For men

Preserving fertility before cancer treatment

For young men with cancer
who wish to have children in the future

What is fertility?

Fertility is defined as "the ability to reproduce".
Cancer treatment may affect your reproductive functions, but there are many fertility preservation options available.

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Introduction

Recent advances in cancer treatment have aided many in overcoming cancer. Yet, despite these advances, some treatments can cause damage to testes and spermatogonia, which may lead to reduced sperm production or infertility.
This brochure will assist young male patients in making informed decisions about their fertilitypreservation options.

Fertility Preservation Checklist

- [ ] **1.** I understand the process and prospects of my cancer treatment, and how they may affect my fertility.
- [ ] **2.** I understand my fertility preservation options and what they involve.
- [ ] **3.** I understand the commitment and costs of fertility preservation, as well as its potential effect on my cancer treatment.
- [ ] **4.** I should consult my oncologist and reproductive endocronologist about my fertility preservation options.
- [ ] **5.** I understand that fertility preservation does not guarantee future fertility.

It is important to discuss all of these points with your partner, family, and any others who may be affected by your decision.

Cancer treatment and fsertility preservation

The balance between cancer treatment and fertility preservation

Starting an appropriate cancer treatment regimen is of utmost importance. Although fertility preservation may be an important consideration, proper cancer treatment should be prioritized over family planning. If time allows, effort should be made to consult with one's partner, family, oncologist and reproductive endocrinologist so as to make an informed decision about fertility prior to undergoing cancer treatment.

When should I start fertility preservation treatment?

You should first discuss your fertility preservation options with your doctor to understand both the merits and disadvantages of all preservation options. As preservation treatments must be performed before cancer treatment can proceed, it is sometimes necessary to adjust the treatment schedule if this is a possibility.

How cancer treatment affects testicular functions

Effects of chemotherapy and molecular targeted drugs

For males, gonadal dysfunction can occur due to direct toxic effects of chemotherapy and radiation therapy on spermatogonia, the primordial germ cells that mature into sperm during spermatogenesis. Some kinds of chemotherapy, radiation therapy, and surgery can cause damage to the testes and spermatogonia and reduce or stop sperm production.

Effects of chemotherapy on sperm production

Risk	Cancer treatment
High Risk	Any alkylating agent + TBI Any alkylating agent + pelvic radiation, or testicular radiation Cyclophosphamide >7.5 g/m^2 MOPP >3 cycles, BeACOPP >6 cycles Protocols containing Temozolomide BCNU + Cranial/ brain radiation
Intermediate Risk	Protocol containing cisplatin BEP x 2-4 cycles Cumulative cisplatin dose <400 mg/m^2 Cumulative carboplatin dose ≤2g/m^2
Low Risk	ABVD, CHOP, COP Combination chemotherapy for leukemia Anthracycline + cytarabine
Very Low/ No Risk	Vincristine
Unknown	Monoclonal antibody Tyrosine kinase inhibitor

Endocrine treatment for prostate cancer may affect sperm production. While there are reports suggesting some molecular targeted drugs may not affect male gonadal function, the influence of molecular targeted drug on sperm production is uncertain.

Effects of radiation therapy

Spermatogonia are extremely sensitive to radiation. Radiation therapy can lower sperm production when it is targeted towards the testicles, pelvis, pituitary gland, and brain, as can total body irradiation (TBI).

Effects of radiation therapy on sperm production

Risk	Cancer treatment
High Risk	TBI before stem cell transplantation >2.5Gy in men >6Gy in boys Cranial radiation ≥40 Gy
Intermediate Risk	Testicular radiation dose 1-6 Gy (due to scatter from abdominal/ pelvic radiation)
Low Risk	Testicular radiation dose 0.2-0.7Gy
Very Low/ No Risk	Testicular radiation due to scatter from abdominal/pelvic radiation) <2Gy

Effects of surgery

Removal of both testicles stops sperm production forever, while an orchiectomy does not affect sperm production.

Surgery on the prostate, bladder, large intestine, spine, or rectum can damage the nerves and cause erectile dysfunction and ejaculatory dysfunction. These surgeries often cause retrograde ejaculation or semen backflow towards the bladder.

Fertility preservation options

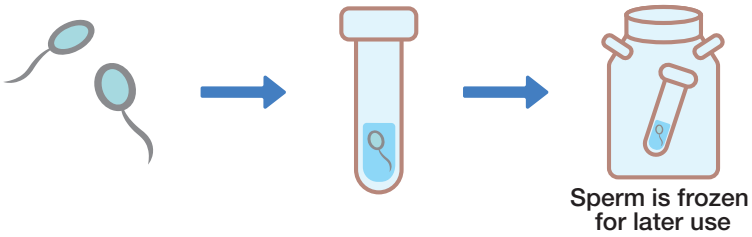
Sperm cryopreservation before starting cancer treatment is an established clinical option for male fertility preservation. Masturbation is the most common semen specimen collection method for postpubertal males.

Fertility preservation for males

	Adult	Children
Established methods	Sperm cryopreservation	After puberty, you can select sperm cryopreservation
Pre-clinical	Cryopreservation of testicular tissue	Cryopreservation of testicular tissue
Non-recommendation	Hormonal therapy	

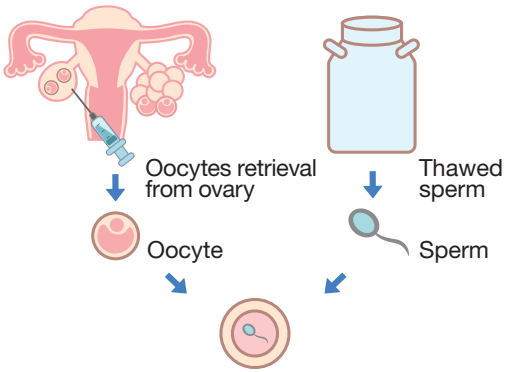
Even before treatment, testicular cancer can itself lower sperm counts. When sperm collection for cryopreservation is not possible, sperm can be removed using testicular sperm extraction (TESE) or microsurgical epididymal sperm aspiration (MESA) procedures. When deciding whether to go through with reproductive medicine, it is important to know that this procedure is not covered by insurance. If sperm preservation is not an option for you, consult with your oncologist and reproductive endocrinologist.

