

# IVF and ICSI

## **What are IVF and ICSI?**

IVF is short for in vitro fertilisation and ICSI is short for intracytoplasmic sperm injection. Both are forms of what is typically referred to as 'assisted conception' and involve the fertilisation of an egg by sperm outside the body. The first IVF baby (Louise Brown) was born in Oldham (England) on 25 July 1978 following the pioneering work of a gynaecologist (Patrick Steptoe) and a scientist (Robert Edwards). The techniques have been refined over the last three decades making it possible for many couples to now achieve their dream of having children. Over twelve thousand babies are born in the UK each year from IVF and ICSI.

## **Who are they for?**

IVF was originally introduced to help women with blocked or damaged fallopian tubes achieve live births. ICSI was subsequently introduced to help men with abnormal sperm parameters including low count, poor movement, abnormal sperm forms and anti-sperm antibodies. It is also utilised when IVF treatment is unsuccessful due to poor or failed fertilisation. Since those early days it has come to represent the ultimate treatment for any form of infertility that fails to respond to other conventional treatment. The law as it currently stands in the UK allows any woman below the age of 55 years to have IVF treatment. We are comfortable treating women below the age of natural menopause i.e. 51 years.

## **How is it regulated?**

IVF/ICSI treatment is regulated by the Human Fertilisation and Embryology Authority (HFEA) in the UK. The HFEA was established in 1991 to license clinics to offer these treatments, monitor the treatment, and regulate research that involves human eggs, sperm and embryos (fertilised eggs). It publishes an annual guide of clinics that offer IVF treatment and couples can access this information on [www.hfea.gov.uk](http://www.hfea.gov.uk).

## **How is IVF/ICSI performed?**

IVF/ICSI treatment involves a long process that may take up to 6 weeks from start to finish and even longer to know whether it is successful. Appreciation of and adequate preparation for this will help couples cope with the often rigorous demands of the treatment.

### ***Initial assessment***

This includes full interview with both partners as well as general and pelvic examinations of the female. Blood tests are performed to establish the woman's hormone profile (FSH, LH, Oestradiol and Anti-Mullerian Hormone), rubella status, blood count and blood group. The couple undergoes a virology screen for HIV, hepatitis B and hepatitis C. The male's sperm sample is assessed for sperm count, movement, proportion of normal forms and antibodies. Cervical swabs are obtained to exclude genital tract infections.

### ***Counselling***

Counselling is available to couples undertaking the IVF/ICSI journey and can be of immense help in coming to terms with some of the difficulties they are likely to encounter. Although not a compulsory requirement, couples are encouraged to utilise the opportunity for counselling.

### ***Ovarian stimulation***

The mainstay of IVF/ICSI treatment is controlled stimulation of the ovaries to generate growth of many eggs. This is achieved using two different types of injections, one to suppress the ovaries so that the woman does not ovulate before this is desirable and the other to stimulate growth of eggs. These are typically started at two specific points in the menstrual cycle; on day 2 in short cycles and on day 21 in long cycles. Pelvic ultrasound scans and blood tests are used to monitor the response to stimulation. This continues until the eggs are mature enough to be ripened and collected.

### ***Egg collection***

The mature eggs are collected from the ovaries in theatre under sedation or general anaesthesia. The eggs are gently sucked out through a long needle that is guided into the ovaries through the vagina. Rarely, the eggs are collected by laparoscopy (keyhole surgery). Women typically spend half a day in hospital and are able to return home later that day.

### ***Mixing/injecting eggs with sperm***

The male is required to produce a semen sample by masturbation on the day of egg collection after a 3-4 day abstinence from ejaculation to ensure good quality sperm. The sperm is specially prepared to select the best quality ones for use. For IVF, the sperm is mixed with eggs and the mixture is left overnight in an incubator. For ICSI, a single sperm is injected into the centre of each mature egg using a specially designed needle. The inseminated/injected eggs are checked the next morning to see how many have fertilised (become embryos). We usually commence a five-day course of antibiotics from the egg collection.

