

IVF

A Guide for Women and Couples

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www.expertfertility.org

What is IVF?

IVF – *in-vitro* fertilization – is a medical treatment that has been in use for **more than 40 years**. It was first invented to allow pregnancy where a woman's fallopian tubes are blocked. Today, the technology of IVF has been developed to the point where it may be used for many different conditions. IVF is used to treat not only infertility in women, but in men, and in the treatment of genetic (inherited conditions), as well as to preserve fertility in cases of cancer. In Australia, almost 14 000 IVF babies are born every year.

In an IVF treatment, eggs are collected directly from a woman's ovaries. In the IVF laboratory, the eggs are fertilised to become embryos. Embryos either are replaced in the woman's uterus to allow pregnancy, or can be frozen for use in the future.

To achieve these things, a number of scientific techniques have been developed to allow modern IVF treatment to be safe and very effective.

For most women, a single egg develops and is released from the ovary each month. IVF uses the same hormone that women naturally produce – FSH, or 'follicle stimulating hormone' – is given but injected each day in a higher dose that usually occurs naturally. Growth and development of the eggs is checked with regular blood tests and ultrasound test. Safety is paramount in any IVF treatment.



What occurs during an 'IVF cycle'?

A 'cycle' of IVF treatment can mean different things, but in general refers to a complete round of treatment through until either a pregnancy test or, if no embryo is transferred back to the uterus, when one or more embryos are frozen.

In a **stimulated cycle** of IVF, a course of injections of the hormone FSH is given – usually one injection each day – until the eggs have developed to maturity and are ready to collect. The eggs are bound to the inside of the ovarian follicles, so to allow them to be collected a 'triggering injection' is given. This process takes about 36 hours, so typically a triggering injection is given in the evening and the eggs are collected 36 hours later in the morning. The egg collection is technically a simple procedure. An ultrasound is used in the vagina to find the ovaries, and a needle is passed through the vagina into the ovary with gentle suction used to collect the eggs. The eggs are either mixed with, or injected with, sperm to allow fertilization. In modern IVF, the fertilized eggs (embryos) are grown in specialized nutrient fluid until about the fifth day of development. At that point, healthy embryos may either be placed in the uterus (an 'embryo transfer') or may be frozen ('cryopreserved') to be stored and thawed in the future.

The basic IVF cycle allows for many other varied treatments. In some circumstances – cancer, for example – eggs may be frozen for use in the future. Embryos may be tested before being frozen: this might be done to test whether the embryo is affected by a genetic (inherited) disease; or, to determine whether the embryo has the correct number of chromosomes. Donated eggs or sperm sometimes are used. IVF has many variations.

A typical 'stimulated cycle' of IVF

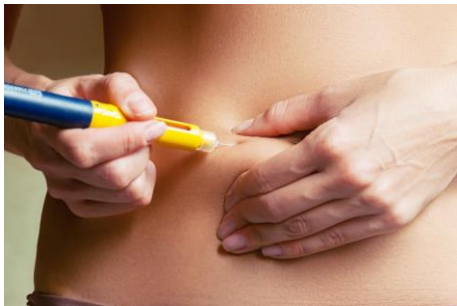
'Day One'

The first day of your period is called 'day one.' On that day, you would come in to the IVF Unit to have a **blood test**. This is to confirm that your hormone levels are at the right level for an IVF treatment to work. Once the blood test results are available and checked, you can begin a daily inject of FSH hormone.



A daily injection

For somewhere between ten and 15 days – this varies according to a woman's response to the treatment – a daily injection of FSH is given. This will stimulate growth and development of follicles in the ovaries. It is within follicles that the eggs grow and mature.



Preventing ovulation

The body will naturally want to release the developing eggs – this is called 'ovulation.' Of a woman ovulates before the eggs can be collected, the eggs usually are lost. To stop this happening, a second daily injection is given once the developing follicles reach a certain stage of development. This second injection is called an 'antagonist.'

Checking your progress



It is important to check how your body is responding to the IVF injections – both an over-response (which can make you ill) and an under-response (where few or no eggs develop) are potential problems. Your response to the injections is assessed by blood tests and ultrasound. These may be required every two or three days during an IVF treatment cycle. Typically, these monitoring tests are done in the morning. They allow fine-tuning of injection doses, and timing of an egg collection.

