Preserving Fertility

Research Promotion of Fertility Preservation for Childhood and AYA Generation Cancer Patients

Context

- Cancer treatment can affect reproductive organs, the ovaries and testes; reduced fertility is a major concern to young patients. Collecting and freezing embryos (fertilized eggs), unfertilized eggs, ovarian tissue, and sperm for future use is possible, though costly. Without reimbursements by national medical insurance, the procedures impose a heavy economic burden particularly on young cancer patients.
- Furthermore, more evidence on the efficacy of freezed unfertilized eggs and ovarian tissue as means of fertility preservation are required.
- Support for fertility preservation therapies differ between local governments, national policies are required.

Project Summary

- An initiative to promote research on fertility preservation therapy will begin in fy 2021. There will be subsidies for fertility preservation therapy. Clinical information will be accumulated as evidence on the efficacy of fertility preservation therapies, and guidelines on the long-term storage of specimens from patients will be drafted.
- Whilst accumulating evidence, nationwide initiatives will be launched to fulfill the wishes of young cancer patients to have children in future after fighting cancer.

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Preservation Options

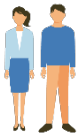
Fertilized egg

Eggs fertilized in vitro or microscopically, and developed, frozen and stored

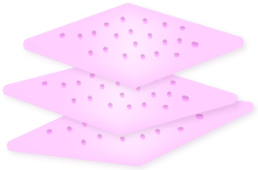
Single:
- ✓ menstruating
- ✓ transvaginal egg retrieval possible

Egg (Unfertilized)

Eggs frozen and stored before in vitro or microscopic fertilization



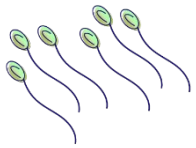
Married:
- ✓ menstruating
- ✓ transvaginal egg retrieval possible



Ovarian tissue

Ovarian tissue extracted, the entire egg production function including oocytes are frozen and stored

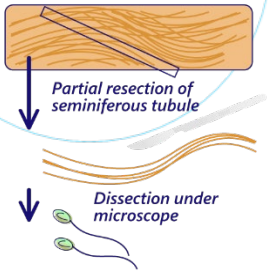
Unmarried/married:
- ✓ menstruation not required
- ✓ transvaginal egg retrieval not required
- ✓ laparoscopy offers shortened treatment



Sperm

Sperm frozen and stored for future in vitro or microscopic fertilization

Capable of ejaculation, sperm present



Testicular sperm extraction

Sperm collected directly from the testicles, frozen and stored

Capable of ejaculation, but sperm not present sperms formed, w/o ejaculation capacity

* Clinical records of all procedures, with cases resulting in pregnancy and birth in Japan and overseas are available
* Freezing of testicular tissue (testicle tissues extracted, the entire sperm production function including the spermatocytes are frozen and stored) is under research, but not yet ready for clinical use.
* Common-law/civil partnerships also eligible to freeze embryos (fertilized eggs)

(Partially revised extract from materials provided by Dr Nao Suzuki)

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- Promotes fertility preservation research by collecting clinical information from patients to generate evidence of the efficacy of preserving fertility, and developing guidelines for long-term specimen preservation, whilst reducing the cost burden of preserving fertility.

- Encourage young cancer patients fight the disease, support nationwide measures to assist having children in the future, whilst accumulating its evidence on effectiveness.

