Preserving Fertility In Young Cancer Patients: A Medical, Ethical And Legal Challenge

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ABSTRACT

Modern cancer treatment, while often producing lifelong cures, can also result in permanent damage to many organ systems. Although more than 70% of children and young adults can be cured of their cancers, infertility, which frequently accompanies curative therapies for many common types of cancer, is one of the most devastating long-term complications. In this paper we discuss the medical, legal, and ethical ramifications of attempting to prevent this side effect and present some of the challenges that remain.

INTRODUCTION

More than 70% of children and young adults with cancer can be cured. This remarkable statistic is the result of more than 35 years of collaborative laboratory and clinical research in the United States and abroad. As a result, it has been estimated that as many as 1 in 250 adults under the age of 45 will be a long-term survivor of childhood cancer by the end of this decade.[1] Thus, we are currently caring for a unique population of aging cancer survivors. However, this success has come at the price of late- and long-term side effects, from both the initial disease and from the sequelae of curative treatment. One of the most devastating of these complications is infertility. Two real-life examples from our institution are illustrative (we have changed their names for confidentiality purposes).

When Jessica was 17 and a senior in high school, preparing to try out for the girl’s tennis team, she noticed that her left leg was weak and her toes were numb. She shrugged it off as many teenagers are wont to do, but during the subsequent months, the symptoms steadily got worse. She finally told her mother, who immediately took her to see their family physician. Her doctor was quite worried about Jessica’s physical examination, which showed a pronounced neurologic deficit in her left leg, accompanied by pain in her tailbone and the back of her left thigh. Her doctor immediately scheduled
Jessica was referred to the Duke University Medical Center, which is where Dr. Rosoff met her. A biopsy revealed she had a peripheral primitive neuroectodermal tumor, a relatively uncommon type of cancer affecting teenagers and young adults. Fortunately, there was no evidence of metastatic disease. She was treated with intensive chemotherapy (including the drugs cyclophosphamide and ifosfamide) and local radiotherapy. The latter used a specialized, 3-D, CT simulator to limit the size of the radiation field to as small an area as possible. While Jessica endured many side effects during her treatment that resulted in numerous stays in the hospital for short-term complications, she did remarkably well.

Jessica is now a lively and intelligent 22-year old young woman attending a renowned university in Virginia; she has an excellent chance of being cured. She is playing tennis again and is generally feeling well. Unfortunately, she most likely will be unable to have her own biological children due to the effects of chemotherapy and possibly the radiation. One must wonder whether there was any way this could have been avoided.

When Ben was 14, he noticed a painful lump in his right wrist. An x-ray showed what appeared to be a malignant tumor arising from the radius. A CT scan confirmed the existence of a tumor. A biopsy revealed an osteosarcoma, a type of bone cancer, the same kind Teddy Kennedy, Jr. had. Luckily, the cancer had not spread. Ben was treated with intensive chemotherapy and surgery, and he, like Jessica, has done extremely well. Ben is now a 16-year old high school junior. He, too, is probably cured and will grow up to be a healthy man just like his father. Unlike his dad, however, it is almost certain he is sterile, a result of the ifosfamide chemotherapy he received to cure his cancer.

Jessica and Ben are but two of the thousands of patients who have been helped to live their lives, relatively healthy and free of cancer, but are unable to have biological children. A significant percentage of long-term survivors suffer this complication.[2] Like other people with infertility, the psychological effects can be consuming.[3] One commentator has explained these effects occur because:

*Parenthood is an integral part of the life most individuals envision for themselves. This vision is deeply rooted in American culture and is continually reinforced by social norms. The biological link between parents and children is a fundamental part of this vision - - most people assume that someday they will have their ‘own’ children. Women are raised to see themselves as future childbearers; men, to understand fertility as central to masculinity. As a result of this socialization, most Americans consider biological parenthood as an essential component of a fulfilled life.[4]*

Consequently, because “the desire to have children must be among the most basic of human instincts, and denying it can lead to considerable psychological and social difficulties,”[5] infertility often creates one of the most distressing life crises for the individual(s) dealing with it.[6] The long-term inability to conceive a child can evoke
significant feelings of loss and hopelessness.[7] The literature on the psychological consequences of infertility shows that infertility can be a devastating experience, especially for women.[8] Studies have revealed that there are significant differences between fertile and infertile women, with the latter having generally higher stress-levels and lower self-esteem.[9] Infertile women have similar levels of anxiety and depression as compared to women with cardiac disease, cancer, hypertension, and HIV, thus revealing the intense impact that infertility can have on an individual’s psychological health.[10] In addition, coping with the multitude of medical decisions and the uncertainties accompanying infertility can create great emotional upheaval.[11] Thus, the psychological effects of infertility may be even more overwhelming in the population of childhood cancer survivors who have already survived life-threatening illness and have dealt with numerous medical decisions and treatment.

Some might say that young cancer survivors should be grateful they are alive and shouldn’t worry about this “minor” problem, for they can always adopt children or take advantage of the latest assisted fertilization and reproduction techniques using donor eggs and sperm. Moreover, when one views dispassionately the severity of known late effects of chemotherapy and radiation, some of which can be life-threatening, infertility tends to pale by comparison. But this attitude ignores the fact that most people prefer to have their own biological children. Indeed, the experience of one of the authors seeing adults in our Long Term Follow-Up Clinic has convinced us of the personal tragedy that infertility due to cancer treatment is for many survivors. This is especially true for people who were treated as children, but also applies to young adult women who suffer the same consequences. Even if services to preserve fertility were available at the time, it is uncommon for patients and families to have been consulted or informed of this possibility of this side effect. All-too-often we have seen young women and men devastated by the knowledge that, in addition to the potential for treatment-related heart disease and second cancers, they will not be able to bear or father children. Oncologists who care for children and young adults spend a lot of time thinking of ways to avoid both the short- and long-term complications of treatment. Can the sterilizing effects of intensive chemotherapy and radiation be avoided?

