

Patient Information on Fertility Preservation

Women's natural fertility

A woman's natural fertility is highest in her late teens and twenties. There are many reasons why having a baby at this stage of life is not the chosen option. Although a woman will ovulate every month almost until the age of 50, her actual fertility (chance of getting pregnant) declines significantly from her early thirties. Of course individuals vary enormously, and lifestyle factors like smoking and increased body weight, play an important (negative) role too.

The reduction in fertility is not only due to the decline in the number of eggs left in the ovary over time, but it is also related to an increase in the proportion of abnormal eggs. This leads to both a lower chance of conception and also an increased risk of miscarriage.

The indication that the problem lies with using 'older' eggs can be deduced from the interesting scientific model seen when older women receive eggs donated from a younger woman.

Table 1, below, shows that women in their 40s perform poorly in an IVF programme with pregnancy rates <10% per cycle. However, when they are provided with donor eggs from younger women, they can achieve pregnancy rates nearer to 50% per cycle, which result in live birth rates in excess of 35% per cycle, throughout the age range.

Table 1. Live birth rate per IVF cycle (HFEA 2003-04 – Published in 2006)

Age (years)	< 35	35-37	38-39	40-42	> 42
Live birth rate (%)	28.2	23.6	18.3	10.6	3.2

In developed and developing countries there is now a steady shift towards having babies later in life and we expect that it will become common practice to freeze eggs as an insurance measure.

Fertility Preservation

In the past, individuals could only freeze embryos (eggs already fertilised with sperm), which of course required a stable heterosexual relationship. The embryo is a collection of small cells which survive the freezing process quite well. On the other hand, the mature human egg is a large cell with a complex internal structure which is often irreparably damaged by conventional freezing methods.

Recently, methods have been developed that allow safer freezing of mature eggs which survive freezing and thawing, and lead to successful pregnancies at a rate similar to frozen embryos. These methods have been adopted in some centres over the last few years, and the results are encouraging.

Although only a few hundred babies have been born worldwide so far, the reports are satisfactory and reliable.

Egg Vitrification

The latest breakthrough on this technology is the use of a process for storage called vitrification. It works by removing nearly all the water from the egg cell by osmosis. The egg can then be stored at the same low temperatures as frozen eggs without damage. Published results indicate that there is negligible damage to the egg caused by these procedures, resulting in success rates, after fertilization, which are

identical to fresh eggs. GCRM has now adopted this method as the preferred means of storage.

It is important to realise that the decline in fertility is due to the “age of the eggs”, and therefore fertility preservation should apply only to women who are **less than 35 years of age**. There are exceptional circumstances (eg AMH \geq 16.0 pm/L) when it may be a viable option up to the age of 38 years.

What is involved?

The procedures for putting your fertility on ice are very similar to a standard IVF cycle. It involves a course of daily fertility drug injections for approximately 2 weeks followed by an operation to remove the eggs. The eggs are then carefully vitrified and put into store in liquid nitrogen at -196°C . They can be kept under these conditions without deteriorating for an indeterminate length of time.

When you decide that it is time to use these eggs, they will be thawed at the appropriate time of your menstrual cycle, fertilized using ICSI (‘intracytoplasmic sperm injection’; the injection of a single sperm into the egg), and transferred to your womb a couple of days later.

Objective statistics and expectations, using vitrification

These simple statistics are based on a single treatment cycle yielding enough eggs to provide a reasonable chance of success. If you respond to treatment by obtaining 10 eggs, we would expect that on average, 8 of these will be mature and suitable for freezing. We would anticipate that all of these would survive the freezing and thawing processes successfully. Upon thawing, the eggs are subjected to ICSI and fertilization would be confirmed the next day. We can estimate that this would yield approximately 6 viable embryos.

On average, depending upon age at freezing, each of those viable embryos has a 15 to 30% chance of leading to a live birth. Therefore the original collection of 10 eggs, should lead to a 60% to 80% chance (cumulative) of a live birth. Of course there will be wide individual variation around each of those figures, but they do indicate the potential success of the treatment. Younger women would expect to produce more than 10 eggs, each of which would have a higher expectation of implantation than older women. Hence, the younger the woman at the stage of treatment – the better results can be expected.

The age of the woman at the stage of thawing and implantation has a negligible impact upon outcome.

WHAT IS INVOLVED IN THE TREATMENT FOR EGG FREEZING / VITRIFICATION?

Prior to undergoing the procedure, we would assess your ability to respond to the fertility drugs (*ovarian assessment*), as a small number of individuals, although normally fertile, do not respond with sufficient eggs in any one cycle. As can be seen from Table 1, the earlier you decide to undertake the procedure the better chances of success.

