

# RECEIVING DONATED EGGS IN THE IN VITRO FERTILISATION (IVF) PROGRAMME

*A guide for patients receiving donated eggs, July 2009*

## HOW TO USE THIS BOOKLET

This booklet aims to provide information on receiving donor eggs as part of in vitro fertilisation (IVF). It not only covers IVF itself, but also embryo freezing, sperm microinjection (ICSI), and the various options for culturing embryos. We have put the general information first, and detail about treatment later. ***Really important points are written in bold italics, like this.*** There is a glossary at the end where you can check out unfamiliar words or jargon.

When it does not answer particular questions you may have, the members of the Fertility Associates team will be very willing to help you. There will be many opportunities to discuss issues should you proceed with donor egg treatment. No question is too dumb!

***If you need information of advice in a hurry, please ring the clinic. If the clinic is unattended, the telephone message will tell you whom to contact and how.***

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## IS DONOR EGG AN OPTION FOR ME?

### Who makes use of donated eggs?

'Donor eggs' offer women whose ovaries have stopped working (sometimes called 'ovarian failure') or who do not have ovaries the only means of having a pregnancy. Donor eggs can also be used for women who have genetic disorders that can affect a baby or reduce the chance of a pregnancy. Donor eggs may also be an option for people who have not become pregnant after in vitro fertilisation (IVF) perhaps due to poor quality of their own eggs.

## EGG DONORS

### Who can become a donor?

Donors can be either:

- 1 Friends or close relatives of the potential recipient. These donors are called '**personal donors**'.
2. Women who wish to donate eggs to someone they do not know. These donors are recruited through the clinic, either in response to an advertisement placed directly by a potential recipient, or by the clinic. When the recipient places the advertisement, the clinic processes the responses. These donors are called '**clinic recruited donors**'.

Donors should be aged between 21 and 35 years and have no history of serious inheritable disease. The upper age limit is because a woman's fertility declines in her late thirties, while the chance of congenital abnormalities such as Down Syndrome increases especially after the age of 37. Fertility Associates strongly prefers all donors to have completed their own family before donating.

It is possible for personal donors to be a little older than 35 years, as long as the donor and recipient accept the issues involved.

### Recruiting a personal donor

Asking a person to be a donor for you carries its own issues, and we strongly encourage you to discuss the matter with us before you approach your prospective donor.

Personal donors have to go through the same screening process as any other donor, and need to provide the same non-identifying information for any child. The same 'stand-down' period of three months applies. The stand-down period is explained in the section on counselling.

### Advertising for an egg donor

If you do not have a personal donor we recommend that you advertise for a donor. We can give comprehensive advice and guidance on options available, including magazines that are most likely to provide the best response. Recipients who place their own advertisement are given 'first choice' of the donors it recruits. The clinic also advertises in general for egg donors.

Fertility Associates usually receives 10 to 30 responses from each advertisement. At the initial contact, clinic staff give prospective donors an overview of the IVF/Donor Egg process and they briefly assess the person's suitability as a donor. This involves taking into

account their age, number of children, family history, whether they have completed their family, general health status and their motivation for wishing to donate. An information booklet is sent out to each suitable respondent with details of how to proceed further by making an appointment with a nurse, counsellor and doctor. As part of their first appointment potential donors have screening bloods taken. These need to be repeated three months later before a donor is cleared to donate.

It is important to note there is a high attrition rate in donor recruitment. For example, only three in 30 women who answer an advertisement about being a donor go on to make clinic appointments. Of those three, on average only one completes the necessary appointments and screening. Because becoming a donor is fully voluntary, our policy is to not follow up those that do not attend their appointment.

### **Paying for donor costs**

Egg Donors are reimbursed for the following costs associated with the donation:

- Travel to the clinic (based on Mileage),
- Visits to the laboratory for blood tests,
- Parking,
- Pharmacy items and GP visits related to treatment.

The recipient will receive an invoice at the end of their treatment, to pay for the above donor expenses.

Publicly funded treatment includes an allowance of up to \$400 for reimbursement of egg donor's expenses. Recipients of a publicly funded treatment will be required to pay for expenses incurred by their donor beyond this amount.

### **How are donors and recipients linked for treatment?**

The clinic's staff help donors and recipients put together a profile about themselves. In addition, donors can describe what sort of people they are happy (or unhappy) about receiving their eggs, and recipients can describe their preferences for a donor.

The nurses and counsellors associated with the donor egg programme coordinate the linking of a particular donor and recipient. Generally, a donor views the profiles that the recipients have supplied about themselves and decides whether she is comfortable about donating to that person or couple. The recipient is then given the donor's profile. If both are acceptable to each other, plans for the timing of the IVF/Donor Egg treatment cycle may begin.

Sometimes a potential recipient and a donor ask to meet before or during treatment – you can decide whether you want to do this and how much information to give about yourself. Any meeting or sharing of identifying information should be done through the clinic after an explanation from a counsellor about the implications.

A donor's eggs will only be donated to one recipient in a particular cycle of treatment. Donors have the right to change their mind about donating up to the time of egg collection. Once embryos are created from donated eggs, any further decisions about the use or disposal of the embryos will be made by the recipient woman and her partner.

### **What further information can donors have?**

Donors may know the outcome of their donation, and the sex of any child, but to preserve anonymity we do not give them details of when a birth occurs, unless the recipients agree to exchange this information.

### **What further information can recipients have?**

Each donor completes a questionnaire containing non-identifying information, such as interests, how they would describe themselves, etc. Most recipients want to look at this information before confirming their choice of donor. This information is also available to the child if he or she requests it.

All our donors must be potentially identifiable which means that the donor agrees to be contacted by the clinic on behalf of the parents or any children that may result from her donation and to then consider giving more information about herself. This is not a guarantee that the donor will agree to divulge her identity. Although we encourage identifiable donors to keep the clinic informed of any change of address, not all will remember to do so!

### **COUNSELLING**

Being prepared for the issues raised in donor egg is very important. Receiving donor eggs has far-reaching implications. A consultation with a counsellor helps you to examine the implications for you and your family. You must see a counsellor to discuss the issues involved with donor egg before committing to treatment.

You will probably find that being on a treatment cycle is an emotional as well as physical experience. Treatment can trigger grief about your infertility and maybe other life experiences too. It can sometimes be an emotional roller coaster where hope and fear reflect the ups and downs of treatment. Many people benefit from having some practical coping and relaxation strategies – even if it is only what to tell family, friends, and workmates. Our counsellors can help you find your own answers, drawing on many years of experience talking with others in the same situation.

Although counsellors are part of the Fertility Associates team, their conversations with you and any notes they take are kept confidential from the rest of the staff, unless they have concerns about you becoming an egg recipient or there are issues of safety.

Fertility Associates recognise that, for the long term interests of all involved, including the potential child, it is important to resolve the issues that arise from DO as a treatment, prior to treatment commencing. A minimum of two counselling consultations are required before patients start their first treatment with an individual donor. When first setting up treatment with own donor (donor recruited by the patient) a minimum of two counselling consultations for the donor are also required. A joint session with the donor may be indicated as well. For privately funded treatments, counselling charges for patients and for the donor in preparation for treatment are the responsibility of the recipient. An additional counselling consultation is available free of charge with every IVF cycle so please make use of this important service. These consultations are provided for support and information and are not an assessment. Partners must attend counselling.

In some situations, an application for ethical approval is required by the National Ethics Committee on Assisted Human Reproduction (NECAHR) before treatment can proceed. The counsellors will prepare the required documentation. No identifiable information is given to NECAHR.

### **Information sharing**

Whom to tell and what to tell the child are often questions asked by concerned parents. The question of “who am I?” is fundamental to everyone, and there is ongoing debate about people’s right to know their beginnings and genetic inheritance. If a procedure such

as donor egg is concealed, there is always the risk that it will be discovered later, causing trauma to the child. It is the belief of those working in the field of infertility in New Zealand that it is generally better to be open and honest and to tell the child. However, different cultures may have a different perspective on this issue. There are books that suggest creative ways of telling your child.

You also need to think about whether, or when, to tell your family and friends. Although you may want to keep your treatment private, it also helps to have the support of friends and family.

### **Information sharing with your child**

Because conception through the use of donor oocytes has only been possible since the mid 1980's, there are no long-term follow-up studies of children conceived through donor oocytes. However, there are parallels between donor oocytes and donor sperm and in the latter case the consensus of those working in the field would be that it is better to be open and tell the child. The issues involved with donor insemination, and paralleled by donor eggs, are developed very well in a book called 'Gift of a Child', which we strongly encourage you to read if you wish to proceed.

The chance of a child from the donor egg treatment meeting one of the children of the anonymous donor is very low. Any risk is reduced by your willingness to be identifiable.

## **LEGAL ASPECTS**

There are a number of legal issues concerning donor egg treatment. It is essential that participants consent in writing to the procedure. With this consent, the child is the legal child of the woman and her partner (if she has a partner).

The Status of Children At 2004 recognises the woman carrying the child as the legal mother of the child. The woman's partner at the time of birth, whether by marriage, civil union or de facto, is also a legal parent of the child. Neither the child nor the donor have any rights or liabilities in relationship to each other.

The practice of IVF and donor eggs is governed by the Human Assisted Reproductive Technology (HART) Act 2004. An important principle of the Act is that offspring conceived through the use of donor eggs (or donor sperm) should be made aware by their parents of their genetic origins, and be able to secure information about the donor and her identity.

For pregnancies arising from eggs donated after 20 August 2005, Fertility Associates is obliged to give the Registrar-General of Births Deaths and Marriages identifying information about the child and the donor. After the age of 18 a child may ask the clinic or the Registrar-General for the identity of the donor, and this information will normally be given. The child may ask for the identity of any other children conceived using the same donor, and the donor may ask for the identity of all persons born as a result of her donation. In these cases, both or all the parties need to agree before the information can be given. There are provisions for children getting information from the age of 16, and for parents to get information about the donor too.

For eggs donated before this date, the Act has made provision for donors and offspring to voluntarily join a register to be maintained by the Registrar-General that offers similar opportunities for linking.

The HART Act affects two other aspects of donor egg treatment:

- Embryos cannot be stored for more than 10 years unless the person or couple storing the embryos gains permission to do so from the ethics committee.
- The Act has substantial penalties (fines and imprisonment) for paying for, or providing financial inducement for, donor eggs.

Fertility Associates is accredited by the Australian Reproductive Technology Accreditation Committee (RTAC) and abides by their guidelines. RTAC inspects clinics every three years, and their inspection includes looking at patient records. The members of the RTAC team sign a confidentiality agreement.

### **Confidentiality**

The clinic's notes are only available to staff, and are not removed from the building. If you are referred elsewhere (e.g. if you move or want obstetric care) and copies of your medical records are requested, we would not provide any information about your donor egg treatment unless it was clear that you had given us authority to do so.

Donors are identified only by a number throughout our records, so that there is no way that you can learn the donor's identity or vice versa unless you and your donor agree to this.

## **PREPARING FOR DONOR EGG TREATMENT**

There are many important issues to consider before agreeing to be the recipient of donated eggs. To help make this decision, appointments are arranged with the nurse who coordinates donor egg treatment, a doctor, and a fertility counsellor. During these meetings potential recipients have the opportunity to gather the information needed and talk over the implications of being an egg recipient.

Our nurses and counsellors are always happy to answer any questions

### **Seeing a doctor**

Before starting any treatment, you will need to see one of our doctors. The doctor will go over treatment options, what treatment entails, costs, and ethical issues.

### **Seeing a nurse**

One of our nurses will go over the practical aspects of treatment. Often this is done following the doctor's appointment, but sometimes it is better to book a separate time, especially if the details of treatment may depend on the results of tests that the doctor has arranged.

### **General health check**

Some people have medical conditions that may affect the safety of carrying a pregnancy. A common example might be diabetes; a less common example might be a heart condition. We strongly advise you to have a general health check with your GP before starting fertility treatment and to disclose any medical condition to your doctor at Fertility Associates. Your Fertility Associates doctor will focus on your medical history related to the chance of becoming pregnant, which may not cover the same aspects as a general health check from your GP.

### **Seeing a counsellor**

Seeing a counsellor is required before embarking on donor egg treatment. The counsellor can also help you prepare for, and cope with, your treatment and its outcomes. The counsellor is an ideal person to go over the issues raised in the consent forms.

### **Consent forms and legal aspects**

Both the donor and recipient and their respective partners must sign consent forms before starting any aspect of treatment, including starting the drugs. You can withdraw consent at any time, or change your mind after treatment begins. If you do this, you will need to change the original consent or fill out a new form. We will give you a copy of each consent form you sign.

There are separate consent forms to use for using donor sperm and for thawed embryo replacement.

### **Risk questionnaire**

Every woman fills out a risk questionnaire before treatment to help us identify any potential problems.

### **Tests**

Before starting treatment, the doctor or nurse will organise some routine investigations for the recipient, the donor and where appropriate their partners.

**Rubella** All female patients are tested for rubella (German measles) immunity. If there is no natural immunity to rubella then vaccination is required before starting treatment. Vaccination eliminates the risk of rubella infection in early pregnancy, which can result in birth deformities.

**Blood count and blood group** These are important tests for pregnancy that can identify potential problems.

**Hepatitis B and C** We test both men and women for these viruses so we can minimise the risk of hepatitis being transmitted to a child. We also want to prevent contamination of laboratory equipment.

