

Effects of cancer therapy on fertility and Ovarian function

The aim of this Information sheet is to help answer some of the questions you may have about fertility preservation. It explains the benefits and risks of the different options as well as what you can expect when you come to hospital. If you have any questions or concerns, please do not hesitate to speak to a doctor or nurse caring for you.

What is fertility preservation for women undergoing cancer therapy?

Recent advances in treatment mean a larger number of women can hope to recover or be cured of cancer. However, the chemotherapy and/or radiotherapy used to treat the disease can in many cases affect future fertility or permanently affect the ovaries.

We can offer fertility treatment before the chemo/radiotherapy which may give you an opportunity to try for a baby when you have completely recovered. The likelihood of the ovaries being affected is different for different women. It will depend upon your age and the type of treatment you will have. Your doctor can refer you to the fertility clinic to discuss this further. We realise that the diagnosis of cancer and coping with the treatment can be a difficult time for you and we will be happy to answer any queries you may have.

Will my chemotherapy have to be postponed in order to have fertility treatment?

Fertility treatment takes two to three weeks from the start of the medications to stimulate your ovaries.

Your doctor can refer you to discuss fertility preservation, if your cancer treatment can be deferred for this period of time. There are different options of fertility preservation interventions that are available. At your consultation, the fertility doctor will discuss which method is the most suitable for you.

What are the options for fertility preservation?

The options are listed below. Your doctor will be able to discuss each in more detail with you and give you an information leaflet.

IVF and embryo freezing

This option is suitable if you have a partner and are in a stable relationship.

In Vitro fertilisation (IVF) involves stimulating the ovaries with dally hormone injections to produce several eggs, which are then recovered by a minor operation.

In the laboratory, the eggs are mixed. with sperm provided by your partner. The resulting fertilised eggs (embryos) are then frozen in the laboratory by a process called vitrification. These embryos can be stored for up to 10 years in the first instance. Storage may then be extended depending upon individual circumstances.

1



When you have recovered completely after chemotherapy, and are ready to try for a family, the embryos can be thawed (defrosted) and replaced in the womb either in your natural cycle or after preparing your womb by taking hormone therapy. On average one in three - four women will become pregnant using this method.

Freezing of oocytes (unfertilised eggs)

This is suitable for women without a partner or for young girls who are sexually mature. It is different from embryo freezing because your eggs are recovered and stored without being fertilised. In the future when you wish to try for a baby the eggs will be thawed (defrosted) and mixed with sperm from your partner to create embryos. After creating the embryos, they will be cultured in the laboratory and transferred to the womb after preparing the womb with hormonal treatment.

This option is generally less successful than frozen embryos because unfertilised eggs do not survive the freezing process as well as the embryos. However, these techniques are Improving all the time and recent literature reports good survival rates (with between seven and eight out of 10 eggs surviving) after thawing.

The success will largely depend on the age of the woman when the eggs were frozen.

Ovarian tissue cryopreservation

This is mainly indicated for pre-pubertal girls diagnosed with cancer.

This procedure is still in an experimental state and this treatment and is not currently offered in our unit. However, your doctor may be able to provide information if this procedure is being offered elsewhere.

A surgeon removes a small portion of your ovary and freezes it. The operation is done under general anaesthetic (when you are asleep) and the surgeon will insert a telescope into your abdomen to remove the ovarian tissue. The tissue is then frozen. Later when you have recovered after chemotherapy, the tissue can either be transplanted into you/ body or the eggs from the tissue matured in the laboratory.

Hormonal therapy

If you are having chemo/radiotherapy, it is thought that the ovaries may be protected by temporarily switching them off. This is done by giving you injections of a drug (GnRH agonist). The injection is given every four wee s while you are undergoing chemotherapy. Your periods are likely to stop completely during that time.

It does not have any serious risks or side effects, but you may experience some symptoms similar to the menopause, which can last as long as you are having the injection.

This method may not be suitable for everyone. It is also currently an experimental procedure, and we cannot be sure that the treatment will protect your ovaries. It may be considered if you do not have enough time to undergo IVF before starting chemotherapy.



