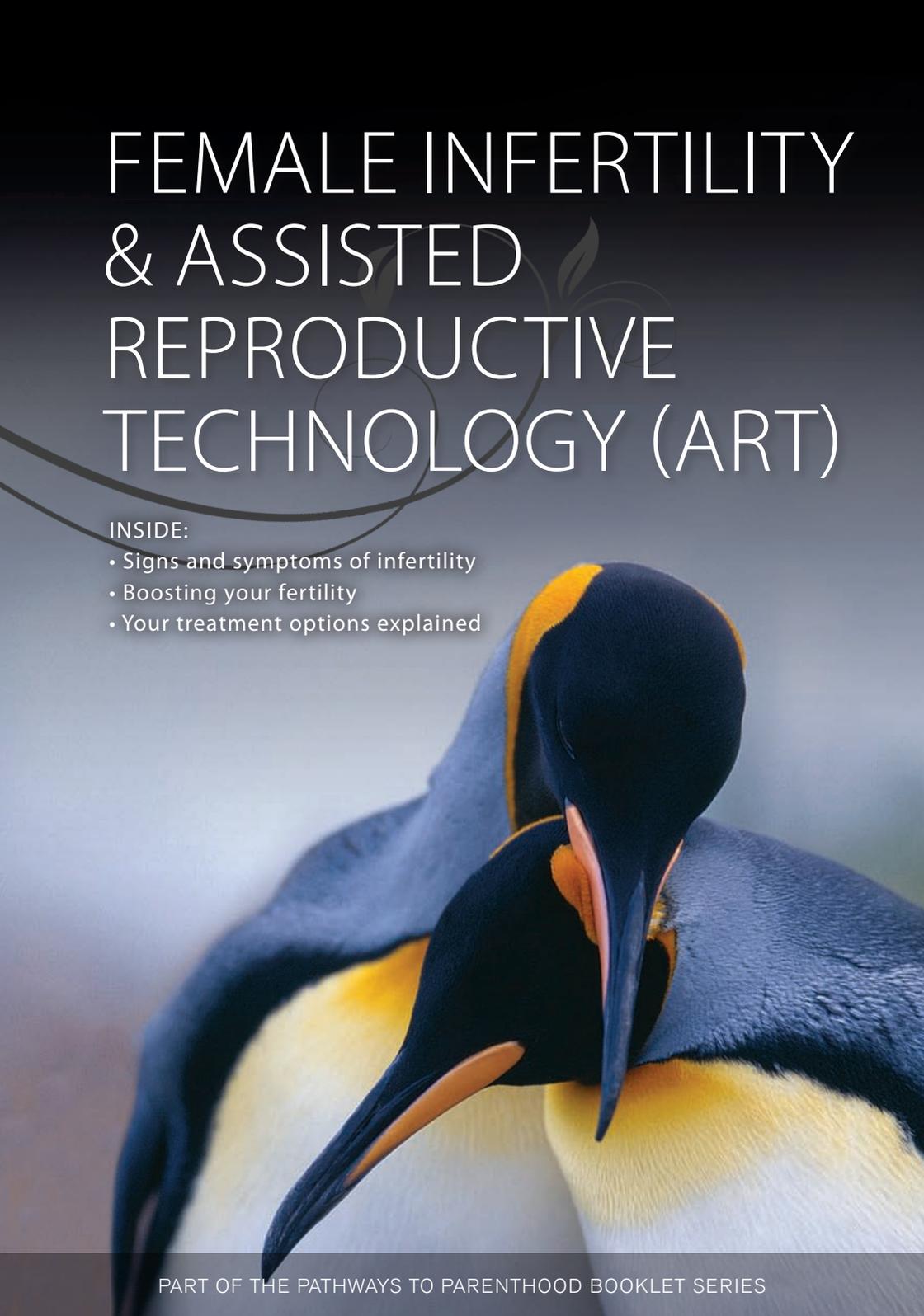


# FEMALE INFERTILITY & ASSISTED REPRODUCTIVE TECHNOLOGY (ART)

## INSIDE:

- Signs and symptoms of infertility
- Boosting your fertility
- Your treatment options explained



# ABOUT THIS BOOKLET

This series of booklets has been developed and written with the support of leading fertility clinics across Australia, and AccessAustralia – a national organisation that provides numerous services for people having difficulty conceiving. We also acknowledge the many people who spoke openly about their own experiences with assisted conception in order to help others experiencing a similar journey. Merck Serono thanks the many individuals, couples and Australian healthcare professionals, including fertility specialists, specialist nurses and psychologists who shared their knowledge and expertise during the production of these booklets.

**Important notice:** The information provided in this booklet does not replace any of the information or advice provided by a medical practitioner and other members of your healthcare team. If you have any further questions about female infertility and assistive technologies, please contact your doctor.

*Please note that throughout this booklet, the generic name of a medication will be stated first followed by the brand name in brackets.*

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# INTRODUCTION

If you are concerned about your fertility, the first thing to understand is that you are not alone. Up to one in six couples worldwide have difficulty conceiving in the first 12 months of trying.<sup>1</sup> It is also important to recognise that becoming pregnant is not that easy for everyone. Many couples believe that once they stop taking precautionary measures, they will fall pregnant very quickly. In reality, there is only a fairly short time each month within the menstrual cycle when conception is possible.

Scientific advances over the past three decades have helped millions overcome problems with fertility. Treatments ranging from medications to assisted reproductive technologies (ART), including *in vitro* fertilisation (IVF) are achieving unprecedented success. In this booklet you will find information about the potential factors that may affect your ability to conceive, how to boost your fertility naturally and also an overview of the many assisted reproductive technologies (ART) available.

A diagnosis of infertility can naturally leave you feeling shocked and lead to a whole range of emotional reactions, which are often very strong and, at times overwhelming. This is normal and while most of the time you will be able to cope with the stress and pressure of the situation, there may be times when you need extra support, reassurance or some coping techniques to help you manage the challenges and your stress levels. It is important that you talk to your partner and other friends and family members about how you are both feeling throughout the diagnosis and treatment process. Your healthcare team, including counsellors and the support organisations listed in the back of this booklet will also be able to help with any concerns or questions you may have.

**Scientific advances over the past three decades have helped millions of women overcome problems with fertility.**

# WHAT IS INFERTILITY?

The term 'infertility' is used when the ability to become pregnant is diminished or absent. It does not mean that you are unable to have children but that you may require treatment or assistance to achieve a pregnancy. Infertility is generally used if a couple has not conceived after 12 months of regular unprotected intercourse, or after six months for women aged over 35.<sup>1</sup> There are two types of infertility. The first is known as **primary infertility** and this is where a couple has never achieved a pregnancy before. **Secondary infertility** is where a couple is unable to conceive after they have already had a pregnancy or child.

While the rate of infertility has not increased in recent years, we are now more aware of the issue as more and more women and men seek treatment. In reality, about one in six couples have trouble conceiving and about half of these couples will require medical assistance to overcome this problem.<sup>2</sup>

Many couples who have difficulty conceiving may have a specific medical condition hindering the woman's ability to become pregnant. In 40% of cases the issue is attributable to the female, while in 40% of cases the issue is traced back to the male.<sup>3</sup> In about 10% of cases, fertility problems are linked to both partners, resulting in both requiring some form of treatment.<sup>3</sup> The remaining 10% of infertility is unexplained, even after exhaustive testing.<sup>4</sup>

If after a year of trying, you have had trouble conceiving you should consult your local general practitioner (GP). If you are a woman aged over 35, it is best to seek medical help after six months. Your doctor will probably want to run some tests (see page 16), discuss your lifestyle and refer you to a fertility specialist or fertility clinic.