Table 1: Cryopreservation subsidies

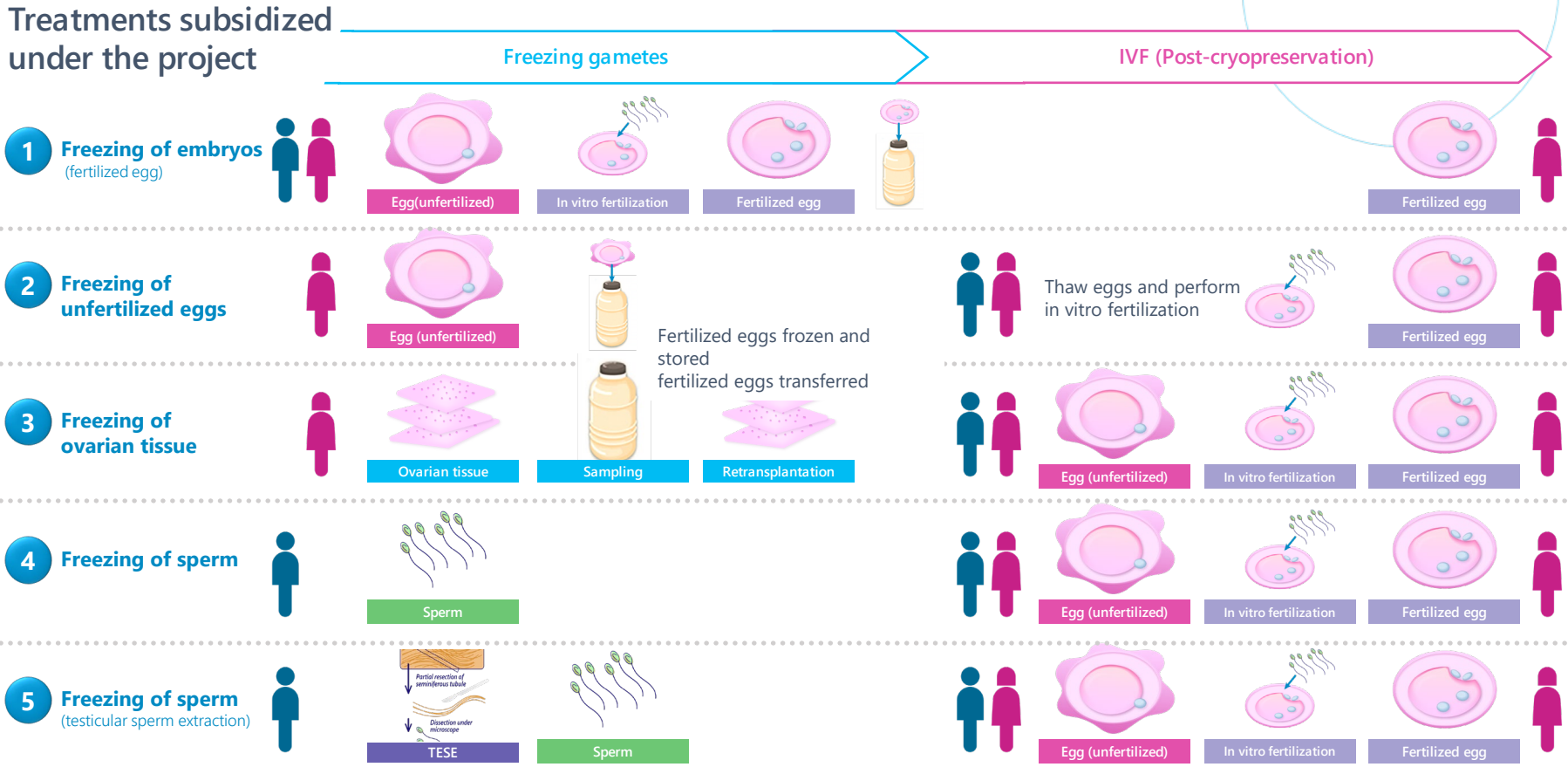
Treatment	Maximum (per treatment)
(1) Freezing of embryos (Fertilized egg)	350,000 yen
(2) Freezing of unfertilized eggs	200,000 yen
(3) Freezing of ovarian tissue	400,000 yen
(4) Freezing of sperm	25,000 yen
(5) Freezing of sperm (Testicular sperm extraction)	350,000 yen

Table 2: IVF (post-cryopreservation) subsidies

Treatment	Maximum (per Treatment)
Using embryos frozen (1)	100,000 yen
Using unfertilized Eggs frozen (2)	250,000 yen
Post reimplantation of frozen ovarian tissue (3)	300,000 yen
Using frozen sperm (4) and (5)	300,000 yen

Partially revised from documents submitted to Study Group on Preserving Fertility for Children and AYA Cancer Patients (11 Mar 2022)

Research on Fertility Preservation for Childhood and AYA Generation Cancer Patients - Initiatives



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Research on Fertility Preservation for Childhood and AYA Generation Cancer Patients - Eligibility

1. Age

- Preserving gametes
  under 43 years of age (at time of cryopreservation)
- IVF (post-cryopreservation)
  females under 43 years of age at start of treatment
  (common-law/civil partnerships eligible)

2. Treatments/Diseases

- Treatments for reduced fertility in childhood and AYA patients classified as high-, intermediate-, and low-risk, on oncology clinical practice guidelines (2017 Japan Society of Clinical Oncology)
- Cancers requiring prolonged treatment, such as breast cancer hormone therapy, which may impair ovarian reserve
- Hematopoietic stem cell transplantation treatment for aplastic anemia and other non-cancer diseases
- Alkylating agents administration for systemic lupus erythematosus and other non-cancer diseases

3. Screening

- Requiring deliberations by both the physician in charge of the primary disease, and a reproductive medicine physician (IVF specialist)

4. Consultation and consent

- Written consent of the patient, or for underage patients, of guardians

Research on Fertility Preservation for Childhood and AYA Generation Cancer Patients - Medical Institutions Requirements

1. *Collaborative Network for Cancer and Reproductive Medicine* established in the prefecture

Collaborative Network for Cancer and Reproductive Medicine

- A collaborative network between **cancer treatment/reproductive medicine facilities and local governments** in each prefecture
- Information on regional networks in 47 prefectures available on website of the Japan Society for Fertility Preservation

2. Designation of Medical Institutions

- In general
  full time medical physicians with relative accreditation on staff, guidelines observation, follow-up clinical information registration, participation in regional cancer-reproductive network, reproductive medicine treatment/support
- Eligibility - gametes cryopreservation
  Designated as a medical institution for preserving fertility (specimen storage) by the Japan Society of Obstetrics and Gynecology or the Japanese Urological Association, and by prefectural governments
- Eligibility - post-cryopreservation IVF
  Designated by the Japan Society of Obstetrics and Gynecology, and by prefectural governments
- Responsible for providing information, consultation services and psycho-psychological support to the patient, liaising with the medical institution treating the primary disease
- Responsible for entering data including clinical information, into the Japan Oncology and Reproductive Medicine Registry System (JOFR), and for periodical follow-up of subjects. Information on reproductive status, outcome of the primary disease is also to be entered into the system.

3. Primary disease care

- Provide medical indication reports, provide information, consultation service, and psycho-psychological support to patients, working with colleagues including from other institutions.