

## Patient Overview: In Vitro Fertilisation

### Overview

IVF stands for in-vitro fertilisation i.e. literally fertilisation in a glass dish. You may also hear the term ART used which stands for Assisted Reproductive Technologies. IVF is a subset of ART and the two are often seen to be synonymous although this is not necessarily true. There are many other forms of assisted reproduction that Monash IVF and Gynaecologists use not all of which are IVF.

### Why Perform IVF?

The world's first IVF pregnancy and birth was achieved in the UK in 1980. The girl born, Louise Brown, has recently had a baby herself. IVF was initially developed as a treatment for blocked fallopian tubes. However its use has been generalised to various other situations, as technology and treatments have improved. Other indications for IVF may include severe male factor infertility (low or absent sperm count), endometriosis, abnormal or infrequent ovulation, early ovarian failure or poor ovarian reserve in which case sometimes donor eggs are required and commonly, unexplained infertility. Often several of these factors exist at the same time and the decision to proceed towards IVF reflects a sum total of my assessment of your potential fertility, combined with your desire and time course over which you would like to conceive a child.

IVF has become exceptionally common as it has become more successful and, in Australia, we are lucky that many IVF cycles are still subsidised by Medicare, although this is not the case in all countries. In Australia we also have some of the world's best success rates and this, combined with relatively modest cost and government rebates, means that IVF is a very attractive option for many couples. As success rates continue to improve it is easy to see that cycle numbers will increase and the reason for using IVF will extend.

IVF has a high success rate but statistically has some potential disadvantages. No medical treatment, or indeed most things in life, are completely risk free and the risk that we commonly talk about with IVF reflects those of over stimulating the ovaries, ovarian cysts, small chances of multiple pregnancies and possible increase inside pregnancy complications such as premature birth, small for gestational age babies, ectopic pregnancies or a small increase in birth defects. The term birth defects is used very generically and can reflect all from the most trivial to more severe problems. However, in my experience I have never known a couple to be dissuaded from using IVF because of the small chance of these problems occurring.

## Overview of In Vitro Fertilisation

Undertaking IVF treatment through Monash IVF consists of several steps. At the time of first consultation I will take a detailed history and examine you to try to determine a cause for your particular problems. After performing assessment of both partners, we will then meet again and I will summarise the results and assess your wishes and requirements in order to decide how to proceed. Assuming you proceed to IVF, this must be preceded by a compulsory counselling session with one of the counsellors at Monash IVF. You must register with Monash IVF and before this can be done, you must also undertake, according to new legislation, a Police Record check and Child Protection Order check, on both partners. Please note that this is different from a Working With Children check, which many patients now have acquired due to their work. The police record and child protection order checks need to be sent in with the registration form at the outset.

Basically, then, the steps in IVF consist of counselling, stimulation of the ovaries to produce several eggs, treating the eggs, fertilizing the eggs with sperm, growth of the embryos in the laboratory for something like two to six days and transfer of one or two embryos at a time into the uterus. The average lag time from sign up to commencing treatment is around four to six weeks. It is important to realize that pregnancy rates for the first stimulation cycle vary widely and according to the circumstances. However it probably goes without saying that an IVF cycle gives you a greatly increased chance of pregnancy compared to no treatment at all and most other forms of fertility treatment. Generally speaking a normal cycle has around 25% per month chance of falling pregnant. This is very low when you consider that rabbits and other animals may have as high as 80% chance. The average IVF cycle through Monash IVF will have around a 40% pregnancy rate per cycle however this will be less in some couples and greater in others.

## Ovarian Stimulation

Ordinarily every month a woman's ovaries aim to produce one egg which is extruded from the surface of the ovary (ovulation) in the middle of the month. In IVF, to increase our chances, we choose to stimulate the ovaries more than occurs in the natural state producing many more eggs which are then fertilised.

This is generally preceded by a period of so called down-regulation. There are various drugs that may achieve this but one of the most common and effective means of doing this is to simply commence the oral contraceptive pill. I must admit this does sound queer when one is trying to conceive however the function of the oral contraceptive pill is to give the ovaries a rest and switch off all of the developing follicles so that they may then all develop in synchrony during the IVF cycle. It is usually necessary to be on the contraceptive pill for around two weeks before commencing stimulation.

The second stage then consists of receiving injections of medications classed as GnRH agonists or nasal sprays, which will further prevent the body from prematurely releasing hormones that would stimulate the ovaries to cause premature ovulation. This is usually started at approximately one week after starting the oral contraceptive pill. So called down regulation is confirmed by blood test and ultrasound. Following down regulation, you will commence injections of synthetically made follicle stimulating hormone (FSH) generally in the evening. The dose range of FSH varies widely according to the ones that we estimate that you will get from your ovaries. After a few days of injections you will have further blood tests and ultrasounds to measure follicle growth, ultrasounds and blood tests may be repeated several times within the cycle.

The goal of stimulation is to have several follicles that are approximately 15-18mm in size. After around five to ten days of FSH when we have estimated the follicles are ready you will be instructed to give yourself an injection of HCG to trigger ovulation. HCG stands for human chorionic gonadotropin and there are various brand names including, Ovidrel, Pregnyl. HCG's are generally injected under the skin at a particular time in the evening, which prepares the follicles for egg pick up, generally scheduled for around thirty six hours later.

## Potential Problems with Treatment

The FSH injections don't cause side effects themselves however the sometimes large number of follicles developing on the ovaries may. Ovarian hyper stimulation syndrome (OHSS) may occur in around 1-2% of patients and is sometimes unpredictable. Sometimes we can anticipate this developing by a rapid rise in blood hormone levels and an IVF cycle may be cancelled.