# SIGNS AND SYMPTOMS OF FEMALE INFERTILITY

Apart from the fact you may have been trying to become pregnant for six to 12 months, there may be no obvious signs or symptoms of what is causing the problem. However, the following are good reasons to visit your doctor as soon as possible:

- irregular or absent menstrual periods
- history of pelvic infection
- two or more miscarriages
- history of using an IUD for birth control
- sterilisation reversal
- difficulties with sexual intercourse
- chronic pelvic pain
- breast discharge
- history of sexually transmitted disease
- excessive acne or facial hair.

## The impact of age

While the rate of infertility has not changed, the increased number of couples seeking treatment may be due in part to more women who, for career, financial or other reasons, are waiting until they are in their mid-30s before starting a family. According to Australian Institute of Health and Welfare statistics, the proportion of mothers aged 35 years and over increased from about 16.3% in 1999 to about 23% in 2008.<sup>5</sup> Mothers aged 40 years and over made up almost 4% of all women giving birth in 2008 compared with 2.4% in 1999.<sup>5</sup>

We also know that the average age of women undergoing ART treatment using their own oocytes (eggs) was 35.7 years in 2008.<sup>6</sup>

Many couples do not realise that fertility will be lost at a relatively early age. A woman is most fertile between the ages of 15 and 24.5.<sup>7</sup> Women will begin to lose their fertility (the quality and quantity of viable eggs) from age 35 years onwards with it becoming very obvious at age 40. In contrast to women, male fertility can persist into old age even though sperm counts and semen quality start to deteriorate in men over the age of 45.

An age-related decline in the number of healthy eggs in a woman's ovaries is one of the reasons for infertility. A woman is born with all the eggs she will ever have – about 400,000. By the time she reaches puberty, each month, during her reproductive years, about 20 eggs are used even though usually only a single egg matures and is released. This process, called ovulation, contributes to the numbers of eggs decreasing, but the majority of eggs are slowly absorbed by the body. By the fifth or sixth decade of life, most women will have depleted the egg supply they were born with.

As women grow older, other changes affecting fertility include:

- menstrual cycles can become irregular and shorter
- the endometrium (lining of the womb) may become thinner and less able to nurture a fertilised egg
- vaginal secretions can become less fluid and more hostile to sperm
- some conditions can damage the reproductive organs as time passes, or worsen if not treated properly, including endometriosis and polycystic ovary syndrome
- frequency of sexual intercourse may decrease due to a decline in interest and the increasing duration of a couple's relationship.

If a pregnancy occurs, older women are more likely to develop medical disorders including diabetes and high blood pressure. The baby is more at risk of having a chromosomal abnormality, such as Down syndrome and there is an increased risk of women over the age of 35 having a miscarriage.

## 'BUT I DON'T LOOK MY AGE...'

Despite the biological facts, many women aged over 35, do successfully become pregnant and have a baby without any complications. However, it is important to realise that age **does** matter in becoming pregnant even if you do not look or feel your age. While keeping yourself fit with regular exercise and a healthy diet is important, unfortunately your body knows exactly how old you are and there is no way to reverse the ageing of your ovaries and eggs.



# THE FEMALE REPRODUCTIVE SYSTEM

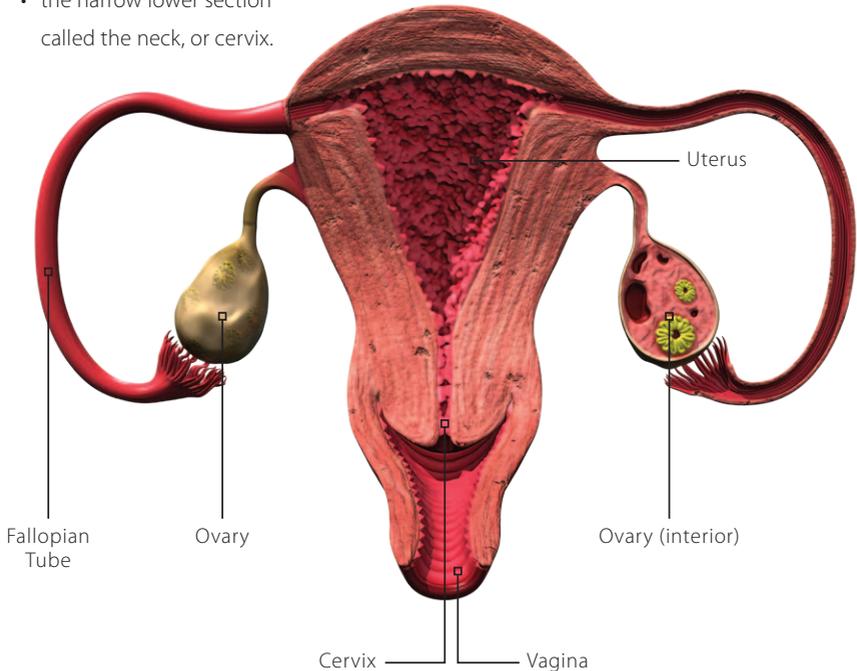
Before we discuss how female infertility is diagnosed, the causes and treatment, it may be helpful to review how the female reproductive system works and the importance of ovulation.

## The uterus

The uterus is a pear-shaped organ capable of undergoing major changes during a woman's reproductive life. From puberty to the menopause, the inner lining of the uterus (the endometrium) provides a suitable environment for embryo implantation and development during pregnancy. The endometrial lining thickens during the first half of the menstrual cycle. If the egg is not fertilised, or implantation does not occur, the endometrium is shed and excreted from the body via the vagina during menstruation and is slowly replaced in the course of the next menstrual cycle. The uterus also undergoes powerful, rhythmic contractions during labour, resulting in the delivery of the fetus at birth.

The uterus is composed of two main parts:

- the bulging upper section called the body
- the narrow lower section called the neck, or cervix.



# The ovaries

The ovaries produce, store and release mature egg cells or **ova**. The female body contains two ovaries that are located on either side of the uterus (womb). They resemble a large almond in size and shape. Beneath the surface of the ovaries are thousands of microscopic structures called ovarian follicles. The follicles contain the eggs. Each month only one egg is released from a follicle. The ovaries also release the female sex hormones, oestrogens (which encourage the eggs to mature and help prepare the uterus for pregnancy) and progesterone, which also helps prepare the uterus for pregnancy by maturing the lining.

# Fallopian tubes

The fallopian tubes consist of two tubes approximately 10 cm long that lead from the uterus and end in finger-like projections called fimbriae. The fimbriae 'hover' over the ovaries but are not attached to them. During ovulation, the end of the fallopian tube receives the mature ovum (egg) that is released from the ovary. The ovum remains in the fallopian tube for a few days. Fertilisation normally takes place in the fallopian tube, as can be seen in the figure on this page.