**HIV** We test both men and women for HIV, because special precautions should be taken if treatment is to be considered. The test detects antibodies to the HIV virus, so a negative test does not absolutely eliminate the possibility of infection. Before having an HIV test, you may wish to see a counsellor to consider the implications of the test results. The cost of HIV counselling is not included in the cost of treatment.

We also test male partners of women having donor egg in the same way. This is to stop the clinic wrongly attributing an infection to the donor.

### **Thyroid Function Test**

Abnormal levels of thyroid hormones can interfere with ovarian function. Thyroid disease can also result in illness during pregnancy or cause birth abnormalities.

**Auto-antibody antibody screen** Sometimes an auto-antibody screen is indicated. Some antibodies are associated with a higher risk of miscarriage, and their presence requires extra care during pregnancy.

**Semen analysis** We need to know about sperm quality to decide whether conventional IVF or sperm microinjection (ICSI) is more appropriate, and we often ask you to do a semen analysis in our laboratory even if you have had one done elsewhere. Our embryologists have experience picking up subtle signs of sperm quality. Sometimes we recommend a trial sperm preparation to check whether enough sperm can be isolated for treatment.

If you are concerned that you might be unable to produce a semen sample on the day, we may be able to freeze a back-up sample. This needs to be done well in advance so we can see how well the sperm survives freezing and thawing. There is a separate charge for sperm freezing (unless it is done for medical reasons as part of publicly funded treatment). You will also need to complete a consent form for freezing and for using the frozen sperm. *Sperm will not be frozen for backup unless you request it.*

**Cervical smear and vaginal swab** All women should have a copy of the results of their most recent cervical smear forwarded to the Fertility Associates. If a smear has not been taken in the last twelve months, would you please contact your GP to arrange one and request that a copy of the results be forwarded to Fertility Associates. Cervical screening can detect early pre-cancerous changes that should be treated before treatment.

We also ask for a vaginal and cervical swab just before or during each donor egg cycle to detect bacteria that may increase the chance of pelvic infection when the embryo transfer catheter is passed into the uterus.

## **OPTIMISING SUCCESS**

Some lifestyle changes can improve the chance of pregnancy.

### **Smoking**

There is good evidence that if a woman smokes cigarettes her chance of conception during IVF treatment is halved. Smoking cigarettes probably reduces the number, and perhaps the quality, of the eggs that develop in the ovaries, and may reduce blood flow to the uterus. Miscarriages are more likely in women who smoke. We strongly encourage women to give up smoking well before starting fertility treatment.

There is some evidence to suggest that tobacco may affect sperm production.

### **Caffeine and alcohol**

There is some evidence that even quite small amounts of caffeine can reduce the chance of pregnancy, so you may wish to reduce the amount of tea, coffee, cola or energy drinks you consume. There is conflicting evidence whether modest amounts of alcohol (1-5 drinks a week) can reduce a woman's fertility.

### **Weight**

Being over-weight can lead to a higher chance of problems in pregnancy. Fortunately, even a relatively small loss in weight (often just 5-6 kg) with some exercise can be very beneficial. Your doctor will give you advice if necessary.

### **Medications**

Some medications may interfere with fertility or treatment. Please tell us if you are using tranquillisers such as Stelazine or Haloperidol, drugs for migraine, nausea or vomiting, such as Maxolon, or cortisone-type steroid drugs for asthma, rheumatoid arthritis, allergies of skin conditions.

### **Drugs and sperm quality**

Narcotics, tobacco, marijuana, or heavy alcohol use may impair sperm production in men. Sperm production can also be temporarily affected for up to three months after some antibiotic therapy or a high fever such as during the flu. Please tell us if any of these factors apply to you.

Some doctors suggest men take a zinc supplement for three months prior to IVF treatment. Your doctor will advise you if this is beneficial.

### **Folic Acid and vitamins**

We encourage all women wanting to become pregnant to take folic acid. Folic acid can prevent up to 70% of cases of neural tube defects in babies. Neural tube defects occur when the spine does not develop properly. Sometimes the skin does not close over the spinal cord as well, such as in spina bifida. Tablets of 0.8 mg folic acid per day are sufficient, and should be taken from the beginning of treatment until 7 weeks into pregnancy. Folic acid is available from pharmacies without a prescription. Women on anticonvulsant drugs should take folic acid only under supervision from their doctor. There is no good evidence that other vitamin supplements or multivitamins are beneficial when women have a normal diet. Large doses of some vitamins, particularly Vitamin A, can lead to birth defects. However if you want to use other vitamins, we recommend Elevit, which contains folic acid and which is available from pharmacies without a prescription.

### **Aspirin**

There has been considerable interest in whether low-dose aspirin may improve blood flow to the ovary and uterus, and therefore improve the chance of pregnancy during IVF treatment. Despite an early study in favour of this theory, extensive studies have shown that there is no benefit in taking aspirin during IVF treatment, so we do not advocate the use of aspirin during IVF treatment.

### **Heparin**

Your doctor may prescribe low-dose heparin if you have autoantibodies.

### **Alternative therapies**

Many patients try alternative therapies such as Chinese herbs, aromatherapy, naturopathy, acupuncture or reflexology. We suggest you stop alternative therapy for the duration of treatment. We do not support alternative practitioners who plan therapies during treatment. Of particular concern is the use of herbs, which are essentially drugs in their natural state. Most herbs have not been tested scientifically for their effect on hormone production, sperm, eggs or embryos, or on the receptivity of the uterus to an embryo implanting during infertility treatment. There are a few studies showing particular herbs inhibit sperm and egg function.

### **Sexual activity**

We do not think that sexual intercourse during your donor egg cycle will harm your chance of pregnancy. Do not forget that we recommend two to three days abstinence before producing the semen sample on the day of the donor's egg collection.

## WHAT HAPPENS DURING IVF AND DONOR EGG TREATMENT?

### The six steps in IVF

1. The donor uses drugs to stimulate the ovaries to produce several mature eggs.
2. We monitor the stimulation of the donor's ovaries and the timing of egg collection.
3. We collect eggs from the donor's ovaries.
4. We add the recipient's partner's sperm to the donated eggs and grow the embryos in the laboratory.
5. We transfer the resulting embryos into the recipient's uterus.
6. We use drugs to help the recipient's uterus be receptive to embryos.

### Using drugs to stimulate the donor's ovaries

There are several ways to stimulate the ovaries. The 'long course' or 'down regulation' approach works best for most women.

**'Long course'** Treatment starts with the use of a drug called a GnRH agonist - the most common versions are injections that have the trade names 'Buserelin', 'Lupron', 'Leuprolide', 'Lucrin' or 'Zoladex', or a nasal spray that has the trade name 'Synarel'. For simplicity we just refer to Buserelin in this booklet.

This injection of Buserelin is usually started on Day 21 of a menstrual cycle. During the first few days of Buserelin treatment, the pituitary gland releases large amounts of two hormones called follicle stimulating hormone (FSH) and luteinising hormone (LH). The pituitary gland becomes over-stimulated and stops producing FSH and LH. The pituitary is now said to be 'down regulated' (switched off). We check this has happened with a blood test 14-18 days after starting Buserelin.

When the pituitary gland is down regulated, injections of FSH are started. The trade names for FSH are 'Gonal F' and 'Puregon'. FSH stimulates the growth of follicles in the ovaries. Follicles are fluid-filled sacs in the ovary, each containing an egg. The aim of the FSH injections is to stimulate about 6-12 follicles to grow to maturity.

During the 9 to 15 days or so of FSH treatment, the follicles grow from about 5 mm in diameter to about 20 mm in diameter. Each follicle contains an egg, but the egg is tiny, less than 1/10 mm in diameter. Follicle growth is monitored by ultrasound scans of the ovaries and by measuring through blood tests for estradiol, which is the main hormone made by the cells of the follicle.

When the follicles are large enough, an injection of the hormone hCG, which has trade names 'Profasi', 'Ovidrel', or 'Pregnyl', is given. This triggers the final stage of egg maturation, and prepares the follicle for ovulation.

Why do we stop the body's own secretion of FSH only to give injections of the same hormone? There are two reasons. One is that the body normally tries to limit the number of follicles ovulated per month to one, and it does this by reducing FSH secretion during the menstrual cycle. If the body's own FSH level is falling, it tends to limit the effectiveness of the FSH injections. The other reason is that Buserelin also turns off secretion of LH as well as FSH, so that the body can no longer trigger ovulation by itself. This prevents premature ovulation, or ovulation, and therefore egg collection, at inconvenient times such as the middle of the night.

**‘Long course after the pill’** A variation of the ‘long course’ protocol has the woman use the oral contraceptive pill from around day 1 until Buserelin is started. This has several potential advantages over not using the pill. These include quicker down-regulation on Buserelin, less chance of a cyst developing, and more ability to adjust the week of egg collection. Fertility Associates clinics plan to make the use of the pill routine with time.

**‘Short course’** The ‘short course’ approach is used when the donor does not respond well to the ‘long course’ approach, or needs larger amounts of drugs. Buserelin starts on day 2 or 3 of the menstrual cycle. The body’s own FSH released during the first few days on Buserelin starts follicle growth, which is continued by daily injections of Gonal F or Puregon. It is sometimes called the ‘flare’ approach, because it uses the initial flare of FSH stimulated by Buserelin.

**‘Microdose flare with pill’** A variation of the ‘short course’ uses a much lower dose of Buserelin, and prior use of the pill for two weeks, to reduce the chance of cysts or a single ‘dominant’ follicle. This protocol is called the ‘microdose flare with pill’ protocol.

**Cetrotide short course’** A different approach uses one of a new family of drugs, called GnRH antagonists. The most common GnRH antagonist is called ‘Cetrotide’. The donor starts daily injections of FSH start on the second day of the cycle, while daily injections of Cetrotide start around day 6. FSH stimulates follicle growth in the ovaries as before, while Cetrotide prevents ovulation. Compared to the ‘long course’, the use of Cetrotide halves the number of days of injections. However, Cetrotide is more expensive than Buserelin, and the pregnancy rate may be slightly lower.

### **Collection of eggs from the ovaries**

Once the trigger injection of hCG has been given, the eggs need to be removed from the follicles around 36 hours later. Any earlier, the recovery rate of eggs is low because the eggs are still embedded in the wall of the follicle. Any later, the follicles will have burst, releasing the eggs into the Fallopian tubes or the abdomen.

At egg collection, a needle is guided along the side of the ultrasound probe in the vagina. The ovaries are usually only 2-5 cm from the top of the vagina, so they are easily reached with the tip of the needle. Once the doctor places the needle into a follicle, he or she gently draws off the fluid in the follicle into a test-tube. The test tube is passed to the embryologist to look for the egg under a microscope. If the egg is not found, the follicle can be gently flushed with culture medium to try to displace the egg. Eggs are recovered from about 80% of follicles.

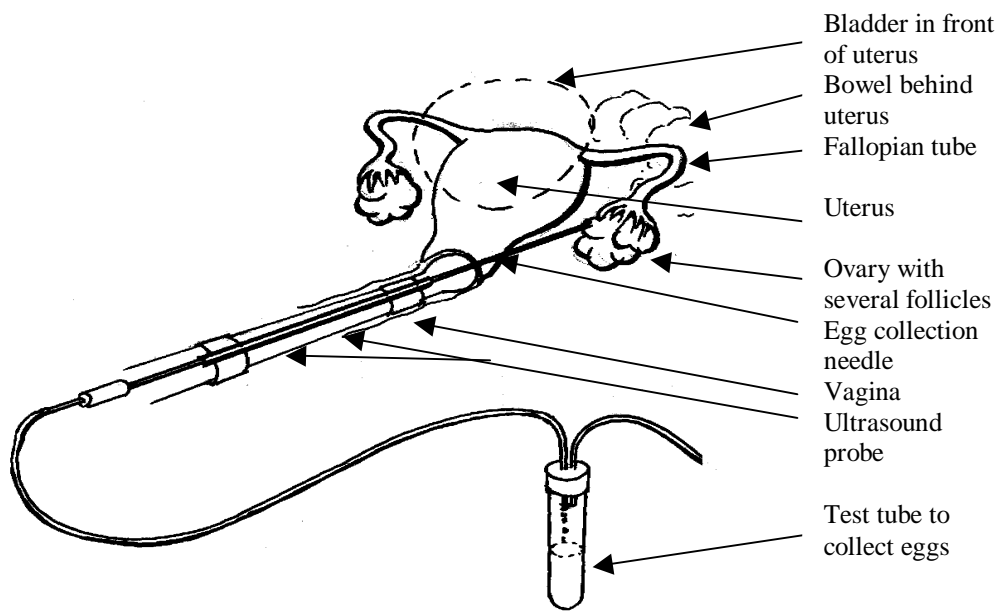
During egg collection, women have pain relief in the form of a short acting intravenous narcotic drug. The most painful part is usually the first time the needle goes into the ovary.

