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Victorian Assisted Reproductive Treatment Authority

Possible health effects of IVF

The first Australian baby conceived through in-vitro fertilisation (IVF) was born in 1980. Since then, over 100,000 babies, who were conceived using IVF and other assisted reproductive technologies, have been born. In 2010, 3.3 per cent of all Australian babies were conceived with assisted reproductive technologies (ART).

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The purpose of this pamphlet

The Victorian Assisted Reproductive Treatment Authority (VARTA) is an independent statutory authority. One of VARTA's roles is to ensure that people considering ART have access to impartial information so that they can make informed decisions.

In the hands of experts, IVF procedures are safe and medical complications are rare. However, as with all medical procedures, there are some possible health effects. This pamphlet was compiled with the assistance of experts in the field of IVF. It provides an overview of the possible physical and emotional health effects of IVF for men and women and of outcomes for children born as a result of treatment.

The information in this pamphlet refers to IVF and intracytoplasmic sperm injection (ICSI) but does not include ovulation induction alone.

The information represents the state of knowledge about health effects of IVF at the time of publication and is drawn from studies published in scientific literature.

Why it is difficult to determine if there are IVF-related health effects

The results of studies examining health effects of IVF can be difficult to interpret. For example, some health effects of IVF may not be related to the procedure itself but to an underlying cause of infertility or the fact that, on average, those who use IVF are older than those who conceive spontaneously.

Another potential problem with studies of IVF-related health effects is the unintentional bias in the way people are selected and assessed. For example, if babies born through IVF are examined more thoroughly and reporting to health registers about them is more complete, then it might seem that health problems are more common than in spontaneously conceived children.

Possible physical health effects of IVF for women

During treatment

Physical complications requiring hospital admission occur in about one per cent of all stimulated treatment cycles. The most common complication is ovarian hyperstimulation syndrome (OHSS). This syndrome can develop as a result of the fertility drugs which are used in IVF to stimulate the ovaries to produce multiple eggs. OHSS is a potentially serious condition which, in very rare cases, can lead to blood clots, kidney failure and death. In 2008, 198 women (0.6 per cent of all stimulated cycles) were hospitalised as a result of OHSS. All IVF programs monitor patients carefully to minimise the risk of OHSS. If a patient develops an excessive number of follicles in response to the fertility drugs the patient's doctor may recommend that the cycle be cancelled before egg collection to avoid OHSS. Or, if the doctor has reason to believe that the patient is at risk of OHSS after the egg collection procedure, the advice may be to freeze all the embryos and then transfer them, one at a time, when the ovaries return to normal.

Surgical complications which require hospital admission, such as bleeding and infection from egg collection, occur in less than 0.5 per cent of IVF cycles.

The risk of serious complications from general anaesthesia and sedation is approximately one in 50,000 treatment cycles.

Possible physical health effects of IVF for women

Long-term

There have been very few studies examining long-term health effects of IVF for women, other than some studies relating to cancer. Those undergoing treatment are often concerned that the use of fertility drugs may increase a woman's risk of cancer.

A number of large studies have investigated the relationship between the use of fertility drugs and breast cancer. Combining these studies, the risk of using fertility drugs has been investigated in over 45,000 women and no overall increase in the rate of breast cancer has been found.

Ovarian and uterine cancers are much more uncommon and therefore more difficult to study. However, most studies have shown no significant increase in the risk of developing these cancers due to fertility drugs.

Some studies have raised questions about whether there is an increase in cancer risk associated with the duration of fertility drug use, or use of specific types of fertility drugs among certain groups of infertile women. To date there is no conclusive evidence that these factors increase the risk of cancer.

Although the findings of these studies are reassuring, it is important to remember that IVF has only been available for just over 30 years and that it is only in the last two decades that IVF has been used by large numbers of women. Therefore, questions remain about the very long-term risks of using fertility drugs, particularly for rare forms of cancer. Also, little is known about the effect of fertility drugs in women with a strong family history of breast or ovarian cancer, or in women with a personal history of cancer prior to fertility treatment.

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Possible physical health effects of intracytoplasmic sperm injection (ICSI) for men

In some infertile men, sperm for intracytoplasmic sperm injection (ICSI) can not be obtained from the ejaculate. In these rare cases, sperm may be retrieved surgically either by needle biopsy of the testicles under local anaesthesia, or open biopsy under general anaesthesia. These procedures are associated with minor risks related to the operation itself and use of anaesthetics. Local bleeding or infection occurs in less than one per cent of open biopsies; needle biopsies carry an even lower risk of complications.

