy and reproduction raises ethical issues for both cancer and fertility specialists, including issues of experimental vs established therapies, the ability of minors to give consent, the welfare of expected children, and posthumous reproduction (1). In some respects, gonadotoxic treatment-related infertility is not markedly different from other kinds of infertility. In other respects, however, the context of cancer gives rise to issues of patient and offspring welfare that do not arise in other infertility settings. This statement seeks to guide specialists who provide gonadotoxic therapy (oncologists, hematologists, rheumatologists, neurologists, etc.) and fertility specialists in attempts to preserve fertility and to aid patients in reproducing after gonadotoxic treatment.

INCREASED SURVIVAL AND REDUCED FERTILITY

Improvements in treating cancer have enabled many younger persons with cancer to survive (2). Five-year survival rates with testicular cancer, hematologic malignancies, breast cancer, and other cancers that strike young people may be 90% or greater. However, treatment of these cancers is often 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 (3).

Female fertility also may be impaired following surgery, chemotherapy, or radiotherapy treatment for cancer (4). 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 the time of treatment (5). An elevated serum follicle-stimulating hormone (FSH) level is the most traditional biochemical indicator of ovarian damage and failure. However, antimüllerian hormone (AMH) and antral follicle count (AFC) are now commonly used as other markers of ovarian aging (6–8).

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 (9). Reducing the radiation dose to the ovary by shielding or surgically moving the ovaries from the field of radiation (i.e., oophoropexy) may preserve ovarian function (10). Suppression of folliculogenesis with GnRHa for fertility preservation has long been controversial

(11, 12). Multiple randomized studies have been conducted as well as a dozen meta-analyses, which have presented conflicting data. Results have been limited by heterogeneous populations, different chemotherapy regimens, and variations in study endpoints. Recently, the first long-term analysis showed that GnRHa did not prevent primary ovarian insufficiency in lymphoma patients (13). However, a meta-analysis of all the randomized trials conducted in breast cancer patients showed efficacy of ovarian suppression in reducing premature ovarian failure and increasing pregnancy rate (14). The National Comprehensive Cancer Network (NCCN) guidelines were updated to acknowledge the use of GnRHa in preventing chemotherapy-induced ovarian failure in estrogen receptor-negative tumors (15), although the American Society of Clinical Oncology (ASCO) did not change its recommendation. If the cancer treatment can be delayed, it is possible to undergo ovarian stimulation and retrieve and cryopreserve eggs (both mature and immature) or produce embryos that can be frozen for later transfer to the patient or a gestational carrier. Ovarian tissue freezing prior to the initiation of gonadotoxic treatment is considered experimental by the ASRM Practice Committee, but over 87 live births have been reported worldwide (16). It is becoming a viable option for prepubertal girls for whom oocyte or embryo freezing is not an option, for women who either cannot delay treatment or for when hormonal treatments are contraindicated.

THE PATIENT'S DILEMMA: BALANCING CANCER AND FERTILITY

A diagnosis of cancer can be a life crisis for any person. Its impact varies with the type of cancer, treatment prospects, and the physical, emotional, and social resources of the patient. Younger persons face the additional potential loss of reproductive function and the opportunity to have children. Surveys of cancer patients reveal a very strong desire to be informed of available options for fertility preservation and future reproduction (17). At the same time that patients who wish to reproduce in the future (and their parents in cases involving minors) receive a diagnosis of cancer, they also must consider possible effects on fertility. To preserve fertility, they may need to accept changes in standard treatment protocols or undertake steps to preserve gametes or gonadal tissue that carry their own risks and uncertainties.

Men in these circumstances sometimes find producing a sperm sample highly stressful. Women have more options, but all are more intrusive. If there is time before treatment, a woman may undergo ovarian stimulation, oocyte retrieval, and oocyte or embryo cryopreservation. The approach of using oocytes to create embryos that can be cryopreserved indefinitely is an option only for women with male partners or women who are willing to use a sperm donor. Both embryo and oocyte cryopreservation require the woman to undergo an invasive procedure at or soon after the time of diagnosis and while she awaits definitive treatment for her cancer. In the future, laparoscopic ovarian biopsy with ovarian tissue

cryopreservation may become established as a therapy to be offered routinely to patients.