### **Adding sperm to the eggs and embryo development**

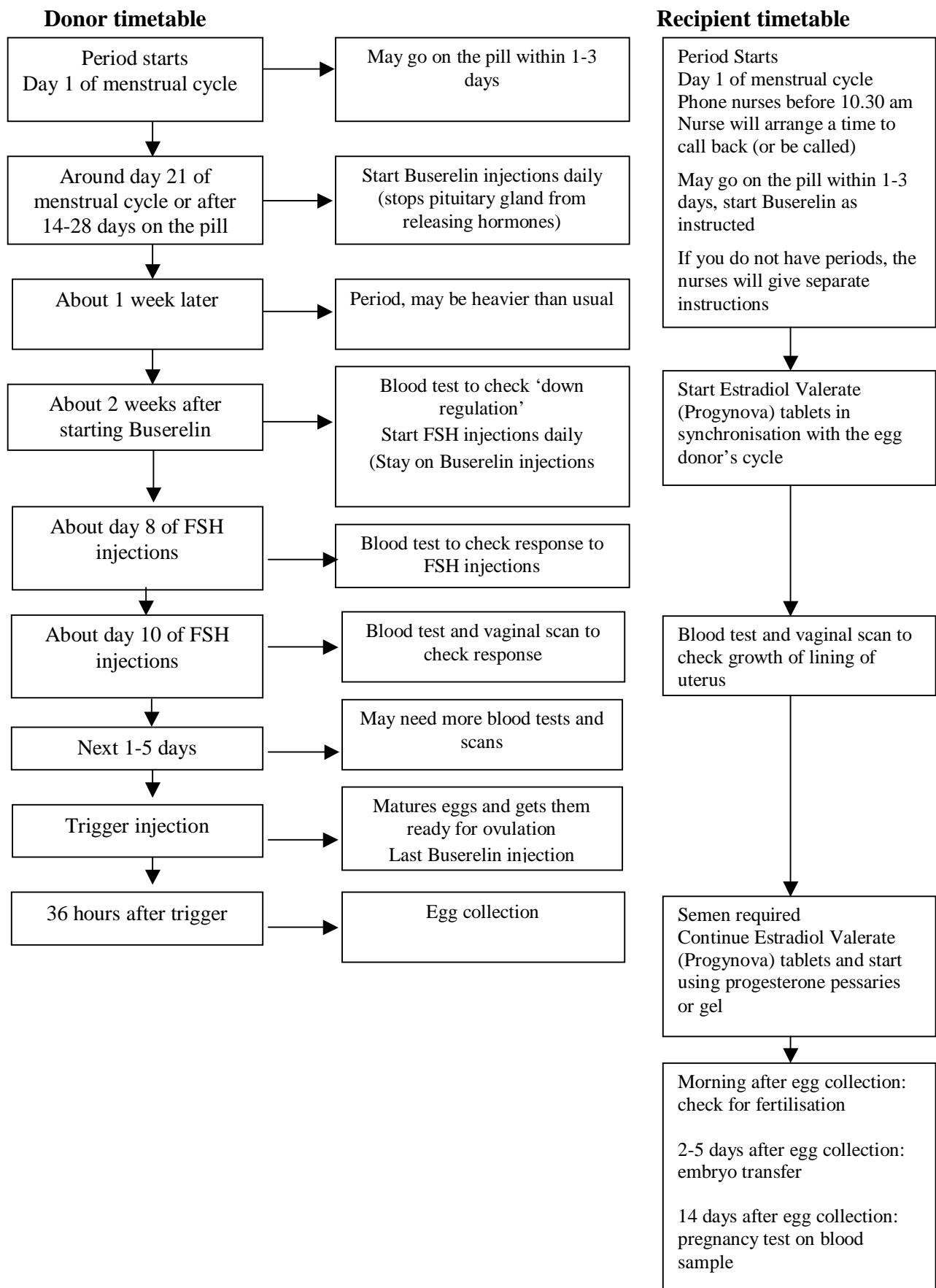
The donated eggs are placed in a fluid called culture medium in an incubator at 37°C in plastic dishes. Sperm are isolated from semen. The culture medium contains a small amount of human serum albumin, a protein purified from blood that has been screened to Blood Bank standards. It also contains low levels of some antibiotics.

In IVF, about 100,000 sperm are added to each dish. If ICSI is used, the eggs are placed in a shallow dish in microdroplets of culture medium under oil, arranged around a central drop containing sperm. The embryologist captures sperm one at a time, using fine glass needles attached to manipulators mounted on a microscope. The embryologist then moves to a drop containing an egg, holds the egg with another fine pipette, and injects the sperm deep into the egg.

**Figure 1. Diagram of egg collection using ultrasound guidance**



**Figure 2. Typical timetable for treatment**



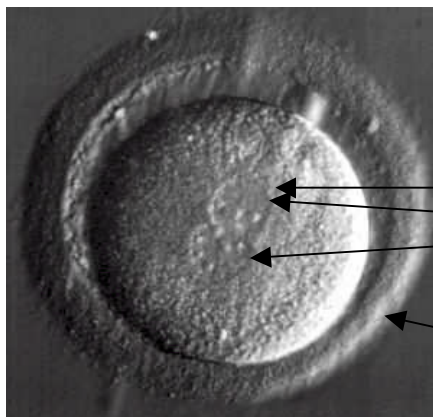
The next day, 16-18 hours after adding the sperm, the eggs are inspected to check for fertilisation, and moved into fresh culture medium.

The cells in the embryo keep dividing over the next few days. On the fifth day a fluid-filled cavity forms in the middle of the cells, so that the embryo consists of an even outer layer and an inner mass of cells. An embryo at this stage is called a blastocyst. The outer layer of cells will become the placenta; the inner cell mass the foetus. In the next day or so the shell that encases the embryo (the zona pellucida) thins, the embryo expands, the zona splits, and the embryo hatches from the zona and implants into the lining of the uterus.

Embryos may be transferred on day 2 or 3 after egg collection, or moved to culture medium of different composition for blastocyst culture. When embryos progress to blastocysts, they are replaced on day 5 or 6.

**Figure 3. Stages of embryo development checked in the laboratory**

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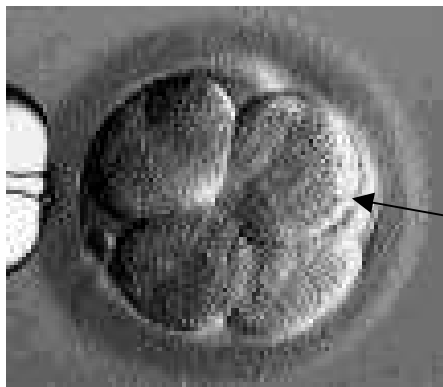


**Fertilised egg, about 18 hours after adding sperm**

This is what is seen at the fertilisation check on day 1

Male and female 'pronuclei' (the genetic material from the egg and the sperm before they join)

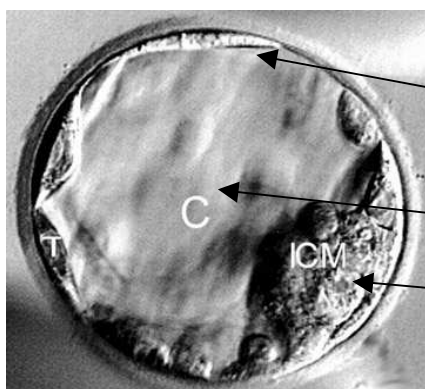
Zona Pellucida (soft shell surrounding the egg)



**8-cell embryo, day 3**

Many embryos are at the 8-cell stage at embryo transfer on day 3 after egg collection

One of the 8 cells



**Blastocyst, day 5-6**

Outer lay of cells, which becomes the placenta

Fluid-filled cavity

Inner cell mass, which becomes the fetus

If there are many embryos, some can be frozen on day 1 for later use, or else any ‘spare’ good quality embryos left after embryo transfer can be frozen.

### **Embryo transfer to the recipient**

Embryos are selected for transfer. Usually only one or two embryos are transferred to reduce the chance of triplets.

Embryo transfer is usually very simple. The embryologist loads the embryos in a tiny amount of culture fluid into the tip of a thin tube. The doctor puts a speculum in the vagina, just as during a cervical smear. The catheter is gently passed through the cervix into the uterus. Usually ultrasound is used to help with the transfer, or to see the size and angle of the uterus. Having a full bladder makes embryo transfer much easier.

### **Using drugs to help the uterus be receptive**

Estradiol Valerate tablets and progesterone pessaries or gel are continued until advised to stop by the nursing staff.

### **Embryo freezing**

Good-quality spare embryos can be frozen, stored in liquid nitrogen, and thawed later to give another chance of pregnancy. Freezing involves adding a ‘cryoprotectant’, or antifreeze solution, to the embryos. The cryoprotectant draws water out of the cells, so that ice crystals are less likely to form inside the cells when the temperature falls below freezing. The embryos are sealed in plastic straws, cooled at a controlled rate, and then stored in liquid nitrogen at  $-196^{\circ}\text{C}$ .

About 50-70% of embryos survive the freezing and thawing process. The figure depends on the quality of the embryos and the stage the embryos are frozen. It can also vary between one woman and another.

Embryos may be stored frozen for up to ten years under the HART Act, although individuals may apply the ethics committee to extend the duration of storage. The clinic reserves the right to dispose of embryos when people have not paid storage fees or cannot be contacted.

## **RISKS AND SIDE EFFECTS**

IVF/Donor egg treatment is a medical and surgical procedure that carries its share of side effects and risks. Side effects are common events that seldom pose a threat to health or life, although they may be unpleasant and painful. Risks are uncommon events that can potentially have serious and permanent consequences. The donor experiences most of the risks and side effects. Those relevant to women receiving embryos from donated eggs are listed below.

### **Risks**

#### **Vaso-vagal reaction**

There is a small chance of a vaso-vagal reaction at the time of embryo transfer. This is an involuntary reflex that causes the heart to slow, blood pressure to drop, and fainting. The embryo transfer is usually stopped and done at a later time.

### **Infection after embryo transfer**

There is a small chance of uterine infection after embryo transfer, which overseas studies put at about 0.2% to 0.4%. When this happens, bacteria that are present in the vagina are transferred into the uterus and cause a local infection. If you feel sore, feverish or unwell within a few days of embryo transfer, call the clinic. Infection usually settles with antibiotics. There have been cases of damage to the uterus or Fallopian tubes, but this is very rare.

### **Bleeding after embryo transfer**

There is a small chance of bleeding from the cervix after embryo transfer, on the day of transfer or the next day. This is not believed to affect the chance of pregnancy.

### **Ectopic pregnancy**

When an embryo implants in the Fallopian tube, the cervix or the abdomen, it is called an ectopic pregnancy. Ectopic pregnancies can be dangerous because the placenta can grow into a blood vessel and cause major internal bleeding. We can usually detect an ectopic pregnancy by the level of hCG in the blood tests and the early ultrasound scan, but not always. *Symptoms include severe, localised abdominal pain – seek medical help immediately.*

### **Multiple pregnancy**

A major risk of having embryos from donated eggs is multiple pregnancy. The subject on how many embryos to transfer is discussed in the section 'Decisions to make' later in this booklet.

Culturing embryos to the blastocyst stage before embryo transfer may increase the chance of identical twins. Sometimes there is exchange of blood between identical twins while they are still in the uterus, which increases the risk that one twin will not develop as well as the other, and increases the risk of complications during pregnancy.

### **Sperm and embryo storage**

Sperm and embryos are stored in sealed plastic straws immersed in liquid nitrogen banks. For many years we have screened people for Hepatitis B and C before banking wherever possible, and from mid-2002 we started routine screening for HIV. When people screen positive to Hepatitis or HIV, their sperm is stored in a separate bank, and extra precautions are taken before embryos straws are frozen. Cross-contamination of viruses, like Hepatitis B or HIV, from one straw to another while in a liquid nitrogen bank has never been reported world-wide, but is a theoretical possibility with sperm.

There is a very small risk that a liquid nitrogen bank will fail, causing the sperm or embryos stored in it to perish. Bank failure has been reported very occasionally around the world. Unfortunately, it is prohibitively expensive to insure against bank failure because of the unusual nature of the risk. Fertility Associates takes reasonable precautions but cannot be held responsible for the loss of sperm or embryos from bank failure.

## **IVF CHILDREN**

### **Chance of Abnormalities**

The chance of congenital abnormalities in children born after IVF is similar to that of children conceived naturally, which is just under 3%. There might be a slightly higher rate of chromosomal abnormality in children from ICSI (see the section on ICSI later in the booklet).

The chance of abnormalities such as Down Syndrome is the same in IVF and ICSI pregnancies as the general population, which shows a sharp rise with age, especially after the mid-30's. With donor egg, the chance of abnormalities is dependent on the age of the donor. If the donor is 35 years or older, you may want to consider prenatal diagnosis by amniocentesis or Chorionic Villus Sampling (CVS) if you become pregnant.

Recent studies suggest IVF and ICSI are probably associated with a higher risk of various rare disorders associated with the 'imprinting' of genes. Imprinting disorders occur in about 1: 10,000 children conceived naturally; with IVF and ICSI the rate probably increases to about 1:2,000. This would mean on average an affected child from IVF or ICSI every three years in New Zealand. Your doctor can provide more information about these disorders.

If some of the cells are damaged during freezing and thawing of an embryo, the chance of that embryo implanting and giving rise to a child is lower, but there is no greater risk of abnormalities. At this early stage of embryo development, each cell of the embryo is capable of giving rise to an individual person.

### **Development of children from IVF and ICSI**

IVF is a relatively recent technique, with the first birth in 1978 and relatively few children born until the mid-80's. There have been several large follow-up studies from the USA and various European countries that altogether included around two thousand children, mainly up to the age of 10. Physical, mental, and social development of IVF children was similar to children conceived naturally. There is no information specifically about children from donor egg treatment and IVF.

