SUPPORTING PATIENTS WITH CANCER:

FREQUENTLY ASKED QUESTIONS

Funding statement: These independent educational activities are supported by an educational grant provided by Pfizer. PCM Scientific is the medical education company acting as scientific secretariat and organiser for this programme. The activity is run independently of the financial supporter and all content is created by the faculty. No funder has had input into the content of the activity.

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Commonly asked questions about cancer, treatment and female fertility

What is fertility?

Fertility is a person's natural ability to have children. Fertility starts at puberty, although the cells that will become eggs and sperm are present in the ovaries and testes from before birth[1,2].

Women are born with a limited number of eggs[3]. Over her reproductive years, a woman will have ≈450 ovulatory cycles, when an egg is released, and she may become pregnant[4]. When the supply of eggs runs out, a woman will no longer be able to fall pregnant and she enters the menopause[2].

Essentials for conception: what do you need to get pregnant?

To achieve a pregnancy, there needs to be a supply of eggs (oocytes), a functioning womb (uterus), viable sperm, and, if conception is to occur naturally, the desire and ability to have sexual intercourse with a partner. You can also use assisted reproductive techniques such as in vitro fertilisation (IVF) and/or intracytoplasmic sperm injection (ICSI).

IVF
– a technique where an egg and a sperm sample containing many sperm are placed in a test-tube or petri dish to allow fertilisation

IVF-ICSI
– a technique where an egg is fertilised by a single sperm using a sperm injection technique

What types of treatments are used to treat leukaemia and how do they affect fertility?

Treatments used for cancers of the blood (white blood cells; ALL, AML, and CML) include[5–7]:

- Chemotherapy
- Radiotherapy
- Targeted therapy – where drugs target specific genes and proteins that are involved in the growth and survival of cancer cells
- Antibody therapy (also known as immunotherapy) – where the antibody binds to a specific site on a cancer cell to activate the immune system. This destroys the cancer cell or blocks the development of tumour blood vessels

Cancers of the white blood cells have a tendency to spread to the ovaries and testes (the primary reproductive organs in the body – the testes in men and the ovaries in women), so therapy needs to be specifically directed to these areas. The risk of therapy-induced fertility problems varies with time and intensity of treatment.

How can leukaemia treatment affect fertility?

The risks of infertility depend on the treatment regimens used[1], and whether they are used in combination with other treatments. It is important to speak to your doctor about this as it can be different for every patient.

Chemotherapy targets rapidly dividing cells – this includes cells in the testes and ovaries[1], hair follicles, and the cells that line the intestines. This is why chemotherapy causes nausea and hair loss and is the reason that fertility is also affected.

Radiotherapy damages the DNA of cancer cells. The radiation also affects the DNA of the surrounding healthy cells, which may include the ovaries and testes[2]. Your doctor will try to minimise this using shields to protect specific areas and keeping radiation 'scatter' to a minimum.

There is currently little information on the effects of targeted therapy and immunotherapy on fertility[2]. It is suspected that these treatments are less damaging than chemotherapy and radiotherapy, but more studies are needed.

How treatment affects sexuality

It is important to note that treatment side effects may affect physical and emotional sexuality:

Physical side effects
Makes the skin more sensitive
Fatigue
Pain
Decrease in vaginal lubrication and changes in the lining of the vagina

Emotional side effects
Treatment worries
Illness worries
Survival worries
Anger

Cancer treatment may affect female fertility in different ways. Chemotherapy has important short-term effects on egg growth and may damage the immature eggs stored in the ovary[1], and radiotherapy can damage both the ovary and the womb[9].

Chemotherapy effects

Chemotherapy can affect the ovary by damaging both growing follicles and the non-growing follicles[1,3].

Growing follicles contain the hormone-producing cells and the maturing egg. Damage to the growing follicles results in loss of hormone production, and you may stop having periods[1].

Non-growing follicles make up the 'reserve' of follicles, some of which start to grow every day: the menopause occurs when this reserve gets depleted.

The ovaries are very sensitive to chemotherapy, with some chemotherapy treatments causing more damage to eggs than others (with greater damage caused by higher doses of treatment)[1].

Radiotherapy effects

The effect of radiotherapy on fertility depends on[10]:

- Location – whether the ovaries are in the area of the body that receives the radiotherapy
- The overall dose of radiation
- Age of the patient

Human eggs are very sensitive to radiation and the probability that fertility problems will develop after treatment is related to the number of immature eggs contained in the ovary at the start of treatment. This declines with age, but also will vary between women[4].

Radiotherapy to the lower abdomen or pelvis may also affect the womb. Before puberty, radiotherapy can prevent later growth of the womb, and in adult women, damage to the blood vessels and the elastic nature of the muscles can affect its ability to grow and support a pregnancy.

Depending on the field of radiation needed, it may be possible to use protective shielding placed over the region of the ovaries and womb to reduce the amount of radiotherapy they receive[11].

