Cryopreservation of Gametes in Young Patients With Cancer

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PAST BARRIERS TO CRYOPRESERVING SPERM BEFORE CANCER TREATMENT

Although successful cryopreservation of sperm became possible in the mid-1970s, banking sperm before cancer treatment was considered impractical until much more recently (1). A major barrier to sperm banking was the concern that the cryopreserved semen would be of little use in establishing pregnancies. Many young male patients with cancer, particularly those with testicular tumors or Hodgkin’s disease, already have reduced sperm counts and motility by the time of diagnosis and the start of treatment (2). Freezing and thawing semen further reduces its quality, because many sperm cells either will not survive or have impaired ability to fertilize an oocyte. Cryopreserved semen with good post-thaw counts and motility can be used with intrauterine insemination (IUI) to produce pregnancy rates of approximately 15% per cycle. If the sample is of lesser quality, success can be enhanced by combining IUI with superovulation, using stimulating hormones to enable the female partner to produce multiple mature oocytes. However, the cryopreserved semen of many survivors of cancer does not even fall into the range in which superovulation has a chance of reasonable success.

Another barrier to banking sperm before cancer treatment was the typical protocol, which recommended collecting 3 to 6 ejaculates, each after 48 to 96 hours of abstinence. Thus, cancer treatment might need to be postponed for 2 weeks to collect enough semen for future infertility treatment.

CURRENT STATE-OF -THE-ART SPERM BANKING

The situation changed dramatically with the 1992 success of a new assisted reproduction technique, in vitro fertilization (IVF) with intracytoplasmic sperm injection (ICSI) (3). With ICSI, one sperm cell is injected directly into each oocyte harvested after the woman undergoes a cycle of ovarian stimulation. Because the female partner in IVF-ICSI is typically young with normal fertility, live births per cycle are higher than those for IVF in general. It is now possible for a man to become a father even if only a few cryopreserved sperm cells remain alive after thawing (4). Furthermore, we know that semen from adult (5) and adolescent (6) patients survives cryopreservation and thawing without any incremental loss of quality even if the initial counts and motility were not optimal. It is also possible to collect semen samples with adequate post-thaw qualities after an interval of only 24 to 48 hours, minimizing the postponement of cancer treatment (7). Because mature spermatozoa are resistant to mutagenic damage from cancer treatment, samples can even be collected during...
the first few days of chemotherapy or pelvic irradiation if the patient feels well enough to try to ejaculate. Banking sperm is not prohibitively expensive. One review suggests that average charges for cryopreservation and 5 years of storage are between $600 and $1,200 in the United States (8). In our experience, private insurers often cover some or all of the costs; however, insurers are not mandated to cover infertility treatment in most states and long-term survivors may end up with a hefty bill if IVF-ICSI is necessary.

THE HEALTH OF OFFSPRING FROM CRYOPRESERVED SPERM

There is no increase in birth defects among children conceived with cryopreserved sperm. In fact, one consideration is that cryopreserved sperm have typically not been exposed to mutagenic chemotherapy or radiotherapy. Some cancer survivors may feel more comfortable using sperm collected before their treatment even if natural conception is possible years later, although preliminary evidence suggests that the genetic mutations in sperm cells produced by Cancer treatment may be transient (9,10). A recent follow-up of the offspring of childhood cancer survivors also supports the existing literature suggesting that rates of genetic problems or birth defects do not increase when a parent has had potentially mutagenic cancer treatment before conception (11). The risk for cancer in the children of survivors also does not appear unusual, except in the few families affected by inherited cancersyndromes (12,13). These favorable findings may allay survivors' fears of having children with major health problems as a consequence of the father's medical history.

SHOULD TEENAGERS BE ASKED TO BANK SPERM BEFORE THEIR CANCER TREATMENT?

Cryopreservation appears to be effective for periods of time without additional of sperm quality, making it worthwhile to store semen samples even if fatherhood will be postponed for many years (4).