If fertilisation occurs, the resulting embryo is held in the fallopian tube until it has developed into a small cell mass (blastocyst). It is then propelled through the fallopian tube by a



combination of rhythmic contractions of the muscular walls of the tube and the action of tiny hair-like projections called cilia. The embryo is swept toward the uterus where pregnancy may be established via implantation.

# Summary of the female reproductive system

Structure	Description	Function
Uterus	Pear-shaped cavity containing endometrial tissue, and a lower portion called the cervix.	Site of embryo implantation and development. Provides muscular contractions to deliver fetus during labour.
Ovaries	Two almond-shaped structures located on the opposite sides of the pelvic cavity.	Produce and store eggs (ova). Produce and release oestrogens and progesterone.
Fallopian Tubes	Ducts that end in finger-like projections that hover over, but are not attached to, the ovaries.	Ova pass through tubes from ovaries to uterus. Site of fertilisation.
Vagina	Canal leading from outside of body to cervix.	Serves as lower part of birth canal. Receives sperm from male.
Vulva	Collective term for external genitalia (e.g. clitoris and labia).	Surround and lubricate opening to vagina.

## Ovulation and the menstrual cycle

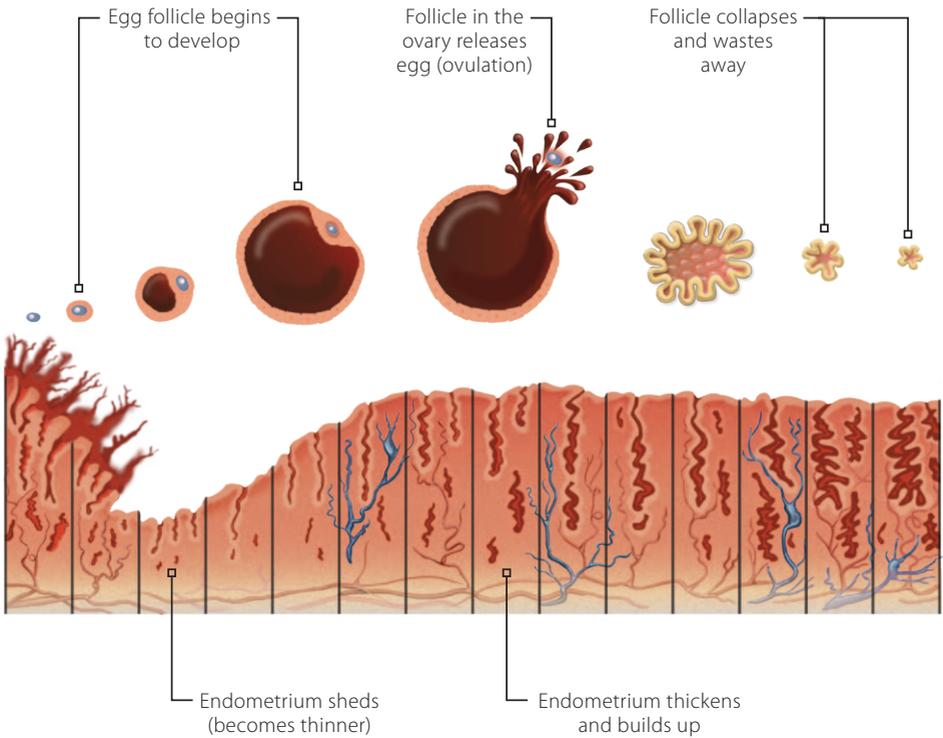
Ovulation is the development and release of an ovum (egg) from a woman's ovaries.

Ovulation is the fertile period of a woman's menstrual cycle. The menstrual cycle refers to the maturing and release of an egg and to the preparation of the uterus to receive and nurture an embryo. A typical cycle takes approximately 28 to 32 days and is divided into three phases:

**1. Follicular (Days 1–13).** On the first day of the cycle when your period begins, the uterus sheds its inner lining (called the endometrium) from the previous cycle. The endometrium provides a suitable environment for embryo implantation and development during pregnancy. The pituitary gland, located at the base of the brain, releases two hormones, **follicle-stimulating hormone (FSH) and luteinising hormone (LH)**. Under the influence of FSH and LH, one of your ovaries selects between 10 and 20 eggs to become possible candidates for release. The chosen eggs begin to mature in the ovary within their own sacs, called follicles.

**2. Ovulatory (around Day 14, depending on the length of the cycle).** The fastest growing follicle ruptures and only one egg is released from the ovary into a fallopian tube. During ovulation, the fallopian tube receives the mature ovum (egg), which is released from the ovary. The ovum remains in the fallopian tube for a few days. Fertilisation normally takes place in the fallopian tube, as can be seen in the figure on page 6.

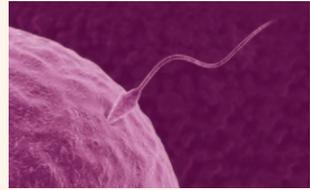
**3. Luteal (Days 15–28).** If the egg meets the sperm in the fallopian tube, conception may occur. The fertilised egg is swept through the tube toward the uterus where the embryo – as it is now called – will implant into the lining about six days after ovulation. It begins to produce a hormone called **human chorionic gonadotrophin (hCG)**, which tells the body it is pregnant. hCG can be detected in urine or blood around the time of a ‘missed’ period. If fertilisation doesn’t occur, the ovum passes through the uterus, the uterine lining will break down and be shed several days later and the next menstrual period begins.



# Egg fertilisation

## Stages of development

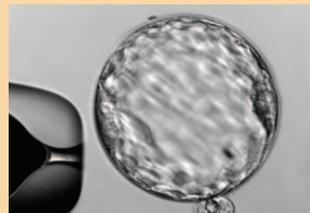
**Zygote:** A single sperm penetrates the mother's egg cell, and the resulting cell is called a zygote. The zygote contains all of the genetic information (DNA) necessary to become a child. Half of the genetic information comes from the mother's egg and half from the father's sperm. The zygote spends the next few days travelling down the fallopian tube and divides to form a ball of cells. The term **cleavage** is used to describe this cell division.



**Morula:** When the zygote reaches 16 or more cells, it is called a morula. The morula is no larger than the zygote, but keeps producing smaller and smaller cells through cleavage.

**Blastocyst:** The morula continues to divide, creating an inner group of cells with an outer shell. This stage is called a blastocyst and consists of approximately 100 cells (taking around four to five days to develop). The inner group of cells will become the embryo, while the outer group of cells will become the membranes that nourish and protect it.

**Embryo:** The blastocyst reaches the uterus around day five, and implants into the uterine wall on about day six. The cells of the embryo now multiply and begin to take on specific functions resulting in the various cell types that make up a human being (e.g. blood cells, kidney cells, and nerve cells).



# BOOSTING YOUR FERTILITY

To give yourselves the best chance of becoming pregnant, it is recommended that you have unprotected intercourse every two to three days.<sup>1</sup> In addition, changing your lifestyle in certain ways and timing intercourse for when you are most fertile are some of the recommended ways to maximise the possibility of conceiving.

