

Walking Two Worlds—Adolescent and Young Adult  
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*Supplement to Cancer*

## Choice in Fertility Preservation in Girls and Adolescent Women With Cancer

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With the cure rate for many pediatric malignancies now between 70% and 90%, infertility becomes an increasingly important issue. Strategies for preserving fertility in girls and adolescent women occur in two distinct phases. The first phase includes oophorectomy (usually unilateral) and cryopreservation of ovarian cortex slices or individual oocytes; ultrasound-guided needle aspiration of oocytes, with or without in vitro maturation (IVM), followed by cryopreservation; and ovarian autografting to a distant site. The second phase occurs if the woman chooses to pursue pregnancy, and includes IVM of the oocytes, followed by in vitro fertilization (IVF) and transfer of any created embryos to the woman's uterus (or to a surrogate's uterus if the cancer patient's uterus has been surgically removed or the endometrium destroyed by radiotherapy). For ovarian autografting, the woman would undergo menotropin ovarian stimulation and retrieval of matured oocytes (likely by laparotomy, but possibly by ultrasound-guided needle aspiration if the ovary is positioned in an inaccessible location). The ethical challenges with each of these phases are many of fertility preservation and include issues of informed choice (consent or refusal). The lack of proven benefit with these strategies and the associated potential physical and psychological harms require careful attention to the key elements of informed choice, which include decisional capacity, disclosure, understanding and voluntariness, and to the benefits of in-depth counseling to promote free and informed choice at a time that is emotionally difficult for the decision makers. *Cancer* 2006;107(7 Suppl):1686–9.

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**W**ith the cure rate for many pediatric malignancies now between 70% and 90%,<sup>1–3</sup> infertility, a common side effect of cancer treatment,<sup>4,5</sup> becomes an increasingly important issue. Recently it has been suggested that strategies for preserving fertility should be available routinely to girls and adolescent women with cancer prior to radiation therapy or chemotherapy.<sup>6–8</sup> All strategies for preserving fertility in girls and adolescent women have at least 2 distinct phases that may be separated by several decades. The first phase includes oophorectomy, usually unilateral, followed by cryopreservation of ovarian cortex slices,<sup>7,9,10</sup> or individual oocytes<sup>10–13</sup>; ultrasound-guided needle aspiration of oocytes, with or without prior menotropin stimulation,<sup>14</sup> or in vitro maturation (IVM) followed by oocyte cryopreservation; and ovarian autografting to a distant site (removed from the field of radiotherapy).<sup>10,15,16</sup> The second phase occurs if the woman chooses to pursue pregnancy, in which case

her treatment would involve in vitro fertilization (having been preceded by IVM if the oocytes are premature) and transfer of any created embryos to the woman's uterus (or to a surrogate's uterus if the cancer patient's uterus has been removed surgically or the endometrium destroyed by radiotherapy). For ovarian autografting, the woman would undergo menotropin ovarian stimulation and retrieval of matured oocytes, likely by laparotomy (or possibly by ultrasound-guided needle aspiration if the ovary is positioned in an accessible location).

Use of these strategies raises a number of ethical challenges for informed choice (consent or refusal). For example, who should be the one to accept or refuse a proposed fertility-preserving intervention—the child (or adolescent), the parents (or legal guardian(s)), or both the patient and her parents (or legal guardian(s))? What might she/they be choosing—a research intervention, a therapy or a nonvalidated practice—and on what basis? These are complex questions that deserve critical attention, especially since none of the strategies for safeguarding future fertility are benign interventions.

### Decisional Capacity

It is widely accepted that persons with decisional capacity (the terms competence and incompetence are not used in this article to avoid potential problems of equivocation between the moral and legal constructs) must consent to interventions before these can be undertaken. It is also widely accepted that persons lacking decisional capacity are to have such decisions made for them on the basis of substituted judgement (when their prior wishes are known or knowable) or best interests (when there are no prior wishes or these are unknowable).<sup>17</sup> With children and adolescents, a complicating factor can be uncertainty about decisional capacity. In some jurisdictions there is an age of consent that can be used to clarify who the decision-maker is in any specific instance. In many jurisdictions, however, including most Canadian provinces, there is no age of consent; for all patients there must be an individual determination of capacity.

Deciding to pursue or forego interventions that are first steps towards fertility-preserving strategies requires a high level of decisional capacity, because this decision involves future planning and because it is complex. Most girls and some young adolescents will lack such decisional capacity, which involves the ability to reflect upon and weigh complex options in light of personal goals for the future. What they may lack in particular is the ability to estimate whether they want a future that includes pregnancy and par-

enthood, and if so whether the future child they imagine having and caring for need be genetically related to them. One cannot simply assume (as some authors do) that parenthood will or would be part of the life that they would choose for themselves.

Some adolescents may know (or claim to know) that children are important to them, but genetic ties are not. If so then adoption or assisted human reproduction using donor gametes may be legitimate alternatives to unproven fertility-preserving strategies. However, there may be practical difficulties with both of these options. For example, while use of donor sperm is relatively common for men who have become infertile following cancer treatment, the option of donor oocytes may not be meaningful for women because of the small number of altruistically donated oocytes likely to be available (as suggested by recent European experience).<sup>18,19</sup> The complexity of the decision-making suggests that, in many instances, surrogate decision-makers (parents or legal guardians) may be called upon to make decisions in the best interests of the child or adolescent cancer patient.