To attempt to circumvent the sterilizing effects of chemotherapy and radiation on children who have cancer, we have suggested that fertility preservation services should be available and offered to all patients who are either of childbearing age at the time of their diagnosis or have the potential to be so in the future. Patients under the age of 18 would be provided with the option of having their sperm or ova collected and cryopreserved (frozen) until they are adults, at which time they would have the option of using their preserved gametes to have their biological children. For boys and men, the collection would be obtained using standard techniques of masturbation, and at least one specimen would be obtained for cryopreservation. The collection for females would be more invasive and would need to be done through a surgical procedure since the “usual” way of obtaining eggs via the time-consuming process of hormone stimulation cannot be used (see below). Oocytes would be gathered as ovarian cortical slices using laparoscopic techniques.[12] Thus, the age range for the girls who could use this service would be based on whether the physician believed he/she could obtain a
sufficient tissue specimen. For girls who would be having abdominal surgery as part of their cancer treatment or for another reason (usually diagnosis, or possibly oophorectomy for pelvic radiation therapy), the laparoscopy would occur at the same time. However, the girls who would not need abdominal surgery would need to undergo a separate laparoscopy to obtain the cortical slice. For both procedures, the girls would have to be sedated under general anesthesia. Finally, only one ovary would be biopsied in each female patient due to both the low, but real, risk of ovarian damage, and the fact that more than enough eggs can be harvested.

However, as simple as this proposal might appear on first review, there are many pitfalls and potential roadblocks that arise when practical implementation looms near. In the remainder of this article, we will discuss the medical, ethical and legal aspects of fertility preservation in cancer patients, especially children: all three areas present challenges that need to be addressed and overcome in order to provide the highest quality of care to this vulnerable population and thus attempt to not deprive them of one of life’s greatest fulfillments. Finally, we will discuss the program we have created at Duke that we suggest could serve as a model at other institutions.

THE MEDICAL AND ETHICAL CHALLENGES

We believe that boys, girls, men, and women should be offered the opportunity to take advantage of fertility preservation services, but the implications of participation are different for the two sexes. Thus, we will discuss the access to gamete preservation by boys and young men first, since they are relatively straightforward. Let us first describe exactly how this is done and some of the obstacles.

The technology to collect semen by masturbation and then to store it by cryopreservation has existed for some time and is quite successful. With advanced assisted reproduction techniques like intracytoplasmic sperm injection, the number of viable sperm available upon thawing is not as crucial as it once was when artificial (in vivo) insemination was the only available method. Cryopreservation of sperm is fairly simple and straightforward, does not require enormous amounts of equipment, and is also relatively inexpensive. Semen can be stored in this way almost indefinitely, or at least for many years without significant loss of viability.

For typical semen collection in healthy adult males, multiple samples are taken over a two to three week period.[13] Delays of this length of time before initiating cancer therapy for children are usually not possible due to the necessity for starting treatment quickly because most cancers in young people are very aggressive and rapidly growing.[14] Consequently, boys may only be able to provide one or two ejaculates at best. Furthermore, the size or volume, and thus the number of viable gametes, may be affected by both the age of the child and the severity of his illness. Having a small sample, however, does not decrease the potential benefit of the entire process because “a single ejaculate, even if of poor quality, will usually contain at least a few million living
sperm” that can be cryopreserved for later use.[15] Some young cancer patients may have a difficult time ejaculating, which could also be an impediment to successful collection.[16]

There are biological reasons why it is difficult to collect viable sperm from pre-pubertal boys, but this has not stopped some investigators from either doing testicular biopsies[17] or using the technique of electroejaculation (this approach is most often used in paraplegic men who wish to father children and are impotent due to their spinal cord injuries).[18] While the former has not been reported in the literature to have been tried in the United States, where the proscriptions against using unproved and risky technologies on minors are widely observed, perhaps we may need to reconsider this policy in this special population of boys. However, there is no question that the chances of success (defined as obtaining viable spermatocytes) using invasive techniques are very low in pre-pubertal boys due to the lack of spermatogonia and other cellular machinery necessary for sperm production. It is possible that these approaches should be reserved for boys who have entered puberty but may not be capable of producing an ejaculate by masturbation for any number of physical or psychological reasons. Likewise, these technologies may circumvent some of the religious or social proscriptions against [A1] masturbation in which many people believe (see below).

In our Reproductive Endocrinology Clinic, like many others around the nation, private rooms are equipped with a television and a videocassette player, along with sexually explicit (some would call them pornographic or obscene: see below) tapes and magazines. In the United States, few societal taboos exist about allowing consenting adult men to view sexually explicit materials (if they wish) to masturbate to produce one or more semen samples, although many people of faith find this disturbing. There may be moral, ethical, physical and religious obstacles to collecting semen samples from male minors by the same methods used for adults, i.e., using sexually explicit materials as masturbatory aids. Boys would require their parents’ consent to the procedure and collection (and thus their permission to masturbate), which could cause them and their parents psychological discomfort, embarrassment, or possibly humiliation. It is unlikely, however, that these feelings would be so severe as to cause the collection procedure to be labeled “risky,” especially because it would seem that masturbation in this setting would be less “taboo” and more clinical. However, proper counseling should be available to these boys to lessen the risk of any possible psychological harm and to increase the potential benefit of the entire process. What this counseling should consist of is less clear. In our experience, consultation with male physicians, adult friends, fathers, and even members of the clergy has been helpful.

However, religious beliefs against masturbation may create major obstacles for boys and men, as some religions teach that masturbation is a sinful activity. For instance, Orthodox Jews believe it is sinful and immoral to masturbate because it “waste[s] the seed.”[19] The Church of Jesus Christ of Latter-day Saints, which believes that propagating children is an obligation of their faith, is adamantly opposed to masturbation.[20] The Church declares that “[m]asturbation is a sinful habit that robs one of the Spirit and creates guilt and emotional stress.”[21] Roman Catholicism
teaches that procreation should occur only in the sanctity of a marriage between a man and a woman.[22] So, traditionally in Catholicism, "any form of reproductive manipulation is considered morally wrong."[23] In fact, in 1987, the Vatican issued an encyclical entitled Donum Vitae ("Instruction on Respect for Human Life in Its Origin and on the Dignity of Procreation"), expressing the Church's moral opposition to techniques of procreation that deliberately severed the procreative and unitive ends of sexuality, including donor insemination and in vitro fertilization.[24] In addition, all Catholic sexual acts rest on the principle that procreation in an essential aspect of human sexuality, so the church believes every genital act must be open to the possibility of conception, which is why masturbation has been forbidden.[25] However, with the new Catechism issued in 1999, the Catholic Church declared that masturbation is not necessarily sinful.[26] Many, if not all, evangelical Protestant faiths in the United States and elsewhere, proscribe masturbation as sinful. Thus, different religions espouse different views on masturbation that could be an impediment to the boys and young men taking advantage of this technology. Indeed, we believe that the thoughtful input of clergy and theologians should be an integral component of any comprehensive fertility preservation program.