The first births using ICSI did not happen until early 1993. Studies that have examined the health and development of ICSI children in their first and second years of life have not revealed any obvious problems.

A study of over 5000 children conceived after IVF showed a similar rate of childhood cancers to children conceived naturally.

## **COMMON PROBLEMS DURING DONOR EGG TREATMENT**

IVF/Donor egg treatment is complex – even with the best knowledge, unexpected things can happen. We will always discuss options with you before any decision is made. Future treatment cycles will benefit from what is learnt.

### **Slow down regulation by the donor**

Sometimes the Buserelin injections given to the donor cause follicles to grow, so that the ovary is still making estrogen at the down regulation blood test. Usually another 4-7 days of Buserelin is all that is needed. If a follicle persists, an injection of hCG will nearly always cause it to ovulate. An alternative to waiting for down regulation is to stop the cycle and try again in 1-2 months time.

### **Stopping treatment for under-stimulation by the donor**

If only one or two follicles develop in the donor, or if the blood test results are low, it may be best to stop treatment, and try again later using more drugs. We advise stopping because of poor response to drugs in about 10-20% of cycles. If your donor has a poor response during a publicly funded cycle, we will make the decision whether to stop, and whether we can offer her another attempt at egg donation.

### **Stopping treatment for over-stimulation by the donor**

Occasionally treatment is stopped because too many follicles develop, meaning there would be an increased risk of Ovarian Hyperstimulation Syndrome (OHSS) if the donor went ahead with egg collection. Not having the trigger injection prevents any chance of OHSS.

### **Ovulation before egg collection**

Although follicles are not supposed to ovulate within 36 hours of the hCG trigger injection in the donor, ovulation will happen in about 0.5% of cycles.

*It is important to understand that the donor has no control over these events.*

### **Donor herself stops**

Due to unforeseen personal circumstances or a change in mind, a donor may choose to stop. This is an uncommon occurrence.

### **No or low fertilisation**

As long as 3 or more eggs are collected, then the chance of not having embryos to transfer is less than 2%. Low or no fertilisation can be due to an unexpected sperm factor or an egg factor. Very occasionally (about 0.2% of cycles) the semen is contaminated by bacteria that are resistant to the antibiotics in the culture media. Since this tends to be an intermittent problem, and since most semen samples contain some bacteria, it is not practical to screen routinely for bacteria.

## **DECISIONS TO MAKE**

### **Frozen or fresh embryos**

Donors are screened for HIV and for Hepatitis B and C, but it is possible for a donor to contract one of these diseases between the screening test and treatment. The safest approach is to freeze all the embryos, store them for six months, and then ask the donor to do another set of screening tests before thawing the embryos for transfer. However, embryos often sustain some damage during freezing and thawing, and the pregnancy rate with frozen embryos is substantially lower than with 'fresh' embryos. For this reason, most people opt to use fresh embryos, instead of quarantining them for six months.

### **How many eggs to add sperm to?**

On average, only 75% of mature eggs fertilise in IVF or ICSI. Of the embryos formed, some will be of poor quality and will not be suitable for transfer or freezing. Unless you have an ethical objection to discarding 'poor quality' embryos or to freezing 'spare' embryos, adding sperm to all the eggs maximises the chance of having at least two good quality embryos for transfer.

### **How many embryos to transfer?**

The reproductive system in women has evolved to support and grow one baby at a time - normally only one egg ovulates each month more than 98% of pregnancies from natural conceptions are a singleton.

From the early days of IVF, people have increased the chance of pregnancy by transferring more than one embryo. But transferring more than one embryo introduces the possibility of multiple pregnancies with their adverse consequences.

For a long time it was common to restrict the number of embryos transferred to three, but as methods improved, the number of triplets increased. Triplets soon changed from being seen as "IVF miracles" to a serious problem - about 30% of triplet pregnancies miscarry before 20 weeks gestation before the babies can possibly survive. And of those that progressed past 20 weeks, many children are born prematurely with a high chance of death or handicap.

More recently, transferring two embryos in younger women was seen as a reasonable compromise between improving the chance of pregnancy and limiting the risk of multiple pregnancy, but even twin pregnancies carry increased risks of death and handicap, as shown below.

As well as the medical risks, having twins can have a significant social and emotional impact. This includes more marital stress and depression than among couples with IVF or ICSI singletons, more relationship crises, thought of divorce and increased perception of difficulties with the children. Younger mothers with low birth weight children are most at risk. Despite the extra stress with twins, some research suggests that parents of IVF or ICSI twins have a lower divorce and separation rate than parents of non-IVF twin, perhaps indicating a strong marital relationship.

The table below summarises medical risks with twins (mostly for twins in general), and some data from an American study on family stress with IVF twins.

**Table 1. Risks to the mother and child(ren) in singleton and twin pregnancies**

<b>Risk</b>	<b>Singleton pregnancy</b>	<b>Twin pregnancy</b>	<b>Risk for twins</b>
<b>To the mother</b>			
Hospitalisation for ovarian hyperstimulation syndrome (OHSS) in an IVF pregnancy	4.6 % of pregnancies	9% of pregnancies	2 times higher
Mother dying in childbirth	5 per 100,000 births	15 per 100,000 births	3 times higher
<b>To the child(ren)</b>			
Stillbirth or death soon after birth (neonatal and perinatal death)	2.8% of children	6.3% of children	2.5 times higher
Baby admitted to neonatal intensive care unit (NICU) after birth	15% of children	48% of children	3 times higher
A serious brain haemorrhage around birth			5 times higher
Serious infection			3 times higher
Respiratory distress			6 times higher
Cerebral palsy	0.23% of children	1.3% of children	5 times higher
Some handicap	2.5% of deliveries	7.4% of deliveries	3 times higher
<b>Overall medical risks</b>			
Estimate of any problem (death, abnormality, or some handicap)	6% of deliveries	20% of deliveries	3 times higher

**To the family**

Difficulty meeting material needs	2.4%	18.2%	8 times higher
Lower quality of life	4.7%	12.1%	2.5 times higher
Maternal depression	15.9%	22.9%	1.5 times higher
Maternal stress	7.1%	13.8%	2 times higher
Lower marital satisfaction	7.8%	11.8%	1.5 times higher

With the improvements in IVF pregnancy rates from advanced methods in the last few years, Fertility Associates now strongly advises single embryo transfer (SET) when the donor is aged 35 or younger and when there is at least one reasonable quality 8-cell embryo on day 3.

Having twins also carries considerable costs for public hospitals – the average hospital cost of birth and neonatal care in New Zealand is \$5000 for a singleton birth, but \$31,000 for a twin birth. For this reason and to improve the health of IVF children, the Ministry of Health now requires SET for people who meet the criteria above when they have publicly funded IVF treatment. A second publicly funded donor egg cycle is offered if the first does not lead to the birth of a child.

Transfer of two embryos may be considered when:

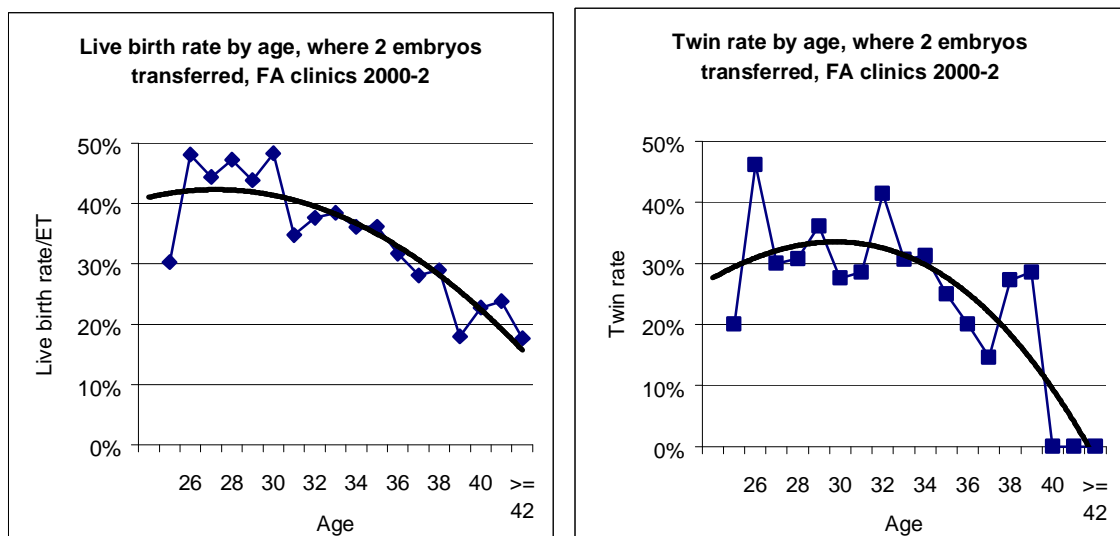
- The donor is 36 or older
- The donor is 35 or younger AND none of the embryos meets the criteria above.

Transfer of three embryos may be considered when the donor is aged 40 or older.

If you do not want the possibility of twins, you should have only one embryo transferred, although it is still possible to have identical twins after the transfer of one embryo.

The following graphs may help you decided whether to have one or two embryos transferred, by taking into account the chance of pregnancy and the chance of twins when two embryos are transferred. The curves show the overall trends.

**Figure 4. Live birth and twin rates with two embryos transferred**



The decision on how many embryos you want to transfer should be made before or early in your donor egg treatment cycle. This gives you time to ask your doctor about your situation and to talk with a counsellor about the implications of SET and its alternatives. The implications of SET include:

- What to do if embryo quality on the day of embryo transfer were not sufficient for the clinic to recommend SET.
- How you would feel if you had twins after switching to the transfer of two embryos under these circumstances.
- The possibility of the 'second' embryo not surviving freezing and thawing in a subsequent treatment.

### **At what stage to transfer embryos?**

The longer embryos are left to develop in the laboratory, the better the choice, since embryos can be chosen on their ability to keep growing at the right rate. On the other hand, conditions in the laboratory are unlikely to be as good as in the body, so longer periods of culture may be detrimental.

Generally embryos are transferred on day 3, depending on the number of embryos available, their appearance, rate of growth, and also the time of day the egg collection was done. We usually like to observe embryo development for at least 44-46 hours before choosing which embryos to transfer.

At this stage, embryos are mainly being selected on their physical appearance – the number of cells, the evenness of the cells, and the degree of 'fragmentation'. The cells in human embryos seldom divide without throwing off a few 'blobs' of cellular material, which are called fragments. Embryos with a higher grade do have a better chance of resulting in a pregnancy, but the relationship between appearance and pregnancy is only approximate.

In theory the best selection would come from culturing embryos for 5-6 days to see which developed into high quality blastocysts. The option of blastocyst culture is covered in a later section of this booklet.

### **Embryo freezing**

Most couples choose to freeze 'spare' embryos of good quality to give them another chance of pregnancy later on, but a few do not like the idea of having embryos frozen. There is the possibility that you will become pregnant after transfer of the fresh embryos, and not want to use your frozen embryos. The consent form asks what we should do with frozen embryos if you and your partner separate, or die, or can not be traced by the clinic. The clinic reserves the right to discard your embryos if you lose contact with the clinic for two years or more, or do not pay annual storage fees.

Embryos frozen on day 1 have a higher chance of survival than embryos frozen on day 2 or 3, so if there are many embryos (say more than 8), some may be frozen on day 1 leaving a reasonable number to choose from for transfer on day 2 or 3. Any good-quality 'spare' embryos after transfer can also be frozen. If blastocyst culture is planned, all embryos are usually cultured, and any 'spares' frozen only if they become blastocysts.

Embryos may be stored frozen for up to ten years under the HART Act, although individuals may apply the ethics committee to extend the duration of storage. The clinic reserves the right to dispose of embryos when people have not paid storage fees or cannot be contacted.

### **How many embryos to transfer after embryo freezing**

Although the chance of pregnancy using frozen embryos is lower than using fresh embryos, there is still a high chance of twins when two thawed embryos are transferred.

An analysis of birth rates from Fertility Associates showed quite similar birth rates when one or two embryos thawed embryos were transferred, and when the embryos were undamaged by thawing, or had sustained only moderate damage, such as the loss of only 1-2 of 8 cells.

We strongly recommend single embryo transfer (SET) for women who had embryos frozen when they were 35 or younger.

Transfer of two embryos may be considered when:

- The woman was 36 or older at the time of embryo freezing
- The woman was 35 or younger at freezing, but when the first embryo is thawed, more than 25%-50% of the cells are damaged.

Transferring of three embryos may be considered when the woman is aged 40 or older.

## **STEP-BY-STEP THROUGH A DONOR EGG CYCLE**

### **Synchronising and manufacturing a recipient's cycle**

If you have a normal menstrual cycle and are receiving fresh oocytes, your cycle needs to be synchronised with that of the donor. This can be done with the use of a drug called a GnRH agonist - the most common versions are injections that have the trade names 'Buserelin', 'Lupron', 'Leuprolide', 'Lucrin' or 'Zoladex', or a nasal spray that has the trade name 'Synarel'. For simplicity we just refer to Buserelin in this booklet. Buserelin effectively turns off the reproductive functions of the pituitary gland, and hence the ovaries. Women who have ovarian failure will not need to use Buserelin.

