Cancer and Fertility: Ethical and Legal Challenges

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Preserving the fertility of younger cancer patients requires coordinated efforts and attention to ethical issues by oncologists and fertility specialists. Although sperm is easily stored, freezing eggs or ovarian tissue is still experimental and should not be offered except as part of an experimental protocol. When gametic material is stored for later use, written directives for posthumous use may be given effect, and subsequently born children may be recognized as legal offspring of the deceased. Concerns about the welfare of offspring resulting from an expected shortened life span of the parent are not sufficient reason to deny cancer survivors assistance in reproducing. [J Natl Cancer Inst Monogr 2005;34:104–6]

Improvements in detection and treatment have enabled many younger persons to survive cancer, but successful treatment may also impair fertility. The intersection of cancer and reproduction raises ethical issues for oncologists and fertility specialists, and legal and policy issues for society.

The Patient’s Dilemma: Balancing Cancer and Fertility

A diagnosis of cancer is a life crisis for any person. During the stressful period of receiving a diagnosis and treatment plan, patients (and their parents, in the case of a minor) must also consider possible choices to preserve fertility. They may be given the option of more conservative treatment for the cancer or the chance to preserve gametes or gonadal tissue. Each choice carries risks and uncertainties.

If treatment brings cure or remission, cancer survivors may consider having children. Some couples even choose to become parents when one spouse has died or is dying of cancer, for example, by using cryopreserved sperm to conceive. If they are unable to reproduce coitally, they may seek reproductive assistance, including the use of stored gametes or tissue. They may also consider donor gametes, gestational surrogacy, adoption, or childlessness.

The Oncologist’s Role in Preserving Fertility

Physicians treating younger patients for cancer should be aware of the adverse effects of treatment on fertility and of ways to minimize those effects. If gonadal toxicity is unavoidable, they should also be knowledgeable about options for fertility preservation and offer referrals to patients.

Although many physicians treating cancer in younger patients are sensitive to these issues, oncologists have traditionally focused more on providing the most effective treatments available, and less on the patient’s posttreatment quality of life. All oncologists may not be as attentive to issues of fertility as the patients might like. A recent survey of oncologists at two major medical centers showed that close to half rarely or never raised the issue of fertility or sperm preservation, even though these are the easiest options that exist (1).

Oncologists may also be unaware of the options available for women or to whom to refer their patients for further advice. Fertility and survivor groups should work with oncology organizations to make sure that information is appropriately conveyed and options explained to younger patients faced with cancer.

The Role of Fertility Specialists

The fact that a 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, and recommended treatments (i.e., chemotherapy, radiation, bioimmunotherapy, surgery) require that each case have its own treatment strategy. Consultation with the patient’s oncologist will often be essential.

Preserving Gonadal Tissue and Gametes: Safety and Efficacy of Procedures

A main role fertility doctors play with cancer patients is preserving gametes or gonadal tissue for use at a future time. The only established clinical option for preservation of male fertility is cryopreservation of spermatozoa in sexually mature males. When it is not possible to obtain ejaculate, sperm can be retrieved by epididymal aspiration or testicular biopsy. With advances in assisted reproduction techniques, and in particular intracytoplasmic sperm injection, freezing of even one ejaculate before starting cancer treatment provides a reasonable chance of having a biologic child. A case of a child born with sperm frozen for 21 years after treatment for testicular cancer has even been reported (2). However, several recent reports from sperm-banking facilities concer that less than 20% of men who store sperm before cancer treatment end up using it to try to conceive (3–6). Given that insurance rarely covers the costs of cryopreservation, patients should be made aware of the financial costs as well as the benefits of sperm banking.

Preserving ovarian function when chemotherapy or radiation to the ovaries cannot be avoided is more problematic. The only successful technique currently available is to undergo a cycle of in vitro fertilization and create embryos for later use, but this option is available only if a person has the resources, there is time before treatment, and it is safe to use hormonal drugs to stimulate the ovaries—a controversial issue for women with breast cancer. A spouse, partner, or willingness to use donor sperm is also necessary. Women without a partner who are...
unwilling to use donor sperm have only experimental options with a poor track record of leading to pregnancy (i.e., cryopreserving mature, unfertilized eggs or freezing ovarian tissue for later retransplantation or in vitro maturation of oocytes).