We next discuss female patients, whose situation is much more complicated and involved. Treatment damage to ovarian function can take many forms, and it can be difficult to accurately predict, except in certain circumstances, whether a woman would maintain fertility years after therapy has ended. The baseline infertility rate for couples in the United States is about 10-15%, so one would have to assess increased risk above this rate for young women due to cancer treatment. Indeed, an accurate assessment of the risk of infertility in girls and young women as a consequence of cancer treatment is exceedingly difficult to construct because of the paucity of well-designed studies to address this question. Whereas the data for the dose-response toxicity relationship for alkylating agent chemotherapy for males is reasonably well established, the same cannot be said for females, leaving both clinicians and researchers to estimate (or simply guess) the risk. Thus, much more research will be required to obtain this information before it can be applied in a clinical setting. Nonetheless, female cancer patients, even those who may not be at high risk for infertility, are increasingly demanding fertility preservation. This topic is of great relevance and urgency due to the proliferation of commercial infertility clinics offering to preserve fertility by cryopreservation of ovaries and oocytes (see below). Even though these techniques are unproven that has not prevented many of these companies and clinics from selling these services to this extremely vulnerable population of young women (see, e.g., http://www.givf.com/ovary.cfm).

From a technical perspective, gamete preservation for girls is, for a variety of reasons, more challenging than for boys. Unlike sperm preservation, where collection and freezing techniques have been used in healthy males for years, and the use of frozen sperm to later produce healthy babies is well-documented, the collection, freezing, and use of ovarian tissue for purposes of reproduction, is still highly experimental. In addition, the collection of ovarian tissue is much more physically intrusive, and requires surgery. These two factors – a greater level of medical intrusiveness and risk, and less
likelihood of a successful outcome – mean that designing a program for girls and young women requires heightened sensitivity to the ethical concerns. The principles of beneficence and nonmalificence are paramount in our treatment of minors, especially when they (and their parents) are as psychologically vulnerable as those who have just been told they have cancer, the treatment for which could cause infertility. Special care must be taken to not take advantage of these patients and families, even for such a noble cause.

For instance, while it highly likely that Jessica is infertile, it is by no means definite. The accepted definition of infertility is “one year of frequent and unprotected coitus without conception, suggesting a diminished capacity to conceive and reproduce.”[27] This definition is most applicable to females since the ability to get pregnant is dependent upon a number of mutually dependent and independent factors, including successful ovarian follicle formation and ovulation, transit of the mature egg down the fallopian tube and fertilization in the uterus followed by implantation. Meanwhile, all men have to do is produce sufficient functional sperm that can fertilize an egg. However, in a significant percentage of infertile couples the problem does not lie with the female partner, as the male could have a low sperm count, for example.

Current technology has allowed physicians who specialize in infertility to overcome many potential obstacles associated with conception. For instance, women who are capable of ovulating but who have blocked fallopian tubes (from prior infection, for example) can have mature oocytes harvested by laparoscopy, fertilized in vitro, and embryos inserted into the uterus for implantation. However, in Jessica’s case, if she were infertile, it would be impossible to say whether it was due to some pre-existing condition, her treatment, or some combination of the two.

Chemotherapeutic agents or radiation can cause ovarian damage; because of this it would be preferable to obtain oocytes before starting therapy. If one could wait for several weeks to start anti-cancer therapy, and if the primary disease would not contraindicate giving hormones to induce super-ovulation, then one could potentially harvest hormonally mature eggs, fertilize them in vitro, and freeze the embryos for later use. This is possible because the technology for cryopreservation of embryos is well established, although cryopreservation of immature oocytes from ovarian tissue is still experimental. Presumably, this approach could be used for a woman who knew she wanted to have children (or more children) and had a male partner (or not) available. However, having the time to undergo these procedures and having a male partner to fertilize their eggs is a rare situation for these young women. For minors and women without partners, this is impossible. Furthermore, for some patients, the use of high doses of hormones that stimulate hyper-ovulation might be contraindicated due to the potential for increasing the rate of cancer cell growth, clearly something that we would not want to do. Young women with estrogen receptor-positive breast cancer would fall into this group.

More commonly, treatment must be started right away, and there is little time available to obtain hormonally mature eggs. Many reproductive endocrinologists have begun to
offer to take ovarian cortical slices (biopsies) by laparoscopy to cryopreserve for later use. Unlike hormonally mature oocytes, which cannot withstand the rigors of freezing and thawing very well, immature eggs are more resistant to thermal stress. The frozen ovarian tissue would then be thawed at a later date and implanted into the same patient (autologous) with the hope that it could function normally. The challenge is that a successful human pregnancy has yet to result from this approach. While this technique has worked to produce offspring in a number of species, such as rodents and ungulates, the same cannot yet be said for humans. It is encouraging, however, to note that ovarian slices have been successfully “auto-transplanted” into several women to restore hormonal function, including ovulation, although not pregnancy. Although we suspect it is only a matter of time before this technique is perfected for women, it has not stopped commercial (and a few academic) centers from offering this “service” (ovarian cortical slice harvesting and freezing) to women and, in at least one report from England and Israel, to girls under the age of 18 years.[28]

What about providing the service to girls under the age of 18 in the United States? From the medical standpoint, it would be theoretically possible to obtain ovarian tissue from even very young children (< 8 years of age), and maybe even babies. However, the ability to even find the ovaries in small girls would be a challenge. If one could find them, their size most likely would preclude taking only part of the gland, meaning a unilateral oophorectomy (total removal of the ovary) would be necessary. Furthermore, the ability to do this procedure with a laparoscopic approach diminishes with decreasing age. Thus, young girls may have to undergo open pelvic surgery to obtain oocytes to cryopreserve for later use. If the child needed abdominal surgery anyway (say to biopsy or resect an abdominal tumor), one could make the argument there is minimal-to-no added risk in removing part or all of an ovary at that time. It may, nonetheless, be less controversial to offer ovarian cryopreservation to pubertal girls. While the laparoscopic surgery they would undergo is low-risk as far as surgery goes, it still involves some risk of bleeding and infection, which might not be a risk the girls (or their parents) are willing to take.