A recent case-series from Germany (6) found that boys as young as 14 were able to discuss the decision to bank sperm, had semen parameters no different from adult patients with cancer, and with few exceptions, were able to masturbate to provide samples. The current report from Denmark in this issue of the Journal of Pediatric Hematology/Oncology (14, see pages 429-430) suggests that boys unable to produce a sample by masturbation may be able to bank sperm through technologies that have proven successful for men with spinal cord injuries: the use of a strong vibrator, or using a rectal electric probe that can stimulate ejaculation but must be used under anesthesia to avoid pain. We encourage routinely offering semen cryopreservation as an option not only to young adult patients with cancer, but to any boys who have attained a state of puberty such that spermatogenesis is taking place. In the future, it may become possible to remove spermatogonia, the stem cells that produce mature spermatozoa, from the testes of prepubertal boys, cryopreserve these cells during the time of cancer treatment. And later replace them in situ to restore spermatogenesis (15).

CURRENT PRACTICE OF OVARIAN CRYOPRESERVATION

Although techniques for using cryopreserved oocytes to produce pregnancies are not yet perfected, some cancer centers have also begun to store frozen ovarian tissue before cancer treatment in girls and women, hoping that advances in the next few years will justify the effort (16). This practice is acceptable if clear informed consent is obtained from the patient and her family and if out-of-pocket expenses are minimized by subsidizing the cryopreservation with research funding.

HOW TO DISCUSS SPERM BANKING WITH ADOLESCENT PATIENTS

Discussing sperm banking today with teenagers and their families takes patience and sensitivity. It necessitates dwelling on the potential infertility that can result from the very treatment.
we hope will save a young boy's life. It also
involves discussing his prognosis and his wishes
about the disposition of his frozen sperm if he dies.
We advocate including an advance directive in any
informed consent for banking sperm. The wife of a
man with testicular cancer has become pregnant
after his death through IVF-ICS with his
cryopreserved sperm (17). Other cases have
occurred in which a spouse or partner wanted to
use cryopreserved sperm posthumously to conceive
a child, or the patient's parents wanted to create a
grandchild using a surrogate mother (18). If
advance directives are not available, the patient's
wishes may be disregarded in favor of decisions
made by a court of law. Because the issue of using
semen posthumously raises important ethical and
emotional issues, physicians should also try to have
a bioethicist available to talk to families, and
formulate institutional policies to provide limits
and guidance.

Then there are the "brass tacks" of collecting
semen. We suggest bringing up the topic with the
patient and at least one parent present. Parents may
be more interested than the patient in ensuring that
they will have grandchildren. A teenager may have
trouble picturing himself wanting to be a father
some day. Occasionally, parents may think that
banking sperm is inappropriate, although the patient
would prefer to do so. A mental health professional
expert in oncologic issues may be able to help
families resolve disagreements about whether to
bank sperm so that a young patient's wishes can be
honored.

Some time should be spent discussing sperm
banking with the patient alone. Teenagers, may be
embarrassed to admit in front of their parents that
they have tried masturbation, or that they have had
a nocturnal emission. An empathic physician,
oncology nurse, social worker, or mental health
professional can normalize masturbation and help
minimize the embarrassment of collecting semen at
the sperm bank. With young teens, the least
invasive method of collecting semen is always
preferable. If parents will allow it, having some
nonviolent erotic magazines or videos in the
collection room may be helpful. Boys who are
uncomfortable with masturbation can be
encouraged to use less powerful vibrators that are
sold commercially as personal massagers. with the
medical-grade vibrator used in the Danish clinic
available as a back-up.

Teens from ethnic minority groups or with a strong
religious background may be more concerned about
masturbation than average. For older teens who
have a committed partner, allowing the couple to
produce ejaculation in the collection room by
manual stimulation may be a more emotionally
acceptable alternative, although parental consent
would be needed if the couple is not married and
either partner is under 18. Although
electroejaculation can be used as a last resort,
particularly if it can be performed during
anesthesia that is required for another
treatment-related procedure, it should be reserved
for rare cases. We hope that this editorial will
stimulate oncologists to offer sperm banking more
often as an option to young cancer patients. Some
patient education materials are already available
on this topic (19), but more need to be developed
tailored to teenagers and their families. Research
also needs to be conducted on physician and patient
attitudes and knowledge about gamete
cryopreservation before cancer treatment.
REFERENCES