**Freezing eggs.** Freezing human oocytes poses a number of problems, because of their size and structural complexity. Although as many as 100 children may have been born worldwide after insemination of thawed oocytes, success rates remain far lower than those for thawed embryos. As a recent review noted, “the pregnancy rate is not high enough to justify its routine use in clinical practice” (7).

At present, no program should advertise or offer oocyte cryopreservation as an established technique. Programs may, however, offer it experimentally as part of an institutional review board (IRB)–approved protocol, with full disclosure of risks and benefits to the patient–subject.

**Freezing ovarian tissue.** Prepubertal girls or women who cannot delay cancer treatment to undergo ovarian stimulation have no currently effective way to preserve their fertility. Experimental protocols do exist, however, for removing and freezing ovarian cortical tissue. The hope is that ovarian tissue can be thawed and reimplanted after cancer treatment as an autograft, either back into to the pelvic cavity or to a heterotrophic site, so that mature oocytes could be fertilized naturally or harvested for in vitro fertilization. Alternatively, if in vitro maturation of oocytes became possible, primordial follicles in the tissue could be used for that purpose.

Although no births have yet been reported, one team has reported ovulation and a human embryo resulting from ovarian tissue retransplanted to the arm, and further successes might occur (8). A major problem is ischemic damage to the tissue pending transplant and revascularization (9). Another concern is whether autotransplantation of the tissue could reintroduce malignant cells.

Some clinics in the United States are offering cryopreservation of ovarian tissue on an experimental basis, with women paying the costs out-of-pocket. Given the unproven status of this procedure, it is essential that it be offered only as part of an IRB-approved protocol, with full disclosure of risks and uncertainty. Later efforts to thaw and retransplant should also be subject to IRB review until the safety and efficacy of retransplantation or other use of the tissue has been established.

**Minors.** The question of preserving fertility will also arise with minor patients, many of whom will not be competent themselves to consent to such efforts. Ethical and legal norms require that procedures done on minors should serve their best interests (10). If invasive procedures are necessary, a minor who is able to understand the issue must give their assent (permission less than full consent) (11,12). This means that the procedure can be done if the minor agrees, but not if he or she objects. If the patient is too young to give assent, parents may not consent to experimental procedures involving more than minimal risk unless there are positive expected net benefits for the child.

Postpubertal males will ordinarily be capable of ejaculation and can provide sperm for storage. Sensitivity and tact should be taken in discussing this option with them, including discussion outside the presence of their parents. If they cannot ejaculate, in some cases a testicular sperm extraction or epididymal sperm aspiration could be done with their assent and parental consent. In the future, prepubertal boys may be candidates for the harvesting of spermatogonial cells via testicular biopsy.

Postpubertal females should be capable of assenting or objecting to either established or experimental procedures, for example, the choice of whether or not to undergo a cycle of ovarian stimulation to create embryos or freeze eggs or whether or not to agree to an invasive procedure to collect ovarian tissue. If a teenager objects to any of these procedures, they should not be done, despite parental wishes.

If ovarian tissue cryopreservation were safe and effective, prepubertal girls could assent with parent consent to laparoscopy to obtain tissue. For girls too young to give assent (typically, those children under 7 years of age), parents may consent to the procedure if reasonable persons would find that the potential benefit is sufficient to justify the medical risks and discomforts. In such cases it would be advisable to have an ethics committee or similar body review the parental and physician decision to go forward.

The same requirements of minor assent, parental consent, and net benefit would apply when procedures are still experimental (11,12). Because the procedures’ experimental use is intended to benefit the minor subject, they might be done with the minor’s assent and the consent of his or her parents if an IRB finds that the potential benefit of preserving fertility outweighs the burdens of retrieving gametes or gonadal tissue.

### Directions for Disposition of Stored Gametes and Tissue

Persons (or their legal guardians) whose gametes, embryos, or tissue is stored to preserve fertility should give directions for future disposition of that tissue. This might best be done when the gametes or tissue are removed or preserved, but directions can be given at any later time that the patient chooses. It is especially crucial that the patient (or legal guardian) specify what should be done with stored gametes or tissue if the person storing them dies. A written document should specify whether stored materials should be discarded or used by designated individuals for posthumous reproduction.