This is especially true when we are unable to predict the true risk of ovarian damage from various cancer therapies (see above). We are thus faced with a situation in which we have a combination of unproven, yet potentially useful and proven in the future, technologies, a surgical intervention of known risks (laparoscopy), and only a very loose estimate of the risk of infertility due to a particular cancer treatment as the data set upon which we rely for both policy formation and individual patient recommendations. This is true for both girls and women, but especially so in minors. Offering medical interventions to patients for which there is current proven benefit outside of an approved research program is ethically questionable for adults and undoable in children for whom the principle of beneficence outweighs all other considerations. There are exceptions to this rule in which the potential for societal or “class” benefit may apply (Phase I clinical trials of new anti-cancer drugs in children is one such example), but these are uncommon.
The financial impact of fertility preservation is another major consideration. Like most medical services involved with fertility, insurance companies, and government health care payers rarely, if ever, cover the costs of the procedures. While the freezing and storage of ovarian tissue is probably not that much more expensive than the analogous service for sperm, the costs associated with surgery, anaesthesia, and hospitalization are considerable and must be totally borne by the patient and/or her family. At many institutions, this cost can approach $5000 or more.[29] Does this mean that we can only offer the (potential) preservation of fertility to people who can afford to pay for it? Such a prospect undoubtedly raises issues already at the forefront of discussions about disparities in access to medical care based upon socioeconomic, racial, and ethnic factors. Unfortunately, this point is almost completely academic, as there are few medical centers that take care of adults (and even fewer pediatric centers) that have programs in place to offer gamete cryopreservation to all their patients who may be at risk.[30] However, we have had to confront this challenge at our own institution and develop a unique solution (see below).

THE LEGAL CHALLENGES

In order for any individual to take advantage of the service of collecting and cryopreserving his or her gametes, the law requires that the patient provide informed consent to undergo the procedures. The purpose of informed consent, which requires a physician to disclose to the patient “all the facts which mutually affect the rights and interests of [the patient] and the surgical risks, hazards, and dangers, if any . . . ,”[31] is to protect the rights of the patient, while promoting bodily integrity and self-determination among patients.[32] Thus, “[u]nder the informed consent doctrine, physicians are obligated to provide each patient with information necessary to enable the patient to make an intelligent decision about whether to undergo a recommended procedure, consent to an alternative treatment option, or refuse treatment altogether.”[33] The following represent the six types of information typically required for consent to be considered informed: (1) the diagnosis; (2) the nature and purpose of the treatment or procedure; (3) the expected outcome and probability of success; (4) the material risks, benefits, and consequences of the proposed treatment or procedure; (5) the alternatives to the proposed treatment and supporting information regarding the alternatives; and (6) the effect of no treatment or procedure, including the effect on the prognosis and material risks associated with no treatment.[34]

For children to use a fertility preservation service, their parents must provide consent. The parents must consent because children are considered to be immature; consequently, the law assumes they are unable to make important decisions affecting their lives.[35] The law, therefore, provides adults with the authority to make decisions for children that adults are free to make for themselves. The premise of this law is that the parents are the first best caretakers of the child and that they have an interest in this role that warrants legal protection.[36] Thus, the requirements of informed consent that would apply to competent adults, such as explaining the nature of potential benefits,
would simply apply to informing the parents about their decision to permit their children to use the service.

Although it is not legally required, children should be given the chance to voluntarily agree to use the service, by giving their “assent.” However, if this is done as part of a research program, Institutional Review Boards are required to demand minor assent as part of informed consent. “The assent process should be tailored to the age, maturity and psychological state of the children involved and should be easy for the children to understand.”[37] It should also include a discussion of any discomforts and inconveniences the child may experience if he/she uses the service.[38] Such assent allows the child to feel empowered and to feel as if he is taking part in making decisions about his treatment. It may, therefore, make him feel more at ease about what he will endure.[39] The process is not just about getting the child to agree to use the service, but rather it is about making sure the child understands the procedures and what it means to preserve his gametic material.[40] These details may differ in other countries.

Three consent situations could arise with respect to offering this service to children: (1) the child assents and the parents consent to use the service; (2) the parents consent to the child’s use of the service, but the child does not assent; and (3) the child assents and wants to use the service, but the parents will not consent. In the context of informed consent, with respect to the first scenario, there should be no problem with the child using the service, so long as there really is informed consent. Under the law, if the second scenario were to happen, the parents would have the right to force the child to use the service. However, we do not believe that this situation would happen very often, and it would be highly unusual for a physician to force a child to undergo these procedures. Finally, the third scenario presents the most problems, not only legally, but also ethically. Due to a child’s unique status in the law, doctors should not treat the children against their parents’ wishes, although they may desperately want to.

In addition to the principle of informed consent, legal issues exist surrounding disposition and ownership of specimens. Are the frozen gametes property, and if so, who owns them and what can they do with them? These issues take on even more complications and have more ramifications when analyzing collecting and freezing gametes from minors. One of the major issues is whether the gametic material should be classified as “property.”

