

Guideline for cryopreservation of unfertilized eggs and ovarian tissues in Japan Society of Reproductive Medicine

Ethics Committee in Japan Society of Reproductive Medicine

1 | INTRODUCTION

The Japan Society of Reproductive Medicine (JSRM) issued the guideline for cryopreservation of unfertilized eggs and ovarian tissue in 2013. The Japan Society of Obstetrics and Gynecology also announced the society opinions concerning cryopreservation of unfertilized/fertilized eggs and ovarian tissue in 2016, independently. To integrate these statements and to reflect the development of current therapeutic modalities in Japan, ethics committee of JSRM revised the guideline for cryopreservation of unfertilized eggs and ovarian tissues.

First, considering that medical interventions for the treatment of malignancies might cause iatrogenic ovarian dysfunction, medical indication for cryopreservation of unfertilized eggs and ovarian tissues was specified. Second, the guideline of cryopreservation of unfertilized eggs and ovarian tissues for women that do not apparently possess malignancies and hope to preserve probable future fecundity was also described. Furthermore, requirements to be obeyed by facilities of reproductive medicine were raised to avoid the easy execution of these treatments.

We hope that this new guideline could help the specialists of reproductive medicine in their daily practice and also would be helpful for women that definitely desire to preserve future fecundity.

2 | MEDICALLY INDICATED CRYOPRESERVATION OF UNFERTILIZED EGGS AND OVARIAN TISSUES

(Eligible persons)

1. If gonadal hypofunction may be caused by medical intervention, eg, treatment of malignant tumors (hereinafter referred to as the underlying disease), it is allowed to cryopreserve unfertilized

eggs and ovarian tissue (hereinafter referred to as unfertilized eggs, etc.) upon request of the concerned person (the cryopreservation technique is hereinafter referred to as this method). If the implementation of this method is not considered to considerably disadvantage the concerned person's fertility preservation and treatment of the underlying disease, the person shall be deemed eligible for this method.

2. Prior to the implementation of this method, the attending doctor treating the underlying disease is required to provide appropriate written information and grant permission for the intervention to provide an understanding of the effect of the intervention on the treatment of the underlying disease.
3. If a malignant tumor is found in the ovary scheduled for cryopreservation, cryopreservation of the ovarian tissue will not be performed.
4. Cryopreservation of ovarian tissue is allowed based on the consent of the concerned person if she is an adult or based on the consent of the concerned person and person with parental authority if she is a minor. In the latter case, if the concerned person reaches adulthood, her willingness to continue the cryopreservation of her ovarian tissue shall be confirmed and her written consent shall be reobtained.
5. To obtain consent, both the attending doctor treating the underlying disease and the doctor specializing in reproductive medicine shall provide information and adequately explain the methods of collection and cryopreservation of unfertilized eggs, etc., and assisted reproductive technologies (ARTs) using frozen unfertilized eggs, etc., verbally and in writing, and then obtain informed consent (IC).

(Implementing facilities)

1. As a rule, the facility where the preservation of unfertilized eggs, etc., is performed and the facility where ART is implemented with the use of these tissues should be the same.

^aEthics Committee in Japan Society of Reproductive Medicine Participating members are given in the Appendix.

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2. It is desirable to implement this method in an ART-registered facility located within the facility where the underlying disease is treated; however, if there is no ART-registered facility within the facility where the underlying disease is treated, this method may be implemented at another ART-registered facility that can work together with the facility where the underlying disease is treated.

(Preservation of unfertilized eggs, etc.)

1. For the preservation of unfertilized eggs, etc., each facility is required to have the equipment to preserve the unfertilized eggs, etc., for a sufficiently long period of time. It is also desirable that the facility regularly confirms the concerned person's willingness to continue the preservation of the unfertilized eggs, etc.
2. Unfertilized eggs, etc., shall be discarded if the concerned person expresses the wish to discard the unfertilized eggs, etc., or dies. The facility may discard preserved unfertilized eggs, etc., after notifying the concerned person of the plan to discard unfertilized eggs, etc., when she has passed her reproductive age.
3. If the ART-registered facility is no longer able to continue the preservation of the unfertilized eggs, etc., the facility shall consider continuing the preservation of the unfertilized eggs, etc., at another ART-registered facility as far as possible in cooperation with the facility where the underlying disease is treated after obtaining the concerned person's consent.

(Others)

1. The sale, purchase, or transfer of cryopreserved unfertilized eggs, etc., is not allowed.
2. It is not allowed to use unfertilized eggs, etc., for other purposes than the concerned person's reproduction. However, frozen unfertilized eggs, etc., may be used, as an exception, only after the necessary procedures, including IC obtainment, are taken in accordance with the laws and national and ministerial guidelines if the concerned person expresses willingness to discard her unfertilized eggs, etc., and grants permission to utilize her frozen unfertilized eggs, etc., for research that contributes to the development of reproductive medicine.
3. Medical institutions that deal with medically indicated cryopreservation of unfertilized eggs, etc., are required to file an application for registration (facilities and cases) with the Japan Society of Obstetrics and Gynecology.

Notes

To obtain the IC set forth in the above item 5), the doctor specializing in reproductive medicine shall explain the following points.

1. The details of this method, expected results, and potential effects on the prognosis of the underlying disease.
2. The duration of cryopreservation of unfertilized eggs, etc., and the procedure of discarding the unfertilized eggs, etc.

3. The details of ART using frozen unfertilized eggs, etc., the chance of a future pregnancy, and the safety of the pregnancy.
4. The costs involved with this method.

