Edinburgh Fertility Preservation - What we do

Scroll down for further information on each procedure.

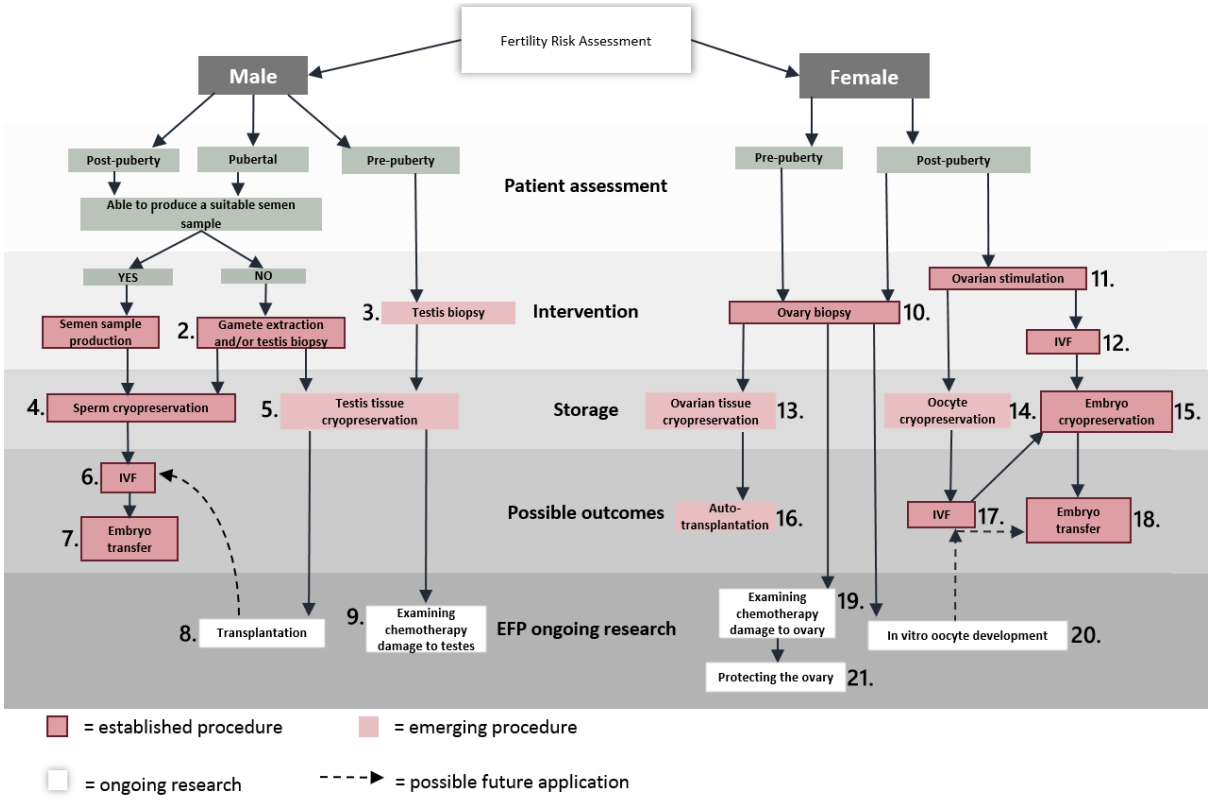

Image adapted from Adapted from Anderson et. al, 2015, Lancet Diabetes and Endocrinology, found at http://www.thelancet.com/journals/landia/article/PIIS2213-8587(15)00039-X/abstract.

Procedures

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1. Fertility Risk Assessment

With the considerable costs of storing frozen tissue and the invasive and experimental nature of some of the techniques involved, there is little point in a patient opting for fertility preservation unless there is a strong chance their fertility will actually be compromised by their treatment plan.

A fertility risk assessment will consist of looking at factors including the age and development stage of the patient, the prognosis, and the intended treatments.

Treatments known to have the most clinically significant risk to fertility in both male and female patients include:

- total body irradiation
- chemotherapy conditioning before bone marrow transplantation
- radiotherapy to a field that includes the sex organs
- specific chemotherapy drugs

2. Gamete extraction and/or testis biopsy

For individuals from whom it is not possible to obtain a semen sample without intervention, gamete extraction and/or testis biopsy can be used to obtain sperm and testis tissue for cryopreservation. Gamete extraction usually involves the surgical removal of mature germ cells i.e. sperm. A testis biopsy is the removal of a small amount of testis tissue, which can be preformed in pre-pubertal boys who have not started producing sperm yet.

3. Testis biopsy

For a prepubertal boy or adolescent male from whom no sperm sample can be obtained, a sample of testis tissue - a 'biopsy' – can be taken instead. This is usually done under general anaesthetic. The tissue biopsy can be frozen and stored for possible future use in restoring fertility.

4. Sperm cryopreservation

Sperm cryopreservation is one of the most established techniques for assisted reproduction, having first been carried out successfully in 1953. If an individual is unable to produce a semen sample there are alternative procedures available for gamete extraction. The cryopreserved sperm, when needed, can then be thawed and used for IVF to create an embryo.

5. Testis tissue cryopreservation

Testis tissue cryopreservation involves obtaining a testis tissue biopsy from a boy or adolescent male prior to treatment which may compromise their fertility. The biopsy samples are treated with protective chemicals and frozen at a very low temperature and stored until needed. Restoration of fertility from frozen immature testis tissue has been shown to work in animal studies, and research is currently underway to develop similar strategies using human tissue.