Sperm cryopreservation



Fertility after cancer treatment

Infertility may occur immediately or within a few months after cancer treatment and can last for months or years; in some cases, infertility is permanent. The extent and speed of recovery of spermatogenesis following a cancer treatment are dependent on the agent used and the dose received. When semen parameters are insufficient for natural pregnancy, frozen sperm with advanced reproductive technologies (ART) such as IVF and intracytoplasmic sperm injection (ICSI), can be used to achieve fertilization with a low number of viable sperm.



When sperm collection for cryopreservation is not possible, sperm can be removed using testicular sperm extraction (TESE) procedures. It is important to follow up your fertility after cancer treatment with your oncologist and reproductive endocrinologist.

When should I receive reproductive medical care after cancer treatment?

You should consult with your oncologist because the scheduling needs to be coordinated with your cancer treatment plan.

Family planning after cancer treatment

- Ask your oncologist about fertility before cancer treatment.
- Natural pregnancy is possible in some cases.
- Since natural pregnancy may be difficult depending on pre-treatment fertility and cancer treatment, ask reproductive endocrinologist about fertility preservation options.
- It may be difficult to have a child in a situation of illness, health condition after treatment, original infertility and so on.
- Even if you do not receive fertility preservation treatment before cancer treatment, fertility after treatment may be possible, so consult your reproductive endocrinologist.
- You may have to think about a lot of things and feel burdened. Please do not hold it alone and talk to the medical staff about your feelings.

For patients who do undergo fertility preservation treatment

- Please carry out the renewal procedure for cryopreserved sperm as necessary.
- If you wish to conceive using cryopreserved sperm after cancer treatment, please consult with the reproductive medical institution.
- Please be aware that it may be difficult to transfer cryopreserved sperm to other medical institutions.
- Using fertility preservation before cancer treatment does not guarantee future fertility.

For partner

- It is important that the partner is in good general health.
- In case of death or divorce, preserved sperm cannot be used.
- Frozen embryo, eggs or sperm cannot be used without the consent of the patient.

Flow chart for fertility preservation options

1. Ask your oncologist, nurses, pharmacists, medical social worker or psychologists about fertility preservation.

2. Ask your oncologist whether your reproductive function will be affected by your cancer treatment.

3. Select a reproductive endocrinologist.

4. Request a letter of introduction from the oncologist to the reproductive endocrinologist.

5. The reproductive endocrinologist will explain your current fertility and preservation options. (Your health insurance may not cover this fee. Please contact your reproductive medical institution for details.)

6. **If you opt for fertility preservation**
   You will undergo treatment at a reproductive medical institution.
   If you select not to pursue fertility preservation prior to treatment
   You may contact a reproductive endocrinologist after cancer treatment as needed.

7. After consulting about your fertility, you are ready to start cancer treatment.

How to find reproductive medical institutions

Consult your oncologist first. Several resources are available to you.

- **Japan Society for Fertility Preservation（JSFP）**
  日本・がん生殖医療学会　https://www.j-sfp.org/

- **Information Center for Cancer Patients**
  がん・情報サービス　https://ganjoho.jp/public/index.html

- **Oncofertility for Children and Adolescents**
  小児・若年がんと妊娠　https://www.j-sfp.org/ped/index.html

Costs for fertility preservation

Reproductive medicine is not covered by insurance.
Be advised that you will receive this treatment at your own expense.

Standard costs

- Counseling : First visit　Thousands to 10000 yen
- Oocytes cryopreservation : 200,000 yen to 400,000 yen
- Embryo cryopreservation : 300,000 yen to 500,000 yen
- Ovarian tissue cryopreservation 600,000 yen to 800,000 yen
- Sperm cryopreservation : 50,000 yen
  (If testicular extraction is required 400,000 yen to 500,000 yen)
- Annual storage fee for cryopreservation : 200,00 yen to 600,00 yen
- Micro insemination using cryopreserved sperm : 350,000yen to 400,000 yen

— Infertility treatment is covered by insurance from April 2022 in Japan, while fertility preservation for cancer patients is not covered by insurance.

— The Ministry of Health, Labour and Welfare launched the "Project to promote Fertility Preservation for Children and AYA Cancer Patients" from April 1, 2021. You can receive some subsidies for the fertility preservation treatment. For more information, please contact your local government.

Questions you should ask your oncologist

Reproduction medical institutes will need the following information from your oncologist.

- **Primary site of cancer**
- **Stage, prognosis**
- **Scheduled start date of cancer treatment**
- **Treatment (Chemotherapy, Operation, Radiation therapy)**
- **Urgency of cancer treatment (Time needed for fertility preservation)**
- **The risk of infertility by cancer treatment**
- **Contact information of oncologist for reproductive endocrinologist**

Please review the five checkpoints on page 2 after you talk with your reproductive endocrinologist to check whether you now have full information to make your own decision.

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Working Panel Tasked with Compiling Evidence Regarding the Fertility of Long-Term Survivors of Cancer during Childhood or Adolescence and with Developing a Reproductive Medicine Network (Organizer: Yoko Miyoshi)

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