Estrogen and progesterone are then given to mimic the hormone levels found in a normal menstrual cycle, to make sure the uterus is receptive to the implantation of a viable embryo. The regimen will consist of Estradiol Valerate taken orally three times daily, from cycle day 1.

Progesterone will start from the day the donor has her egg collection.

The progesterone usually comes in the form of 'micronised' progesterone pessaries with the trade name 'Utrogestan'. The usual dose is two pessaries at a time, three times a day, which means every eight hours. These pessaries are placed in the upper vagina. Crinone is an alternative form of progesterone that comes as a gel in a pre-filled vaginal applicator. The usual dose is one applicator worth of Crinone every day, placed in the upper vagina. Some women will get a slight discharge when using Utrogestan or Crinone. Please tell us if irritation occurs, although studies show this does not occur very often with Utrogestan or Crinone.

Utrogestan is used all over the world for IVF. However, it is not registered as a drug in New Zealand because of the low level of use and the high cost to pharmaceutical companies of registering drugs. Because it is not registered in New Zealand, it is mentioned separately in our consent forms, and we are legally required to provide the names of everyone who uses it to the Ministry of Health. No other information goes to the Ministry. If you have any comments about your use of Utrogestan, please let us know.

Sometimes women have some bleeding before their pregnancy test is due – this does not necessarily mean that you are not going to be pregnant. ***Do not stop using the Estradiol Valerate tablets and progesterone pessaries or gel until we tell you the results of the pregnancy test! If you are pregnant, you will need to continue taking Estradiol Valerate and the progesterone pessaries or gel until around the 12<sup>th</sup> week of pregnancy.***

### **Consent**

One of the Fertility Associates staff will go through the consent form with you to ensure you understand the treatment and its options, and will act as a witness. We will give you a copy of each consent form you sign.

***You must have your consent form and risk questionnaire completed before you start any drugs. Remember – no consent, no treatment!*** You can always change things later, such as the number of embryos to transfer, if you want to.

### **Starting a treatment cycle**

Once you have all the information, the clinic's donor egg coordinator will work out a timetable for you to start and when to contact us.

We will review your medical records to plan when you should start your drugs, the dose of the drugs, and other details.

***You must be able to be contacted by the clinic from the time you start ovarian stimulating drugs such as Gonal F or Puregon until the day of embryo transfer.***

### **Paying for private treatment**

The clinic will tell you the cost of treatment for you and your donor, well before you start. Any drugs that are used need to be paid for by the time they are picked up, or before we courier them to you if you live out of town. We will also invoice you for the IVF or ICSI part of treatment early in the cycle, and this fee needs to be paid before the donor has her egg collection.

There are separate information sheets explaining the fees associated with donor egg treatment. You pay for an IVF cycle, plus the fees for donor eggs – the donor egg fees depend on whether you have a personal or clinic-recruited donor.

The IVF or ICSI fees are refunded if the cycle is stopped before egg collection (e.g. for poor or over-response to the drugs), and instead you pay a management fee for the blood tests, ultrasound scans and staff time.

If your donor has an egg collection but you do not get to embryo transfer, you must pay the IVF or ICSI fees, but there is a refund for the embryo transfer part of the cycle. If all your embryos are frozen, the refund is used to cancel out the fee for embryo freezing

There are separate fees if you have embryos frozen, store sperm, or need to have sperm screened for antibodies.

### **Timetable for drugs and blood tests**

The nurse will tell you when to start drugs, when to have your first blood test, and when your first scan is likely to be. We will provide a planning sheet for the treatment cycle. Be sure to write everything down! The nurse will also arrange a time for you pick up the drugs or will arrange to send the drugs by courier.

The nurses will tell you when to start each type of drug, and the dose to take. There is a separate instruction sheet on how to give yourself injections if you require them. Our nurses will show you how to do this, or you can arrange a local nurse to provide instructions.

### **Blood tests**

We will tell you when you need to have blood tests and where to go for them. Many people come to the clinic early in the morning (the time varies from clinic to clinic, but is usually around 8 am to 9 am), but tests can be organised at other laboratory collection rooms.

Each clinic has a list of the places where you can have blood tests taken; these include most cities in the North Island. If you want to have your blood taken somewhere other than the clinic, please ask the nurse to make sure that this is feasible. The nurses can give you times and places for tests so that the results will be available on time.

### **Ultrasound scans**

Ultrasound scans are usually done between 8 am and 9 am, but later times in the morning can occasionally be arranged in special circumstances. Each clinic has its own way of recording when you arrive so that the doctor doing the scanning knows who is waiting. The nursing or reception staff can help you.

Ultrasound scanning uses an ultrasound probe placed in the vagina, and you need to have an empty bladder.

### **Telephone calls to keep track of progress**

The team meets around 12:30 pm each day to analyse the results and to decide the next step in the management of your cycle. You need to ring the clinic every day that you have a blood test or an ultrasound scan for the day's instructions, or the clinic will need to ring you. The nurses will tell you when your instructions will be available – it is usually from about 1:30 pm onwards, but may be different in the weekend or if you have had your blood test done outside the clinic. Both you and the clinic need to know how and when you are going to contact each other.

Please ask as many questions of staff as you want during treatment.

### **Triggering for egg collection**

The final maturation of the donor's eggs is induced by a trigger injection of hCG. This is given 36 hours before egg collection is planned.

### **Egg collection ('Day 0')**

When we arrange the hCG trigger injection for your donor, we will also arrange a time for the egg collection and a time for your semen sample to be delivered to the lab. We invite you to deliver a gift for your donor on this morning. Arrangements can be discussed with the donor egg co-ordinator.

On the morning of egg collection the recipient starts progesterone pessaries or gel (as well as continuing the Estradiol Valerate tablets).

### **Providing a semen sample**

On the morning of your donor's egg collection, the nurses will tell you what time you need to arrive at the clinic. Please produce a sperm sample before leaving your home or accommodation, and bring it to the clinic with you. The quality of the sperm sample is

best if it is possible for you collect the sample within one hour of arriving at the clinic. We have a room in the clinic if it is more convenient than collecting it at home. Please tell us where you are going to be during the day, in case we need to contact you about the quality of the sperm.

Please pass urine, and then wash your hands before producing semen. This reduces the amount of bacteria from the skin entering the semen. The semen must be collected in the container we give you.

Sexual abstinence of around three days allows the number of sperm to build up to optimal levels. Longer periods have no further advantage, and can sometimes be detrimental because of the accumulation of aged sperm.

If you are concerned that you may be unable to produce a semen sample on the day, we may be able to freeze a back-up sample. This needs to be done well in advance so we can see how well the sperm survives freezing and thawing. There is a separate charge for sperm freezing (unless it is done for medical reasons as part of publicly funded treatment). You will also need to complete a consent form for freezing and for using the frozen sperm.

### **The fertilisation check ('day 1')**

On the morning after the egg collection, an embryologist will check your eggs to see how many have fertilised normally. We have arranged a time for you to ring, or for us to ring you with these results. At this time we may be able to confirm a time for the embryo transfer.

### **Embryo transfer ('Day 2-6')**

You will need to arrive at the clinic about a quarter of an hour before the embryo transfer is scheduled. You will be able to see your embryos down the microscope before they are transferred. This is a special time for most people, and you will probably want to be together at the transfer.

*Please have a fairly full bladder for embryo transfer* – this can help make the transfer easier, especially when the doctor uses ultrasound to help place the catheter containing the embryos. Embryo transfer is usually painless, very seldom needs any drugs, and usually takes less than a quarter of an hour.

Afterwards you can continue your normal activities – the embryos will not drop out! We do not think intercourse will do any harm.

### **Take home packs and waiting**

Following embryo transfer, a nurse will talk to you about continuing your Estradiol Valerate tablets and progesterone pessaries or gel over the following two weeks to maintain the lining of the uterus.

Sometimes women have some bleeding before their pregnancy test is due – this does not necessarily mean that you are not going to be pregnant. ***Do not stop using the Estradiol Valerate tablets and progesterone pessaries or gel until we tell you the results of the pregnancy test! If you are pregnant, you will need to continue taking Estradiol Valerate and the progesterone pessaries or gel until around the 12<sup>th</sup> week of pregnancy.***

Waiting to see whether you are pregnant can be the most stressful part of treatment. Please feel free to call the nurses or one of our counsellors.

## **Review**

We will provide a written summary of your treatment cycle. Some doctors prefer to do this as a letter to your GP with a copy to you; others prefer to provide you with a written summary at transfer. We strongly encourage you to make an appointment with your doctor to review how things went or to plan pregnancy care. This review consultation is free if you had publicly funded treatment. We can help you make this appointment at the time of embryo transfer.

## **PREGNANCY TEST (Day 14) AND EARLY PREGNANCY CARE**

Nearly two weeks after embryo replacement we organise a pregnancy test. At this stage a blood test will give a more reliable result than a urine test, especially if you have had hCG injections in the past two weeks. You can find out the result of the pregnancy test by ringing the nurses at the usual time, usually after 2 pm, or we can give you the result in a sealed envelope.

Because we try to detect pregnancy on day 14, which is the earliest stage that pregnancy can be detected, we look for a very low level of the pregnancy hormone hCG. Sometimes it may be possible for a low level of hCG to be present even though there is no pregnancy, and so sometimes it may be difficult to tell from just one blood test whether you are pregnant.

If the pregnancy test is positive (or ambiguous), we will arrange another test four days later. This test can help decide whether you need to continue taking Estradiol Valerate tablets and progesterone pessaries or gel. We may want to track the progress of pregnancy with further weekly blood tests.

We will arrange an ultrasound scan at 7 weeks to see whether the pregnancy is progressing normally, and to check whether the pregnancy is single (one baby) or multiple (twins or more). Fertility Associates prefers to be responsible for your early pregnancy care, such as this scan and any hormone tests to monitor pregnancy. If your treatment was publicly funded, our early pregnancy care is free. Otherwise the options are for Fertility Associates to provide this personalised care for a fee, or for your doctor to refer you privately to an ultrasonography service.

### **Pregnancy follow-up**

We have an obligation to know the outcome of all pregnancies from our treatments – we will ask you whom we can contact to get this information. Please tell us if you change address.

### **Pregnancy loss**

About 20-30% of treatments that lead to a positive pregnancy test on 'day 14' will result in miscarriage. The rate will be even higher if the eggs came from an older donor.

The majority of miscarriages are probably due to genetic abnormalities in the embryo that cause the embryo or the placenta to stop developing at some stage. Very early pregnancy loss is sometimes called a 'biochemical' pregnancy, because the pregnancy was detected by biochemical pregnancy tests only. When pregnancies reach 6 weeks or more, they are called clinical pregnancies because the pregnancy can be detected by ultrasound scanning. If the scan shows a sac (the fluid inside the membranes and placenta) but no fetus, the pregnancy is sometimes called an 'empty sac', or a 'blighted ovum'.

Most miscarriages are recognised by bleeding accompanied by some pain. However, as many as 30% of normal continuing pregnancies have some degree of bleeding in the first three months. Warning signs of miscarriage are bleeding that continues, becomes heavier, and/or the woman has low, cramping, period-like pains. The sudden disappearance of pregnancy symptoms may signal a miscarriage some days later. If you have any of these symptoms or are concerned about miscarriage, ring the clinic for advice.

Sometimes levels of beta-hCG hormone give some indication that the pregnancy may not be ongoing, well before symptoms develop. If you are having weekly blood tests the clinic staff will be able to warn you if your beta-hCG levels look problematic.

Often the first indication that a pregnancy may not be ongoing comes from the ultrasound scan at 7 weeks – if the scan is unclear another scan will be arranged in 3-7 days.

Most miscarriages occur before 10 weeks or so, and seldom need a D&C (dilatation and curettage of tissue from the uterus).

A miscarriage, no matter at what stage of pregnancy, is the loss of a potential baby, and the grief can be severe. Some people experience a change in emotions for a long time afterwards. If you have a pregnancy loss, please consider using the clinic staff as a source of help and emotional support. Our counsellors are especially experienced in helping people at this very difficult time.

## **USING FROZEN EMBRYOS**

It is important to recognise that only 50-70% of embryos survive freezing and thawing. Sometimes none of the embryos survive thawing. It can also be disappointing to find that most or all of the embryos have sustained some degree of damage. Like other clinics, we consider that an embryo has survived freezing and thawing if 50% or more of the individual cells survive. This definition is based on the observation that pregnancy rates are reasonable if 50% or more cells survive, but almost nil if fewer than 50% survive. The loss of cells within the embryo only affects the chance of pregnancy; it does not increase the chance of congenital abnormality, since each cell is capable of giving rise to a complete person.

### **Decisions to make and giving consent**

Like IVF itself, there is the decision of how many embryos to transfer, and the same principles hold for the transfer of thawed embryos as for fresh embryos.

As explained earlier in this booklet, we strongly recommend single embryo transfer (SET) for women who had embryos frozen when they were 35 or younger.

Transfer of two embryos may be considered when:

- The woman was 36 or older at the time of embryo freezing
- The woman was 35 or younger at freezing, but when the first embryo is thawed, more than 25%-50% of the cells are damaged.

Transferring of three embryos may be considered when the woman is aged 40 or older.