But how does one decide what is in the child's or adolescent's best interests? For example, it is possible that parental decision-making about fertility-preservation reflects a personal interest in avoiding possible recriminations from their daughter if she becomes an infertile adult. Although a young cancer patient may want to avoid additional surgery out of fear or exhaustion brought on by cancer therapy, she may later regret having missed an opportunity for fertility preservation and blame her parent(s) for this loss, irrespective of whether she chose to forego the surgery or her parent(s) did so on her behalf.

Alternatively, the parent(s) might say that they want to attempt fertility preservation in order to preserve their daughter's choice. However, their decision may ultimately be motivated by an interest in having their daughter fulfill what they perceive to be one of women's social roles: childbearing. Thus, rather than enhancing autonomy, the decision would promote societal expectations about women and childbearing.

Parental consent to fertility-preserving surgery might also be motivated by an interest in becoming a grandparent, rather than any specific interest of the child. From the point of view of the parent(s), it is quite possible that childlessness is a tragedy to be avoided at all costs. Alternatively, as the parent(s) suffer through the experience of having a daughter with cancer, they may believe that having children is emotionally risky and that childbearing is to be avoided. The ethical worry in either case is that the

judgement of the parents may not reflect the future best interests of the patient.

Whenever possible it is imperative that the child or young adolescent with cancer be involved in the decision making about fertility preservation.<sup>20</sup> Ideally, counseling should be available to both the child and the parent(s), and not reinforce norms about the role of women.

### Physical and Psychological Harms

In addition to decisional capacity, informed choice requires disclosure and understanding. In decision-making about fertility-preservation, the patient and/or her parents must be told about, and understand, the nature and objective of the fertility-preserving strategies. Specifically, they need to know and understand that, although fertility-preserving interventions are currently offered to girls and adolescent women in a treatment context (as a way to mitigate one of the side effects of cancer therapy), data regarding the safety of fertility-preserving strategies are incomplete and evidence of their efficacy is lacking.<sup>15,21-24</sup> For this reason alone, fertility-preserving strategies should be offered only in the context of well-designed research studies.

In addition to the need for information about the nature and objective(s) of any proposed fertility-preserving strategy, there is a need for full disclosure and adequate understanding of the physical and psychological harms associated with each strategy and of the option of no intervention. The harms relevant to making a truly informed choice at phase one of fertility preservation include *future* physical and psychological harms, rather than only initial harms. (Some of the future harms are also relevant to informed choice at phase two.) To make an informed choice about something that will have a significant impact on one's future, one must know what the future will hold if one chooses that thing or does not choose it. The relevant harms, then, are initial and future physical harms and initial and future psychological harms.

Initial physical harms include those associated with the surgery to retrieve ovarian tissue,<sup>25,26</sup> autografting ovarian tissue,<sup>27</sup> or the retrieval of oocytes after menotropin stimulation.<sup>14</sup> A relevant consideration here is whether the surgery, such as oophorectomy, or autografting, will be performed at the same time as any required cancer surgery or whether an additional laparotomy or laparoscopy, and anesthesia will be required.

Future physical harms, when later trying to achieve a pregnancy, include the side effects of

menotropin stimulation and oocyte retrieval<sup>14</sup> on women with autografted ovaries, and the remote risk of implanting malignant cells, cryopreserved with the ovarian tissue<sup>28-30</sup> or, even more remotely, transmitted in the liquid nitrogen tank from another cancer patient's ovarian tissue (in most units ovarian tissue from cancer patients is cryopreserved in a designated liquid nitrogen tank, as has been recommended for sperm and embryos of carriers of infectious disease).<sup>31,32</sup>

Lastly, there are the potential physical harms to offspring born following successful fertility preservation. They may have an increased risk of cancer related to a genetic predisposition to cancer.<sup>33</sup>

Initial psychological harms may include the potential for false hope, not only in regard to fertility preservation, but also in regard to the cancer treatment. It is important to recognize that discussion of fertility-preserving strategies may impact the patient's and parent(s)'s understanding of information relevant to the cancer treatment. Patients and parent(s) who are asked to consent to the retrieval and preservation of ovarian tissue for later transfer could easily interpret the request as indirect assurance of long-term survival following cancer treatment. But such assurance "rais[es] expectations at a time when patients are most vulnerable and pressured to make a myriad of life altering medical decisions."<sup>21</sup>

Potential future psychological harms associated with infertility include significant feelings of loss and hopelessness, higher levels of stress, and lower self-esteem.<sup>34-36</sup> Treatment of infertility may add additional stress,<sup>37,38</sup> especially since it is often unsuccessful.

### CONCLUSIONS

The long-term survival of girls and adolescent women undergoing cancer treatment is now common place, with cure rates for many pediatric malignancies between 70% and 90%. This fact behoves us to carefully examine available fertility-preservation strategies, not only from a clinical perspective, but also from an ethical perspective. Most important in this regard are concerns about informed choice.

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