Can I get help to deal with the process?

Your oncology team will be able to refer you to a fertility centre if you are considering a fertility preservation procedure before you start treatment, or to discuss it further.

Following completion of treatment, you should also discuss any fertility concerns with your care team, who will be able to refer you to a fertility centre.

What should I do about contraception?

Contraception during and after treatment

During treatment, it is very important to use contraception. Some anti-cancer treatment drugs may pass through the placenta and affect the developing baby[12]. Barrier contraception, such as the condom/femidom, is recommended as it is unknown whether treatment drugs may be passed on to a partner[13]. Oral contraceptives, whether progestin-only pills or the combined pill, have no effects on treatment and are safe to use; however, if you are having gastrointestinal problems as a side-effect of chemo- and radiotherapy, this may reduce the effectiveness of oral contraceptives[13].

Intra-uterine contraceptives that require insertion into the womb (copper IUD and levonorgestrel IUD) or injection under the skin (etonogestrel implants) should be avoided to prevent bleeding problems[13], although devices placed prior to diagnosis may be left in the body during treatment. IUDs and injections may not be appropriate for blood cancers where bleeding and clotting responses are suppressed[14].

After treatment, it is recommended to continue with contraception for at least 6 months in case there have been effects on growing eggs, and to ensure you are fully recovered. Your doctor may advise you to stay on contraception for a longer period of time[13]. Talk to your doctor to find out what is right for you.

What is fertility preservation?

Fertility preservation is a series of techniques and steps taken to collect and store reproductive tissue and/or cells to help you have a biological family in the future, after a disease-free interval.

Fertility preservation procedures are normally performed prior to treatment, and it is important to discuss whether this is relevant and possible for you with the oncology team regarding the risk to your fertility of the planned treatment, and any potential delay to treatment due to the fertility preservation process.

What approaches are there for fertility preservation?

Egg banking

The established and gold-standard technique for female fertility preservation is egg cryopreservation[15]. This involves daily hormone injections to stimulate the ovaries (just like for IVF treatment), for about 2 weeks. Once the eggs have got to the right stage of maturity, as judged by an ultrasound scan, the eggs

can be removed[16]. This involves a further internal (vaginal) scan, with a needle passed through the top of the vagina into the ovaries. You will be given a light anaesthetic for this.

Egg cryopreservation by means of very rapid freezing (vitrification) provides the highest yield of eggs for later use[17].

Time scale

To allow time for the stimulation and egg collection, chemotherapy would need to be delayed for 2–3 weeks. The timing of the menstrual cycle is not important and stimulation of the ovaries to induce ovulation can be started any time in your cycle[18].

Using the eggs

When the woman is ready for pregnancy, the eggs will be thawed and a single sperm from your partner (or a donor) injected directly into each egg by IVF-ICSI. The fertilised eggs will develop into embryos over the next few days, and normally 1 (or sometimes 2) would be replaced into your womb 5 days later. If you have more good quality embryos, these can be frozen again to use later.

Embryo freezing

Alternatively, after collection of the mature eggs they can be fertilised to form embryos before freezing. This requires sperm from your partner, or a donor. When the woman is ready for pregnancy, the embryo will be thawed and placed directly into the uterus.

Eggs vs embryos: which is right for you?

Some women in a partnership will prefer to freeze an embryo, but other women do not want to freeze embryos for many reasons (i.e., do not have a partner and do not wish to use sperm donors, or do not wish to freeze an embryo for religious reasons)[16]. The freezing of eggs rather than the freezing of embryos allows women a choice and also gives ownership of the eggs to the woman rather than shared ownership of an embryo[16]. It is essential to recognise that an embryo created from a woman's egg and her partner's sperm is their joint property, and both need to consent to its subsequent use, at the time of use[19]. This means that if the relationship breaks down and the man does not give permission for that embryo to be used, it can't be used[19].

Ovarian tissue cryopreservation

This is an option for adolescents and women for whom treatment is very urgent, as it does not require ovarian stimulation so doesn't delay cancer treatment. The whole or part of an ovary is removed, sliced into strips and frozen[20].

Using frozen tissue

After treatment finishes and when the woman wishes to fall pregnant, the tissue is thawed and transplanted back[20]. This fertility preservation option may also restore both hormonal and reproductive ovarian functions following cancer treatments[11]. Once the transplanted tissue is functioning again, after

	Cryopreservation method	
	Slow freezing	Fast freezing
Alternative names	Controlled rate Slow programmable	Vitrification
Time frame for sample being cooled to -196˚C	Several hours[23]	Few minutes[23]
Used for preserving	Sperm[25]	Eggs[17]
Why is this process used?	Allows the storage of large sample volumes[25]	Prevents the formation of ice crystals in the egg[23]

approximately 2–9 months, natural conception may occur, or eggs can be collected and IVF or IVF-ICSI procedures can be performed.