Will the ovarian stimulation for IVF Increase my cancer risk?

The hormonal medications used to stimulate your ovaries during the IVF will increase the oestrogen level in your body. However, the level will return to normal within few days after the treatment in over. So, you can expect a rise in the oestrogen level for the couple of weeks when you will take the hormonal injections to stimulate your ovaries.

Since the ovarian stimulation lasts for only a short duration (approximately 2 weeks), the risk to cancer flare up is very low.

For those with oestrogen sensitive tumours. the risk of cancer flare can be reduced by giving another medication (letrozole) during the stimulation process, which reduces the oestrogen level without having any impact on the success of the IVF stimulation.

Do I need any tests before I can freeze embryos I eggs?

There is a theoretical risk of viral (HIV, Hepatitis B & C) cross-contamination between samples that are stored in liquid nitrogen. Though there have been no reported incidences of such cross-contamination between frozen samples, you (and your partner) will be screened for HIV and Hepatitis B & C before we freeze embryos/eggs.

Can I discuss fertility preservation before treatment?

You can be referred to the fertility specialist to discuss the options of preserving fertility. In many cases there may not be enough time to complete fertility treatment before starting the chemotherapy. If there is, the consultant will discuss and advise treatment that is appropriate for you. An ultrasound scan, and ovarian reserve test will be undertaken to assess your present fertility status. You will also have screening blood tests. All the relevant consent forms need to be completed by you/and your partner before treatment is commenced.

Are there legal implications of storing embryos/eggs?

Under the terms of the Human Fertilisation and, Embryology Act (1990) you are required to give written consent regarding:

- Storage of your embryos/eggs.
- The period of time for which they may be stored.
- The purposes for which your embryos/eggs can be used.
- Your partner will also be required to complete the treatment and storage forms H embryos are to be stored.
- To state wishes over any embryos created/eggs stored.
- What should be done with your embryos/eggs in the event of your death or if you become incapable of varying or revoking your consent.



If you have stored embryos, it is important to remember that in the future, both partners involved in the initial treatment, must provide written consent at the time when the embryos are replaced. If your partner withdraws his consent. it will not be possible for us to replace the embryos.

If you have stored eggs and wish to have fertility treatment in the future, you and your future partner can do so after signing new consent forms.

Is this treatment available on the NHS?

There is currently no special funding available for fertility preservation. The criteria for funding are the same as that of any other couple seeking fertility treatment. If you are eligible for fertility treatment (meaning if you are diagnosed with infertility), then funding will be provided for fertility preservation.

NHS funded treatment will not be available if you already have a child.

What happens if I cannot have fertility treatment before my Chemo/radiotherapy?

It is possible that as a result of the cancer treatment the ovaries stop working permanently or the duration of treatment may place you into an age of natural menopause.

If it was not possible to store eggs/embryos before treatment some couples may wish to consider using donated eggs. You will need treatment with IVF, where the donated eggs would be fertilised with sperm from your partner. The resulting embryos would be replaced in your womb. If it is successful, the pregnancy should proceed as any pregnancy, and you would give birth to the baby.

How will I know if my ovaries recover their function?

In some young women the ovaries may start functioning after many months or years. You will have the option to be seen in the follow-up clinic to assess whether the ovarian function has resumed. If the ovaries recover, there may be a need for contraception, which can be discussed at that time.

What happens If my ovaries do not recover?

For some women the ovaries may never recover. This is known as premature ovarian failure (if you are under the age of 40). You may have hot flushes, night sweats and sleep disturbance. These symptoms can be relieved with hormone replacement therapy (HRT). However, HRT might be contraindicated in some cancer patients.

The diagnosis of cancer and coping with the treatment can be stressful, creating difficulties in physical and emotional relationships. Following premature ovarian failure or after radiotherapy to the pelvis, you may have a low sex drive, or sex can be uncomfortable.



You may feel differently about yourself, and concerned about how your partner feels about you. Many young women and men are embarrassed or feel it not the most thing to discuss with the doctor.

