Fertility Preservation Options for Women Undergoing Oncology Treatment

This leaflet is for you if you are in the process of having, or have had oncology treatment. It discusses some of the treatment options available for fertility preservation.

Introduction

Fertility preservation is the process by which oocytes (eggs) undergo an intervention to preserve their use for future attempts at conception. Fertility preservation is considered for patients who may undergo treatment that causes the destruction of oocytes (eggs) leading to infertility.

Those with the greatest need to consider fertility preservation techniques are women with cancer undergoing chemotherapy or radiation. Fertility preservation may also be discussed with women who will be undergoing surgical removal of both ovaries (oophorectomy) or anticipated chemotherapy for other medical reasons that may impact future fertility.

The most common indications for fertility preservation include breast cancer, cervical cancer, cancers of childhood and youth (such as leukaemia), patients planning bone marrow transplant or stem cell transplant, planned bilateral oophorectomy, planned pelvic radiation, planned chemotherapy for non-cancer diagnoses such as severe lupus glomerulonephritis or other autoimmune or haematological diseases.

After oncology treatment women can have normal fertility, fertility followed by an early menopause, compromised fertility, or ovarian failure (menopause).

There is no testing that can be completed to predict your fertility response to treatment. Infertility risk will depend on type, duration, and dose of chemotherapy; location on the body and dose of radiation; location of surgery; cancer type; age of patient, and fertility status prior to starting treatment.

For all patients desiring fertility preservation, options must be individualized.
Female fertility preservation options currently available

- Embryo cryopreservation
- Oocyte cryopreservation (egg freezing)
- Laparoscopic oophoropexy (ovarian transposition) (key hole surgery)
- Ovarian suppression
- Radical trachelectomy (cervical cancer)

Other methods, however, are gaining wider acceptance, but still need to be established, such as in vitro maturation of oocytes and ovarian tissue freezing in females.

Ovarian suppression

Research is looking into using hormone treatment to protect the ovaries from chemotherapy. This means having injections of hormones called luteinising hormone blockers (LH blockers-also known as GnRH analogues), for example goserelin (Zoladex), while you are having chemotherapy. The aim is that the LH blockers stop your ovaries working during the time you have treatment.

Once your treatment has finished you stop the injections and your ovaries start working again. The evidence so far is mixed and we need more research to find out whether this does preserve fertility.

GnRH analogues, however, can be helpful in decreasing menstrual bleeding during cancer treatments.

Laparoscopic Oophoropexy (Ovarian transposition)

Laparoscopic oophoropexy is utilized as a fertility preservation technique when there is expected pelvic radiation without chemotherapy in premenopausal women. The goal is to move the ovary(ies) and their blood supply to a fixed point at least 3cm outside the area of radiation exposure; this would not be the normal anatomic location for these gonadal structures.

Collaboration with radiation oncology is critical. The surgical procedure involves laparoscopically suturing (stitching) the ovary with permanent sutures to the lateral anterior (front) abdominal wall. Titanium clips are placed at the site of transposition so that the location of the ovary(ies) can then be seen by the radiation oncologist.

Success rates vary between 15% and 90% depending on various clinical factors.

Oocyte cryopreservation (egg freezing)

Oocyte cryopreservation is the process by which eggs themselves are cryopreserved. This has been technically challenging, as compared to embryos, because of the large water content of the oocyte which is prone to intracellular ice formation and spindle disruption.
There are two methods to freeze eggs: Slow freeze and vitrification (fast freeze). Slow freeze has an approximately 2% live-birth rate per oocyte thawed and vitrification has an approximately 4% live-birth rate per oocyte thawed (patients usually have multiple oocytes available). A male partner is not required.

Egg freezing often involves the freezing of mature eggs. This process can be completed on post-pubertal females. It requires that gonadotropins are given to stimulate the growth of follicles which are then aspirated in an oocyte retrieval procedure.

The eggs are then frozen and, at a time determined by the patient, the eggs can be thawed and used for In-vitro fertilisation (IVF)/Intra-cytoplasmic sperm injection (ICSI). ICSI must be incorporated to help increase fertilization rates.