Some men with severely reduced sperm production have low testosterone levels, or risk developing testosterone deficiency later in life. Biopsies of the testes can, in rare cases, further reduce testosterone production, resulting in the need for lifelong testosterone replacement therapy.

Possible emotional health effects of IVF

IVF treatment is psychologically demanding and emotional health effects are common. In Australia, counselling services are available in all IVF clinics. Women who have IVF treatment and their partners are encouraged to use these if they experience emotional difficulties.

Women often experience symptoms of depression and anxiety during IVF treatment, particularly when waiting for results after embryo transfer and when treatment fails. For some people, deciding whether to continue or stop treatment can be difficult. Couples who have frozen embryos that they are not intending to use often find it hard to decide what to do with these embryos.

For some couples the strain of IVF causes relationship problems but others describe feeling closer and able to support each other through the demands of treatment.

In the first few months after giving birth, women who conceive with IVF have a higher rate of parenting difficulties than women who conceive spontaneously, including anxiety about caring for the baby. However, these difficulties improve with time. The rate of exclusive breastfeeding three months after the birth is lower after IVF than spontaneous conception and this may be related to worry about the ability to nourish the baby.

When IVF fails, people often feel very disappointed and sad. However, follow-up studies show that within a few years of ending treatment, there are very few differences in terms of emotional wellbeing and life satisfaction between those who had a baby as a result of IVF and those who did not.

Outcomes of IVF pregnancies

The risks of pregnancy loss and adverse birth outcomes after IVF must be viewed in the context of how often problems occur in spontaneously conceived pregnancies in Australia.

Current Australian data for all pregnancies shows that approximately:

- one pregnancy in six will miscarry
- one baby in 14 will be premature
- one baby in 25 will have a birth defect
- one baby in 100 will die around the time of birth
- one baby in 400 will have cerebral palsy and be disabled.

As discussed below, some of these are more common after IVF. If you are proceeding with treatment you should discuss these and other risks with your infertility specialist, who can provide advice relevant to your particular circumstances.

Although most pregnancies after IVF proceed without complications, studies show that women who conceive with IVF are more likely to:

- experience bleeding during the pregnancy
- develop blood clots in early pregnancy
- develop high blood pressure and diabetes in later pregnancy
- deliver prematurely.

Birth outcomes for babies born as a result of IVF

The following statistics relate to single babies, as opposed to twins or other multiples.

It is important to know that the vast majority of babies born as a result of IVF are healthy and have no short or long-term problems. However, Australian statistics show that compared with spontaneously conceived babies, IVF-conceived babies have a higher risk of certain outcomes. In 2010 nearly 10 per cent of single babies born after IVF were pre-term (born before 37 weeks gestation) compared with 8 per cent of spontaneously conceived babies. Also, 7 per cent of IVF-conceived single babies were low birth weight (weighed less than 2,500g) compared with 4.7 per cent of spontaneously conceived single babies.

Recent studies have found that the risk of bleeding during pregnancy, premature birth, and low birth weight is lower among babies born as a result of transfer of a frozen/thawed embryo than among babies born as a result of a fresh embryo transferred in a stimulated cycle.

A single IVF baby is more likely to be born by caesarean section than a single baby conceived spontaneously. There are a number of possible reasons for this but the important implication is that a mother's physical and emotional recovery following caesarean birth may be slower than after a vaginal birth.

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Birth outcomes for babies born as a result of IVF

Twins and more

Multiple births are about eight times more common after IVF than they are after spontaneous conception. A multiple pregnancy creates a greater risk for the mother and her babies than a pregnancy with one baby. A major risk is pre-term delivery. Other risks include bleeding during pregnancy and high blood pressure, or pre-eclampsia[1] of pregnancy.

Babies born from a multiple pregnancy are more likely than those from single pregnancies to have cerebral palsy or to die close to the time of birth, mainly due to the higher risk of pre-term birth. The risks for the baby are substantially greater in a triplet or quadruplet pregnancy than in twin or single pregnancies.

There are higher rates of psychological distress in mothers of multiples because caring for more than one baby is more difficult than caring for a single baby.