## Lifestyle changes

**Give up smoking.** Smoking can cause problems for virtually all areas of the reproductive system. **Women** who smoke are more likely to have difficulty conceiving, may not respond as well to infertility treatments and are at increased risk of miscarriage, complications during the birth and of having a baby with a low birth weight.<sup>8,9</sup>

For **men**, smoking may affect the development and quality of sperm, decrease the sperm count and reduce the volumes of semen.<sup>10</sup> In addition, there is a higher risk of impotence (erectile dysfunction).<sup>10</sup>

For information and advice on how to stop smoking, visit Quit Now at [www.quitnow.info.au](http://www.quitnow.info.au) or call the Quitline on 131 848.

**Restrict alcohol intake.** As drinking excessive amounts of alcohol may affect sperm count and increase the risk for miscarriage and birth defects, it is recommended that both male and female partners take a conservative approach to alcohol while trying to become pregnant. If you choose to drink, the Australian Alcohol Guidelines recommend that **women** should have less than seven standard drinks in any week and no more than two standard drinks on any one day.<sup>11</sup> Having two alcohol free days each week is also recommended.<sup>11</sup> For **men**, the recommendation is to drink no more than two standard drinks on any day, with two alcohol free days.<sup>12</sup>

**Say no to drugs.** Illegal drugs such as cocaine and marijuana have been known to disrupt the menstrual cycle and ovulation process.<sup>13,14</sup> Marijuana can also affect sperm count.<sup>13,14</sup>

**Exercise with caution.** Exercising heavily every day may interfere with the regularity of the menstrual period. For men, prolonged cycling can cause damage to the groin and there is also the risk of damage to the testicles from contact sport.<sup>14</sup>

## Lifestyle changes (cont.)

- ❑ **Well-balanced diet.** There is no special eating plan for becoming pregnant. A sensible diet that includes plenty of fruit, vegetables, grains, meat, poultry and seafood is advised.
- ❑ **Cut back on caffeine.** The studies are divided on this subject, but caffeine may interfere with the natural ovulation process and even a modest amount of coffee (one or two cups daily) may decrease fertility and affect sperm count.<sup>14</sup>
- ❑ **Mind your weight.** For both men and women, being overweight, or underweight can cause fertility problems, especially if your weight is influenced by another condition such as diabetes, or polycystic ovary (ovarian) syndrome (PCOS) – see page 20. For **women**, a body fat level just 10-15% above or below normal can contribute to infertility.<sup>15</sup> The good news is that a large percentage of women diagnosed with infertility related to being overweight or underweight conceive spontaneously when their weight normalises. Dieting while you are trying to become pregnant may throw out your body's natural balance so it is best to embark on a weight loss program before you start trying to conceive.

For overweight **men**, losing weight may help increase your sperm count.<sup>14</sup>

- ❑ **Increase your intake of folic acid.** For women, increasing your intake of folic acid (known as folate in its natural form) before conceiving and for the first three months of pregnancy can reduce the risk of having a baby with neural tube defects such as spina bifida. Folic acid is readily available in tablet form from pharmacies (at least 0.4–0.5 mg of folic acid each day) or you can eat more folate rich foods such as green leafy vegetables (spinach, broccoli), oranges, bananas, avocado, berries and eggs.<sup>16</sup> Many foods, such as cereal and bread have

added folic acid – look for this on packaging.<sup>16</sup>

If you have a family history of neural tube defects, or take epilepsy medications, you may need a higher dose of folic acid.



- **Discuss your medications.** As some medications may affect male or female fertility, please discuss with your doctor any prescription, over the counter medications, or complementary therapies that you may be taking.

## Getting the timing right

Known as the 'rhythm method' or 'calendar method', this process involves calculating when you are ovulating (when an egg is released from one of the ovaries) based on your menstrual cycle. If you are having regular cycles (regardless of the length of the cycle), subtract 14 days from your average cycle length. So if your cycles are 28 days, you will ovulate on day 14, but if your cycles are shorter, e.g. 25 days, by subtracting 14 days, you will ovulate on day 11. It is recommended that you have intercourse at least three or four days prior and on the day of your ovulation day in order to maximise your likelihood of becoming pregnant. There are many ovulation calendars available online which automatically calculate your most fertile days based on your provided dates. Try [www.babycenter.com.au/tools/ovu/](http://www.babycenter.com.au/tools/ovu/) or [www.mydr.com.au/tools/OvulationCalculation](http://www.mydr.com.au/tools/OvulationCalculation)

### HOW OFTEN IS ENOUGH?

Not having intercourse for five days increases sperm count but may affect the motility (active movement of the sperm). Having intercourse more than once a day is probably too much.<sup>14</sup>

To be on the safe side, when you are close to ovulating, have sex at least every other day, if not once every day.



## WHERE'S THE FUN?

The focus on timing intercourse around ovulation can take the spontaneity and fun out of sex. 'Baby sex' can often feel like a chore rather than something pleasurable and can lead to a lack of desire and sometimes erectile problems in men, and vaginal dryness in women. Try to keep the romance alive and make a conscious effort to give each other lots of attention and praise. Do things that you enjoy doing as a couple and remind yourself that you have a life together beyond trying to become parents.

## Changes in cervical mucus

At the beginning of your menstrual cycle, the mucus is sparse, cloudy and dense but when you ovulate, this fluid becomes more plentiful, clear, slippery and stretches easily – often described as being the consistency of raw egg white. This mucus is easier for the sperm to swim through.

## Best positions

The best positions for conception aim to expose the woman's cervix to as much sperm as possible. The missionary position (man on top) is believed to be good for conceiving as it allows for the deepest penetration, placing sperm closer to the cervix. Rear-entry (man entering woman from behind) or lying side-by-side can also deposit sperm close to the cervix and aid conception.

To expose the cervix to the maximum amount of semen, the woman can also try elevating her hips with a pillow and lie there for about 15 minutes before getting up to go to the bathroom.

## PEAK TIMES

Studies suggest that the number of quality sperm peaks in the late afternoon and that women are also most likely to ovulate between 3–7pm.

# DIAGNOSING FEMALE INFERTILITY

When you decide to seek medical advice about trying to conceive, your first visit should be to a general practitioner (GP). Depending on your GP, they may want to discuss some of the recommended lifestyle changes or whether you are trying to conceive at the best time (as discussed in the previous pages). Sometimes your GP may run some preliminary tests (see below) or they will refer you to a gynaecologist who specialises in reproductive health. Alternatively your doctor may refer you to a fertility clinic, many of which can be found in large hospitals.



For your first appointment with a specialist or fertility clinic, it is best to go as a couple. Your specialist will initially ask you detailed questions about your medical history and your sex life and may conduct a physical examination including a breast and pelvic examination. If you have not had one done recently, a routine pap smear may also be done to rule out infection or any pre-cancer or cancerous cells on the cervix (lower part of the uterus). Your partner will probably be tested at the same time or another appointment will be made.

## What are we testing for?

When evaluating a couple, a specialist is trying to determine which of the following five essential conditions required for pregnancy may not be functioning correctly.

Your doctor will check for:

1. The right balance of hormones to allow egg and sperm development and support.
2. A healthy mature female egg (female oocyte or gamete) and whether ovulation regularly takes place.
3. A good quantity and quality of male sperm (male gamete).
4. A functioning reproductive tract (uterus and fallopian tubes), which allows for the egg and sperm to meet and fertilise.
5. The ability of the female body to allow for implantation of an embryo and to maintain and nourish that embryo.