The opposite is poor ovarian response or under stimulation. Sometimes and unpredictably an IVF cycle may need to be cancelled when it is anticipated that the response will be too poor in order to obtain a meaningful number of eggs. We always hope that you get a maximum value out of a cycle for your cost, time and inconvenience expended and if we anticipate a poor result from a cycle then cancellation will give us a chance to regroup and perhaps change the protocol for your next cycle in order to achieve a better result.

## Egg Retrieval: VPU (Vaginal Pick Up)

This is scheduled for around 36 hours after your HCG triggering injection. Both male and female partners will attend one of the Monash IVF facilities. The female partner undergoes VPU under a light sleeping anaesthetic or sedation. Whilst you are asleep we will perform a trans-vaginal ultrasound where it will be readily apparent where the ovaries and follicles are. There has generally been some growth of follicles, since your most recent ultrasound several days prior. A very fine needle is inserted, under ultrasound guidance beside an ultrasound probe and used to suck out the fluid contents of each follicle in each of which there should be at least one egg although this can vary. The VPU procedure takes around 10 – 15 minutes. It is common to experience minor lower abdominal cramping, or vaginal spot bleeding after a pick up procedure. After the procedure you will be monitored in the recovery area for a few hours and then allowed to go home. On the day of the VPU, the male partner will also be required to produce a further semen specimen. This is then re-examined by the embryo scientist in our laboratory, and fertilisation of the oocytes undertaken. You will be instructed to call the lab the following day where it will give you an idea of the success rates of fertilisation. Occasionally, even though we previously considered a semen analysis to be adequate, rather than allowing the semen to spontaneously fertilise an egg we will recommend ICSI (intracytoplasmic sperm injection) where a single sperm is injected into an oocyte in order to achieve fertilisation. We may expect around 50% of the eggs harvested to fertilise.

## Embryo Growth in Culture

There is a lot of science and also art involved in growing embryos in culture. Fortunately, in Monash IVF we have some of the best embryo scientists in Australia and probably the world. The embryos are observed and have a qualitative grading system where each embryo is assigned a number and an estimate made of the embryo's potential to lead to a pregnancy. The embryos are grown in culture usually from anything between two and seven days. Later embryos, called blastocysts, have higher pregnancy rate after transfer. However not all embryos will be suitable for allowing us to progress to blastocyst stage in culture and will be transferred earlier.

Therefore after around two to five days after retrieval one or two eggs are transferred back into the uterus. This is quite a simple procedure, not unlike having a Pap smear, and is done under ultrasound guidance. A plastic speculum is inserted and a very fine plastic tube passed through the cervix into the bottom part of the uterus, and you will be able to see the embryo being injected into the uterus in a bubble of fluid. This is a very exciting time, and after the transfer many women actually feel that they are pregnant however actual confirmation of pregnancy will require subsequent blood testing.

Subsequent to the transfer, it is usual to support the pregnancy with progesterone gel, (Crinone) for a couple of weeks.

## How many Embryos are Transferred?

Monash IVF is committed to having one healthy pregnancy per IVF transfer cycle however for subjects over 40 years of age sometimes a double embryo transfer is performed. Again we are aiming for one successful pregnancy at a time however allowing for an attrition rate with transferred embryos, obviously transferring two embryos has a high chance of ending up with one child reaching term. It is also important to remember however that after transfer of two embryos, occasionally triplets may result due to splitting of an embryo. This is however very uncommon. We will need to have a detailed discussion regarding the number of embryos transferred prior to proceeding with your treatment. In Australia, it is illegal to transfer more than two embryos at a time.

## Storing Unused Embryos

Embryos that are not transferred are commonly frozen. This is called cryopreservation and again in Monash IVF we have amongst the best cryopreservation techniques in the world. Embryos may be stored in this way indefinitely. If they are successfully thawed, frozen

embryos have just as high success rates for resulting in a pregnancy than fresh embryos. However not all embryos survive the thawing process.

After successfully completing your family, if you have frozen embryos in storage, Monash IVF has detailed printed guidelines for you to decide what to do with the embryos. Options include disposal, donation to another couple, donation to medical research, or ongoing storage for a fee.

### What Happens after the Embryo Transfer?

After the transfer blood testing will be performed on you in order to determine whether a pregnancy has occurred. Unfortunately home urinary pregnancy testing is not sensitive enough. If the first blood test or HCG level is  $<5$  it is safe to say that you are not pregnant. If the first HCG level is  $>10$  then we are confident that a pregnancy has occurred. This is often correlated with blood progesterone levels. The blood tests are generally then repeated 48 hours later and we expect the HCG level to double around every 48 hours during the first few weeks after embryo transfer. After a few weeks, if HCG levels increase as expected, an ultrasound will be done in order to check the wellbeing and dates of the embryo.

In skilled hands a foetal heart beat is generally visible after five to six weeks of gestation which correlates with three to four weeks after embryo transfer. At that stage it would be time to start thinking about your ongoing pregnancy care.

### What if my First Cycle is not Successful?

If, unfortunately you do not achieve a pregnancy after your IVF cycle then we will meet again in order to discuss your IVF cycle, and your future course of treatment. In some cases this will involve a complete change to your protocol, and in some cases further investigation may be needed. If you have frozen embryos at your disposal after your first cycle then it is usually a simple matter to arrange a natural cycle frozen embryo transfer.

I always find starting up a patient on her first IVF stimulation cycle very exciting, and naturally our hopes run high for a successful pregnancy after her first cycle. However we have to remember that there is a significant chance that you won't achieve a pregnancy after your first cycle and first embryo transfer. Indeed it may take two or three cycles to do so. There are many emotional ups and downs with IVF treatment and the first cycle is always the most stressful. However I am always happy to talk to you about your requirements, your experiences and don't forget that your patient co coordinator is always an invaluable source of support.