### ***Embryo replacement***

The best quality 1-2 embryos are replaced in the womb on days 2, 3 or 5 after egg collection. We do this in theatre under ultrasound guidance. The embryos are gently sucked into a soft tube that is passed through the cervix into the womb and expelled near the top of the womb. The procedure does not usually require any

anaesthetic or sedation. We discuss and agree the number of embryos to be replaced beforehand but generally encourage most women to have single embryo replacement. Any good quality embryos that have not been utilised for treatment will be frozen for the couple's use in future.

### **Afterwards**

We advise women to take things easy following embryo replacement but there usually is no need to take time off work. Hormone injections or pessaries (vaginal tablets) are given afterwards to help the developing embryos. If treatment is unsuccessful a period will begin usually between 7 and 14 days after the replacement. Women who have not had a period by this time are offered pregnancy tests and if positive, pelvic ultrasound scans three weeks later.

### **What can go wrong?**

About 3 out of 4 women will complete this treatment without any difficulties or problems. Common problems encountered include:

- **Poor response to stimulation** - this affects about 1 in 10 women with development of very few or no eggs at all leading potentially to cancellation of treatment cycles. Although the ovarian reserve test we perform gives us an indication of likely response and allows us to adjust the stimulation drugs accordingly, we often encounter unexpected poor response. There is the option to use a higher dose of stimulation drugs in a subsequent cycle.
- **Excessive response to stimulation** - this can result in a condition called 'ovarian hyperstimulation syndrome' that affects up to 1 in 10 women. It is fortunately mostly mild but can cause abdominal pain and bloating, vomiting, shortness of breath and tiredness. We make every effort to prevent its occurrence by responsible ovarian stimulation and sometimes sadly have to cancel cycles on account of this condition. Hospital admission is necessary for severe cases. Very severe cases may become life threatening, but this is fortunately now rare.
- **Injuries during egg recovery** - the needle used for the egg recovery may cause injury to the organs in the pelvis (such as the bladder, intestines, and blood vessels) but this is extremely rare.
- **Pelvic infections** - there is a small risk of infection following the egg collection and severe cases may result in pelvic pus collection. We give antibiotics after egg collection to help prevent this.
- **Multiple pregnancies** - there is a risk of multiple pregnancies with IVF/ICSI treatment particularly with replacement of more than one embryo. We make every effort to limit the occurrence of this to fewer than 20% of live births and this effort explains why we encourage women to have single embryo replacement.
- **Abnormalities in babies** - it is now clear that babies born following ICSI treatment have greater risks of inherited genetic, epigenetic and chromosomal abnormalities.

### **Donated sperm, eggs and embryos**

IVF/ICSI can be undertaken with donated sperm and/or eggs. Alternatively, already formed embryos can be donated by one couple for use by another. The HFEA has strict regulations governing treatment with donated gametes and these will be discussed with any couple to whom they apply. Some women cannot produce their own eggs because they have undergone the menopause prematurely and so need donated eggs or embryos. Women with abnormal eggs and those with a genetic abnormality that they do not wish to pass on to their children can also use donated eggs or embryos. Men who cannot produce their own sperm for any reason can utilise donated sperm. Any healthy man, woman or couple that is free of genetic or transmittable diseases can potentially donate their gametes. Potential donors undergo a screening process that includes detailed history and examination, blood tests for chromosomes and infections like HIV, hepatitis B, hepatitis C, syphilis and cytomegalovirus, and cervical swabs. Practical details of how these are undertaken will be discussed with couples for whom they are relevant.

### **Egg sharing**

Egg sharing is a special form of egg donation whereby two women undergo IVF/ICSI treatment simultaneously that is mostly paid for by one woman (the recipient) and both share the eggs produced by the other woman (the donor). This treatment is beneficial in situations where a female with good ovarian function who cannot afford to pay for IVF/ICSI treatment is paired up with another female (the recipient) who can afford to pay for treatment but has poor ovarian function. The recipient effectively pays for the treatment and the eggs retrieved from the donor are divided up between donor and recipient using a previously agreed formula. All previously described processes for IVF/ICSI remain the same.