If cancer survivors are not able to reproduce coitally, they may seek medical assistance, including the use of stored gametes or tissue. They also may consider donor gametes, gestational carrier, adoption, or not having children.

THE ROLE OF ONCOLOGISTS AND OTHER MEDICAL SPECIALISTS IN PRESERVING FERTILITY

Physicians treating younger patients for cancer and noncancerous conditions must 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 cancer 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. There can be great variability in how cancer treatments affect fertility and it may be difficult to predict with certainty an individual's risk; patients should be counseled about this uncertainty.

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 (18). 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. It is important that discussions about fertility preservation start as early as possible in the planning of cancer treatment. Fertility preservation can usually be completed in 2–3 weeks; if started promptly, it can often be done without a delay in cancer treatment.

Research has shown that patients desire their oncologists to be attentive to issues of fertility (19). If gonadal toxicity is likely, clinicians might not always inform patients of options for gamete, embryo, or gonadal tissue storage. In a recent study of male cancer patients, for example, only 29% of patients received fertility counseling and 11% attempted sperm banking (19). Another study showed that although 60% of oncologists reported an awareness of 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 (20). 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). Reproductive endocrinologists should collaborate with

oncologists, updating them regarding available technologies and facilitating consultations with patients newly diagnosed with cancer. To further these alliances, education about fertility preservation should be incorporated into training programs for oncology and reproductive endocrinology.

Fertility preservation is a core component of cancer care in younger persons with treatable 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, pediatric and adolescent gynecologists, 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 must 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.

Having just been diagnosed with cancer or surviving the acute or extended phase of coping with cancer distinguishes the cancer patient from other fertility patients. Variations in type of cancer, time available until the 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 has 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 may be included in the discussion, but it is also advisable to discuss these issues with the patient individually.

PRESERVING GONADAL TISSUE, GAMETES, AND EMBRYOS: SAFETY AND EFFICACY OF PROCEDURES

The main role of fertility specialists with cancer patients is counseling and providing preservation of gametes, embryos, or gonadal tissue for use at a future time. The only established clinical option for preservation of male fertility is cryopreservation of spermatozoa obtained either via ejaculation or surgical sperm retrieval. The feasibility depends upon the sexual maturity of the patient. When it is not possible to obtain an ejaculate, sperm can be retrieved by epididymal aspiration or testicular biopsy in sexually mature

men. Not infrequently, sperm produced by cancer patients at the time of diagnosis are of poor quality. With advances in assisted reproduction techniques, in particular intracytoplasmic sperm injection (ICSI), freezing of even one ejaculate before starting cancer treatment provides a plausible chance of having a biological child.

In most instances, preservation of sperm obtained by masturbation poses no particular ethical problem, but may not be allowed in some religious or cultural settings. Where ejaculation is not possible, questions also will arise about the permissibility and circumstances under which electroejaculation, testicular biopsy, testicular sperm extraction, or epididymal sperm aspiration may be appropriate.

Preserving ovarian function when chemotherapy or radiation to the ovaries cannot be avoided is more problematic. The most established strategy for preservation of female fertility is for a woman to undergo a cycle of in vitro fertilization (IVF) and create embryos for later use. This option is available only if there is time before treatment to undergo a cycle of stimulation to obtain oocytes and a safe method of ovarian stimulation exists. Willingness of spouse, partner, or patient to use donor sperm for this purpose also is necessary. When embryo cryopreservation is not feasible or desired, women who have the time and ability to undergo a stimulation cycle should be offered oocyte cryopreservation. Freezing ovarian tissue for later retransplantation or in vitro maturation of oocytes may still be offered with appropriate institutional review board (IRB) oversight when other more established options are not feasible.

Oocyte Cryopreservation

The option for postpubertal females who lack a male partner, do not wish to use donor sperm, or object to embryo cryopreservation is to undergo ovarian stimulation and oocyte retrieval to obtain oocytes that can be cryopreserved and warmed at a later time when the patient is ready to have offspring. Women with a partner also may wish to cryopreserve all or a portion of their oocytes unfertilized in the event that their current relationship dissolves. Oocyte cryopreservation, once deemed experimental due to the technical challenges associated with the size and structural complexity of oocytes, has now seen higher success in many programs as evidenced by recent literature. With the use of cryoprotectants and cryotools in combination with rapid cryopreservation techniques (vitrification) and fertilization with ICSI, multiple clinics have reported increasing pregnancy rates using cryopreserved and warmed oocytes (21, 22), including women who have had gonadotoxic therapy (23). In presenting the option of oocyte cryopreservation, the physician should clearly explain their practice's own experience with oocyte cryopreservation, including pregnancy rates.