It is a good idea to discuss how you want your embryos thawed with an embryologist before you complete your consent form. The consent form has a space for you to write how many embryos you want thawed and what to do if not all embryos survive freezing and thawing, or if some sustain a moderate level of damage.

***Both partners must give their consent to thaw embryos on the consent form for thawed embryo replacement, regardless of what you have consented to on previous consent forms. Your consent form must be completed before we can thaw your embryos.***

### **Types of cycles**

The focus of a frozen embryo cycle is replacing the embryos at the right time in a menstrual cycle, or manufacturing an artificial menstrual cycle using hormones. There are several ways of doing this.

**Blood tracking** Daily blood tests for LH from a particular day in the cycle (the actual day depends on your average cycle length) is the most reliable way of detecting ovulation and therefore when to transfer embryos. It means coming to the clinic daily, or going to community labs that can offer this test and then send the results to Fertility Associates the same day. Getting blood taken over the weekend may be difficult so other options may be needed, such as travelling to the clinic, or using Clearplan.

**Twice daily 'Clearplan'** 'Clearplan' is an easy to use do-it-yourself test for measuring LH in the urine at home. When used morning and evening it is almost as reliable as blood tests in timing ovulation in about 90% of cycles. Clearplan is an option for people living away from the clinic.

**Manufactured cycle** Instead of using a normal menstrual cycle, drugs can be used to prepare the uterus. The advantage of a manufactured cycle is that the embryo transfer can be planned for a particular day quite independently of your menstrual cycle, and you normally need only one blood test. The disadvantage is that if you become pregnant you will need to take the drugs up to the 10<sup>th</sup> week of pregnancy. It is more reliable than a natural menstrual cycle in women who have irregular ovulation, or if you want to have a thawed embryo cycle immediately after an IVF cycle. It is especially useful for people who do not live in the same city as the clinic, because daily blood tests are not needed.

**Travel arrangements** Because it is possible that none of your embryos will survive thawing, we aim to tell people whether there are any embryos to transfer before they start their trip into the clinic. Once the blood tests or Clearplan indicate when thawing should be done, we will arrange a time for you to contact the clinic, or for the clinic to contact you, to see if the embryos have survived and to confirm a time for transfer.

### **Moving embryos**

Embryos can be transported between the clinics in a portable liquid nitrogen container if it would be more convenient to have your embryo thaw cycle at a different clinic. Transport needs to be arranged by the clinic holding the embryos. The clinic charges a fee for arranging transport in addition to the courier fee. There is a small risk that the liquid nitrogen container will be damaged or its delivery delayed, leading to the embryos thawing prematurely and thus not surviving.

### **Starting a cycle**

Please telephone the clinic before 10 am on day 1 of your cycle. Day 1 is the first day of your cycle that you wake up with your period. For instance, if your period starts in the afternoon, the next day is 'day 1'. If your period starts at the weekend, wait until Monday for ringing. It is very useful to have a record of your six previous 'day 1' dates when you ring for your first cycle of treatment. These period dates can help us to decide when to start blood tests or Clearplan if you are using these methods to detect ovulation.

If you do not have regular menstrual cycles, please telephone the clinic to plan your frozen embryo thaw cycle.

We will review your medical records and previous treatment. The nurse who takes your call will arrange a time for you to call back.

The nurse will tell you when to start drugs if you are having a manufactured cycle. Be sure to write everything down!

### **Blood tests**

We will tell you when you need to have blood tests and where to go for them. Many people come to the clinic early in the morning (the time varies from clinic to clinic, but is usually around 8am to 9am), but tests can be organised at other laboratory collection rooms.

### **Thawing the embryos**

Once the likely time of ovulation has been established or the uterus is ready from drugs you have been given, the embryologists will work out when to thaw your embryos. We will arrange a time with you to ring the clinic to find out whether your embryos have survived freezing and thawing, and the likely time for embryo transfer. Please leave a contact number with the nurses in case the embryologist doing the thaw wants to ask your advice about how many embryos to thaw. Although you will have specified the maximum number to thaw in your consent form, sometimes fewer embryos survive than anticipated, and it can be useful to reassess your original request.

The time for embryo transfer can be confirmed when you ring the clinic to find out whether the embryos have survived thawing.

### **Embryo transfer and after**

Embryo transfer after thawing embryos is just the same as after IVF with fresh embryos – see the instructions in the IVF section on embryo transfer, pregnancy test, and review.

If you have had a manufactured cycle, a nurse will talk to you about continuing to take progesterone pessaries or gel until your pregnancy test. Sometimes women have some bleeding before their pregnancy test is due – this does not necessarily mean that you are not going to be pregnant. ***Do not stop using the pessaries or gel until we tell you the results of the pregnancy test! If you are pregnant, you will need to continue taking the pessaries or gel until we tell you it is safe to stop.***

### **Review**

We will provide a written summary of your treatment cycle. Some doctors prefer to do this as a letter to your GP with a copy to you; others prefer to provide you with a written summary at transfer. We strongly encourage you to make an appointment with your doctor to review how things went or to plan pregnancy care. This review is free if you had publicly funded treatment. We can help you make this appointment at the time of embryo transfer.

## SPERM MICROINJECTION (ICSI)

In conventional IVF the eggs are placed in culture medium in a plastic dish. Sperm are isolated from semen, and about 100,000 sperm are added to each dish. If there are very few sperm or if the sperm do not function normally, the chance of sperm fertilising the eggs in this way is very low.

In sperm microinjection, a single sperm is injected into the middle of a single egg. The technique is often called Intra-Cytoplasmic-Sperm-Injection (ICSI).

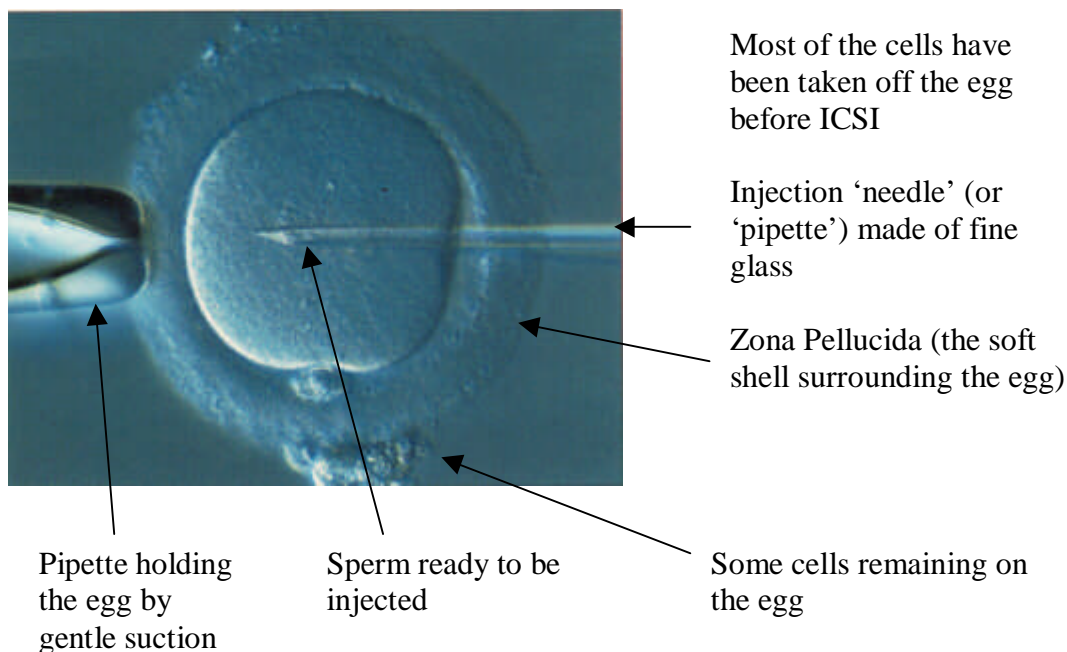
### About ICSI

Normal fertilisation involves a complex sequence of events, initially controlled by the sperm. ICSI bypasses the work the sperm otherwise has to do during fertilisation. During the ICSI procedure, the embryologist breaks the egg's membrane to trick the egg into thinking it has been fertilised in the normal way, and breaks the sperm's tail before injection to allow signalling chemicals to escape from the sperm into the egg.

ICSI can work because in most men the genetic make-up of most sperm is normal even though the sperm might be abnormally shaped, unable to move very well, or unable to undertake the steps of normal fertilisation.

Sometimes when many eggs are obtained and the sperm quality is moderate, there may be a place for performing ICSI on some eggs and conventional IVF on the rest. If reasonable fertilisation occurs with normal IVF, then ICSI would not have to be used in a future cycle. This strategy maximises the information gained while giving a good chance of having embryos to transfer.

**Figure 5. Sperm injection in ICSI**



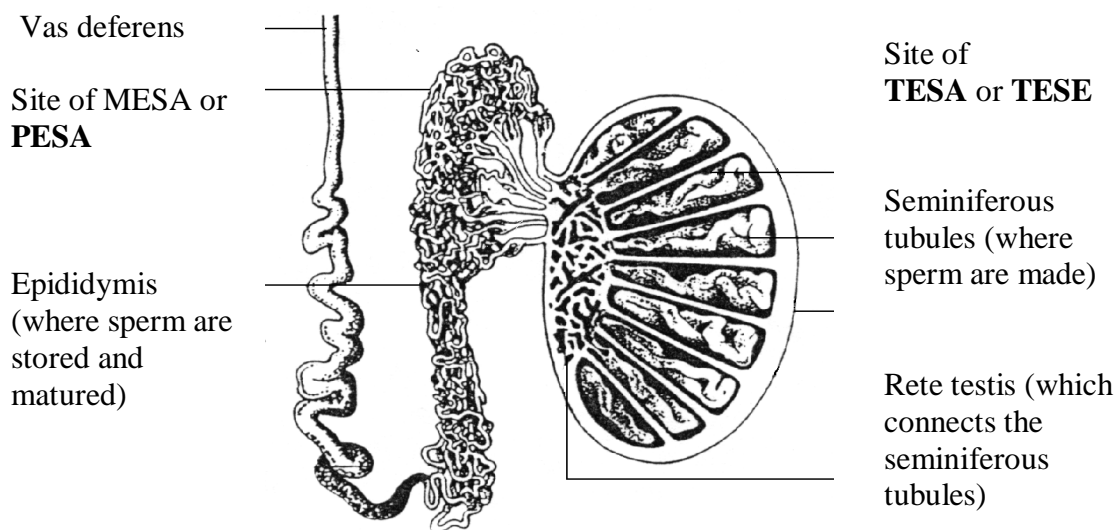
### Getting sperm from the testis

Sperm are produced in the seminiferous tubules in the testes and then pass into the epididymis (see Figure 5). If a man has a blockage in the outflow tract – from infection, vasectomy or even congenital absence of the vas, this is called **‘obstructive azoospermia’**. It is nearly always possible to retrieve sperm from the testis or epididymis from these men.

Other men have sperm production in the testis but the number produced is too few for them to appear in the semen; this is called **‘non-obstructive’ azoospermia**. With non-obstructive azoospermia, sperm can be retrieved for ICSI in only 50% of men, but it can be very hard to predict who they will be. Occasionally there may be few sperm in the ejaculate sometimes but not at other times.

Usually the two types of azoospermia can be distinguished by physical examination and a blood test for the hormone FSH. Occasionally a testicular biopsy can help make a diagnosis. Because a testicular biopsy is not without risk (see the next section), whether to have a biopsy or not needs careful discussion with your doctor. Even when a trial testicular biopsy produces no sperm, sperm can be found in 50% of these men when they try ICSI treatment. This is because many of these men make sperm in small areas of the testis, and it is a matter of luck whether tissue is taken from one of these areas at the biopsy.

**Figure 6. The testis and epididymis, and ways of retrieving sperm**



Sperm for ICSI can be taken directly from the testis in a variety of ways.

**MESA** (Micro-epididymal sperm aspiration) refers to an operation under general anaesthesia in which the surgeon takes fluid from the epididymis with the help of an operating microscope. The operation is expensive, so it is usually only done at the time of vasectomy reversal (or a similar operation). Sperm from MESA is frozen for later use.

**PESA** (Percutaneous epididymal sperm aspiration) refers to passing a fine needle through the skin into the epididymis.

**TESA** (Testicular sperm aspiration) refers to passing a fine needle into the testes, to take a small sample of tissue.

**TESE** (Testicular sperm extraction) refers to taking a larger amount of tissue from the testis through a cut in the skin.

Local anaesthetic usually gives sufficient pain relief for PESA, TESA and TESE procedures.

PESA, TESA and TESE are usually done before the start of an IVF cycle. If sperm are found, they can be frozen and then thawed later for use on the day of egg collection. If we are not sure whether any sperm will survive freezing and thawing, we can thaw one straw from the sample to check it one or two days after sperm retrieval and freezing.

### **Risks and benefits of ICSI**

The benefit of ICSI is increasing the chance of fertilisation when there is a sperm problem or if there has been unexplained low fertilisation in a previous IVF cycle.

The chance of miscarriage may be slightly higher with male infertility. The rate of congenital abnormality in children conceived by ICSI seems to be similar to that for IVF. The chance of pregnancy and miscarriage does not seem to be affected by the number or appearance of the man's sperm.