### **Ethical issues**

There are implications of using donated gametes that all involved parties need to be aware of:

- **Payment of donors** - this is a contentious issue and the legislation concerning it varies from country to country. The family doctor, gynaecologist or infertility specialist will usually be able to advise couples of the current legislation governing this form of treatment in their different countries. The current legislation in the UK holds that sperm, egg and embryo (indeed any body tissue) donation should be performed altruistically and not attract any form of payment, except where this is to cover reasonable expenses incurred by the donor in the process of the donation.

- **Egg sharing** - this practice may make treatment possible for couples that otherwise may not be able to afford it themselves but it has a potential for abuse. Couples contemplating egg sharing should discuss the issues thoroughly beforehand and agree a plan of action especially with regard to how the eggs are shared and any future problems coped with. These include success in one but not the other couple.
- **Anonymity** - the regulations governing this vary according to country. Legislation in the UK has recently changed to give offspring of sperm, egg and embryo donation cycles the right to find out the identity of their genetic parents once they reach their eighteenth birthday.
- **Legal parents** - the legislation governing this may vary from country to country and couples need to seek guidance from their healthcare providers about local regulations. Current legislation in the UK holds that a married man and woman receiving treatment are the legal parents of any child that results. For unmarried couples, both partners are not automatically awarded legal parent status and have to apply for this through the courts.
- **Informing the child** - there is currently no legal requirement in the UK for couples that have been successful with donor gamete treatment to inform the children of their origin. However, most clinics recognize that children have the right to know about their conception. Some units arrange a yearly reunion for children born from this and other forms of assisted conception treatment (including DI, IVF and ICSI) to reinforce the normality of such children. Counselling is available at all licensed clinics to discuss the implications of using donated gametes.

### Frozen embryo replacement

Couples with frozen embryos can have these replaced without the need to undergo another IVF/ICSI stimulation cycle. Frozen embryos have a 60-70% chance of surviving freezing. The embryos are replaced in natural or hormone prepared cycles. Natural cycles are suitable for women with normal regular ovulation while those with irregular periods need preparation of the womb using hormone tablets, pessaries (vaginal tablets) and injections. These artificial hormones used to prepare the womb will need to be continued for some time after the replacement, up to three weeks if treatment unsuccessful and up to the 12<sup>th</sup> week of any resulting pregnancy. Details of replacement procedures, number of embryos replaced, and what happens afterwards will be discussed fully with couples.

### How successful is IVF/ICSI?

The technique of IVF has made it possible for many couples to fulfil their dreams of having children but sadly treatment is not always successful. Factors that improve the chance of IVF succeeding include young female age (particularly if less than thirty years old), previous pregnancies, and short duration of infertility. IVF/ICSI success is measured professionally by pregnancy and life birth rates and current average rates in the UK are detailed in the table below.

Age groups	Fresh IVF/ICSI cycles	Frozen embryo cycles	IUI cycles without drugs	IUI cycles with drugs	DI cycles without drugs	DI cycles with drugs
< 35 years	32%	22%	11%	13%	12%	16%
35 - 37 years	27%	17%	11%	13%	12%	14%
38 - 39 years	19%	18%	9%	10%	10%	10%
40 - 42 years	12%	12%	6%	9%	5%	6%
43 - 44 years	4%	8%	5%	4%	1%	0%
> 44 years	3%	12%	12%	0%	0%	0%

Table 1. Live birth rates for assisted conception cycles in the UK; HFEA published results for - 2008.

### Useful contacts:

#### Human Fertilisation and Embryology Authority (HFEA)

30 Artillery Lane, London, E1 7LS  
Tel. 0207 377 5077; [www.hfea.gov.uk](http://www.hfea.gov.uk)

#### PROGRESS

Campaign for Research into Reproduction, 140 Gray's Inn Road, London, WC1X 8AX

#### Donor Network

P.O. Box 265, Sheffield, S3 7XY  
Tel. 0208 245 4369