The Italian registry of assisted reproductive technology (ART) is the most comprehensive assessment of children born from oocyte cryopreservation to date and shows no apparent increase in congenital anomalies in 2152 live births (24). The Practice Committee of the American Society for

Reproductive Medicine, after reviewing available evidence, concluded that oocyte cryopreservation may be a viable alternative for those women with high potential for ovarian failure for whom embryo cryopreservation is not an option (25).

Ovarian Tissue Cryopreservation

At present, women who cannot delay treatment and undergo ovarian stimulation to create embryos or obtain oocytes for cryopreservation have limited options to preserve their fertility. Protocols do exist, however, for removing and cryopreserving ovarian cortical tissue; the ASRM Practice Committee considers this an experimental procedure. It is anticipated that ovarian tissue will be thawed and implanted after cancer treatment or that techniques for maturing oocytes in vitro will be developed in the future. Although ovarian tissue cryopreservation is still experimental, the technique is promising as a fertility-preservation option and there have been over 87 live births reported from cryopreserved ovarian tissue (16). Major problems include ischemic damage to the tissue pending transplant and revascularization and the theoretical possibility of reintroducing malignant tumor cells. If these and other problems are overcome, this technique may be used without delaying treatment or using hormones to stimulate the ovaries in patients healthy enough to undergo a laparoscopic ovarian biopsy or oophorectomy. Given the experimental state of this procedure, it should be offered only as part of an IRB-approved research protocol, with full disclosure of risks and uncertainty of benefits to the patient.

Issues in Minors with Cancer

The question of preserving fertility also will arise with minor patients, many of whom will not be competent to consent to such efforts. Ethical and legal norms require that procedures done on minors serve their best interests. If invasive procedures are necessary, minors who are able to understand the choice presented must give their assent (permission that is less than full consent). Accepted methods of preserving gonadal material for minors should be offered to parents in the informed consent process and also in accord with the American Academy of Pediatrics' statement on pediatric assent, according to which children should be involved in a developmentally appropriate manner in health-care decisions (26, 27). Investigational methods should be offered to parents only under an IRB-approved protocol.

Postpubertal males ordinarily will be capable of ejaculation and can provide sperm for storage. Care and tact should be taken in discussing this option with them, including discussions outside of the presence of their parents. If the children cannot ejaculate or are too young, then an epididymal sperm aspiration and testicular sperm extraction can be done with their assent and parental consent, as long as this is recognized as a safe and effective way of maintaining male fertility. At some point, testicular tissue cryopreservation in prepubertal males also may be feasible. Testicular tissue cryopreservation in prepubescent

males is considered experimental and only should be performed under the auspices of IRB or surgical innovation committee oversight.

With females, the question of fertility preservation could arise first with postpubertal minors who would be capable of assent or objection. If a stimulation cycle may occur safely, they could assent to oocyte retrieval and cryopreservation to provide oocytes for storage. If ovarian tissue cryopreservation also becomes feasible, they could assent to laparoscopy to obtain ovarian tissue. If minors object to any of these alternatives, the procedures should not be done, despite parental wishes.

If ovarian tissue cryopreservation is shown to be safe and effective, efforts to preserve the fertility of prepubertal females also may be possible. As with older females, both parental consent and the child's assent to ovarian tissue cryopreservation procedures would be necessary. If the child is too young to give assent, parents may consent to removal of ovarian sections if the procedure is deemed to offer a potential benefit to the child. Although persons might differ on this question, reasonable persons could find that the parents' choice to preserve the child's fertility in this way is a reasonable one in light of the relatively limited intrusion (laparoscopic ovarian biopsy) that would be necessary.