The law provides people with the right to control their property. “Property rights are viewed as a ‘bundle of rights,’ including ‘the right to possess, the right to exclude, the right to use, the right to dispose, the right to enjoy the fruits or profits, and the right to destroy’ the property in question.”[41] Because the law in the United States has been slow in recognizing these property rights in human biological materials, such as sperm, ova, embryos, and other cells, it is unclear how the gametic material of the children who use the proposed service would be treated.[42] Some courts, however, have recognized at least quasi-property rights in human biological material.
At least one court has considered the issue of whether sperm is property and determined there is a limited property interest in human sperm. In *Hecht v. Superior Court*, 20 Cal. Rptr. 2d 275 (Ct. App. 1993), a man who had been storing his semen in a sperm bank gifted fifteen vials of his sperm to his girlfriend in his will and then committed suicide. His adult children challenged the gift, arguing the sperm should be destroyed because there were no property rights attached to sperm. The court did not accept his children’s argument, holding the sperm was property for the purposes of devise and for the probate court to have jurisdiction over. The court, however, refused to apply more general property principles, such as the law of gifts of personal property, to the gift the man bequeathed to his girlfriend. In making its decision, the court noted sperm banks generally treat sperm as property, and it acknowledged the American Fertility Society’s position that “gametes and conceptuses are the property of the donors.”[43] In addition, it relied upon the American Fertility Society’s declaration that donors “have the right to decide at their sole discretion the disposition of these items, provided such disposition is within medical and ethical guidelines . . . .”[44] The court then analogized sperm to embryos and concluded that sperm stored solely for the purpose of artificial insemination is “unlike other human tissue because it is gametic material that can be used for reproduction.”[45] The court reasoned further that the value of sperm lies in its potential to create a child after fertilization, growth, and birth.[46] Ultimately, the court did not award the sperm to the girlfriend, because the issue before the court was simply whether a lower court properly ordered the sperm to be destroyed. Instead, the court reversed that order, holding the sperm was entitled to be distributed in probate. Thereafter, the probate court ruled that the girlfriend, based on a distribution formula in a settlement agreement, was entitled to 20% of the frozen semen.[47]

Although the issue of sperm as property is unsettled and complicated, the issue is even more problematic with respect to eggs, primarily because it is rare for unfertilized eggs to be cryopreserved. Nonetheless, the analysis of the *Hecht* court in finding a limited property right in sperm and finding the value of sperm to be in its potential to create a child could be similarly applied to the eggs harvested through the service that will be used later for reproduction. Moreover, given the American Fertility Society’s position on gametes as donor property, it would be inconsistent for them to view eggs as anything other than property.

The *Hecht* court was very concerned that gametic material should be used as the donor intended. One way to enable individuals to have their materials used as intended is by recognizing human biological materials as property, thereby giving the owner an enforceable stake in them.[48] Yet, many people are opposed to recognizing property rights in the human body, arguing that it commodifies the body and demeans human dignity.[49] One can argue, however, that property rights in human biological materials should be recognized because of the protective value of the rights, and because it will provide a relatively unified approach to settling the complicated issues that arise when the status and disposition of human biological materials are concerned.[50]
Furthermore, it has been argued that with respect to the question of whether sperm and eggs are property, the answer should be a resounding yes. If both are property, the children should have rights to control the materials, even if only through their parents. But, to use the services we propose, we believe that children and their parents should sign a consent form declaring that they will destroy the materials if the child dies before reaching his or her majority. Similarly, adults will be asked to consent to this stricture, although the ability to enforce this mandate in adults may be questionable. We suggest such a provision because it directly raises the issue of what to do with the frozen sperm (ovarian tissue) in the event of the child’s death, and requires the parents (or adult donor) to think about the issue before entering the program, rather than having it possibly come up for the first time in the emotionally-charged period following a death. The parents and the child might feel uncomfortable with being forced to make this decision because, as the American Fertility Society recognizes, donors should be able to control the disposition of their gametes, and they might, at some future point, argue that as a result of the consent form, they no longer have such control. Thus, parents and children should be able to determine legally that if the children die, the gametes will be destroyed, or to determine that they will be stored until age 18, at which time the children should have control over their disposition.[51] If both sperm and eggs are property, then it seems that the donors should be able to contract, through their parents, for the disposition of the materials, although this is unclear.

On the other hand, many modern American courts have applied contract law, instead of applying laws concerning property rights, to help resolve disputes concerning human biological materials.[52] One case that considered how to treat gametic materials is the case of *Davis v. Davis*, 842 S.W.2d 588 (Tenn. 1992). In that case, a husband and wife created embryos that were cryopreserved without specifying for the disposition of the embryos if one of them died or if they got divorced. The couple then got divorced, and both parties wanted control of the disposition of the embryos. The husband wanted to destroy the embryos because he vehemently did not want to become a father, and the wife wanted control of them to give them to another couple for implantation. The Supreme Court of Tennessee held that the embryos were neither property nor persons under the law; instead, they held an intermediate status and were entitled to special respect because of their potential for human life. The court also held that the husband’s right not to procreate and his right to avoid parenthood outweighed the wife’s right to see the labors of the in vitro fertilization procedures she endured create a child. Finally, the court expounded that disputes in Tennessee involving the disposition of embryos should be resolved by examining the dispute in the following manner. The court should first look to the preferences of the progenitors. If their wishes cannot be ascertained, or if there is dispute between their wishes, then any prior agreement regarding their disposition should be followed. If no prior agreement or contract exists, however, the relative interests of the parties in using or not using the embryos must be weighed to divine a result, while giving more weight to the party who wishes not to use the embryo to procreate.

Although *Davis* concerned the legal status of and disposition of embryos, an extension of that court’s legal reasoning could be applied to the gametes that would be preserved
through the service we propose. As a result, if a conflict were to arise concerning the disposition of the gametic material of a child who used the proposed service, and if a court considered the case, it might follow Davis and permit whatever party did not want to use the material to create a child to destroy the material. Applying Davis to the wishes of a party involved in this service is complicated by the fact that there are potentially three parties: the child, the child’s parents (assuming they both want the same result), and the service providers. Perhaps, then, a court would rely on the second step set forth by the court in Davis and look at any prior agreements concerning the disposition of the gametic materials. Because this might be the manner in which a court would determine the appropriate disposition, we will require both the children and the parents to sign a contract dictating how the gametes will be disposed of in different situations.

Even different results could occur than in Davis because it seems that court’s primary reason for finding the materials were not property was that the eggs had already been fertilized and, therefore, had the potential to become persons. The materials we would preserve would not yet be fertilized, so while they would still have the potential for human life, that potential would be less than for embryos because gametes differ from embryos in that they do not have the potential for life without fertilization. As a result, if a dispute were to arise concerning the disposition of a child’s materials, a court might determine that gametes are property instead of quasi-property. If this were the case, the child (or, if he is still a minor, his parents) would have the right to possess, use, dispose of, and/or destroy his own property. One also could argue, however, that because the gametes are the materials from which life is created, they do have the potential for life even if only through fertilization, such that a court would hold they have intermediate, quasi-property status.

