

The Royal Children's Hospital Fertility Preservation Service Testicular Tissue Cryopreservation (TTCP) Information Sheet for Leukaemia Patients

Impact of treatment on fertility

Some cancer treatments affect fertility. Children and adolescents who receive treatment for Leukaemia receive medication called alkylators which are known to affect fertility. Treatment can affect sperm count and the cells that make sperm. The risk to fertility can be low, medium or high risk, depending on many factors including the dose of treatment received, age and gender.

For a young biological male who has not reached puberty, we believe the risk to fertility becomes moderate after receiving 4g/m² of Cyclophosphamide. Unfortunately, we can't be exact about the risk estimate due to insufficient data. Doses of around 5g/m², and particularly doses exceeding 10g/m², are strongly associated with a reduced likelihood of parenthood.

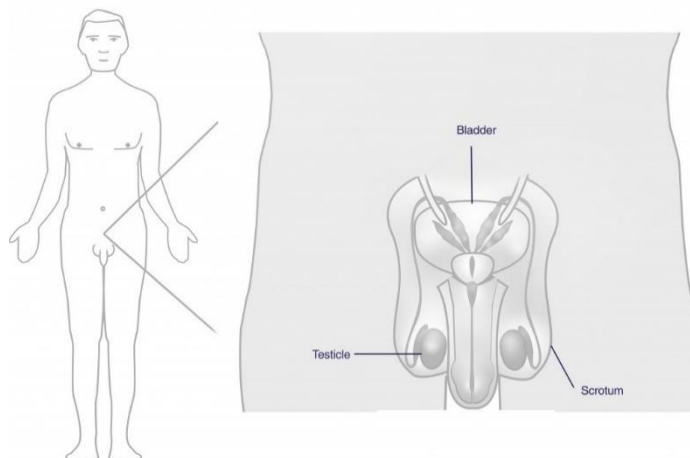
To many parents and young people, fertility is important to them, and many people ask about ways that fertility could potentially be protected.

What Is Fertility Preservation?

Fertility preservation is a process that aims to give patients the opportunity to freeze sperm, eggs or reproductive tissue. It is hoped that this may protect a person's ability to have a biological child in the future. Some of these procedures are proven to assist fertility with live births recorded, and others are considered experimental. Testicular Tissue Cryopreservation (TTCP) is the only fertility preservation procedure available to try and protect fertility for prepubertal males. However, this procedure is experimental.

Reproduction in Biological Males

The testicles of a pre-pubertal child do not contain sperm, they contain germ cells. When puberty begins, usually between the ages of 9 & 15, the pituitary gland (located near the brain) secretes hormones (FSH sperm production & LH testosterone) that stimulate the testicles to produce testosterone and mature sperm.



Testicular Tissue Cryopreservation (TTCP) – what is it?

TTCP involves the collection of healthy testicular tissue prior to starting treatment that may harm the testes. The tissue, which contains immature germ cells, is harvested via a small incision made in the scrotum, where part of the testicle is removed (approximately 30% of the testicle). It is then preserved and frozen until your child is ready to think about starting a family.

This procedure is not routinely undertaken for those at low risk for infertility unless there are special circumstances. This is because:

- 1) It is an experimental procedure. It is important to understand that there is no guarantee that the freezing of testicular tissue will lead to successful pregnancies and/or live births. There are no live births to humans to date.
- 2) Furthermore, in someone receiving only low risk treatment, we would hope that there are other options for saving fertility down the track. For example, collecting a sperm sample later in life.
- 3) Sometimes people are too sick at the start of cancer treatment. In this situation, urgent chemotherapy without any delays can be lifesaving.
- 4) There are risks of the surgical procedure which may be made worse at the start of treatment when counts are low. These include:
 - a. Risk of a general anaesthetic
 - b. Infection
 - c. Bleeding
 - d. Haematoma (collection of blood)
 - e. Risk of a second operation to address any of the above issues

Special Considerations

For patients with Leukaemia there are special considerations. There are only two ways to try and use the tissue.

- One way is to implant the tissue back into the body in the hope that it will produce sperm. Unfortunately, tissue that has been collected from patients who have been diagnosed with Leukaemia are not able to have this tissue reimplanted due to the risk of malignant cells being present and reintroducing Leukaemia back into the body.
- Another way is to try to mature the tissue outside the body in the IVF lab via a process called In-Vitro Maturation (IVM). Unfortunately, we do not know how to develop mature sperm from this tissue in humans.

Who Is Eligible For TTCP?

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

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

What Other Options Are Available?

- Your child can have their testicular function assessed later after treatment in follow-up clinic.
- Sperm donation from father, brother, male relative or other donor in the future.
- Fostering or adoption.
- For post pubertal males, freezing of mature sperm is an option.
- If the situation changes and the doses of treatment will become moderate or high risk to infertility, and surgery is deemed safe, then TTCP may be considered at a later date.

What does TTCP surgery involve?

The tissue, which contains immature germ cells, is harvested via a small incision made in the scrotum, where part of the testicle is removed (approximately 30% of the testicle). The procedure takes

approximately 20 minutes and is usually coordinated with another procedure. The incision will be closed with dissolving stitches and may have a small dressing. Recovery time is usually a few days.

Currently, scientists from the Reproductive Services Unit at The Royal Women's Hospital (RWH) collect the tissue from theatre and process it at their centre. A small piece is sent for histopathology to see if there are any malignant cells in the tissue. It is then sliced, placed in liquid and frozen until required for future fertility treatment. Sometimes the tissue is dissected for mature sperm in children who are going through puberty.

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 can only be used by your child. In the unfortunate event of the death of your child, the tissue cannot be donated to research or be utilised by anyone other than your child. Therefore, the tissue must be either:
 - Disposed of
 - Released to a nominated funeral director for burial/cremation with your child

Who Do I Contact For Further Information?

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

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