Please speak to the fertility nurse or doctor, as help and support is available.

Is a counselling service available?

We can refer you to an experienced and confidential counselling service.

What Is the procedure for egg/embryo freeze?

Full cycle information will be given to you at consultation outlining the tests required, forms required, process and potential risks. The initial steps (1-4) are similar to that in an IVF cycle

Step 1: Ovulation induction

FSH Injections to stimulate the ovaries to produce multiple follicles (each follicle potentially containing an egg), over a period of approximately 2 weeks.

Step 2: Monitoring response

3-4 scans (with blood tests) over this period to monitor the number and size of the follicles. to help us correctly time when we should collect them.

Step 3: Preparing for collection

Trigger injection when the leading follicle reaches 17-22mm, to mature the eggs in preparation for collection.

Step 4: Egg collection

The eggs are collected using a minor vaginal procedure performed under general anaesthetic/sedation and under ultrasound guidance.

Step 5: Egg freezing

Following collection, the cells around the eggs are stripped away to identify which eggs are mature. These mature eggs are then cryopreserved using the vitrification process.

Step 5: If you are considering Embryo freezing

A semen sample will be required from the male partner on the day of the egg collection. The eggs are then fertilised by either conventional in-vitro fertilisation (IVF) or intra-cytoplasmic sperm injection (ICSI). After either IVF or ICSJ the eggs are incubated overnight, and the embryologists will assess for successful fertilisation the next morning. Fertilised eggs will be frozen on the same day.



Step 6: Future use

If you have frozen eggs, then these eggs can be thawed and fertilised using micromanipulation techniques (ICSI) that are required as the freeze / thaw process leaves the outer layer of the egg (zona pellucida) hardened. These fertilised embryos are cultured and those of highest quality chosen for transfer into the prepared lining of the uterus. Any top-quality embryos not transferred can be frozen for later use.

If you have frozen embryos, then one embryo would be thawed (defrosted) and transferred in your natural cycle or after preparing your womb with hormones.

When can I consider pregnancy after completing breast cancer treatment?

It is advisable to wait for at least two years from completion of active cancer treatment before becoming pregnant. This is because the possibility of the cancer coming back can lessen over time, and you may be at greatest risk in the first two years after completion of treatment.

It is not recommended to get pregnant for at least four to six months alter chemotherapy treatment.

If you have been advised hormonal therapy (tamoxifen) to prevent recurrence of breast cancer, you might need to take a break from hormone treatment if you want to try to get pregnant. This must be individualised according to your risk and you should discuss with your cancer specialist. Getting pregnant on tamoxifen is not recommended.

If you're planning to get pregnant after you've finished taking the hormone therapy, it's advisable to wait at least two months to allow time for the drug to leave the body completely. The targeted therapy trastuzumab (Herceptin) is normally given for a year and is not thought to affect fertility. However, you should avoid becoming pregnant while taking trastuzumab and for at least six months after treatment has finished. This is because of the possibility of harm to a developing baby.

If you cannot/don't want to take a break from your hormone treatment to become pregnant because of higher risk of breast cancer recurrence, then you can choose to have Surrogacy, which involves another woman carrying a baby for you.

What would I need to do if I am considering surrogacy in future?

If you are considering surrogacy in future, then you would have to consider extra tests and consent forms, which will be clarified in the clinic. Both of you would also have to repeat the tests in 3-6 months' time to release the embryos.

In case of eggs, only the female partner would need to repeat tests in 3-6 months' time.



The following information sites may be helpful:

HFEA - UK regulating authority of licensed conception and treatment centres. <u>www.hfea.gov.uk</u>

Infertility Network UK - National charity providing information & counselling for people with fertility issues www.infertilitynetworkuk.com

Breast cancer support groups: Breast Cancer Now -Charity to support women with breast cancer. https://breastcancernow.org/information-support/support-you

Save My Fertility: An American patient information resource provided by the Oncofertility Consortium. http://www.savemyfertility.org/

Fertility Friends: An online community discussing infertility, adoption. parenting after infertility and moving on. www.fertilityfriends.co.uk