The Davis court also noted that agreements regarding disposition of embryos should be presumed valid and should be enforced in the event of contingencies, such as the death of one of the parties. However, in a Massachusetts case, a couple divorced after harvesting frozen embryos.[53] The wife wanted to use some of the leftover embryos, but the husband did not. Although consent forms and forms providing for the disposition of the embryos were signed at the beginning of the process, declaring that the wife could use the eggs in the event of a separation, the husband then changed his mind. The court found in favor of the husband, indicating the signed forms were unenforceable contracts.[54] These contrasting conclusions by courts in different states highlight the legal uncertainties facing all parties involved in all aspects of the proposed service.

The foregoing legal analysis would be applicable primarily in situations where there is a dispute over disposition and ownership of specimens between the service providers and the child whose materials were preserved. A potential dispute could also arise regarding the disposition of the gametes if the donor child dies but the child’s parents’ desire to have possession of the materials to be used to create their grandchild. Although we would require the signing of a consent form, which would indicate that upon the death of the gamete provider, the sperm or eggs will be destroyed, it is unclear whether a court would enforce the contract over objections by other parties, such as the service
providers[55] or the parents, or how a court would determine how to enforce a contract when the gamete provider is still alive.

Although it might seem unusual that a parent of a deceased child would want to create a grandchild from the deceased child’s biological materials, it would not be the first time that such a request has been made. For example, Pamela Reno of Reno, Nevada was devastated when her 19-year-old son killed himself playing Russian Roulette.[56] Although her son had wanted to donate his organs in the event of his death, she refused to permit doctors to take them unless they harvested her son’s sperm. The doctors collected and cryopreserved his sperm, which she plans to use to impregnate her son’s childhood friend and then raise the children – her grandchildren – herself. Reno explained she desperately wanted grandchildren and that her son always wanted to have children, so she was merely fulfilling his wish by creating his son. While this situation is slightly different from one that could arise with respect to the materials of deceased child-participants, in that the materials have already been collected and preserved, it underscores the fact that even previously unimaginable issues can arise in the context of assisted reproductive technologies. Thus, although this scenario is quite bizarre, we must realize issues such as this could arise if a child who used the service we propose dies, because, as the doctor who harvested Pam Reno’s son’s sperm stated, this is “a request that is becoming more frequent.”[57]

According to a survey of fertility clinics by researchers at the University of Pennsylvania Center for Bioethics, 82 requests have been made by wives, girlfriends, or parents for post-mortem procurement of sperm from deceased individuals who ranged in age from the early 20s to late 30s, with two of minor age and one 60-year-old man.[58] Like the situation with Ms. Reno, in these scenarios, the men from whom sperm was requested to be retrieved were dead; however, with respect to individuals who use the proposed services, their gametes will have already been preserved. Having the gametes cryopreserved prior to the donor’s death eliminates one of the problems with posthumous reproduction, specifically obtaining and using an individual’s reproductive material without his advance consent.[59]

There have been situations where individuals with serious or terminal illnesses preserved their gametic materials, and the materials were used to create a child after their deaths. In one case, a man preserved his sperm in advance of chemotherapy so that he and his wife could have children if the treatment made him sterile.[60] He died three months later, and although there were no signed documents concerning the disposition of the materials, his wife claimed that he told her before his death that “there could always be a child for you.”[61] His wife then was inseminated with the sperm and gave birth to a daughter a year after her husband’s death.

Similar situations regarding posthumous reproduction could arise once the children who used this service reach the age of majority, as they would likely be able to determine what they want to have done with their gametes. For example, if a child gets married after he/she turns 18, then he/she might desire to stipulate that his/her spouse should obtain possession of the materials in the case of his/her death. Thus, although this
scenario would not be as unusual as individuals creating a grandchild from their deceased child’s gametic materials, it still raises issues of whether posthumous reproduction is appropriate and whether we should be facilitating such activity.

The potential for cryopreservation of ova may extend the options for posthumous reproduction to the use of cryopreserved oocytes, similar to using sperm for posthumous conception.[62] Posthumous reproduction by men is technically simpler and more common than posthumous reproduction with women. With advances in cryopreservation technology, however, more women could consider the possibility of producing a child with her genetic material after death.[63] This process could be carried out, because there are currently no statutes prohibiting posthumous reproduction by women.[64] Thus, as one can ascertain from this discussion, providing this service could cause legal and ethical dilemmas with respect to the disposition and ownership of gametes.

As already stated, the issues concerning the control and disposition of gametic material are complex and legal doctrines and rules in the area are unsettled. Consequently, if conflicts were to arise, perhaps courts would resolve the problems by applying property theories, maybe they would strictly adhere to the contract (e.g., the consent form), or maybe they would make a determination based on the concern that gametic material be disposed of as the donor intended, as the court wanted to do in Hecht. Regardless of how a court would decide a dispute over ownership of the gametes, one should be aware that not all courts have enforced contracts providing for the disposition of human biological materials. It is not clear, therefore, whether ownership disputes could be prospectively handled through a consent form.

Aside from the control and disposition issues, another legal and ethical concern arises from collecting the children’s gametic material. Taking organ tissue from girls and young women with cancer, which is very often a systemic disease, could be highly problematic in that there could be tumor present in the ovarian slices removed. Upon auto-implantation at a later date, one could be giving cancer back to the patient who was otherwise thought to be cured. At least one study has attempted to evaluate this in experimental animals and has found the risk to be non-existent, at least for Hodgkin’s Disease, a disorder with a high cure rate and where therapy is a not-infrequent cause of infertility.[65] However, one will not be able to conclusively prove that the cryopreserved tissue is tumor-free; thus, patients will have to assume that risk, small as it may be.