3 | NOT MEDICALLY INDICATED CRYOPRESERVATION OF UNFERTILIZED EGGS OR OVARIAN TISSUES

(Eligible persons)

1. If gonadal hypofunction may be caused by aging and other factors, it is allowed to cryopreserve unfertilized eggs or ovarian tissue (hereinafter referred to as "unfertilized eggs, etc.").
2. Eligible persons for cryopreservation of unfertilized eggs, etc., are female adults who are preferably aged under 36 years at the time of collection of the unfertilized eggs, etc.
3. To obtain consent, the doctor specializing in reproductive medicine shall adequately explain the methods of collection and cryopreservation of unfertilized eggs, etc., and assisted reproductive technologies (ARTs) using frozen unfertilized eggs, etc., verbally and in writing, and then obtain informed consent (IC) from the concerned person.

(Implementing facilities)

1. As a rule, the facility where the preservation of unfertilized eggs, etc., is performed and the facility where ART is implemented with the use of these tissues should be the same.

(Preservation of unfertilized eggs, etc.)

1. For the preservation of unfertilized eggs, etc., each facility is required to have the equipment to preserve the unfertilized eggs, etc., for a sufficiently long period of time. It is also desirable that the facility regularly confirms the concerned person's willingness to continue the preservation of the unfertilized eggs, etc.
2. Unfertilized eggs, etc., shall be discarded if the concerned person expresses the wish to discard the unfertilized eggs, etc., or dies. The facility may discard preserved unfertilized eggs, etc., after notifying the concerned person of the plan to discard unfertilized eggs, etc., when she has passed her reproductive age.

(Others)

1. The sale, purchase, or transfer of cryopreserved unfertilized eggs, etc., is not allowed.
2. It is not allowed to use unfertilized eggs, etc., for other purposes than the concerned person's reproduction. However, frozen unfertilized eggs, etc., may be used, as an exception, only after the necessary procedures including IC obtainment are taken in accordance with the laws and national and ministerial guidelines if

the concerned person expresses willingness to discard her unfertilized eggs, etc., and grants permission to utilize her frozen unfertilized eggs, etc., for research that contributes to the development of reproductive medicine.

3. Concerning the use of cryopreserved unfertilized eggs, etc., adequate consideration shall be given to age-related increases in perinatal risks.
4. Medical institutions that deal with not medically indicated cryopreservation of unfertilized eggs, etc., are required to file an application for registration (facilities and cases) with the Japan Society of Obstetrics and Gynecology.

Notes

To obtain the IC set forth in the above item 3), the doctor specializing in reproductive medicine shall explain the following points.

1. The methods of cryopreservation of unfertilized eggs, etc., and the expected results and risks.
2. The duration of cryopreservation of unfertilized eggs, etc., and the procedure of discarding the unfertilized eggs, etc.
3. The details of ART using frozen unfertilized eggs, etc., the chance of a future pregnancy, and the safety of the pregnancy.
4. The costs involved in cryopreservation.

4 | REQUIREMENTS TO BE SATISFIED BY FACILITIES PERFORMING CRYOPRESERVATION OF UNFERTILIZED EGGS AND OVARIAN TISSUES

The Japan Society for Reproductive Medicine deems it necessary, as essential requirements, for a facility that clinically implements the concerned medical practice (hereinafter referred to as the implementing facility) to have sufficient premises and equipment, have appropriate personnel appointed to the related tasks, and to be organized with an appropriate medical system as well as a registration and reporting system. The Japan Society for Reproductive Medicine therefore requires the implementing facility to satisfy the individual requirements listed below.

1. The implementing facility must have filed an application for registration as “medical institutions to provide assisted reproductive technologies (ARTs)” with the Japan Society of Obstetrics and Gynecology (hereinafter abbreviated as “JSOG”) and already have been approved and certified as a facility registered to perform “medically indicated cryopreservation of unfertilized eggs, embryos (fertilized eggs), and ovarian tissue.”
2. The implementing facility must have renewed the registration procedure at least once after the initial registration with JSOG, satisfy the latest requirements set forth in the “Opinions/views on registration as a medical institution that may provide assisted reproductive technologies (ARTs) and reporting,” and have

records that prove fulfillment of its reporting duty without delay over the previous three years.

3. For the clinical implementation of cryopreservation of unfertilized eggs and ovarian tissue, the implementing facility must seek review by the Ethics Committee of the facility in conformance with the “Ethical Guidelines for Medical and Health Research Involving Human Subjects” on whether or not the clinical cryopreservation of unfertilized eggs and ovarian tissue should be implemented, and obtain the prior approval of the committee.
4. The implementing facility, in cooperation with the attending doctor treating the underlying disease, shall provide the person who wishes to undergo the necessary intervention for cryopreservation of unfertilized eggs and ovarian tissue for such reasons as cancer treatment with the necessary environment for continued and close consultation, advice, and instruction. In particular, if several facilities cooperate with the cryopreservation of unfertilized eggs and ovarian tissue, these facilities shall arrange opportunities to regularly discuss the operation of the system.
5. The implementing facility shall have at least one full-time specialist in reproductive medicine to provide persons requesting cryopreservation of unfertilized eggs and ovarian tissue the opportunity to provide their informed consent appropriately based on adequate information provision and counseling. It is also desirable that each facility has a professional counselor.
6. The implementing facility shall not only organize safe and secure equipment and a management system for the implementation of the cryopreservation of unfertilized eggs and ovarian tissue, but also prepare the necessary measures to archive detailed records of the concerned person as well as her frozen unfertilized eggs and ovarian tissue for a sufficiently long period of time and disclose these upon request of the concerned person and/or her child in the future.
7. The implementing facility shall organize a system that regularly confirms the concerned person's willingness to continue the preservation of cryopreserved unfertilized eggs and ovarian tissue.

CONFLICT OF INTEREST

Members of Ethics Committee in Japan Society of Reproductive Medicine have no conflict of interest.

APPENDIX

Ethics Committee in Japan Society of Reproductive Medicine

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