# Common tests

Your doctor will decide which of the following tests are the most appropriate for you.

**Blood tests** – A series of tests will establish if there is a hormonal basis for a couple's infertility. These tests are also to check for:

- rubella (German measles)
- syphilis
- blood group
- HIV
- antibodies (a compound in the blood, cervical mucus or semen which interferes with normal sperm function)
- hepatitis B & C.

**Ultrasound scan (also called a transvaginal ultrasound)** – Using a long, slender probe inserted into the vagina, your doctor or nurse will check for the following factors:

- anything that may be affecting your cycles such as the presence of ovarian cysts or endometriosis (see page 19)
- how thick the uterine lining is and how well the uterus is responding to hormone production
- how big your ovaries are and the number of follicles present in your ovaries.



**Hysterosalpingogram (HSG)** – This is a procedure in which a dye ('contrast') is injected into the uterine cavity. X-rays are then used to visualise the uterus and fallopian tubes to determine if any blockages are present. It is used less commonly now due to improved ultrasound techniques.

**Laparoscopy** – A small telescopic instrument is inserted through a cut in the navel to examine the areas around the woman's uterus and fallopian tubes.

**It may take two or three visits to the clinic or specialist to complete the necessary tests, and may take between one to six months to establish a diagnosis.<sup>1</sup>**

# CAUSES OF FEMALE INFERTILITY

Once the diagnostic tests have been completed, your doctor will have a clearer idea of what is causing the difficulty with conceiving and will then start treating the condition, or recommend a procedure that may assist you in becoming pregnant.

We have already discussed some of the lifestyle factors that can affect your fertility.

In addition some of the ovulatory or structural causes include:

- problems with ovulation
- blocked fallopian tubes
- endometriosis
- fibroids
- polycystic ovary syndrome
- cervical problems.

## Problems with ovulation

As we have discussed, becoming pregnant is dependent on the release of a healthy egg capable of being fertilised by a healthy sperm. However, if your period is irregular or absent then your production and release may be affected. About 40% of women who are infertile will suffer from ovulatory problems.<sup>1</sup> Infrequent periods (oligomenorrhoea) or the absence of periods (amenorrhoea) are most often caused by deficiency in one of the controlling hormones. These can be successfully treated with medications (see page 22). Problems are also associated with extremely low body weight, being overweight, or a significant change in weight. In addition, ovulation problems can arise if the ovaries themselves are resistant to normal levels of hormones. Absent, damaged or diseased ovaries will also prevent ovulation.

# Blocked fallopian tubes

The fallopian tubes are delicate structures of only about the same thickness as the lead of a pencil. Because of this, they can easily become blocked or damaged. This can interfere with the sperm reaching the egg, a proper embryo development and implantation in the uterus. Blockages may arise as a result of scarring due to infection or previous abdominal surgery.

**Pelvic inflammatory disease** (PID) due to sexually transmitted diseases such as chlamydia or gonorrhoea, is the main cause of tubal infertility. In addition, PID is associated with an increased risk of subsequent ectopic pregnancy – when the fertilised egg implants in the fallopian tube, ovary or abdominal cavity (instead of the uterus).

Tubal infertility can sometimes be treated by surgery, but if this is not possible, or if surgery is unsuccessful, *in vitro* fertilisation (IVF) – see page 28 – may be the solution.

# Endometriosis

This is a major cause of infertility and occurs when tissue that normally lines the inside of the uterus grows in other places of your body where it doesn't belong, such as on the ovaries, fallopian tubes, outside surface of the uterus, bowel, bladder and rectum. The symptoms of endometriosis may include heavy, painful and long menstrual periods. Because this tissue still acts the same as that found in your uterus and responds to changes in your hormones during your menstrual period, the tissue breaks down and bleeds causing pain before and after your period, scarring and adhesions (organs sticking together).

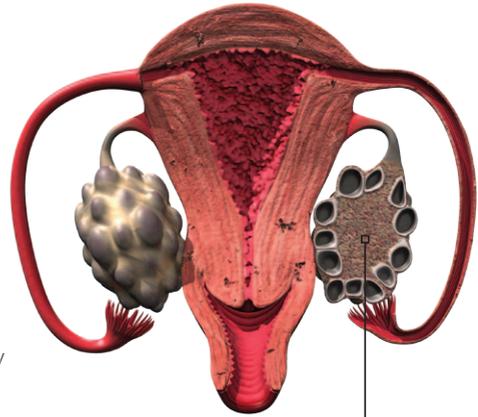
A laparoscopy (see page 17) is used to identify endometriosis and there are several forms of treatment available, involving both medications and surgery.

# Fibroids

Uterine fibroids or uterine myomas occur in up to 70–80% of women by the age of 50.<sup>18</sup> A fibroid is a non-cancerous growth of the muscle in the uterus. These may require treatment if they are causing problems with fertility.

# Polycystic ovary syndrome

Polycystic ovary (ovarian) syndrome (PCOS) is a condition in which the ovaries are enlarged, with a smooth but thicker than normal outer cover. Many small cysts cover this surface, which are themselves harmless, but may cause infrequent or absent periods, resulting in infertility. Polycystic ovaries are most easily seen by an ultrasound scan. The condition may be treated with medication or larger cysts may need to be surgically removed.



Polycystic Ovary

## Cervical problems

Cervical problems may be related to the consistency or not having enough cervical mucus. 'Mucus hostility' may arise as a result of a vaginal infection or the presence of antisperm antibodies in the mucus.

## Unexplained infertility

Unexplained (idiopathic) infertility is defined as not being able to conceive after one year, even though the cycle is normal, semen is normal, laparoscopic findings are normal and there is normal sperm-mucus penetration. In about 15% of couples, a cause for infertility may not be found even after thorough investigation of both partners.<sup>19</sup> Emotionally, this is the most frustrating and stressful diagnosis of all because there is no cause or management plan to focus on. Depending on a woman's age, couples may continue to try to fall pregnant naturally, 'fast track' to assisted reproductive technologies or consider other options, such as living child-free or adoption.

**For more detailed information on endometriosis or polycystic ovary syndrome, ask your doctor for a copy of the *Pathways to Parenthood* booklet specifically on those topics.**

# How might you feel?

## Testing and diagnosis

The testing period can be stressful, invasive, and expensive, and you may feel uncomfortable, guilty, and even fearful about the possible results. These are normal reactions to an overwhelming experience.

## Common feelings include:

- loss of control: a sense that doctors and tests are taking over your life
- anger at your body, your partner, or others who are pregnant or have children
- self-punishment: 'What did I do to deserve this?', 'What could I have done differently?'
- shame and embarrassment over not functioning 'normally'
- need for secrecy, resulting in isolation from friends and family
- sense of being misunderstood by those who have children or are pregnant
- shock, numbness, and/or relief when a problem is confirmed

## Coping strategies:

- Read as much as you can about infertility, its causes, and treatments
- Communicate fears and emotions to your partner regularly
- Support one another, but understand that at times this will be difficult
- Acknowledge that periods of depression and anxiety may happen
- Cut down on stressful activities and avoid social gatherings (especially those involving babies and children like Christenings)
- Allow yourself private time
- Try sharing your problem with supportive friends or family members
- Ask your partner to go with you to medical appointments so you both understand what is happening and write down the questions you would like to ask your doctor

Infertility is a couple's problem not an individual's. Blaming yourself or your partner doesn't achieve anything. By asking for and relying on the support of your partner and by communicating openly with them throughout the evaluation, diagnosis and treatment phases, you may find that your relationship grows stronger.