In addition, an objection could arise to using sperm from a boy or young man who has cancer or using an egg from a girl or young woman who has cancer to create a child, in that there could be a heightened chance the child created from that preserved material will be predisposed to having cancer. Should we be concerned about the potential preservation of “flawed” genetic material? By this we mean genomic DNA (contained in oocytes and sperm) that may predispose future off-spring to an increased risk for disease (cancer)? While the former practice of eugenics and its associated forced sterilization of the “unfit” is a thing of the past, the withholding of gamete preservation from children and adults for whatever reason is akin to prohibiting them from having
biological children (“forced” sterilization). Furthermore, there appears not to be an increased cancer risk in the children of long-term cancer survivors.[66]

Legally, at least two scenarios could arise from the concern of creating a child with “flawed” genetic material: a “wrongful birth” action and a “wrongful life” action. An action for wrongful birth is one brought by parents of a child born with some defect or disease who allege that the negligence of prenatal health care providers or genetic counselors deprived them of the ability to make an informed decision about whether to have the child who had a likelihood of being born in an impaired state.[67] This action is brought by the parents to recover damages accruing to them from having to endure having an “impaired” child. Not all states recognize a cause of action for “wrongful birth,” but even in those that do, the only way a person who had taken advantage of the proposed service would be able to sustain this cause of action is if he/she were not properly warned of the risk of passing cancer onto his/her potential child. Thus, if doctors properly warn of any risks associated with an individual who had cancer passing it on to his/her offspring, a wrongful birth cause of action should be precluded. A “wrongful life” cause of action, however, would not necessarily be unavailable.

“Wrongful life” claims, as they would apply to this scenario, would be claims by “abnormal” or unhealthy children (or the parents on the children’s behalf) asserting that but for the physician’s negligent advice or treatment, the child would not have been born to experience the pain and suffering of living with such an impairment.[68] For such a cause of action to be viable for a child who is afflicted with cancer and who is born from the gametic materials of an individual who used the proposed service, he/she would have to establish that using the cryopreserved material was negligent.[69] We think it is unlikely a court would determine that using the material was negligent, especially if the now-adult survivor was counseled about the risks and chose to have the child anyway. Moreover, very few states permit recovery for this cause of action, and many of those that prohibit recovery do so because it is too difficult to determine whether a disabled existence is worse than non-existence.[70] Thus, another reason the cause of action would likely fail is that the law is hesitant to declare an imperfect life to be less valuable than an unimpaired life.

So, we have addressed the legal problems that could arise with respect to the child created from the cryopreserved materials, but what about the moral problems? We have touched on many of the ethical issues throughout this discussion, but there are a few that assume the greatest importance, and thus the greatest challenge. The most serious issue with this whole project is that vulnerable young girls and their parents have to make major decisions with very little information to help them. While there is a large amount of reliable data about the success rate of pregnancies resulting from the use of frozen semen specimens, the same is not true for cryopreserved oocytes. This places a moral burden on clinicians and researchers to do a better job of collecting this information for the informed use of patients and their families: information such as the likelihood of risk from surgery (including the risk that a child could be made sterile by a surgical procedure intended to preserve fertility!) and the likelihood of a successful outcome (i.e., a pregnancy) using the tissue. Given the fairly low success rate of in vitro
fertilization procedures in general, is it realistic to think that any female survivors will actually end up with a baby? At the present time, this cannot be guaranteed, so the doctrines of beneficence and nonmalificence would prohibit collecting ovarian tissue in minor girls in any situation that could cause harm or increased risk.

Are the issues any clearer for young women over the age of 18? They, too, will have to make decisions very quickly and under very stressful circumstances. The difference lies in their legal ability to consent to procedures that are “elective,” even if they are of no proven benefit, such as the cryopreservation of ovarian tissue. Is consent to undergo laparoscopy, at some risk, any different that agreeing to pursue medically unnecessary operations such as certain types of cosmetic surgery? Both may provide psychological comfort to the patient, and both entail a degree of risk with a successful outcome equally elusive. As mentioned previously, for-profit fertility clinics have taken advantage of this situation and are currently offering ovarian tissue collection and storage for cancer patients.[71]

Another ethical concern is whether by helping these cancer survivors have their own biological children, the physicians are helping them pass on possible “cancer genes”, thus resulting in the birth of children with a higher risk of getting cancer. This ethical concern has two parts: the first is from the point of view of the individual who is preserving his/her gametes, and the second is from the view of the wider society. In the first case, the gamete donor has to make a decision about cancer risk in his or her child-to-be, and key factors in making that decision will be the quality of information he or she is provided and his or her view about whether the fact that the child may have an elevated cancer risk outweighs the parents’ (or parent’s) desire to have a biologically-related child.

As evidenced by our support of the services proposed herein, our position is life – even if impaired by cancer – is better than no life at all, which is why we want to enable the adult survivors of childhood cancer to have the opportunity to be able to create a life that is biologically related to them. If the individuals who endured cancer themselves believe no life is better than life with cancer, it is unlikely he/she will choose to use his/her stored material to create child. In fact, he/she might never choose to have his/her gametic material collected and stored in the first instance. Consequently, the resolution of this issue lies in an individual’s choice, which, we believe, is better than being left with no choice at all.

Given the lack of clear evidence about an increased risk of a cancer survivor’s offspring getting cancer (indeed, what data there is suggests that the risk is no greater than the rest of the population except in rare situations such as patients with hereditary retinoblastoma, the Li-Fraumeni Syndrome, or BRCA mutations, etc.), one might argue that there is some moral duty on the part of the researcher/clinician not merely to tell a would-be participant that their child might be at higher risk of cancer, but to actually try to collect data to help people truly understand what that risk might be. The second issue might be society’s concern over the “passing on” of “flawed genes.” However, since
people pass on all sorts of undesirable genes, and there is no restriction on that, this eugenics argument appears fairly weak.

For boys, the physical procedure of collecting sperm does not represent any increased risk, but it does raise issues of morality for many people, usually within a religious framework. It is only when balancing the perceived good of an outcome (the preservation of fertility) versus the believed evil (masturbation, viewing sexually explicit materials) that these dissonant beliefs can be resolved. Even so, we are asking families to make moral choices within short spans of time in which the atmosphere is emotionally charged from the outset because of the new diagnosis of a life-threatening disease.

Not being able to bear children is devastating for cancer survivors. For boys, the freezing of sperm offers a good possibility of fathering a child in the future. Although for girls the success rate (of producing a baby) might be low, freezing the tissue provides the girl with some choice in the future, while NOT doing it means no choice at all. In order to offer these choices in the most ethically responsible fashion, programs should be conducted as part of a comprehensive a research protocol, gathering data to help answer the unknowns.

