

Taskforce 7: Ethical considerations for the cryopreservation of gametes and reproductive tissues for self use

The ESHRE Task Force on Ethics and Law*¹

This seventh statement of the ESHRE Task Force on Ethics and Law considers ethical questions and specific dilemmas surrounding the cryopreservation of gametes and reproductive tissue. This is of particular relevance with advancing techniques for cryopreservation and the desire of many individuals to preserve fertility after cancer, chronic illness, iatrogenic complications of treatment or simply with advancing age.

Key words: ethics/fertility/gamete cryopreservation/tissue cryopreservation

Introduction

This taskforce addresses the cryopreservation of gametes and/or reproductive tissues in order to preserve fertility.

The subject is especially relevant at this time for the following reasons: (i) the increased longevity of patients (both females and males) whose reproductive potential is threatened by cancer, chronic illness and/or the iatrogenic complications of treatment; (ii) the wish of women to be able to reproduce at a later age with their own oocytes; (iii) the availability of safe and reliable cryopreservation of sperm and adult testicular tissue, as well as the current hopes, based on experimental data, that cryopreservation of female gametes and reproductive tissues may be successful for the preservation of fertility in the aforementioned cases; and (iv) the currently increasing practice of offering the possibility of storing reproductive tissues.

Part 1. The facts and definitions

Survival after cancer therapy has improved enormously in the last decade, both for adults of reproductive age and younger children or adolescents. Most children who survive cancer (85%) are potentially fertile, but a significant minority have a high risk of being sterile. In the case of adults, the prognosis for their fertility depends on the initial pathology (type and site of cancer), their age and the type of treatment needed (radiotherapy or chemotherapy alone or in combination), as well as the duration and dosage of treatment.

1.1 Females

In the female, the most common option at all ages is storage of ovarian strips or biopsies. In post-pubertal women, there is the added choice of cryopreservation of immature or mature oocytes. The third possibility is the cryopreservation of human embryos either with the sperm of their partner or the sperm of an anonymous donor.

With regards to use and treatment, the options are autologous orthotopic or heterotopic transplantation, xenografting, in-vitro follicle culture, in-vitro maturation, IVF and embryo transfer, or embryo transfer. No children have been born so far from the use of ovarian strips. The number of children born both from in-vitro maturation or from frozen-thawed oocytes is limited.

1.2 Males

There are sufficient data concerning the efficiency of sperm freezing, which is generally possible from the age of 12 years (median age for spermatarche 12.5 years).

1.2.1 Pre-pubertal males. The only option here is testicular tissue freezing. Options for use are autologous transplantation, xenografting or in-vitro maturation. No children have been born from the use of pre-pubertal test tissue.

1.2.2 Post-pubertal males. The most common option here is freezing of ejaculated sperm, but storage of testicular tissue is also a possibility. The use of frozen ejaculated sperm in artificial insemination or IVF, and of frozen epididymal and testicular sperm, have proved to be highly effective.

Part 2. Basic ethical principles

2.1 Autonomy

2.1.1 Adults. The autonomy of both males and females should be respected. Each person should be able to take measures to

*The ESHRE Task Force includes: F.Shenfield¹, G.Pennings, J.Cohen, P.Devroey, C.Sureau and B.Tarlatzis.

¹To whom correspondence should be addressed at: Reproductive Medicine Unit, Obstetric Hospital, 2nd Floor, University College Hospital, Huntley Street, London WC1 6AU, UK. E-mail: mfi@easynet.co.uk

preserve his or her fertility whether threatened by disease or voluntary chosen interventions (such as vasectomy) or life-plan considerations (the wish to have a child later).

The moral and legal recognition of autonomy is achieved by obtaining the informed consent of the patient. Obtaining informed consent from adults and children differs because of their different decision-making capacity (competence). There is no need to fix a specific age at which an adolescent becomes competent to make these decisions. In fact, it is more appropriate to speak of emerging autonomy rather than of a specific age to consent.

2.1.2 The child. In the ideal situation the child, parents and caring team agree on the best interest of the child. However, when there is disagreement, the child's decision should be respected if the child is mature and understands the issues at stake.