# TREATING FEMALE INFERTILITY

Discovering the medical reason for not being able to conceive easily and beginning treatment as advised by your doctor, is the start of a new and positive phase of your life. However, it is also important to acknowledge that even with treatment, it may take some time to become pregnant. It can be a long, frustrating and emotional process and you and your partner should prepare yourselves for this (see pages 21 and 31 for some suggested coping methods).

The treatment of female infertility can be categorised into three defined stages. These take the form of consecutive steps. In many cases the first step may be successful, hence the need for further treatment may not be necessary.



**About 85% to 90% of infertility can be treated with conventional therapies, such as medication or surgery. Success rates are continually improving.<sup>20</sup>**

## Hormonal therapy

When you are not ovulating or ovulation is irregular, taking hormonal medications either in tablet form or by an injection, also known as **ovulation induction** is the process where the ovaries or follicles (egg sacs) are stimulated to produce an egg, which can then be fertilised by the male's sperm. Your doctor may also refer to it as 'ovarian stimulation' or when used in conjunction with assisted reproductive technologies as 'controlled ovarian hyperstimulation' or 'superovulation'.

# Oral contraceptive pill

When taken in combination with some of the medications listed on the following pages, the contraceptive pill can help regulate menstrual periods and ensure that egg retrieval happens at a predicted time.

## Clomiphene citrate

If testing indicates that ovulation is irregular or absent, medication that helps you produce eggs will probably be the starting point for treatment. Typically, a doctor will begin what is known as ‘**ovulation induction**’ (the use of medicine to promote ovulation) with clomiphene citrate (also known as Clomid® or Serophene®). It works best for those women whose ovaries are capable of functioning but who need a little assistance.

In a normal cycle, the hypothalamus (part of the brain that controls a large number of bodily functions) releases a hormone called gonadotrophin-releasing hormone (GnRH) at the beginning of your menstrual cycle. If too little or too much is released, normal follicle development will not take place and ovulation will not occur. Clomiphene citrate stimulates the release of GnRH, which in turn causes the pituitary gland to release more FSH and LH. These two hormones promote growth of the fluid-filled sacs (follicles) containing the eggs. Generally if clomiphene citrate is effective then successful ovulation and pregnancy will occur within three to six months.<sup>1</sup> If you do not fall pregnant after three ovulatory responses to treatment, further treatment is not usually recommended.<sup>21,22</sup> Your doctor will advise you on how many courses you should take.<sup>23</sup> If clomiphene citrate is ineffective for you, medications containing FSH and LH, i.e. gonadotrophins (see next page) may be prescribed.

**How is it taken?:** Clomiphene citrate comes in an oral tablet form and is usually taken daily for five days at the beginning of your cycle.

**Side effects:** Side effects may include facial flushes, headaches, breast soreness, nausea and vomiting or abdominal discomfort and bloating.<sup>21,23</sup>

**Success rate:** Clomiphene citrate stimulates ovulation in about 80% of women.<sup>24-26</sup>



## CLOMIPHENE CITRATE AND MULTIPLE PREGNANCIES

According to the American Society for Reproductive Medicine, women who conceive with clomiphene have approximately a 10% chance of having twins.<sup>26</sup> It is rare (<1%) to have more than twins but triplets and higher multiple pregnancies may occur.<sup>26</sup> Careful monitoring is therefore recommended during treatment with clomiphene citrate.

### Gonadotrophins

If clomiphene does not work, the next stage of treatment is usually to start administering a stronger category of medication called gonadotrophins – synthetic forms of FSH, LH and hCG found naturally in humans. Where clomiphene citrate acts to stimulate the release of gonadotrophin-releasing hormone, gonadotrophins act directly on the ovary, promoting follicular development.

Gonadotrophins are also used in conjunction with assisted reproductive technologies including *in vitro* fertilisation (IVF) when more follicles are being encouraged to develop (see page 28).

The injection of high levels of FSH (and sometimes also LH) into your bloodstream stimulates your ovaries to develop multiple follicles and eggs. Ideally no more than one to two eggs should develop to maturity – more than this may lead to a high risk of multiple birth. The growth of your eggs will be carefully monitored through ultrasound.

**Follicle stimulating hormone (FSH)** stimulates development of the fluid-filled sacs (follicles) containing the eggs. It includes the medications Gonal-f®, Puregon®, Elonva®, Pergoveris® (a mixture of FSH and LH) and Menopur® (a non-synthetic hormone containing both FSH and LH activity).

**Luteinising hormone (LH)** is sometimes used together with FSH to stimulate the development of follicles. It includes the medication Luveris®.

**Human chorionic gonadotrophin (hCG)** causes the final maturation and release of an egg. It includes the medications Ovidrel® and Pregnyl®.

**How is it taken?:** These medications are taken by a self-administered injection under the skin, usually via an easy to use pen-type device.

**Side effects:** These may include mood swings, abdominal discomfort, backaches, fatigue and tender breasts.<sup>26</sup>

## What can help?

### Injections

Some women find the thought of having a regular injection quite scary. However, today's technology means that most of the injections are given just under the skin with a pen-like device, which is very easy to use and painless. You will probably be instructed at your clinic or be sent home with a video and clear step-by-step instructions on how to inject in the correct way. You might prefer that your partner does the injection for you or that you do it yourself. Either way, you might feel more comfortable if you both have a practise run in front of one of the nurses at your fertility clinic or gynaecologist's office.



## Gonadotrophin-releasing hormone (GnRH) agonists

Daily administration of a GnRH agonist (or GnRH analogue) will first stimulate the pituitary gland at the base of the brain to make extra FSH and LH, but then causes these hormones to drop right down. As a result, after around two weeks of daily administration, your normal menstrual cycle, hormones and ovulation are all shut down. This helps control premature ovulation and can also relieve the pain of hormonally controlled conditions such as endometriosis and fibroids. When used in combination with injected gonadotrophins (see previous page), it allows for more reliable timing of the egg collection and usually an increased number of eggs being available for *in vitro* fertilisation (IVF). It includes the medications nafarelin acetate (Synarel®) and leuprorelin acetate. Synarel is given by nasal spray morning and night. Leuprorelin is given by a daily subcutaneous (under the skin) injection.

## GnRH antagonists

A newer class of injectable medication, GnRH antagonists – cetrorelix acetate (Cetrotide®) and ganirelix acetate (Orgalutran®) – work by dropping the levels of FSH and LH without first causing an increase in these levels (as do the GnRH agonists). This means they can be given for a shorter period of time. Using this medication allows the continued stimulation of follicle growth whilst preventing the risk of premature egg release prior to egg collection.

## Progesterone

Progesterone may be prescribed in the form of pessaries (inserted vaginally) or as a vaginal gel (Crinone® gel) to better prepare the lining of the uterus for implantation of the embryo.