After you make the decision to proceed, a few tests are required, for different reasons and you will also have to provide your consent to undergo the treatment.

Assessments and Tests

1. Rubella - German measles (blood sample)
2. A recent cervical smear test
3. Hepatitis B & C
4. HIV

Test 3 and 4 are required by all cases of gamete or embryo storage to ensure that only virus free tissues are stored in the same container.

THE TREATMENT CYCLE - CONTROLLED OVARIAN STIMULATION

A high egg yield is normally required to maximise the potential of any treatment cycle. This normally attained by using a procedure called "controlled ovarian stimulation with the GnRH-agonist".

In some cases we may recommend the use of an alternative approach using a GnRH-antagonist.

Controlled Ovarian Stimulation with GnRH-Agonist

Stage 1

GnRH-agonists are used to prevent premature ovulation – this down-regulation injection is given around day 21 of a menstrual cycle.

*In the protocol using the GnRH-Antagonist the "down-regulation" is introduced after starting the **FSH** injections.*

Following your period you will have a blood test and a scan prior to starting your daily injections of follicle stimulating hormone (**FSH**)

You will be taught how to give these injections.

We monitor your response to the injections by taking blood samples and transvaginal ultrasound scans.

The average number of days to be on injections is 10-12 days.

Once the monitoring indicates that an adequate number of maturing follicles are present, a final hormone injection, the HCG, will be given to complete the maturation process. The timing of this HCG injection is critical and it **must** be given at the time specified by the GCRM staff. It is also self-administered.

Stage 2

- On the day arranged, report to the GCRM at the appointed time. You are required to fast before the procedure, as sedation is used.
- Do not eat or drink anything after 12 midnight on the day of surgery, although you may have a glass of water 2 hours prior to admission.

Sedation

For your comfort this procedure is performed under sedation. The anaesthetist will take a history of your general health and discuss the procedure with you. An intravenous cannula (venflon) will be placed in your hand, through which your sedation will be given. You will feel yourself drifting off to sleep, although you may still be aware of noise and touch. The anaesthetist is present throughout the procedure to control your sedation and monitor your wellbeing.

Procedure

The stimulated ovaries are visualised on the ultrasound monitor. A fine needle is passed down a specialised guide attached to the ultrasound probe. The needle is directed into the centre of each follicle (the structure containing the egg) and suction is applied to aspirate the contents of the follicle. The fluid is examined by the

embryologist to look for the egg. The follicle is washed out with special flushing medium which is also checked. The procedure is finished when all the follicles have been aspirated. The procedure takes about 20 - 30 minutes.

You will be transferred to the recovery room and allowed to rest until you feel ready to go home, usually 2-3 hours.

You will need to be collected by a responsible adult as you are not allowed to drive for the next 24 hours, as the effects of sedation will still be in your system.

Possible Side Effects

Common side effects of down-regulation drugs are hot flushes, headaches and mood swings. These symptoms are due to low oestrogen levels. Oestrogen is the hormone normally produced by the ovary in the early phase of the menstrual cycle and symptoms are short-lived and subside when the injections start. They may recur after treatment, as you are not having further hormone support following the egg retrieval.

Ovarian Hyperstimulation Syndrome (OHSS) - Despite careful monitoring, a small number of women may over-respond to the injections. This can result in a condition known as OHSS which can vary in severity. In most cases the symptoms subside spontaneously.

In a mild form - the ovaries are slightly enlarged and you may feel abdominal 'cramps'. If so, please notify nursing staff when attending the unit.

In the severest form - the ovaries are very enlarged and fluid can gather in the abdominal cavity causing discomfort or pain. Admission to hospital may be required for observation and appropriate treatment. However, this is highly unlikely in cases of egg preservation because embryos are not replaced.

Ongoing Research Programmes

Infertility treatment is continually advancing and improving. This is mainly due to research and its findings. In this unit we undertake research projects which we hope will benefit future treatments and outcomes.

You may be asked to participate in research at any stage of your infertility treatment but you are **never** under any obligation to do so.

If you feel that fertility preservation might be for you, and would like to learn more about your options, we would be pleased to see you.

Suggestions and Complaints Procedure

At the GCRM our aim is to develop, improve and maintain the quality of the service. We value any suggestion that you have which would contribute to the wellbeing of all we care for.

If you have any questions or difficulties, please discuss them with any member of the GCRM team. We are here to help and support you throughout your treatments.

We also want to hear from you if you have any cause for complaint. You should speak to Sister Pat Ambrose or Dr. Marco Gaudoin who will discuss the matter with you and may, if appropriate, make a written record of the details.

If you are not satisfied with the care provided by the clinic, you should write to:

Mrs Dorothy Lucas, Complaints Officer, GCRM