**Embryo cryopreservation**

Embryo cryopreservation is the standard technique by which gametes (reproductive cells: in females these are eggs and in males sperm) can be utilised in an attempt to preserve future fertility. Quoted data in the current literature shows that thawed non-donor embryo transfers resulted in a 44% live birth rate for women under 35 years of age, 40% live birth rate for women aged 35-37 years old, and 35.7% live birth rate for women aged 38-40 years old. This data is reflective of most of the infertility population, and thus no specific data for embryo cryopreservation as used in fertility preservation known on a country-wide basis. Pregnancy rates would be expected to approximate the live birth rate for infertility patients.

Embryo cryopreservation requires a male partner unless the patient is prepared to use donor sperm. This process is similar to the IVF process used for infertility patients. Usually two to six weeks is necessary to complete a cycle depending on last menstrual period and response to gonadotropins. This time is needed to develop mature oocytes that are removed during the oocyte retrieval and then combined with sperm in the embryology lab to create embryos that are then frozen.

Embryo cryopreservation would not be an option for patients who are ethically opposed to freezing of embryos.

**Tests needed**

Infectious disease screening is done for anybody involved with fertility treatment (human immunodeficiency virus (HIV), Hepatitis B, Hepatitis C, Chlamydia).

**Prognosis and outcome**

You will be able to attempt to achieve a pregnancy once you have been approved by your medical provider. Some women may still be able to conceive naturally after their treatment for cancer. Younger women may be affected less than older women.
If you are amenorrheic (have no menstrual cycle [periods], have oligomenorrhea (infrequent menstrual cycle) or other menstrual irregularities, you should seek a reproductive endocrinology consultation for evaluation for premature ovarian failure (ovarian insufficiency), with possible testing to include an ultrasound scan for antral follicle counts and blood tests for anti-mullerian hormone (AMH), and/or day 2-5 follicle stimulating hormone (FSH)/estradiol.

If you have normal menstrual cycles then you can attempt conception for 12 months (or six months if you are aged more than 35 years of age) prior to seeking fertility evaluation.

Risk of nonsurgical ovarian failure after childhood cancer occurs at an earlier age than in siblings.

If you are diagnosed with ovarian failure you should seek follow-up for discussion regarding hormone replacement.

**Outcome**

Children born to cancer survivors are not at an increased risk for congenital malformations, cancer, or chromosomal syndromes unless your primary cancer was part of a genetic syndrome.

There is no known increase in primary cancer recurrence except in the case of ovarian tissue transplantation in leukemia patients.

If you have received chemotherapy or radiation that may impact cardiac or pulmonary function, then testing is advisable before you undergo conception attempts. For example, in childhood cancer survivors who have been treated with anthracyclines, an echocardiogram (ECG) is advised for women who are planning pregnancy. In such cases there will be periodic follow-up in pregnancy.

There is no difference for cancer survivors with regard to sex ratio of offspring to childhood.

Females should wait six months to five years after cancer treatment to attempt conception, depending upon recommendations made by your oncologist. This recommendation is based on the current diagnosis and takes into account the expected risk of recurrence for that particular disease and clinical circumstances of the patient's medical history (i.e. stage).

Contraception should be discussed if you no longer desire a pregnancy (even if you think you are infertile, as return of oocyte production can occur).

**If screening blood tests were done, we will write to you and the fertility unit as soon as possible.**
**Benefits**
You might be able to use stored oocytes or embryos in the future to start a family.

**Risks**
Complications of fertility preservation management include:

- Procedural risks
- Medication risks
- Pregnancy complications
- Unknown risks

**Procedural risks**

- Venepuncture: discomfort and potential anemia, infection or ecchymosis (bruising) at injection site.

- Transvaginal ultrasound: abdominal or pelvic discomfort.

- Oocyte retrieval (applies to embryo and egg cryopreservation): bleeding, infection, damage to internal organs with possible emergency medical or surgical intervention, possibility of no eggs being retrieved, pain.

- Laparoscopic oophoropexy/transposition: bleeding, infection, damage to internal organs, adhesions, pain, bowel obstruction, ovarian failure, infarction of fallopian tube, dyspareunia (painful intercourse), possible need for future procedure to "release" ovary, difficult positioning of the ovary for egg retrieval if needed, added difficulty with future surgery if ovarian removal is indicated.

- As previously mentioned offspring of patients with cancer conceived after fertility preservation do not have an increased risk of cancer unless the patient has an underlying genetic syndrome. Pre-implantation genetic diagnosis (biopsy of embryos to look for certain genetic diseases) if an inherited cancer is present, can be performed.

**Medication Risks**
Some of the medications used in fertility preservation techniques with their risks are listed below.