This type of hormonal support may also be combined with oestrogen replacement for women who have no ovarian function and require artificial preparation of the uterus ready to receive donated eggs.

## Surgery

Surgery can often be used to improve fertility when the cause of infertility can be traced to past infections or inflammation, which has left scarring or adhesions such as with endometriosis, fibroids and other uterine or tubal problems.

Microsurgery can be used to reverse sterilisation procedures (e.g. tubal ligation). These days, laparoscopic surgery, also called keyhole surgery is usually preferred in which operations in the abdomen are performed through small incisions in the navel or abdomen wall.

## BE AWARE OF OVARIAN HYPERSTIMULATION SYNDROME

**Ovarian hyperstimulation syndrome** (OHSS) is a potentially life-threatening medical condition, which may occur, though rarely, when your ovaries have been overly stimulated by various fertility medications. The ovaries may increase in size and produce large amounts of fluid. It is characterised by pain and bloating in your abdomen and if severe can cause breathing or urinating problems. Contact a member of your healthcare team immediately if you believe you have any of these symptoms.

# ASSISTED REPRODUCTIVE TECHNOLOGY (ART)

If conception has not taken place after approximately three ovulatory responses to treatment with clomiphene citrate and a further three to five cycles with gonadotrophin treatment, your doctor may recommend you consider one of the many assisted reproductive technologies (ART) available. ART is a general term referring to methods used to unite sperm and eggs by artificial or partially artificial means. The most common ART procedures include **intrauterine insemination (IUI)**, **in vitro fertilisation (IVF)** and **intra-cytoplasmic sperm injection (ICSI)**.

## Artificial insemination (AI) & intrauterine insemination (IUI)

**Artificial insemination (AI)**, is a procedure in which the sperm are placed directly into a woman's reproductive tract. A common AI procedure is **intrauterine insemination (IUI)** in which sperm are inserted directly into the uterus around the time of ovulation to assist their journey to the egg. The procedure is often combined with the female partner taking fertility drugs.

IUI is commonly used when there may be endometriosis, problems with semen volume, concentration or motility (movement), physical problems with sexual intercourse or unexplained infertility. After being 'washed' (the sperm is separated from the liquid part of the semen to remove hormones and other substances), sperm is inserted into the uterus to reduce the distance they have to travel to reach the egg. IUI can also be done using donor sperm, either from an anonymous or a known sperm donor (known as DI or donor insemination) – see information page 30.



# In vitro fertilisation (IVF)

*In vitro* fertilisation (IVF) was the first ART procedure and is still one of the most commonly used. During an IVF cycle, eggs and sperm are collected and placed together in a laboratory dish to fertilise. If the eggs are successfully fertilised in the lab, they are transferred into the woman's uterus. Ideally, one of the fertilised eggs will implant and develop, just as in a routine pregnancy.

## IVF is a four-stage process:

### **Stage 1: Ovarian stimulation, monitoring, and ovulation triggering**

Having a greater number of mature eggs available for fertilisation increases the chances of pregnancy. Since a woman's body normally releases only one mature egg every month, certain medications are used to prevent an early release of eggs while other medications are used to stimulate the ovaries to develop more ovarian follicles, usually between five and 10 (see page 24).

### **Stage 2: Egg retrieval**

Once ovarian stimulation is complete and follicles have matured, your doctor will try to retrieve as many eggs as possible, although all the eggs may not be used in the current IVF cycle. Egg retrieval can be performed under mild sedation, a local anaesthesia or, in some cases, a general anaesthesia. The mature follicles are identified using ultrasound, and then a needle is passed through the vagina to withdraw the fluid from the mature follicle with gentle suction. The fluid is immediately examined under a microscope to see if an egg has been retrieved. The process is repeated for each mature follicle in both ovaries. All retrieved eggs are removed from the follicular fluid and placed in an incubator.

### **Stage 3: Fertilisation**

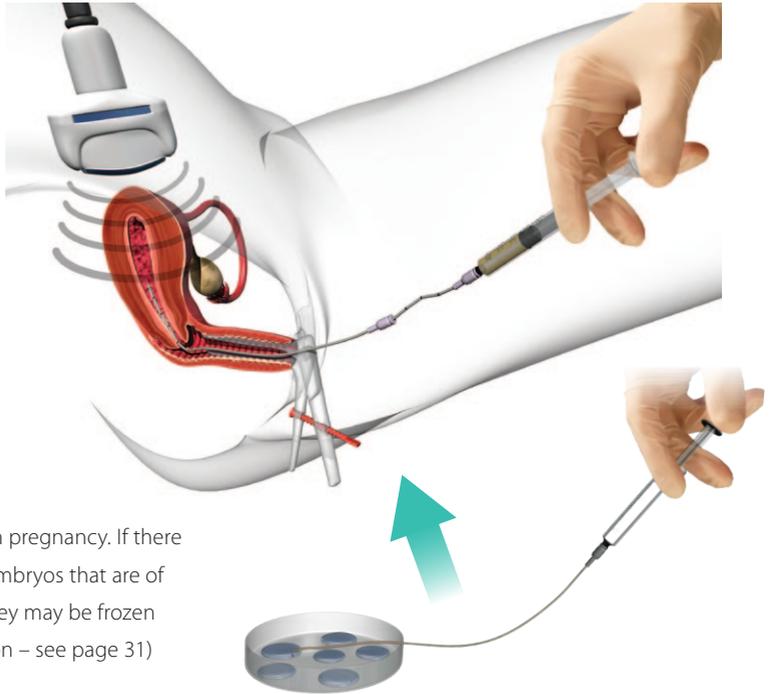
About two hours before the eggs are retrieved, a semen sample is collected from the male partner and processed to select the strongest, most active sperm. The sperm are then placed with the eggs in an incubator set to the same temperature as a woman's body. The next day, the eggs are examined under a microscope to determine whether fertilisation has occurred. If it has, the resulting embryos will be ready to transfer to the uterus a few days later.

#### Stage 4: Embryo development and transfer

Your doctor will discuss how long they will watch embryo development in the laboratory before performing embryo transfer. It is common for transfer to be done between day two (2–4 cell stage) and day five (blastocyst stage – around 100 cells) of development. This allows assessment of embryo cleavage (the way an embryo divides) and ensures the embryo is still developing so that only embryos capable of resulting in a pregnancy are transferred.

Embryo transfer is not a complicated procedure and can be performed without anaesthesia. The embryos are placed in a tube and transferred to the uterus. The number of embryos

transferred depends on a woman's age, cause of infertility, pregnancy history, and other factors. However, in most cases a single embryo transfer is recommended to reduce the risk of a twin pregnancy. If there are additional embryos that are of good quality, they may be frozen (cryopreservation – see page 31) for later use.



# Intra-cytoplasmic sperm injection (ICSI)

Intra-cytoplasmic sperm injection (ICSI) is an identical procedure to IVF except IVF allows the sperm to penetrate the egg of its own accord whereas ICSI directly inserts the sperm into the egg. This is done under a microscope using micromanipulation devices. This technique is used when the sperm is unable to penetrate the egg wall. If the egg is fertilised, the embryo is inserted into the uterus in the same way as described for IVF on the previous page.