Use of Experimental Procedures in Minors

The same requirements of minor assent, parental consent, and net benefit would apply to use of these procedures by minor children when the procedures are still experimental (28). Because their experimental use is beneficial for the minor patient, it might be done with his/her assent if developmentally appropriate or with the consent of the parents, only if an IRB finds that the expected benefits of future reproduction to the child outweigh the burdens of the procedure for obtaining gametes or gonadal tissue. If the child is postpubertal and there is time, then a controlled ovarian stimulation cycle could occur. If there is not time or the patient has not entered puberty, experimental ovarian cryopreservation might be offered as part of an IRB-approved protocol for preserving the fertility of younger female cancer patients with the assent of the patient and parental consent.

DIRECTIONS FOR DISPOSITION OF STORED GAMETES, EMBRYOS, AND GONADAL TISSUE

Persons whose gametes, embryos, or tissue are stored to preserve fertility or their legal guardians should give directions for disposition of that tissue in the future. This might be done best when the gametes, embryos, or gonadal tissue are removed or preserved, but directions can be given or amended at any later time that the patient wishes. For minors, directions should be updated by the gamete provider when they reach the age of majority.

As with directions for storing embryos, the patient should specify what should be done with stored gametes, embryos, or gonadal tissue if he/she dies or otherwise is unavailable; does not pay storage fees; or has abandoned the gametes, embryos, or gonadal tissue. Also important is that patients specify in writing in advance that they want those materials discarded

or used in research, or whether they consent to use of them for posthumous reproduction and by whom. For minors, unless written instructions provide otherwise, gametes should be discarded if the minor does not survive to adulthood.

ASSISTING CANCER SURVIVORS TO REPRODUCE

Persons of reproductive age who survive cancer may seek to reproduce. Discussions about fertility should be incorporated into survivorship programs. If girls or women were not able to cryopreserve oocytes before treatment, they may consider doing this post-treatment if possible. Patients who have retained reproductive function may be able to conceive coitally. If they have diminished reproductive function, they may seek the help of fertility specialists. In some cases, they can make use of previously stored gametes, embryos, or gonadal tissue for that purpose. Other options that may be appropriate include donor gametes, donor embryos, gestational surrogacy, and adoption.

Apart from the risks posed by fertility treatment, physicians may be concerned about the risks posed by pregnancy on cancer recurrence. It is generally recommended that pregnancy be delayed until cancer treatment is concluded because of concerns over the impact of treatment on the fetus. The optimal timing of conception after cancer treatment may be uncertain for some patients.

Reproductive physicians treating cancer survivors should be cognizant of the patient's medical status, treatment plan, prognosis, and potential harmful effects of the therapy. Such effects may occur because of theoretic mutagenic effects secondary to previous cancer treatment, the reproductive techniques themselves, or the risk of heritable disease. They also may arise from psychosocial factors, such as the prospect of recurrence of cancer and a reduced lifespan or the posthumous use of gametes. Physicians also must disclose fully the accepted or experimental status of any procedures offered, as will be the case when cryopreserved ovarian tissue is used to reproduce.

Risks to Offspring from Reproduction

Providing medical assistance to cancer survivors may on occasion raise ethical issues about the impact of their reproduction on future children. One set of issues concerns whether resulting offspring are at a higher risk for congenital anomalies, chromosomal defects, or cancer because of previous treatment or the effects of the assisted reproductive technologies.

Studies that have examined pregnancy outcomes in cancer survivors have found no statistically significant increase in congenital malformations or malignant neoplasms in the resulting offspring (29). These studies, however, primarily evaluated women who conceived spontaneously many years after chemotherapy treatment. Patients should be counseled about the current state of knowledge about the risks of assisted reproductive techniques to the health of offspring.

Posthumous Use of Stored Reproductive Tissue

In some cases, persons who have stored gametes, embryos, or gonadal tissue will die before they have had an opportunity to

use them. Patients, surviving spouses, or family might want to have the gametes or tissue used for reproduction, for donation to others, or for research. If this occurs, it could lead to the deceased person reproducing after death with his or her partner at the time of storage or with other recipients of their donated gametes or embryos.

A relevant question is whether the deceased had consented to posthumous use of his or her stored tissue or gametes in a consent form, advance directive, or another reliable indicator of consent before death. The legal system has recognized that the person's prior wishes about disposition of reproductive material is controlling after death. Instructions that all such material shall be destroyed or not used after death should be honored. Similarly, the law permits gametes and embryos to be used after death if the person has given such directions or if the partner or next of kin has dispositional control of them. Courts have also accepted that children born after posthumous conception or implantation are the legal offspring of the deceased if he or she gave instructions that gametes or embryos may be used after his or her death for reproduction (30, 31).