### Assisting Cancer Patients to Reproduce.

Cancer survivors may wish to become parents. If they have lost reproductive function, they may seek the help of fertility specialists to make use of previously stored gametes or gonadal tissue. Fertility specialists treating cancer patients and survivors should be cognizant of the patient’s medical status, treatment plan, and prognosis, as well as unusual health risks for future offspring and the potential harmful effects, if any, of pregnancy for a female survivor.

**Harm to offspring from reproduction.** Fertility assistance to cancer survivors may raise ethical issues about the effect of their reproduction on future children. One set of issues concerns whether offspring are at a higher risk for physical defects or cancer because of lingering treatment effects, genetic mutation, or the effects of the fertility preservation or assistance process.

A second set of issues concerns the possibility that the cancer patient who appears to have been cured or in remission will have a recurrence of the cancer and die prematurely, leaving a minor child bereft of one parent. Some physicians have questioned whether it is ethical to enable persons to reproduce in situations in which the parent faces a greatly lowered life span or ability to care for a child (13). Ethical analysis, however, yields no convincing reason to deny cancer survivors help in reproducing. Although the effect of the early loss of a parent on a child is
regrettable, many children experience stress and sorrow from other circumstances of their birth. The risk that a cancer survivor will die sooner than other parents does not impose an appreciably different burden than the other causes of suffering and unhappiness that persons face in their lives. Protecting such children by preventing their birth altogether is not a reasonable ground for denying cancer survivors the chance to reproduce (14).

**Posthumous use of stored tissue.** In some cases the persons who have stored gametes or gonadal tissue will die before they have had a chance to use them. Surviving spouses or family might want to use stored gametes or tissue for reproduction or for donation to others, leading to the deceased’s posthumous reproduction.

Although it is desirable that children have two rearing parents, the risks to children of diminished welfare as a result of their being raised by a single parent are not great enough in most cases to make helping single parents reproduce unethical. Whether the gametes used for a single person to reproduce come from a posthumous source, an anonymous living source, or a known living source would not ordinarily be of ethical relevance. If it were, then use by a surviving spouse or partner who had hoped to have children with the deceased would present a strong case for use of those gametes.

A key question is whether the deceased had consented to posthumous use of his or her stored tissue or gametes before death in an advanced directive, a will, or other reliable indicator of that consent. The legal system has recognized that the person’s prior wishes about disposition of reproductive material are generally controlling after death. Instructions that all such material be destroyed or not used after death should be honored. Similarly, gametes and embryos may be used after death if the person has given directions for such use. Several courts and state legislatures now recognize that children born after posthumous conception or implantation are the legal offspring of the deceased if he or she gave instructions while alive that stored material could be used for reproduction after his or her death (15).

Until there is more experience with posthumous reproduction, it is sound policy to allow posthumous reproduction with stored gametes or tissue only when the deceased has given specific consent. It is essential that programs storing gametes, embryos, or gonadal tissue for cancer patients inform patients of the options for making advance directives for future, including postmortem, use. Whether posthumously conceived or implanted offspring will inherit property from the deceased will qualify for government benefits will depend on the law of the jurisdiction in which death occurs.

**Conclusion**

Cancer patients have important needs in preserving and exercising fertility that oncologists and fertility specialists should try to protect. Where treatment damage to reproductive organs is unavoidable, oncologists should inform patients of options for storing gametes or gonadal tissue and refer them to physicians or persons who can provide or counsel them about those services.

Fertility programs should counsel cancer patients and survivors on the risks of cancer treatment on fertility and on the options for preserving fertility and reproducing after treatment. Concerns about the welfare of resulting offspring, whether a result of an expected shortened life span of the parent or of the effects of cancer or infertility treatment, are ordinarily not a sufficient reason to deny cancer patients assistance in reproducing.

Fertility preservation procedures not shown to be safe and effective should be offered to cancer patients only in an experimental setting or in circumstances in which they are fully aware of the limitations of the offered procedures. Parents may act to preserve reproductive options of minor children undergoing cancer treatment as long as the minor assents and the intervention does not pose undue risk.

Programs storing gametes, embryos, or gonadal tissue for cancer patients should request clear and precise instructions about what should be done with stored materials in the event of the patient’s death. If the deceased had previously consented to posthumous use of stored gametes or gonadal tissue, the law should recognize resulting offspring as the natural and legitimate children of the deceased.

**References**