

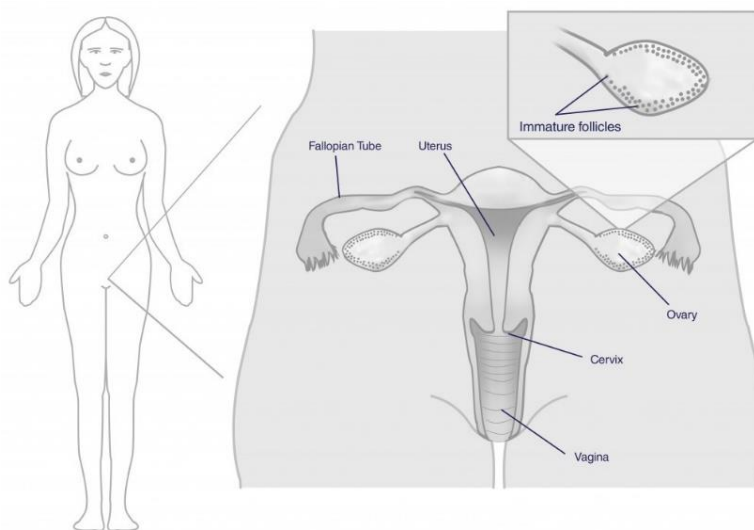
## The Royal Children's Hospital Fertility Preservation Service Ovarian Tissue Cryopreservation (OTCP) Information Sheet

### What Is Fertility Preservation?

Fertility preservation is a process that has the potential to preserve a person's ability to have a biological child in the future. This includes the freezing of healthy ovarian tissue and mature eggs.

### Reproductive System In Biological Females

When a biological female is born, the ovaries will contain hundreds of thousands of immature eggs (follicles). These are all the eggs required for life and they stay inactive until puberty. When puberty begins, usually between the ages of 8 & 14, the pituitary gland (located near the brain) starts making hormones that stimulate the ovaries to make hormones such as Oestrogen. Oestrogen causes breast development, and periods. About once a month, during ovulation, an ovary sends a tiny egg into one of the fallopian tubes. Unless the egg is fertilised by a sperm, a period occurs 2 weeks later.



### Potential Impact on Fertility

Medical treatments such as chemotherapy and radiotherapy, or conditions in childhood such as genetic conditions, may reduce the number of eggs in the ovaries. Depending on the severity, this can sometimes affect hormone production, puberty, periods and fertility. Your doctor will outline the estimated impact of your child's treatment on their fertility (low, medium or high risk). Unfortunately, it can be difficult to be precise about risk this due to limited data.

### How Does Chemotherapy Affect Fertility?

Chemotherapy drugs enter the blood stream and travel around the body searching for cancer cells to destroy. Chemotherapy may reduce the number of eggs in the ovaries. If egg numbers are affected to a large extent there is a possibility that progression of puberty can be affected or menopause may start earlier, affecting fertility.

### How Does Radiotherapy Affect Fertility?

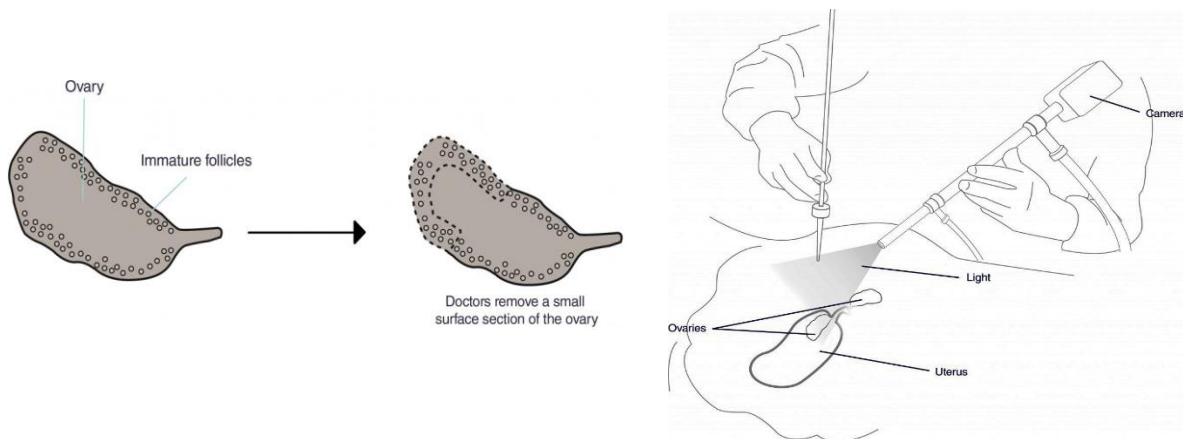
Radiotherapy destroys cancer cells. If the ovaries are exposed to radiotherapy, then eggs can be destroyed. Total body radiation carries a high risk of causing infertility. If radiotherapy is required to treat

a brain tumour, the hormone messages from the brain to the ovaries can be disrupted or lost causing the ovaries to become inactive. However, the ovaries can be triggered into developing mature eggs via hormone stimulation (IVF) in the future.