When the child is immature, the decision to cryopreserve (or not) may be taken by the parents, unless it poses grave prejudice to the wellbeing/welfare of the child. The importance of preserving the possibility of having genetically related offspring in the future is generally recognized, and the parents will have to decide whether this benefit outweighs the current risk of intervention for their child.

Consent and information are the key to autonomy: the parent and the child need detailed information on the risks and benefit involved in the alternatives, including the possibility of death due to the primary disease.

Two considerations may complicate the decision-making of the parents: the possible imperative character of the offer and the principle of parental responsibility. The offer of preserving gametes or tissues may take on an imperative character because of the phenomenon of anticipated decision regret: in decision making, people are led by anticipation of the negative feelings that may follow if they find out later that they made the wrong decision. Secondly, a number of people may think that it is their duty as parents to take up every possibility to promote the future wellbeing of their child, regardless of the possible complications of the intervention. In order to balance this possible bias, the counselling should emphasize both the experimental nature of the procedure and the fact that cryostored reproductive tissue has not been clinically used so far.

2.2 Beneficence and maleficence

In practice the use of standards, codes of practice for gametes and tissue banks is imperative (ESHRE Task Force on Ethics and Law, 2002).

Special care and caution should be paid to the transition from research to treatment: since reproductive tissue storage is still considered experimental and its clinical use involves several important risks, its application should respect safety considerations and the usual standards that apply to the introduction of new therapies.

The potential risks from application of the technique must be weighed against the as yet unproven benefits (use for future reproduction). The risks are the re-introduction of cancer cells in autologous grafting, the risk of animal virus transmission in xenografting, and the risks of prolonged culture on the genetic competence of the in-vitro follicle culture egg.

These considerations apply to storage for medical reasons and to storage for social reasons. Whilst the use of frozen-thawed sperm has become routine, the case is different for reproductive tissue cryopreservation. In view of the lack of success and clinical applications in the case of ovarian tissue, this application should not be offered to women as a means to preserve their fertility potential when there is no immediate threat to their fertility. According to similar reasoning, oocyte freezing for fertility preservation without a medical indication should not be encouraged.

Part 3. Specific ethical dilemmas

3.1 Storage period

The reproductive tissues and gametes should only be stored until the age at which it is considered acceptable to be used for the achievement of a pregnancy, taking into account the welfare of the child and the risks to the pregnant mother. In particular, the welfare of the child is unlikely to be met when both parents are of highly advanced age.

In the case of stored embryos, the storage period proposed in a previous document may be extended to more than 10 years (ESHRE Task Force on Ethics and Law, 2001).

3.2 Posthumous reproduction

Since one category of people who cryostore their gametes or reproductive tissues are patients affected by serious diseases, there is a real chance that some of them will die during storage of their reproductive material. Therefore, the possibility of death of the storage giver due to the primary disease should be raised and talked through in the counselling sessions.

3.2.1 Children or adolescents. In the case of children or adolescents, the reproductive tissue and gametes should be discarded on the death of the provider. The parents do not have the right to decide about the (reproductive) use of the genetic material of their child after his/her death.

3.2.2 Single adults. In the case of a single adult with serious disease, the material should be discarded on the death of the provider. In the case of a single healthy adult, posthumous donation to others is acceptable with prior consent in the case of sperm.

3.2.3 Couples. in the case of couples, posthumous use of the sperm by the surviving partner may be acceptable if there is prior written consent of the deceased partner to this disposition. Posthumous oocyte donation is not recommended as it involves both a less reliable technique and the use of surrogacy.

3.3 Donation

3.3.1 Donation for research. After implication counselling, all gametes or tissue providers or their proxy may donate the reproductive material for research.

3.3.2 Donation for reproduction by others. After implication counselling, this is only acceptable for adults who are healthy at the time of freezing.

3.4 Interdisciplinary consulting is mandatory

All specialties present in the caring team (oncologists, paediatricians, reproductive specialists, psychologists/counsel-

lors) should be heard during decision-making about the best procedure.

Conclusions

In view of the transition time during which research becomes therapy, the considerations of the taskforce will need revision when new evidence is available, specifically in the case of cryopreservation of reproductive tissues, in-vitro maturation and in-vitro follicle culture. Consent needs to be obtained

within a research context rather than for therapy or preservation of fertility *per se*.

References

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