Preparing for an egg collection

Using the results of the blood and ultrasound tests, a decision will be made about the best time to collect the eggs. The eggs have a firm attachment to the follicle in which they are growing – the process by which the eggs are released into the follicle is called 'ovulation.' To begin this process, a 'trigger' injection is given. **Timing of this injection is critical.** If the egg collection procedure is undertaken **too early**, the eggs may still be immature and not have separated from the follicle thus cannot be collected. If the timing is too late, the eggs may be released from the follicle completely and can't be collected. Optimal timing for the egg collection is usually about 36 hours after the triggering injection.

Collecting and fertilizing the eggs in IVF

The egg collection procedure



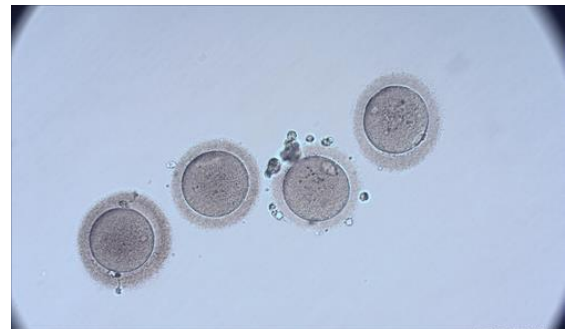
Most egg collection procedures are performed in the **morning**, to allow the laboratory staff time during the day for the fertilisation and other procedures required in IVF.

The egg collection procedure typically does not take very long, usually less than half an hour. Different units have different protocols, but some pain relief is given then an internal ultrasound is used to find the follicles. A needle is passed through the vagina into the ovary, and the fluid within the follicles is carefully suctioned out. The eggs are found in the follicular fluid.

Once the egg collection procedure is finished, it is usually to rest in the recovery area for a while, then provided all is well you can go home and rest for the day.

Taking care of your eggs

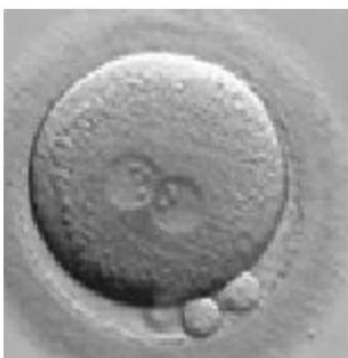
The IVF scientist will carefully assess each of the eggs and select the mature healthy eggs for fertilization. In some cases the eggs and sperm will be mixed together overnight, in other cases individual sperm are selected and injected into the individual eggs – a process known as ‘intracytoplasmic sperm injection,’ or ‘ICSI.’ The choice of method for fertilizing the eggs depends on a number of factors and is very individual.



From eggs to embryos

The fertilized eggs – ‘embryos’ – are nourished and cultured in a highly specialized environment in incubators. Not all embryos will continue to develop, but a number will grow and become ‘blastocyst’ embryos, usually on about day five of development.

Fertilized embryo



Day three embryo



Day five embryo



Transferring the embryo back to the uterus

The aim of IVF is pregnancy, so an embryo will be transferred back to the uterus. This procedure is typically done when the embryo is about five days old – at the ‘blastocyst’ stage of its development.

The embryo transfer procedure typically takes only a few minutes and feels much like a Pap smear. An ultrasound is used to allow accurate placement of the embryo in the uterus. Women usually can return home, or to work, immediately after the procedure with few restrictions.



Storing embryos – ‘Cryopreservation’



Often, more than one embryo will grow and develop. Because the safest policy for women and babies is single embryo transfer (‘SET’), in many cases a number of embryos will develop and be healthy on Day 5.

At this stage, embryos may be suitable for ‘cryopreservation’ – a process in which the embryo is ‘snap frozen.’ Embryos can be stored indefinitely, giving women and couples great flexibility.

Looking after yourself until your pregnancy test

Waiting for a pregnancy test in an IVF cycle can be a time of stress and excitement. It is important to aim to be as healthy as possible. A balanced healthy diet, and regular exercise are important. Managing stress is also a key component of navigating this time.

Many women use mindfulness techniques and meditation, or even treatments such as acupuncture. Getting plenty of sleep, and not spending too much time on stressful work activities, all can help with coping. In some cases, women and their partners will seek counselling. All of these ways of dealing with a challenging week of waiting are healthy.