CONCLUSIONS AND PROPOSAL

This entire discussion presupposes minors would want to have biological children when they grow up. Is that assumption based in fact? How could we make this determination in an accurate manner? What data there is suggests strongly that cancer survivors are not all that much different than the rest of us: they wish to have biological children.[72] An overwhelming percentage of adults do father or bear children, but is that enough of a reason to suppose these young cancer patients would want to do the same? We might answer that by saying that preserving gametes for future use preserves not only the cells, but also the choice of whether to use them. However, is this preservation of choice morally persuasive enough to place children at some small, but definable risk (say, a surgical procedure, or perhaps exposure to psychologically damaging photographs), in order to maintain the ability to make a future decision that could negate the acceptance of that risk?

Unfortunately, we cannot know what our children will choose to do with their lives when they grow up, whether it is their choice of college, spouse, or to have children or not. Since adoption is always an available option for parenthood, a choice that involves no risk to minor patients, one could make the argument that it is unethical to place children at any risk whatsoever. These are important questions that need to be addressed. There is convincing evidence that infertility is a psychologically devastating event for survivors of childhood and young adult cancer, and thus providing them the possibility of preserving their fertility is a worthwhile endeavor. But, one must wonder, is there an age at which children may be mature enough to participate in these decisions as active
partners? Is there an age at which children should be permitted to make decisions about preservation of fertility?

Our ability to cure young people with cancer is at an all-time high, and it is likely to improve even more over the next decade. With this success rate has come the price of long-term side effects, including infertility in a population of patients who would otherwise be considered to be in their prime child-bearing years. In this discussion, we have shown this effect of treatment is psychologically devastating to many patients and is one they often only become aware of later in life.

At Duke, we decided to do something about this situation. Like most places that treat large numbers of cancer patients, we did not have a fertility preservation service in place: whether an individual patient was offered sperm banking or possibly oocyte harvesting was highly arbitrary. A program that we would create from scratch should be able to deal with all of the thorny medical, social, ethical and legal issues that we knew could complicate matters, as well as those that might crop up in the future. Furthermore, we wished to be able to measure the success (or not) of any program we set up. We, therefore, recruited individuals on the faculty (and community) who were interested in this issue to create a working group to begin to formulate an approach. Faculty from the School of Law, the Ethics Institute, the Divinity School and the School of Medicine (Pediatric Hematology-Oncology, Medical Oncology, Pediatric Rheumatology, Pediatric Endocrinology, and Reproductive Endocrinology) started meeting regularly to discuss all aspects of fertility preservation in this vulnerable patient population. We were able to come to consensus decisions on most of the issues presented in this article; the one major issue that still confronts us is that of funding for people who cannot afford the cost. We are constantly seeking grants and philanthropy so that the future ability to have a child is not based upon the patient’s (or his or her parents’) income at the time of diagnosis. The end result is the Duke Fertility Preservation Project, which we will be able to offer to all patients meeting the age and consent eligibility criteria. It should be made clear that this program has two interdependent goals: that of a research project to gather data in a large number of medical, social, and ethical areas, and a clinical service. We will be studying the patients who take part in this project in the laboratory, the clinic, and their lives to see how it is working. We believe that it may serve as a model for institutions and physicians wishing to address an issue that can be so vitally important to young cancer survivors.

Technology is available to help preserve the option of having biological children for many, if not most, of these patients, but it must be done in a systematic, planned, and sensitive way so as to address many of the complicated, medical, ethical, and legal issues surrounding this emotionally volatile issue. Commercial infertility clinics rarely spend much time or effort attempting to offer services to patients such as the minors to whom we propose to offer the services described herein. If we have the technology and science available to allow these individuals to preserve such a precious and important life function, then, as a society, it should not be restricted. Cancer centers should recognize and respect the importance this issue has for young cancer survivors. The preservation of fertility should become a standard service offered to all patients in the
future. However, as this paper has made clear, the challenges to making this goal a reality can be numerous and daunting. To overcome them will require carefully planned and coordinated research programs such as we have proposed. If we are going to have increasing success in curing cancer patients, then more and more of them will have futures to look forward to; we should do all we can to ensure that they are as rewarding as possible.

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[7] Id.

[9] Id.


[14] Id.

[15] Id.


[21] Id.
[22] DeLair, supra note 19.

[23] Id.


[33] Id. at 558.


[35] Samuel M. Davis et al., CHILDREN IN THE LEGAL SYSTEM, at 12 (Foundation Press, 1997).

[36] Id. In addition, restrictions on the freedom of minors are justified on many grounds, such as the following: (1) minors are viewed as incompetent to make decisions because
of their immature understanding and judgment and lack of experience; (2) younger children are limited in their decision making ability because of immaturity in their cognitive development; (3) minors may be vulnerable to coercion and undue influence in making choices, so that they might be taken advantage of by adults who do not have their best interests at heart; and, (4) traditional law presumes that if minors were given the freedom that adults have, that they would often make choices harmful to themselves or others. Id. at 99-100.


[39] Id.

[40] Id.


[42] Id.


[44] Id. at 675.

[45] Hecht, 20 Cal. Rptr. 2d at 283.


[51] However, permitting such control could cause substantial legal problems, which we are trying to prevent by requiring for the destruction of the samples if the children die.
[52] Supra note 41, at 452-56, citing Davis v. Davis, 842 S.W.2d 588 (Tenn. 1992). See generally Estate of Moyer v. Moyer (1978) (holding a wife had quasi-property rights in her deceased husband’s corpse for purposes of burial while declining to find an absolute property right to all of his organs).


[54] Id. at 1056.

[55] Cahill v. Cahill, 757 So.2d 465 (Ala. 2000) (holding that three frozen zygotes formed for the purposes of in vitro fertilization during the parties’ marriage were the property of the University of Michigan and not the parties’).


[57] Id.

[58] Andrews & Elster, supra note 5, at 52-53.

[59] Id. at 55.

[60] Id. at 54.

[61] Id.


[64] Id. at 204.

[65] Kim et al., supra note 12.


[69] Id.

[70] See http://www.givf.com/ovary.cfm