## Using donor sperm and eggs

### Donor sperm

Insemination with donor sperm is used when the male partner does not produce sperm, when the sperm is of very poor quality or if there is a high risk of passing on genetic diseases. Donor sperm is used less frequently because of the improvement in techniques which can retrieve viable sperm (e.g. sperm extraction techniques).

Donor sperm may be from a known or anonymous donor. There are many factors to consider such as whether to tell friends or family about using donor sperm and whether the child should know about their origins as they grow up. **AccessAustralia** and the **Donor Conception Support Group** have many resources on the issues relating to donor insemination (see contact details page 32).

### Donor oocytes

Egg donation is one treatment option for those who wish to have a child but are unable to use their own oocytes (eggs). The eggs may be sourced from an anonymous donor or donated by a close friend or relative. The latter may undergo ovarian stimulation to help the recipient. A comprehensive medical and counselling process is undertaken prior to the initiation of such treatment cycles.

## CRYOPRESERVATION

Although your doctor will try to fertilise all available eggs, usually only one or two embryos will be transferred immediately. If there are any remaining embryos, they can be frozen through a process known as cryopreservation. Frozen embryos are frozen and stored and most will remain unchanged for long periods of time. About two in three embryos will survive the process of freezing and thawing.<sup>2</sup> An advantage of cryopreservation is that these frozen embryos can be used in future IVF/ART cycles without having to repeat the first few steps of ovarian stimulation, egg recovery and fertilisation.

## Success rates

According to recent figures from the Australian Institute of Health and Welfare, there were 61,929 assisted reproductive technology (ART) treatment cycles undertaken in Australian and New Zealand in 2008.<sup>6</sup>

Of these cycles, 17.2% resulted in a live delivery (the birth of at least one liveborn baby).<sup>6</sup> In total, 11,538 liveborn babies were born following ART treatment undertaken in 2008.<sup>6</sup>

## How might you feel?

### Surviving the two week wait

After your embryo transfer, it takes around two weeks for pregnancy test results to be accurate. This 'two week wait' – the time before your expected period – is understandably a time of high anxiety, worry, and frustration for women trying to conceive. Here are some 'survival' tips to help you get through this time:

- Try not to obsess about pregnancy symptoms – feeling pregnant does not always mean that you are.
- Keep busy – this may mean working more, or planning meaningful or fun distractions.
- Allow yourself 15 to 30 minutes a day to think about pregnancy, write down your thoughts, search information online or discuss it with your partner or supportive friends/family members.
- Try some relaxation techniques such as breathing exercises or meditation.
- Avoid pregnancy tests – the chance of getting a positive result before your period is late is very slim.

# SUPPORT ORGANISATIONS

## AUSTRALIA

### AccessAustralia

[www.access.org.au](http://www.access.org.au)

Ph: (02) 9737 0158; Email: [info@access.org.au](mailto:info@access.org.au)

AccessAustralia is a national organisation, which provides numerous services and resources for people having difficulty conceiving. Its services include:

- fact sheets, newsletters and personal stories
- putting you in contact by phone or email with others sharing a similar infertility experience
- a register of infertility self-help groups
- listing of infertility clinics accredited by the Reproductive Technology Accreditation Committee (RTAC)
- listing of professional infertility counsellors across Australia
- lobbying governments for equal access to affordable, quality assisted conception treatment.

### Endometriosis Association (Qld)

[www.qendo.org.au](http://www.qendo.org.au)

Ph: (07) 3321 4408; Email: [info@qendo.org.au](mailto:info@qendo.org.au)

This association provides information and news relating to the latest research and treatments for endometriosis.

### Polycystic Ovarian Syndrome

#### Association of Australia (POSAA)

[www.posaa.asn.au](http://www.posaa.asn.au)

Ph: (02) 8850 9429; Email: [info@posaa.asn.au](mailto:info@posaa.asn.au)

POSAA is a 'self-help' association for women with polycystic ovary (ovarian) syndrome (PCOS) and those who suspect they have it. Its website includes information on upcoming workshops, support groups and fact sheets.

### Donor Conception Support Group

<http://www.dcsq.org.au>

Ph: (02) 9793 9335; Email: [dcsupport@hotmail.com](mailto:dcsupport@hotmail.com)

The Donor Conception Support Group of Australia is a self funding organisation run by volunteers. Its members include those who are considering or using donor sperm, egg or embryo, those who already have children conceived on donor programmes, adult donor offspring and donors. It offers a newsletter, information nights, a library of books and articles and telephone support.

## SANDS

SANDS is a self-help support group comprised of parents who have experienced the death of a baby through miscarriage, stillbirth, or shortly after birth. It provides 24-hour telephone support, information resources, monthly support meetings, name-giving certificates and other support.

### Vic

[www.sandsvic.org.au](http://www.sandsvic.org.au)

Ph: (03) 9899 0218 (support) or (03) 9899 0217 (admin);

Email: [info@sandsvic.org.au](mailto:info@sandsvic.org.au)

### Qld

[www.sandsqld.com](http://www.sandsqld.com)

Ph: 1800 228 655 (support) or (07) 3254 3422;

Email: [admin@sandsqld.com](mailto:admin@sandsqld.com)

### SA

[www.sandssa.org](http://www.sandssa.org)

Ph: (08) 8277 0304; Email: [support@sandssa.org](mailto:support@sandssa.org)

(quick response) or [info@sandssa.org](mailto:info@sandssa.org) (general query)

## NEW ZEALAND

### FertilityNZ

[www.fertilitynz.org.nz](http://www.fertilitynz.org.nz)

Ph: 0800 333 306;

Email: [support@fertilitynz.org.nz](mailto:support@fertilitynz.org.nz)

FertilityNZ is New Zealand's national network for those seeking support, information and news on fertility problems. It provides various services including:

- regional support and contact groups
- general advice and contact service
- comprehensive information brochures
- a forum for confidential feedback on any issues or concerns
- a chatroom where you can seek on-line support from people in similar situations.

### Endometriosis New Zealand

[www.nzendo.co.nz/](http://www.nzendo.co.nz/)

Ph: 0800 733 277 (free phone support line);

Email: [nzendo@xtra.co.nz](mailto:nzendo@xtra.co.nz)

Endometriosis New Zealand promotes awareness of endometriosis, offers information, education and raises funds to support endometriosis related initiatives. It includes disease information specifically designed for teenagers, a support group network, regular seminars and workshops and a free phone support line.

### SANDS New Zealand

[www.sands.org.nz/home.html](http://www.sands.org.nz/home.html)

Ph: (06) 868 9514; Email: [contact@sands.org.nz](mailto:contact@sands.org.nz)

The website [www.fertility.com](http://www.fertility.com) has a wealth of information tailored to three different stages of a couple's journey. In addition to personal stories and frequently asked questions, it offers a number of practical 'tools' to assist you including an ovulation calculator, a questionnaire and advice on your most appropriate coping method.

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# Looking for more information?

Ask your doctor for a copy of the other booklets in the *Pathways to Parenthood* informational series.

- Your step by step guide to treating infertility
- Overcoming male infertility
- Endometriosis
- Polycystic ovary syndrome (PCOS)
- Ovulation induction (OI)
- Intrauterine insemination (IUI)
- *In vitro* fertilisation (IVF) & intra-cytoplasmic sperm injection (ICSI)
- Managing the stress of infertility