For many men with non-obstructive azoospermia or severe oligospermia, the cause of infertility may be genetic. If the defective gene is on the Y chromosome, it is very likely that male children will inherit the same type of infertility. There is already evidence for this. Many men who have azoospermia due to a congenital bilateral absence of the vas deferens (CBAVD) carry the gene for cystic fibrosis. Because of this, we screen both partners for cystic fibrosis when the man could have CBAVD. The screening tests used in New Zealand detect 91% of the gene mutations for cystic fibrosis, so a negative test does not totally rule out a person carrying cystic fibrosis.

Children from ICSI have a slightly higher chance of having an abnormal number of X and Y chromosomes - 0.6% instead of 0.2% in the general population. They also have a slightly higher risk of having abnormalities in the number of other chromosomes – 0.4% instead of 0.07%. Some of these abnormalities seem to have little or no effect, while others can be associated with infertility and/or some degree of mental retardation. They can be detected by prenatal tests using Chorionic Villus Sampling (CVS) or amniocentesis between 11-17 weeks of pregnancy.

Up to 15% of men with zero or very low sperm counts have small pieces of the Y chromosome missing. This loss of genetic material (called a 'deletion') usually leads to poor sperm production. As expected, boys conceived of fathers who have a Y deletion inherit the Y deletion themselves, and most will be infertile when they grow up.

Analysis of the man's chromosomes (called a 'karyotype') is advised unless the male infertility is due to an obstruction. A blood test to screen for Y deletions is available, and tests for other genetic causes of male infertility will probably be developed in the next few years.

If you want to explore the implications of possible genetic abnormalities, we can refer you to the local regional genetics service.

### **Side effects and risks of PESA, TESA and TESE**

Nausea and loss of memory of the procedure are common side effects if sedative and narcotic drugs are used during epididymal or testicular biopsy for PESA, TESA, or TESE.

*If analgesic drugs are used during biopsy they will affect your ability to drive safely, so you need to arrange transport. You can not drive or use machinery during the next 24 hours, and we advise that someone remains with you for six hours after the procedure.*

If drugs are used for testicular biopsy, they can reduce the amount of air you breathe and thus the oxygen in your blood. If your oxygen saturation falls too low the doctor will stop the procedure and give oxygen. Very rarely you may require emergency drugs. Brain damage and death are theoretically possible, but so rare that no figures are available.

Bleeding and infection are possible complications of PESA, TESA and TESE, although they are rare. It is not uncommon to feel discomfort for several days, especially if MESA or TESE has been performed, and good scrotal support and Panadol is advised. *If pain persists or recurs two or three days later, contact the clinic.*

TESA and TESE are likely to cause inflammation in the testis that could reduce future sperm production. They can also damage blood vessels. Up to 80% of men having TESE will have inflammation or collection of blood (haematoma) at the site of the biopsy. Complete loss of blood supply and atrophy of the testis has been reported after a TESE procedure. Repeated TESE procedures are more likely to be successful if done at least 6 months after the last procedure, pointing to temporary damage to the testis after TESE. Similar damage on a smaller scale may occur after TESA.

### **Practical aspects of ICSI**

The only difference between ICSI and conventional IVF is the handling of sperm and eggs in the laboratory. The embryologists decide which sperm preparation methods to use and whether to consider conventional IVF with some eggs. Many couples find it useful to talk with an embryologist, as well as the doctors, nurses and counsellors, before treatment.

## **BLASTOCYST CULTURE AS AN OPTION**

Blastocyst culture is not new – Fertility Associates' first pregnancies from frozen-thawed embryos came from blastocysts in the late 1980's. However, it was only in the late 1990's that scientists discovered how to grow human embryos well to the blastocyst stage and get good pregnancy rates. The key has been the use of sequential media, in which the composition of the culture media changes as the embryo's nutritional needs change over the 5 or 6 days of culture. The blastocyst is the final stage of embryo development before the embryo hatches and implants in the uterus to give rise to pregnancy.

Blastocyst culture offers the possibility of a higher pregnancy rate mainly due to better embryo selection. Many embryos, whether they arise naturally or after IVF, have chromosomal abnormalities that we cannot easily detect yet. These abnormalities stop the embryo from developing much beyond the 8-cell stage, or day 3 of development after egg collection. With blastocyst culture embryologists can choose embryos on the basis of their ability to develop, rather than their physical appearance at an early stage.

In addition embryos do not normally reach the uterus until about the 5<sup>th</sup> day of development. While embryos will tolerate being in the uterus before day 5, it may be

better to delay embryo transfer to day 5. Blastocysts pregnancy may also be associated with a lower chance of ectopic pregnancy.

### **Possible disadvantages**

Only 30-50% of all embryos continue to develop to blastocysts, and some will be of poor quality with a low chance of pregnancy. Some people will not have any blastocysts to transfer, even though they may have had good-looking embryos on day 2 or 3. Even with the new culture medium, it is likely that embryo development in the laboratory will not be as good as in the body, so that some people will not have blastocysts even though they may have got pregnant if their embryos had been transferred on day 2 or 3.

### **What is the place of blastocyst culture?**

Blastocyst culture may be more suitable for:

- People with a large number of similar-looking embryos on day 2 or 3, so that making a decision on which embryos to transfer is difficult.
- People who have not been successful despite several cycles of IVF in the past. These people may benefit from a different way of selecting the embryos to transfer.
- People who want or need to reduce the chance of multiple pregnancy.
- People who incur high costs either through time off or travelling, and so want to maximise the chance of selecting the best embryos for transfer in a single attempt.
- Women who have a higher chance of ectopic pregnancy.
- Women in their late 30's who have a lower chance of pregnancy because of their age, so that selection of which one or two embryos to transfer is even more important.

Blastocyst culture is less suitable for:

- People with only a few fertilised eggs
- People who have one or two good quality embryos on day 2 or 3, with the rest of much poorer quality.

### **Practical aspects**

You should decide, with your doctor, whether you want blastocyst culture before you start your IVF cycle. Please feel free to discuss options with an embryologist as well as your doctor.

Even if you plan to have blastocyst culture, the number of embryos or their quality may not make it beneficial. The embryos are carefully assessed and graded daily. If one or 2 embryos have a much higher grade on day 2 or 3, it is best to transfer the embryos at that time. For this reason it is important for patients to keep in contact with the embryologists day-to-day while decisions are being made.

Miscarriage rates are probably no different from those of IVF using day 3 transfer.

Culturing embryos to the blastocyst stage before embryo transfer may increase the chance of identical twins. Sometimes there is exchange of blood between identical twins while they are still in the uterus, which increases the risk that one twin will not develop as well as the other, and increases the risk of complications during pregnancy.

### **Cost**

There is a separate fee for blastocyst culture to cover the additional costs of equipment, the special culture media for growing the embryos, and staff time.

### **Decision-making, emotional impact and support**

Making the decision to choose to try blastocyst culture may not be easy.

It is important to remember that up to 70% of all embryos do not continue to develop to blastocyst stage, so that some people will have no embryos to transfer at all. Some people may find knowing the 'fate' of their embryos before transfer spares them an agonizing two weeks while waiting to discover whether or not they are pregnant. However, after all the effort, energy, hope and expectation invested in an IVF cycle, having no embryos for transfer is indeed a very disappointing outcome.

Blastocyst culture requires people to be more flexible about what may happen and when embryo transfer might take place. Waiting for the day-to-day decisions can be more stressful, and not knowing for sure the day of transfer can be disruptive.

The clinic staff are available to help you to make the right decision for you. Our counsellors can help you explore your options and their implications, and assist you with coping strategies to reduce the stresses and strains of IVF with blastocyst culture.

## **ASSISTED HATCHING AS AN OPTION**

As described in an earlier section, the embryo 'hatches' from its soft shell (the Zona Pellucida) before it implants into the uterus and gives rise to a pregnancy. There is some evidence that a side-effect of growing embryos in culture is hardening of the zona, so embryos are less likely to hatch. Assisted hatching is the name given to a variety of techniques designed to help the embryo hatch.

The most common method of making a small hole in the zona, or thinning the zona, uses 'drilling' with acidic solution. The embryos are placed in small droplets under oil on the same microscope that is used for ICSI. The embryo is held by gentle suction on one side, and a fine tube holding a small amount of acidic solution is brought close to the embryo on the other side. The acidic medium that comes out of the tube quickly dissolves a small hole in the zona. Once the hole is made, the tube is withdrawn, and the embryo is washed to remove any traces of acidic medium.

Assisted hatching is usually done on day 3 after egg collection when the cells in the embryo have formed tight cell-to-cell connections. It is thought that embryos are less likely to be damaged if drilling is done at this time.

The usefulness of assisted hatching is still being debated. The risk of damage to the embryos seems small, but the possibility of an increased risk of identical or conjoined twins ('Siamese' twins) can not be ruled out. Assisted hatching may be more helpful in women who are older, have not become pregnant despite several IVF cycles, or who have a raised FSH level. It may also be helpful for frozen-thawed embryos.

There is a separate consent form for assisted hatching, and an additional fee.

## **COPING WITH THE STRESS OF DONOR EGG TREATMENT**

### **Infertility hurts**

The pain of infertility goes deep and the grief can feel overwhelming at times. So it is not unexpected that you might find treatment stressful!

Your hopes and expectations may be running high. Things can go astray at any stage. Your donor may not respond well to the drugs, you may get fewer eggs than you expected,

the fertilisation rate of the eggs may be low. Hormonal drugs can cause bigger changes in your hormone levels than you are used to – you may feel more fragile and more easily stressed than normal. It is acknowledged that infertility disrupts your sex life, and an IVF/Donor egg treatment cycle may further disrupt this.

During a cycle there can be lots of uncertainty. We cannot tell you in advance the exact day when your donor's egg collection will be, however we can usually indicate in which week it will occur. A semen sample will usually be required on a particular day and time at request.

In addition, the travelling to and from the clinic during busy traffic times adds to the strain and stress.

At the end of it all you may not be pregnant. We try to minimise the stress that the donor egg cycle places on you, and there are also things you can do.

### **Things you can do**

- Talk to our counsellors and nurses for information and support.
- Try to find a few friends or family members with whom you can share your feelings and experiences.
- Consider postponing or cancelling other things that are stressful.
- Try to have some pleasant activities or treats to look forward to, so you can enjoy life outside the treatment cycle commitments.
- Get plenty of rest, because hormone levels from the drugs can make you tired. Stress is also tiring.
- Agree with your partner to make allowances for each other. Talk to each other about your feelings and anxieties.
- Keep a calendar with blood test dates to help plan and manage your time.
- Write down the day-to-day instructions the clinic gives so you do not worry whether you remember what was said correctly.
- Be prepared to take some days off. After embryo transfer some women feel psychologically in need of a day or two off work.
- Do not underestimate how long and hard it can be waiting between embryo transfer and the pregnancy test.

### **Hints for men**

- It is acknowledged that much of the treatment is centred on the woman. It does not mean you need to hide your feelings or that you are redundant in the process of creating a child.
- Men often have just as intense feelings as women about infertility, treatment, and its issues. However, it is common to deal with these feelings differently. You may react to a crisis by doing something (e.g. play sport, keep busy, etc) rather than focus on the crisis. Many men feel they have to remain stoical and in control to support their partner.
- Talking to someone may be helpful. This may be another man, a counsellor, a support group, or a good mate.

- If you are feeling anxious, or become concerned about your partner, do not forget we are here; you are welcome to give us a call.

### **Not being pregnant**

The biggest hurdle for most people is the news that they are not pregnant. Despite everybody's best efforts, this is the outcome for the majority of people. It may take longer than you think to start feeling better. Remember the clinic counsellors are available to you through this time.

### **Being pregnant**

The welcome news of pregnancy often brings a new set of anxieties. We strongly encourage you to use the clinic for early pregnancy monitoring and emotional support.

### **Support after treatment**

The review appointment can be a time where you can check with your doctor where to go from here. It may mean doing nothing for some time; it may mean deciding on when to start the next cycle.

## **SELF HELP RESOURCES**

### **Consumer societies**

Fertility NZ (formerly called the NZ Infertility Society) has branches in Auckland, Hamilton, Wellington, and Christchurch, and support groups in Waikato, Tauranga, Rotorua, Gisborne, Hawkes Bay, Wairarapa, and Otago. The society publishes a quarterly magazine 'Pathways', has a lending library, provides fact sheets, has an 0800 helpline, and is a strong advocate for better provision of fertility services, including public funding. The local branches and support groups also offer information evenings and contact groups. The clinics have the society's brochures and fact sheets. For more information, telephone the Fertility NZ **helpline 0800 333 306**, or visit the **website [www.fertilitynz.org.nz](http://www.fertilitynz.org.nz)**.

The NZ Donor Conception Network is a group affiliated with fertilityNZ which provides members with the opportunity to network and share experiences through contact groups, an internet chat room and social gatherings. It also provides a library, videos, information evenings and a newsletter, and undertakes lobbying on issues that affect parents and children.

### **Books**

Many books are available from public libraries, and some of the clinics also have libraries from which patients can borrow. The consumer societies also have extensive libraries from which members can borrow.

## GLOSSARY OF TERMS

**Abdominal.** The area of the tummy.

**Amniocentesis.** Procedure where cells are taken from the fluid around the fetus to detect abnormalities, usually between the 15<sup>th</sup> and 17<sup>th</sup> weeks of pregnancy.