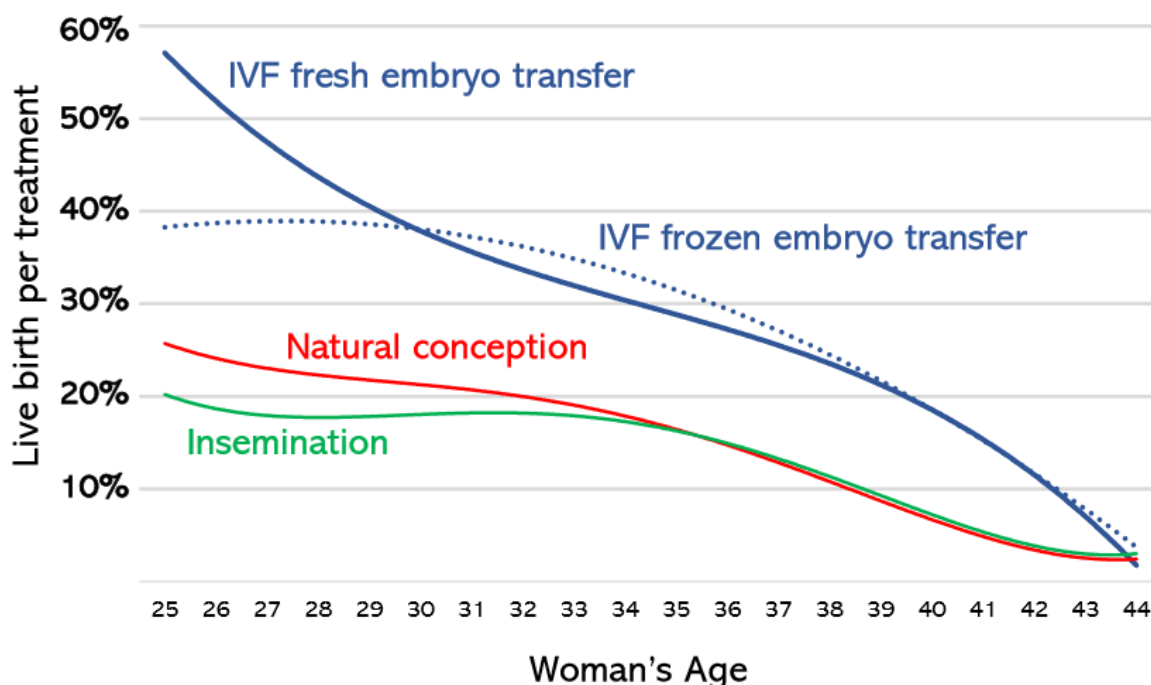
Progesterone in the ‘luteal phase’

Because of the effect of the IVF medications on the endocrine (hormonal) system, in virtually all stimulated IVF treatments additional supplementation of progesterone is given. This is in the form of vaginal pessaries – either ‘micronized’ progesterone or ‘natural’ progesterone. Commonly, blood tests are used to check the level of progesterone and adjust doses.

What are the chances of pregnancy with IVF?

IVF is all about becoming pregnant, so it is important before you make any choices about IVF treatment – or any fertility treatment – to keep in mind the chance that you will take a baby home.

Perhaps the single most important factor that determines the chance of IVF working – the chance of taking a baby home with each treatment – is the age of the woman. The chances are obviously different for different couples, and depend on many factors. Presented below is a graph showing **typical** results according to the age of the woman undergoing IVF treatment, where the embryo that is transferred has not had genetic screening. **These are general results and do not necessarily apply to every women or every couple.**



Graph The 'live birth rate' – the chance of taking a baby home after each treatment – for fertility treatments, compared to the typical live birth rate for natural conception in a healthy couple. In the case of IVF, this is the chance after an embryo is transferred. The IVF figures are separately considered for either a fresh embryo, or a frozen embryo. The comparison in red is with insemination treatment.

Obviously the chances of IVF leading to the birth of a baby are difficult to precisely calculate in every case and for every woman or couple. However, the chances presented here are indicative of the real-world results for woman treated through the IVF unit with which I work.

Before making any decisions about treatment, make sure that you discuss your own individual situation with the doctor providing your fertility care.

If you become pregnant...



A positive pregnancy test in IVF is wonderful news - and also the **beginning** of a journey. Your hormone levels may be monitored through blood tests, and changes may be made to the doses of progesterone. In some cases, further progesterone support is not even needed and can be ceased. An ultrasound test is performed at about seven weeks – usually about a month after the embryo transfer procedure – to check for a heartbeat. Further blood tests and ultrasounds are usually arranged.

... or if pregnancy doesn't happen this time

For many women and couples, the results of an IVF cycle will be disappointing. After all of the emotional build-up, excitement, and stress a negative pregnancy test can be terribly disappointing.

Becoming pregnant through IVF is a journey, and all journeys are a series of individual steps. In some cases, lessons are learned from the IVF treatment cycle. More commonly, everything seems to have gone well – this adds to the disappointment.