Single embryo transfer (SET) is the only way to reduce the rate of multiple births associated with IVF and to give all babies born after IVF the best possible start in life. When several embryos are available after a stimulated cycle, one can be transferred and the remainder frozen. If the first embryo does not result in a pregnancy, frozen embryos can be transferred, one at a time, in subsequent cycles. This way, the cumulative chance of having a baby is the same as if two or more embryos are transferred together but the risk of a multiple birth is almost eliminated. With improved pregnancy rates associated with IVF, single embryo transfer has become more common. The proportion of SET in Australia and New Zealand increased from 40 per cent in 2004 to almost 70 per cent in 2010. As a result the multiple birth rate for IVF-conceived babies in Australia and New Zealand fell to 7.9 per cent in 2010.

The risk of birth defects after IVF

Studies investigating the risk of birth defects in babies born following IVF suggest there is a small increased risk of birth defects compared with spontaneously conceived babies. Between five and six per cent of IVF-conceived babies have a birth defect compared with approximately four per cent of spontaneously conceived babies.

Many of the defects are minor. The severe birth defects that appear to be more common occur in the early stages of foetal development and can often be detected by the ultrasound monitoring of pregnancy. One very rare condition that appears to be more common in children born after IVF is a growth disorder called Beckwith-Wiedemann Syndrome (BWS).

Babies born with BWS are relatively large at birth and have an increased risk of certain childhood cancers. However, with appropriate management, the long-term outcomes for children with BWS are positive. In several studies, BWS has been shown to occur in about one in 4,000 IVF babies compared with one in 14,000 to 35,000 spontaneously conceived babies.

The increased risk of birth defects after IVF may relate to parental characteristics such as age or cause of infertility. It is also possible that the process itself or fertility drugs affect the uterine environment at the time of implantation and impair foetal development.

If difficulty conceiving is caused by a genetic or chromosomal disorder the baby may be affected by the same disorder. For example, about three per cent of men with severe defects of sperm production and low or zero sperm counts are missing parts of the Y chromosome, where genes responsible for sperm production are located. Men with 'Y chromosome microdeletion' may become fathers with the aid of intracytoplasmic sperm injection (ICSI) but their sons will have the same genetic problem and therefore in all likelihood will be infertile.

[1] Pre-eclampsia is a serious disorder of pregnancy characterised by high maternal blood pressure, protein in the urine and severe fluid retention. It is the most common serious medical complication of pregnancy, affecting around 5 to 10 per cent of all pregnancies in Australia. One to two per cent of cases are severe enough to threaten the lives of both the mother and her unborn child.
Better Health Channel
Pre-eclampsia www.betterhealth.vic.gov.au at 8 August 2011.

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Health and development in children born after IVF

Studies of the growth, health and development of young children born after IVF have found few differences between them and other children. However, as multiple births are more common after IVF and children from multiple pregnancies are more likely to be born pre-term and to have a low birth weight than single children, there is an overall increased risk of developmental problems and cerebral palsy. Children who are born very prematurely have more learning difficulties andattention and behavioural problems than those born at term. In adulthood some health problems such as high blood pressure and reduced lung function are more common among extreme pre-term survivors.

Childhood cancer is a rare condition. Most major studies of the frequency of cancer in children born after IVF have shown that the incidence is similar to that in the general population but one recent study reported a slight increased risk. Further studies are needed to investigate the effects of particular forms of infertility and fertility treatments on specific types of cancer.

The very few studies that have followed IVF-conceived children beyond puberty have not detected major differences between them and other young people.

If you have further questions

It is important that you collect information from independent sources and then discuss any questions regarding treatment with your health care provider. This pamphlet provides an overview of the questions that may arise about the use of IVF. If you have other questions that are not addressed here, please raise them with your health care provider or contact VARTA.

Useful sources of information

ACCESS
(Australia's National Infertility Network)
www.access.org.au

Fertility Society of Australia
www.fertilitysociety.com.au

National Perinatal Statistics Unit
www.npsu.unsw.edu.au

Human Fertilisation & Embryology Authority, UK
(HFEA)
www.hfea.org.uk

Andrology Australia
for information on male infertility
www.andrologyaustralia.org

Better Health Channel
www.betterhealth.vic.gov.au

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For more information visit the
Victorian Assisted Reproductive Treatment Authority
at www.varta.org.au or phone 03 8601 5250.