**Analgesic.** Pain killer.

**Azoospermia.** No sperm in the semen.

**Biochemical pregnancy.** A pregnancy that ends at a very early stage.

**Blastocyst.** An embryo 5-6 days after fertilisation, consisting of an outer layer of cells that will become the placenta, and an inner mass of cells that will become the fetus.

**Catheter.** A fine plastic tube used to put sperm or embryos into the uterus through the cervix.

**Cervix.** The lower narrow end of the uterus that connects the uterine cavity to the vagina.

**Chromosomes.** Structures in the nucleus of the cell that carry genetic information.

**Clearplan.** Ovulation detection kit using plastic dip sticks that show changes in the levels of luteinising hormone (LH) in the urine.

**Clinical pregnancy.** A pregnancy that can be detected by ultrasound scanning of the uterus.

**Cryoprotectant.** Special antifreeze solution to enable sperm or embryos to survive freezing.

**Culture medium.** An artificial solution that provides nutrients to sperm, eggs and embryos.

**Chorionic Villus Sampling (CVS).** A procedure where cells are taken from the placenta around 11 weeks of pregnancy to test for abnormalities in the fetus.

**Day 1.** First day of the period. Start of the menstrual cycle.

**Ectopic.** Pregnancy in a place other than the uterus, usually the Fallopian tube.

**Ejaculate.** The semen produced during sex or masturbation.

**Embryologist.** Laboratory staff who look after sperm, eggs and embryos in an IVF programme.

**Endometriosis.** A disease where cells from the lining of the uterus grow outside the uterus, usually in the pelvis or around the ovaries, and causes inflammation and scarring.

**Epididymis.** The twisted tube on the side of the testis through which sperm travel after leaving the testis.

**Estradiol.** The most common type of estrogen hormone produced by the cells of the ovarian follicles.

**Estrogen.** A type of hormone made by the ovaries that stimulates the growth of the lining of the uterus.

**Fallopian tubes.** A pair of tubes attached to each side of the uterus through which the egg travels from the ovary to the uterus. Fertilisation usually occurs in the Fallopian tube. The Fallopian tube is the most common site of ectopic pregnancy.

**Follicle.** Fluid filled structure in which the egg matures in the ovary.

**Follicle stimulating hormone (FSH).** A hormone released by the pituitary gland that stimulates the growth of follicles in the ovary.

**Follicular fluid.** The fluid inside a follicle.

**Fragmentation.** The cellular debris left in an embryo when the cells do not divide evenly.

**Gamete Intra-Fallopian Transfer (GIFT).** Technique where sperm and eggs are placed into the Fallopian tube.

**Hepatitis B and C.** Viruses that may be sexually transmitted, or transmitted by contact with blood and other bodily fluids, that can cause infection of the liver leading to jaundice and liver failure.

**Human Chorionic Gonadotrophin (hCG).** A hormone made by the placenta that is similar to the hormone LH.

**Human Immunodeficiency virus (HIV).** A retrovirus that causes immune deficiency syndrome (AIDS), a disease that destroys the body's ability to protect itself from infection and disease. It is transmitted by the exchange of bodily fluids or blood transfusions.

similar to the hormone LH.

**Insemination.** Placing sperm into the cervix or uterus, or in IVF placing sperm with the eggs in the laboratory.

**Intracytoplasmic sperm injection (ICSI).** A technique that involves injecting a single sperm directly into each mature egg during the IVF procedure to maximise the chance of fertilisation. It involves using fine manipulators and a powerful microscope to see and handle the sperm and eggs.

**In vitro fertilisation (IVF).** A technique that involves combining an egg with sperm in a laboratory dish or tube. If the egg fertilises and begins cell division, the resulting embryo is transferred into the woman's uterus where it will hopefully implant and give rise to pregnancy. IVF is usually combined with drugs that stimulate the ovaries to produce several eggs in order to increase the chance of having at least two good quality embryos to transfer.

**Karyotype.** A test looking at the number and appearance of chromosomes from cells.

**Luteinising hormone (LH).** Hormone released by the pituitary gland that triggers ovulation. Once the LH surge has started, ovulation usually takes place within 12 to 36 hours.

**Neo-natal.** The first few weeks of a baby's life.

**Ovarian Hyperstimulation Syndrome (OHSS).** A disease that can follow from too many follicles being stimulated to grow at once in the ovaries. Fluid moves from the blood into the abdomen and into tissue. Untreated, it can have serious consequences, including stroke and even death.

**Ovarian stimulation.** Stimulating the ovary to produce more than one mature egg in a menstrual cycle by giving fertility drugs.

**Ovulation.** The release of a mature egg from its developing follicle in the ovary. This usually occurs about 14 days before the next menstrual period (ie. around the 14<sup>th</sup> day of a 28-day cycle).

**Pelvic.** The lower part of the abdomen, or tummy.

**Pessaries.** Drugs given in the vagina.

**Pituitary gland.** A gland in the brain releasing FSH and LH.

**Polycystic Ovarian Disease/Syndrome (PCO).** A condition where follicles do not grow past a certain size in the ovary, so ovulation often does not occur.

**Progesterone.** A type of hormone made by the ovary, in the second half of the menstrual cycle.

**Puregon.** Trade name for follicle stimulating hormone (FSH) drug.

**Recipient.** The woman receiving donated eggs.

**Semen.** Fluid that constitutes the ejaculate.

**Seminiferous tubules.** Fine tubes packed in the testis, in which sperm are made.

**Seminal fluid.** The liquid part of the semen, in which the sperm swim around.

**Semen analysis.** The microscopic examination of semen to determine the number of sperm (sperm count), their shapes (morphology), and their ability to move (motility).

**Speculum.** A plastic or metal device, shaped rather like a 'duck's bill', which allows the cervix to be seen.

**Sperm.** The cells (spermatozoa) in the semen.

**Sperm washing.** A procedure to remove seminal fluid from sperm cells before intrauterine insemination or other assisted reproductive technologies.

**TER.** Thawed Embryo Replacement cycle.

**Trigger.** Induction of ovulation with hCG.

**Uterus.** Another name for the womb.

**Vagina.** The canal in the female that leads to the cervix, which leads to the uterus.

**Zona, zona pellucida.** The clear, soft shell surrounding the egg.

## GLOSSARY OF MEDICATIONS

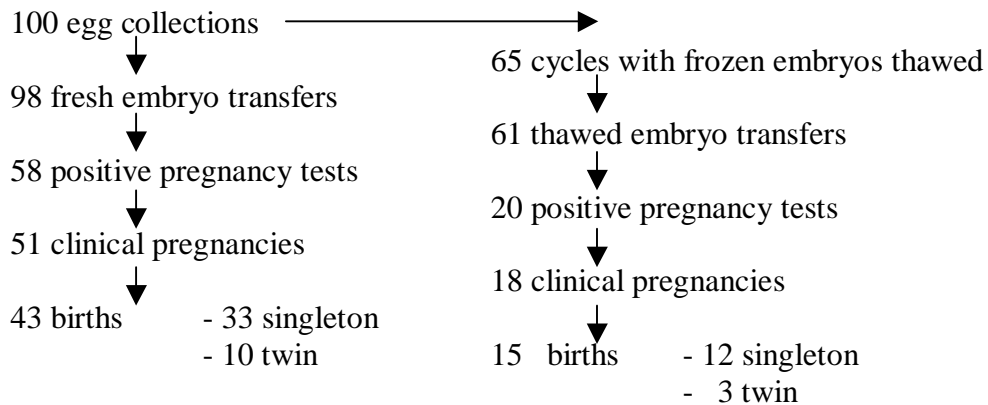
MEDICATION	ADVERSE EFFECTS
<b>BUSERELIN</b> – <i>see GnRH-agonist</i>	Hot flushes, mood swings, dry vagina after prolonged use.
<b>CETROTIDE</b> – <i>see GnRH-antagonist</i>	Nausea, headaches. Local irritation at the injection site.
<b>CRINONE</b> A gel containing progesterone that is inserted into the vagina. Crinone helps to maintain the lining of the uterus in readiness for a potential pregnancy.	Abdominal cramps, headaches, breast enlargement, constipation, nausea.
<b>ELEVIT</b> A multivitamin tablet that contains 0.8mg of folic acid and is safe to use during pregnancy.	Skin rash, constipation, diarrhoea, heartburn.
<b>FOLIC ACID</b> A vitamin taken prior to and during the first 12 weeks of pregnancy that may help prevent Spina Bifida.	Nausea, flatulence, diarrhoea
<b>FSH</b> – <i>see Gonadotrophin</i>	
<b>GESTONE</b> An intramuscular injection containing progesterone. Gestone helps to maintain the lining of the uterus in readiness for a potential pregnancy.	Breakthrough bleeding, change in menstrual flow, amenorrhoea, changes in cervical erosion and secretions, breast changes, oedema, weight gain, acne, mental depression, pyrexia, insomnia, nausea. Local irritation at the injection site.
<b>GONADOTROPHIN</b> An injectable drug used in ART to stimulate the development of ovarian follicles.	Mood swings, abdominal distension. Local irritation at the injection site. Stinging sensation at the time of injection.
<b>GONAL F</b> – <i>see Gonadotrophin</i>	
<b>GnRH-agonist</b> A drug used to suppress the body's production of hormones FSH and LH during ART treatment. May also be used in the treatment of uterine fibroids and endometriosis.	Reversible menopausal-like symptoms including tiredness, headaches and hot flushes.
<b>GnRH-antagonist</b> A drug used to suppress spontaneous ovulation during ART treatment.	Local irritation at the injection site.

<b>MEDICATION</b>	<b>ADVERSE EFFECTS</b>
<b>hCG (HUMAN CHORIONIC GONADOTROPHIN)</b> An injection used to trigger the final maturation of eggs prior to ovulation or egg collection.	Possibility of increased abdominal distension. Local irritation at the injection site. Stinging sensation at the time of injection.
<b>LEUPROLIDE</b> – <i>see GnRH-agonist</i>	
<b>LUCRIN</b> – <i>see GnRH-agonist</i>	
<b>LUPRON</b> – <i>see GnRH-agonist</i>	
<b>MICROGYNON</b> – <i>see Oral contraceptive pill</i>	
<b>NORETHISTERONE (PRIMOLUT)</b> – <i>see Progesterone tablet</i>	
<b>ORAL CONTRACEPTIVE PILL (OCP)</b> A drug that is usually used to prevent pregnancy but can also be used in ART to help time the start of a treatment cycle. May also reduce the development of small ovarian cysts, which can delay the start of ovarian stimulation.	Irregular bleeding, nausea, headache, blurring of vision, breast discomfort, leakage of breast milk, depression, leg pain, glucose intolerance, fluid retention, oedema, intolerance to contact lenses, changes in appetite.
<b>OVIDREL</b> – <i>see hCG</i>	
<b>PREGNYL</b> – <i>see hCG</i>	
<b>PROFASI</b> – <i>see hCG</i>	
<b>PROGESTERONE TABLET</b> Used in ART to induce a withdrawal bleed in women who do not menstruate.	Nervousness, insomnia, fatigue, depression, dizziness and headache. pruritus, irregular uterine bleeding, spotting, and amenorrhoea, nausea, breast tenderness, change in weight,
<b>PROGYNOVA (ESTRADIOL VALERATE)</b> An estrogen tablet that thickens the lining of the uterus, usually in preparation for embryo transfer.	Headaches, irregular bleeding, nausea, breast tenderness and discomfort, leg pain, visual disturbance.
<b>PROVERA</b> – <i>see Progesterone tablet</i>	
<b>PUREGON</b> – <i>see Gonadotrophin</i>	
<b>SUPREFACT</b> – <i>see GnRH-agonist</i>	
<b>SYNAREL</b> – <i>see GnRH-agonist</i>	
<b>UTROGESTAN</b> Pessaries containing progesterone that are inserted into the vagina. Utrogestan helps to maintain the lining of the uterus in readiness for a potential pregnancy.	Possible local irritation or an allergic reaction (rarely).
<b>ZOLADEX</b> – <i>see GnRH-agonist</i>	

## STATISTICS FOR DONOR EGG

These figures combine donor egg cycles from all Fertility Associates clinics for 2002-2004. The total number of donor egg cycles in this period was 136. Most of the egg donors were 37 years or younger.

### Overview where the egg donor was 37 years or younger



### Pregnancy rate by age of recipient

Over this period, birth rates were 44% for women 41 and younger, and 33% for women 42 and older.

### What is the chance of pregnancy with SET?

Widespread use of SET has only since mid-2004, so we do not have experience in egg donation. However, preliminary information from IVF and ICSI from people using their own eggs can act as reasonable guide.

The table below presents actual pregnancy rates and estimated birth rates (in italics), both from transfer of the single fresh embryo, and the transfer of one thawed embryo if there was no pregnancy from the fresh transfer. For egg donation, 'woman's age' applies to the age of the donor.

**Table Pregnancy rates per embryo transfer using SET**

Woman's age	From use of the single fresh embryo			Fresh plus thawed embryo if needed
	Positive pregnancy test	Pregnancy visible on ultrasound	Estimated birth rate	Estimated cumulative birth rate
35 or younger	56%	45%	<i>30%</i>	<i>44%</i>
36 - 39	39%	33%	<i>22%</i>	<i>35%</i>

The estimated live birth rate of 44% using a single fresh embryo and the use of one frozen embryo if there was no pregnancy from the fresh embryo is very similar to the 43 births per 100 egg collections in the flow diagram above.