Until there is more experience with posthumous reproduction, a policy of allowing posthumous reproduction only when the deceased has specifically provided an advance directive and the surviving spouse or other designee agrees is a sound one (32). As a result, it is essential that programs storing gametes, embryos, or gonadal tissue for cancer patients inform patients of the options for disposition of those materials at a future time when the depositor is, due to death, incompetency, or unavailability, unable to consent themselves to disposition. Whether offspring conceived or implanted posthumously will be recognized under the deceased's will or state inheritance laws will depend on the law of the state in which these events occur. Since legal decisions related to posthumous use of stored tissue or gametes may vary between jurisdictions, patients interested in pursuing this option should be advised to consult with knowledgeable legal counsel.

RISK OF POTENTIAL CANCER IN OFFSPRING

As previously noted, there do not appear to be major mutagenic effects in offspring born to patients successfully treated for cancer (29, 33). However, an additional concern can arise in patients with cancer-predisposing germline mutations. Some persons with heritable cancers want to reproduce only if they have reasonable assurance that their child would not have a high risk for their cancer and the burdens entailed in that risk.

Techniques for prenatal diagnosis and PGT provide a way for parents with heritable cancers to prevent transmission of that risk to offspring. Patients intent on minimizing the risk of transmitting cancer genes to offspring may be reluctant to use prenatal diagnosis and termination of pregnancy but would accept PGT for that purpose.

PGT is generally accepted to reduce the risk of the birth of a child with autosomal or X-linked diseases, such as cystic fibrosis, Tay-Sachs disease, sickle cell anemia, and fragile X syndrome. Unlike the early onset of these conditions, the

risk of inheriting cancer might not eventuate until much later in the life of the child, and the gene for the disease may not be fully penetrant. While some persons would argue that the time of onset of disease or variation in risk for inherited cancer has enough ethical weight to justify treating those cases differently, this Committee believes that when the genetic risks are substantial and preimplantation tests for them exist, couples may ethically choose to test embryos to avoid having children with a high risk of those cancers (34).

CONCLUSIONS

Patients facing gonadotoxic treatments have important needs in preserving and exercising fertility that cancer and fertility specialists should try to protect. Oncologists should be encouraged to refer patients to a reproductive endocrinologist early in the planning of treatment. When damage to reproductive organs due to gonadotoxic treatment is unavoidable, health-care providers should inform patients of options for storing gametes, embryos, or gonadal tissue and refer them to fertility specialists who can provide or counsel them about those services. Counseling by a qualified mental-health professional and genetic counselor, when appropriate, also should be offered.

Fertility programs should counsel patients and survivors on the risks of gonadotoxic treatment on fertility and the options for and risks of preserving fertility and reproducing afterward. Fertility-preservation procedures that have not been shown to be safe and effective should be offered to patients only in an experimental setting under IRB oversight. Parents may act to preserve reproductive options of minor children undergoing gonadotoxic treatment as long as they seek the assent of a child able to provide it, the intervention does not pose undue risk, and the intervention offers a reasonable chance of net benefit to the child.

Concerns about the welfare of resulting offspring, whether due to an expected shortened lifespan of the parent or effects of cancer or infertility treatment (in the present state of knowledge) ordinarily are not a sufficient reason to deny cancer patients assistance in reproducing. Programs storing gametes, embryos, or gonadal tissue for cancer patients should request clear instructions about what should be done with stored materials in the event of the patient's death, unavailability, nonpayment of storage fees, or other contingency. Spouses or family members with legal rights to dispose of a deceased patient's stored gametes or other material should use them for posthumous reproduction only if the deceased had previously consented to such posthumous use.

Physicians should assess the likely impact on offspring of cancer treatments and fertility preservation and assisted reproduction procedures and inform patients accordingly. PGT to reduce the birth of offspring with a high risk of inherited cancer is ethically acceptable.

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treatment in all cases. This report was approved by the Ethics Committee of the American Society for Reproductive Medicine and the Board of Directors of the American Society for Reproductive Medicine.

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