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Westmead Fertility Centre

Female Fertility after chemotherapy or radiotherapy treatment

Information for Patients

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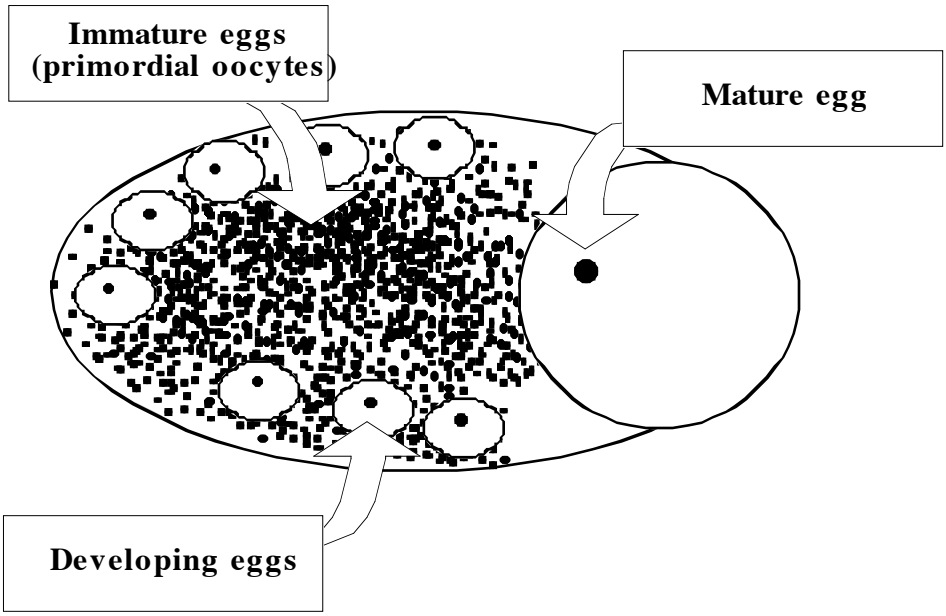
Introduction

Some forms of medical treatment, particularly chemotherapy and radiotherapy, can have an adverse effect on fertility in women. This generally occurs as a result of a toxic effect on the ovary leading to a permanent death of the eggs (oocytes) in the ovary. Other aspects of your fertility such as your vagina, uterus and fallopian tubes are generally not affected to the same extent.

Why is the ovary affected?

When girls are born, they have all the eggs that they will ever have and then continue to use them up through the rest of their life. Unlike men who continually make sperm throughout their lifetime, women cannot make any new eggs. Therefore any eggs, which are lost or damaged through medical treatment, can never be replaced.

How many eggs are there in the ovary?



As shown in the figure, the eggs in the ovary are in three forms:

Immature eggs (primordial oocytes). There are many thousands of these stored within the ovary waiting to be released. They are very immature and currently cannot be matured reliably in the laboratory. Several research laboratories round the world are currently working on techniques to mature

these eggs but a reliable method to achieve this is still not available. These eggs can however be satisfactorily frozen in the tissue in case of any future developments.

Developing eggs. There are approximately 5-20 of these in the ovaries at any one time. These eggs are partially mature and if removed from the ovary at this stage may be matured by culture in the laboratory for several days. This process of partial "in vitro maturation" has been successful in producing mature eggs which will fertilize in the laboratory and these fertilized eggs have resulted in successful pregnancies in a small number of women. However these matured eggs cannot be easily frozen.

Mature eggs. The ovary naturally produces only one (or occasionally two) mature egg in the middle of each menstrual cycle. This is all that is normally required for pregnancy. In theory this mature egg could be collected for storage just before ovulation. However this would provide only a very tiny chance of a future pregnancy and is generally regarded as insufficient to make single egg collection and storage worthwhile. Hormone treatment given by daily injection for about 12 days can be used to allow several eggs to become mature for collection at one time. This is a usual part of IVF treatment. Mature eggs can be fertilised with the partner's semen and the fertilised egg (embryo) can be frozen and stored. Mature eggs can now also be frozen and later thawed before fertilization in the laboratory.

What can be done to give me a chance of fertility?

Chemotherapy and radiotherapy treatment can harm all three of these egg types and therefore may cause irreversible fertility. At present, there is unfortunately no proven way to protect the ovaries against the effects of these treatments.

However researchers are currently investigating a number of strategies to preserve fertility for women needing chemo or radiotherapy treatment and it is possible that these may be of some assistance in the future. **Unfortunately, most of these options are still at the development stage and have not been widely used**. The only treatment which is currently readily available and which offers a reasonable chance of future pregnancy, is to create and store by freezing a small number of fertilised embryos by an IVF procedure.

Currently available options

IVF procedure.

The aim of an IVF procedure is to collect as many mature eggs as possible then fertilise them with your partner's sperm to create embryos. Embryos can be frozen and therefore stored for as long as you need them. In order to collect as many mature eggs as possible, you would first receive hormones by injection. These hormones stimulate all the developing eggs (usually 5-20) to develop and become mature eggs. Once blood tests and ultrasound scans

show that the eggs had developed, the eggs can be collected. This is done in an operating theatre after you have been given a combination of local anaesthetic and sedation. The eggs are collected using a small needle through the vagina into the ovary (under ultrasound vision) to collect the eggs. The procedure takes approximately 20 minutes and you can go home soon afterwards. Once the eggs are collected, they are mixed with your husband's sperm and it takes 24 hours to find out how many have fertilised. Usually about 50-60% of eggs will fertilise although this figure varies and sometimes no eggs at all fertilise. Once the egg has been fertilised, it can be frozen and stored for later use. Later on, the chances of a successful pregnancy for any one cycle of treatment using these embryos is only about 30% It is therefore important to remember that this form of treatment will give you A CHANCE of success but quite clearly does not guarantee pregnancy.