6. **IVF**

In vitro fertilisation (IVF), is a laboratory technique involving bringing the sperm and egg together in a culture dish. It simplifies the process of fertilisation and eliminates a lot of the factors that can prevent it happening naturally, increasing the chances of successful fertilisation. Since the first birth following IVF in 1978, millions of couples who were unable to conceive naturally have used this method to have a child.

7. **Embryo Transfer**

Embryo transfer is a simple procedure in which fertilised embryos are placed in the uterus allowing them to implant and initiate a pregnancy. Anaesthetic is generally not found to be necessary for this procedure. Ultrasound is used to establish the best location for embryo release, and oestrogen injections are administered beforehand to optimally prepare the womb lining for receiving the embryo**.**

8. **Transplantation**

Testis tissue or cells obtained and stored from male patients at risk of infertility may be used in the future to restore their fertility. Research is currently underway to develop strategies to transplant tissue or cells back into the patient after their treatment is completed. Alternatively strategies to make sperm from the tissue/cells in a culture dish are also being developed. Animal studies have already demonstrated that some of these options are feasible but currently there are no established methods to restore fertility using human tissue/cells.

A limited number of centres worldwide are currently undertaking such research. This includes an EU funded collaboration of European clinical research teams, GROWSPERM which includes our centre in Edinburgh as the only UK centre currently involved in such research activity. www.growsperm.eu

9. **Examining chemotherapy damage to testis**

The first step towards the ultimate aim of protecting the testis from chemotherapy damage is to investigate how exactly the different types of drug cause damage to the testis. We have ongoing work investigating this, finding out which drugs are the most toxic to the testis, and what cell types they kill. Current work is funded by Children with Cancer UK.

10. **Ovary biopsy**

For a prepubertal girl or young female adolescent who has not started ovulating yet, a sample of ovarian tissue - an ovary 'biopsy' – can be taken instead of collecting eggs. The procedure is done under anaesthetic. The tissue biopsy can be frozen and stored for possible future use in restoring fertility.

11. **Ovarian stimulation**

Ovarian stimulation is a technique where the ovaries are artificially stimulated to release more eggs than usual so that a substantial number can be collected and stored. It requires injections of different hormones over a period of roughly two weeks and in rare cases can result in ovarian hyperstimulation, where the ovaries overreact to the hormones and produce an abnormally high number of eggs, leading to complications. Collecting the produced eggs is a minimally invasive procedure performed under anaesthetic.

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13. **Ovarian tissue cryopreservation**

Ovarian tissue cryopreservation is a procedure where ovary tissue samples are taken before a female patient undergoes treatment which may damage her fertility. The samples are treated with protective chemicals and stored at a very low temperature until needed. If a patient suffers fertility problems following cancer treatment, the tissue can be transplanted back into the individual to potentially restore fertility and hormone production.

14. **Oocyte cryopreservation**

Oocyte cryopreservation is a procedure where the eggs or 'oocytes,' are stored at a very low temperature in order to maintain them for potential future use in IVF. Although embryos are more suited to cryopreservation than oocytes, oocyte cryopreservation is still preferable for women who are not in a position to create an embryo at the time of consultation.

To retrieve a sufficient number of oocytes for cryopreservation multiple hormone injections stimulate the ovaries to produce more oocytes than they would normally. Ovarian stimulation can take up to two weeks.

15. **Embryo cryopreservation**

Embryo cryopreservation is the freezing of embryos for possible later use in IVF. It is currently the most viable method of preserving a woman's fertility, as oocytes do not freeze as effectively and ovarian tissue cryopreservation is still a relatively novel technique.

16. **Autotransplantation**

Autotransplantation is where tissue is re-implanted back in to the individual from whom the tissue was originally taken. Unlike traditional transplants, the transplanted tissue has the same origin as all the other tissue in the *receiving* body and so there is little risk of it being rejected. Ovarian autotransplants have been shown to be capable of inducing puberty, restoring fertility and postponing early menopause.

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19. **Examining chemotherapy damage to ovary**

The first step towards the ultimate aim of protecting the ovary from chemotherapy damage is to investigate how exactly the different types of drug cause damage to the ovary. Funded by the Medical Research Council, we have investigated many of the drugs most commonly given to young women. The work has shown the great variability amongst drugs, with few drugs directly damaging germ cells.

20. **In vitro oocyte development**

The ability to develop human oocytes from the earliest stages through to maturation and fertilisation outside the body (in vitro) would revolutionise fertility preservation practice. This technique would be most suitable for pre-pubertal girls particularly in cases where ovarian transplantation is not an option.

The aim of our work is to determine whether complete oocyte development can be achieved from human ovarian tissue grown in a multi-step culture system. We have developed a dynamic multi-step culture system that supports:

1. The activation of primordial follicles
2. Growth of multilaminar follicles
3. Oocyte growth out with the large follicular environment

Using this system a population of mature oocytes can be obtained. The challenge now is to improve the quantity and quality of in vitro grown human oocytes and to ensure the safety of this technology before it can be applied in a clinical setting.

21. **Protecting the ovary**

The ideal situation would be if the ovary could be protected from any possible damage by chemotherapy drugs during treatment, thus maintaining fertility. We are using a novel tissue culture technique to investigate a range of potential protectants, in work funded by the European Society of Human Reproduction and Embryology.