### **Ovarian Tissue Cryopreservation (OTCP) - How Is This Procedure Done?**

OTCP involves the collection of healthy ovarian tissue prior to starting treatment that may harm the ovaries. The tissue contains immature follicles. It is then preserved and frozen until your child is ready to think about starting a family. It is important to understand that there is no guarantee that the freezing of ovarian tissue will lead to successful pregnancies and/or live births.

The procedure is performed via laparoscopy (also known as 'keyhole' surgery), which involves a small incision in the belly button, along with 2-3 other small incisions in the abdomen, through which a camera and other surgical instruments are inserted. The surgeon will assess the ovary and then removes about 1/2 to one ovary. The whole ovary is removed if it is very small, or if the treatment is likely to cause a severe impact on future ovarian function. The procedure takes approximately 30 minutes and is usually coordinated with another procedure. Each of the incision sites will have a small dressing on them and recovery time is usually a few days.



Currently, scientists from the Reproductive Services Department at the Royal Women's Hospital (RWH) collect the tissue from theatre and process it at their centre. A small piece is tested for quality assurance to check for malignant cells in the tissue. The remainder is sliced, placed in liquid and frozen until required for future fertility treatment.

### **Using This Tissue In The Future**

There are two techniques being developed to facilitate using this tissue to create a pregnancy. Implanting the tissue back into the body or maturing the tissue outside the body in the IVF lab via a process called In Vitro Maturation (IVM).

#### **Transplanting the tissue back into the body**

Once thawed, the tissue can be implanted into the body next to the ovary. If it develops a blood supply, the tissue will start to work again in response to the hormone messages sent from the brain. These hormones will mature the follicles in the tissue and there is then the potential for a natural pregnancy to occur.

The tissue can also be implanted elsewhere in the body, such as in the abdominal wall, but IVF treatment will be required to create a pregnancy. This would involve undergoing an IVF cycle where mature eggs are collected from the tissue. The eggs are then fertilised with a partner's sperm (or donor sperm) in the IVF lab. Once the egg is fertilised and grows into an embryo, this embryo will then be transferred into the uterus.

Tissue that has been collected from patients who have been diagnosed with Leukaemia are not able to have this tissue implanted due to the risk of malignant cells being present and reintroducing Leukaemia back into the body. For these patients, maturing the tissue via IVM is being developed.

### **Maturing the eggs via IVM**

If the tissue is not suitable to be implanted into the body, the eggs can be matured in the IVF lab, fertilised with sperm and the resulting embryo would be transferred into the uterus. IVM is considered an experimental technique.

### **Who Is Eligible For Ovarian Tissue Cryopreservation?**

Theoretically, there is no lower age limit for Ovarian Tissue Cryopreservation and it can be offered to patients of all ages. However, your child needs to be well enough for surgery. Multiple abdominal scars, bleeding disorders or serious immune deficiency may preclude your child from having the procedure done.

In a very young child, the ovaries will usually be very small and it is highly possible that one entire ovary may need to be removed. We cannot guarantee that the ovarian tissue collected or the remaining ovary will be functional in the future.

### **Outcomes So Far**

Approximately 200 births have been reported worldwide using ovarian tissue cryopreservation technology. Three live births have been reported in women who have had their tissue stored in childhood.

### **Risks and Benefits**

The surgery (Laparoscopy, Ovarian Tissue Cryopreservation, removal of one ovary) is not experimental as this procedure is performed routinely by gynaecologists and surgeons for other indications.

Expected risks of the surgical procedure:

- Risk of a general anaesthetic
- Infection
- Bleeding
- Damage to internal structures (bladder, bowel, blood vessels) which may occasionally require performing an open operation. These risks are likely to be higher during cancer therapy
- Risk of changing from keyhole surgery to a larger incision (laparotomy)

### **What Other Options Are Available?**

- If you decide not proceed with fertility preservation, your child can have their ovarian function assessed later either after treatment in follow-up clinic.
- Egg donation from mother, sister, female relative or other donor in the future.
- Fostering or adoption.
- For post pubertal females, there is the option to have an injection called Zoladex® which is a hormone that suppresses ovarian function and may protect the ovary. Studies in adult women suggest that Zoladex® may have a small protective effect on fertility, but there are no studies in teenagers. Zoladex® is also used to suppress menstruation during chemotherapy.

### **Other Issues to Consider**

- Cost of tissue storage: currently the RWH does not charge for the storage of tissue until your child turns 21. After this, there will be an annual storage fee.
- Cost of IVF treatment if required.
- The tissue may be stored at an alternate IVF centre: there may be storage and transport costs involved.
- The tissue can only be used by your child and, in the unfortunate event of death, the tissue must be disposed of. The tissue cannot be donated to research or be utilised by anyone other than your child.

**Who Do I Contact For Further Information?**

For further information, please contact the Oncofertility team at RCH.

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