- Aromatase inhibitor ie. Letrozole: nausea, vomiting, hot flushes, arthritic pain, back pain, fatigue, hypercholesterolemia (raised cholesterol), formation of ovarian cysts.

- Gonadotropins; FSH or FSH/ luteinizing hormone (LH) i.e Menopur®: breast pain, abdominal pain, nausea, headache, ovarian hyperstimulation (weight gain, pelvic pain, and fluid retention), ovarian pain, constipation, erythema or ecchymosis at injection site, back pain.
- GnRH analogues (also known as LH blockers) i.e. Zoladex®: hot flushes, oedema, headache, insomnia, dizziness, lightheadedness, depression, fatigues, fever, skin reaction, decreased libido, weight loss or gain, nausea, vomiting, diarrhoea, erythema or ecchymosis at injection site, weakness, bone pain.

- Human chorionic gonadotropin (hCG) i.e. Pregnyl®: oedema, depression, fatigue, headache, irritability, restlessness, erythema or ecchymosis at injection site, ovarian hyperstimulation syndrome (weight gain, pelvic pain, and fluid retention).

**Pregnancy complications**

- Chemotherapy: there is no increased risk of miscarriage or low birth weight with chemotherapy. Live birth rates and uterine function are similar for cancer survivors compared to sibling controls.

- Radiation: pregnancy in women who have received pelvic irradiation can be complicated by preterm labor, preterm delivery, low birth weight, placental abnormalities such as placenta accreta, and stillbirth.

**Unknown risks**

- There are unknown risks associated with elevated hormone levels in cancer patients; however, to date there are not any studies that indicate decreased survival or increased risk of recurrence even in estrogen-sensitive tumors such as breast cancer.

- Breast cancer patients who are estrogen receptor and/or progesterone receptor positive can still undergo fertility preservation techniques.

Aromatase inhibitors (for example, letrozole) and selective estrogen receptor modulators (for example, tamoxifen) have been used in combination with gonadotropins for egg/embryo freezing so as to keep estrogen levels low, yet allow maximal egg yield from oocyte retrieval. BRCA screening and pre-implantation genetic diagnosis can be considered.

- There is the unknown risk of progression of disease with pregnancy, although this has not been shown to be an issue in the current literature.

- Also, undergoing some protocols (egg freezing or embryo freezing) may delay cancer treatment for up to six weeks.

- Effects on children born from frozen oocytes and ovarian tissue are unknown, but to date the literature does not suggest any differences in obstetric and perinatal outcomes (mostly egg freezing data).

**Alternatives**

Pregnancies can be established with donated oocytes, or you might opt for adoption.
What should be discussed/what can you ask for?

- Risk of infertility with proposed treatment
- Referral to reproductive endocrinology and infertility specialists
- Prognosis of the ability to undergo a current procedure in the setting of a new cancer diagnosis and the future life expectancy (shortened lifespan is not a reason to deny cancer patients fertility options/treatment)
- Risks for delaying treatment (in the case of embryo or egg freezing)
- Effect of pregnancy on recurrence of disease
- Genetic screening, if indicated and use of pre-implantation genetic diagnosis (PGD) when appropriate
- Use of established versus experimental therapies
- Discuss benefit to minors, if applicable, and their ability to give assent
- Health risks to future offspring
- Fertility preservation techniques
- Posthumous reproduction
- Current funding (treatment, duration of storage)
- Travel to the egg collection centre
- Research (you might want to participate in studies improving results and knowledge)

Contacts/Further information
Cambridge IVF
Kefford House
Maris Lane
Trumpington
Cambridge
CB2 9LG
Tel: 01223 349010

Opening hours:
Monday - Friday
08.00 - 17.00
Saturdays:
10.00 - 14.00

References/ Sources of evidence


Privacy & Dignity
Same sex bays and bathrooms are offered in all wards except critical care and theatre recovery areas where the use of high-tech equipment and/or specialist one to one care is required.

We are now a smoke-free site: smoking will not be allowed anywhere on the hospital site. For advice and support in quitting, contact your GP or the free NHS stop smoking helpline on 0800 169 0 169.

Other formats:
If you would like this information in another language, large print or audio, please ask the department where you are being treated, to contact the patient information team: patient.information@addenbrookes.nhs.uk.

Please note: We do not currently hold many leaflets in other languages; written translation requests are funded and agreed by the department who has authored the leaflet.

Document history
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