Risks

There is a risk with acute leukaemia patients that cancer may be present in the ovarian tissue that is preserved and transplanted, which may cause a recurrence of the cancer[21]. Tests may be able to check whether any cancer is present in part of the frozen ovary tissue sample[22] but can't guarantee the whole sample that would be replaced is clear of cancer.

Cryopreservation techniques

There are two methods of cryopreservation for eggs and sperm – vitrification or slow freezing[23]. In both cases, the sample provided is cooled to -196˚C[24], which places the eggs and sperm into suspended animation until thawing and fertilisation can take place.

Routine testing of samples

In the UK, and in many other countries, a blood sample will be routinely tested for blood-borne viruses (such as HIV and hepatitis C)[24]. This is to ensure safety and prevent contamination of the samples during storage[24] and has no influence on whether samples are frozen and retained.

Written consent for preservation is required

Written informed consent will be required for storage, and you will need to specify how long you want the sample to be stored (in the UK, cancer patients may store their samples for up to 55 years[24]). The consent forms will also include information on what you wish to be done with the sample should anything happen to you[26], and whether the sample is to be used for your own treatment or may be donated to someone else or used for research[26].

Consent can be withdrawn or updated at any point during this process, and you must keep the clinic informed of an up-to-date address to maintain correspondence

Pregnancy after treatment

Studies looking at the return of menstruation have shown that approximately 6% of women resumed menstruation after the end of treatment and the natural pregnancy rate of patients within this group was approximately 20%[27].

How successful is pregnancy after cryopreservation?

Pregnancy resulting from preserved eggs

The success of egg cryopreservation is dependent on the number of eggs that are frozen, and the woman's age[28]. In women aged under 35 at the time of egg freezing, each egg has about a 5% (1 in 20) chance of being able to become a successful pregnancy[29]. This chance is lower in older women[29].

For the children born after assisted fertility treatment, there is no evidence of any issues after a birth achieved from an egg that has undergone cryopreservation.

Pregnancy resulting from frozen embryos

For embryos, the transfer of vitrified and warmed embryos is as efficient as fresh-embryo transfer[30] and embryo storage time after freezing does not affect live-birth rates[31].

Pregnancy complications

In general, women who received chemotherapy have lower pregnancy rates from natural conception than women who have not had chemotherapy. This is potentially due to the side-effects of the cancer treatment, which may cause complications.

There may be a risk of pre-term birth in women with a history of leukaemia: increased monitoring during pregnancy is advised[32].

Women treated with radiotherapy have additional risks to consider. Radiation therapy can cause changes to the blood vessels in the womb, changes to the elasticity of the womb muscles (fibrosis) and can also cause shortening of the cervix[33]. These changes can cause miscarriage or premature birth and may also affect the growth of the baby.

How soon can I try to conceive after treatment?

It is recommended not to try to conceive soon after treatment, as those eggs that are already growing may have been damaged by the treatment you have had[34]. It takes about 6 months for the damaged eggs to be cycled out of the ovaries. Sometimes your doctor will advise waiting longer, perhaps even up to 2 years, to ensure that you have fully recovered from your treatment. Additionally, the risk of the cancer returning is highest in the first 2 years after treatment[13].

There is no increased risk of congenital abnormalities in babies born to women who have had cancer treatment[35].

How am I feeling?

A cancer diagnosis is a difficult and challenging time[26]. You will have to process a lot of complex information about cancer treatment and fertility options in a short period of time[36]. Being told that your cancer treatment may impact on your fertility may be overwhelming and can be stressful and upsetting[37–39]. Speaking with your care team and being involved in the discussion about any fertility preservation options may alleviate some of these feelings and help you to cope with your decisions[40,41].

If you are currently in a relationship, it is advised to involve your partner in fertility discussions[42]. If you are not in a relationship at the moment, please ask your care team for support in developing strategies for communication with future partners. If you feel overwhelmed with any decisions, please speak to your care team who may not realise you need help in coming to a decision[39].

Support services examples

Fertility Network UK	www.infertilitynetworkuk.com
British Infertility Counselling Association	www.bica.net
Human Fertilisation & Embryology Authority	www.hfea.gov.uk
British Fertility Society	www.britishfertilitysociety.org.uk
Leukaemia Care Organisation	www.leukaemiacare.org.uk
Leukaemia Care Organisation "know your rights" toolkits	https://www.leukaemiacare.org.uk/support-and-information/campaigning-and-advocacy/know-your-rights-toolkit/
Macmillan Cancer Care	www.macmillan.org.uk
Cancer Research UK	www.cancerresearchuk.org
Teenage Cancer trust	www.teenagecancertrust.org

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Funding statement: These independent educational activities are supported by an educational grant provided by Pfizer. PCM Scientific is the medical education company acting as scientific secretariat and organiser for this programme. The activity is run independently of the financial supporter and all content is created by the faculty. No funder has had input into the content of the activity.

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