Next steps...

The IVF journey will be different for every woman and couple. For some, it will be quick and direct. For others, the journey will be a longer one and be more demanding.

There are two important ways that you can take **control** of the journey...

Stay well-informed. Make sure you understand every step of the journey by talking with your doctor and understanding why you are having any treatments and what the likely outcomes are.

Share in decision-making. Ask about the evidence for any treatment, consider it carefully, and always make decisions that you are comfortable with.

It's normal to have lots of questions ...

Are children conceived by IVF healthy and normal?

This is an important question asked by most people contemplating IVF treatment. This question has been studied many times. Using Australian data, Davies and colleagues (2016) found that for woman aged less than 29 years the chance of birth abnormalities was slightly higher in IVF pregnancies. For women in their early 30s, there was no difference between IVF babies and those naturally conceived. Interestingly, **for women aged 35 and older, the rate of birth abnormalities was lower than nature**. Since most IVF is used in women aged 30 and older, these findings are very reassuring.

What is hyperstimulation?

Ovarian hyperstimulation is a complication of IVF treatment. When this occurs, the ovaries over-respond to the IVF injections and developed a large number of follicles and very high hormone levels. Fortunately, with modern IVF protocols this is an uncommon complication. By not transferring an embryo, and using medications, most women will have only mild symptoms and will recovery quickly.



Should I have my embryos genetically tested?

Over the last few years, advances in genetic testing have allowed accurate testing of the chromosomes in embryos. By taking a biopsy of some of the cells of the embryo on about the fifth day of development, it is possible to determine whether an embryo has a normal number of chromosome pairs. To answer this question is slightly complex – you can download a separate eGuide called [Genetic Testing of Embryos](#) on the website.

Do I need treatments such as IntraLipid?

There are many treatments that are offered to women as ways of trying to increase the chance of pregnancy in IVF. These include infusions of IntraLipid, an 'endometrial scratch,' acupuncture, steroid therapy, and many others. These are called 'adjuvant treatments.' The evidence to support using these treatments in IVF is of varying quality, and can be difficult to interpret. If you are offered any of these treatments as part of an IVF cycle, make sure you ask your doctor what the evidence is that the treatment will benefit you.

In Summary...

IVF treatment has been used for more than 40 years, and over that time the results have improved dramatically and the conditions that IVF can treat have expanded. For all of these reasons, IVF now is a common treatment – more than 70000 IVF cycles are undertaken in Australia every year and about one child in 25 born in Australia is an IVF baby.

Although IVF is a common, safe, and effective treatment, it is important the you understand a number of issues before having IVF treatment. In the first instance, make sure that understand the reasons that IVF is being offered to you and whether there are other, less-complex options that could work. Secondly, be aware that for younger women – those aged 28 years or less – IVF babies are slightly more likely to have birth abnormalities. Always make sure that you are given a clear and realistic estimate of the chances of taking a baby home when you have IVF treatment. ... and always ask questions of your doctor.

About Professor Steve Robson MD PhD



Steve Robson is internationally recognised as one of the world's foremost specialists. In 2019, Steve was the recipient of the American College of Obstetricians and Gynaecologists highest honour - the **Distinguished Service Award**.

Steve undertook his specialist training in Australia, England, and Canada. In his first year of formal training in IVF and reproductive medicine in 1998 he won the **Young Clinician's Prize** of the Fertility Society of Australasia (FSA).

Steve Robson is the immediate past-President of the Royal Australian and New Zealand College of Obstetricians and Gynaecologists (RANZCOG), and is Professor in Obstetrics and Gynaecology at the Australian National University. He holds two doctorates, both a Doctor of Medicine (MD) and PhD, as well as Fellowships of the Australian, British, and American Colleges of Obstetricians and Gynaecologists.

Steve was appointed by the Health Minister to the National Health and Medical Research Council (NHMRC), as well as to the National Endometriosis Advisory Group – part of the National Action Plan for Endometriosis.

Professor Robson is one of the authors of the *Oxford Textbook of Obstetrics and Gynaecology*, and as a researcher is the author of hundreds of research articles, editorials, reviews, and book chapters. His research has been published in the most prestigious international IVF journals – *Fertility and Sterility*, and *Human Reproduction*.

He has published research papers not only on IVF and assisted reproduction, but also on reproductive surgery and endometriosis surgery.

In addition, Professor Robson is Chair of the organising committee for the International FIGO meeting in 2021, and is a member of the internationally ground-breaking *Mackenzie's Mission* project.