The IVF procedure takes approximately two weeks to complete. Therefore you need to be able to safely delay chemo or radiotherapy treatment for two weeks. Your specialist will advise you if this is possible. For some forms of cancer treatment delay or ovarian stimulation with hormones is not advisable.

Oocyte donation

If your fertility has already been compromised by chemotherapy or radiotherapy treatment, the only option available for you to have a pregnancy is for another woman to donate her eggs to you. The other woman would have to go through an IVF treatment cycle to have her eggs collected as above. Once the eggs had been collected, they would be fertilised with your partner's sperm and the fertilized eggs then belong to you. You could opt to have the embryos transferred when it was appropriate for you.
This option has clear disadvantages; you need someone else who is prepared to go through all this on your behalf and also your child is not genetically linked to you (although he/she would be genetically linked to your partner). However you would give birth to the child and he/she would regard you as his/her parent. Legally you would also be the mother of the child.
Clearly this option has a lot of ethical and emotional consequences for both you and the egg donor. Careful thought and counselling has to be given to all of this.
A separate information leaflet (**Donor oocytes: Information for donors and recipients**) is available from the Westmead Fertility Centre (phone number on the cover of this leaflet) and we will be pleased to send it out to you on request.

Developing New Options

Ovarian tissue storage

By having a small piece of your ovary collected now and stored deep-frozen, you may be able to use it at a later date in one of two ways.

1. Complete oocyte maturation in the laboratory. This is being actively researched in a number of research centres around the world. However, progress has been slow and it is not clear when we will be able to overcome the technical difficulties involved in this process.
2. Surgical re-implantation of the removed piece. A further possibility that has now been used successfully is of surgically replacing the small piece of ovary once the chemotherapy or radiotherapy treatment has been completed. This is an exciting new treatment which has now been used successfully in eight women with the birth of eleven healthy babies so far (December 2009).

The operation to remove ovarian tissue involves a laparoscopy where a camera is inserted into your abdomen under general anaesthetic and part or all of one ovary collected. You can go home about two hours after the operation is finished. It is important to consider the possibility the piece of tissue removed may also contain cells of the cancer for which you need chemo or radiotherapy. Current research is directed at ways of identifying such cells before the ovarian tissue is re-implanted.

Some commonly asked questions.

What are the chances of my ovaries being damaged by treatment?

This is very variable and depends on your age and the type of cancer or other medical treatment you have to have. Return of normal menstrual and reproductive function can often be highly variable. Women whose periods stop altogether after cancer treatment have generally had fairly severe damage to the ovary while women whose periods continue normally have had less or even no damage to the ovary. However even these women may later have an earlier menopause.

Does the damage to my eggs have any other effects on my health?

Yes. Your ovaries need the eggs in order to make the female hormone oestrogen. Therefore if your eggs are lost or damaged through medical treatment, your hormone levels will drop considerably and you will in effect go through a very early menopause. This will have potentially unpleasant side effects such as hot flushes, night sweats and vaginal discomfort as well as possibly affecting your long-term health. Relief of these symptoms can be obtained by taking hormone replacement therapy. In cases where oestrogen hormone replacement therapy cannot be used such as breast cancer, a number of other options can be used to relieve the symptoms of a premature menopause.
In the longer term, a premature menopause may increase the risk of heart disease and the bone disease, osteoporosis. To prevent this, your doctor

may advise you to take hormone replacement therapy up to the time that your menopause would have occurred naturally.

How long can the ovarian tissue be kept in storage?

The ovarian tissue can be stored for as long as you need. Unfortunately tissue can be damaged by the freezing and by the thawing processes. However the risk of such damage is not increased by the length of time spent in freeze-storage. The tissue can therefore be safely left for years if necessary. In addition, we know that children who are born from embryos that have been frozen appear to have a perfectly normal development in later life.

Is there a risk of transmitting cancer cells if surgical re-implantation is carried out?

This may unfortunately be a possibility. Previous work in mice demonstrated that some forms of bloodborne cancer could come back as a result of surgical reimplantation of a piece of ovarian tissue. Surgical reimplantation of ovarian tissue would not be recommended in a woman with a bloodborne cancer (e.g. lymphoma or leukemia) unless this risk could be removed. The situation for a solid cancer in another part of the body (e.g. breast cancer) remains unclear. It may be possible in the future to use genetic tests to screen ovarian tissues for cancer cells prior to replacement of the biopsy.

Are there any costs for these services?

Storage of tissues now (to preserve your options for later) is provided without any charge or commitment to later use of the tissue being necessary. We will contact you every 12 months to check whether you still wish continuation of the storage.

However, as the Sydney West Area Health Service does not support complex (and therefore expensive) fertility treatments, Westmead Fertility Centre may need to levy a charge for some complicated fertility treatments. However this is strictly on a cost-recovery arrangement. Full details are available from the Westmead Fertility Centre on request.