

YOUR STEP BY STEP GUIDE TO TREATING INFERTILITY

INSIDE:

- Recommended lifestyle changes
- Getting the timing right
- Testing and diagnosis
- 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. Your doctor will determine the best medications and course of action for you based on your requirements and conditions.

Prescription medicines have benefits and risks. Use all medications strictly as directed by your doctor and raise any questions or concerns with them before, during or after using prescribed medicines. If you experience side effects consult your doctor.

Full information regarding the medicines listed in this booklet, including how they are taken and side effects, is available from the Consumer Medicine Information (CMI) sheets. These can be found at the TGA website (www.tga.gov.au) for Australian residents and the Medsafe website (www.medsafe.govt.nz) for NZ residents.

Medication availability and funding criteria may differ between Australia and NZ.

CONTENTS

- Introduction** 2
- Step 1. Lifestyle changes** 3
 - Changing your habits – both partners 4
 - Lifestyle advice for women 6
 - Lifestyle advice for men 6
- Step 2. Timing** 7
 - Getting the timing right 7
 - Ovulation and the menstrual cycle 8
 - Home ovulation kits 10
 - Monitoring your basal body temperature 10
 - Changes in cervical mucus 10
- Step 3. Tests** 11
 - What are we testing for? 12
 - Initial examination 12
 - Preliminary testing 13
- Step 4. Diagnosis** 15
 - Causes of female infertility 16
 - Causes of male infertility 18
 - Unexplained infertility 19
- Step 5. Treatment** 20
 - Hormonal therapy – women 21
 - Hormonal therapy – men 24
 - Surgery 25
 - Assisted reproductive technology (ART) 25
- In conclusion** 29
- Support organisations** 30
- Glossary** 32

INTRODUCTION

Whether you have just started thinking about having a baby or have been trying to conceive for a while, the information available on improving your chances of becoming pregnant can often be confusing. This booklet has been developed to help you more easily understand the steps you will go through as you embark on your journey towards parenthood. By providing a step-by-step introduction to treating infertility, we hope to make the process less stressful and give you more control and confidence as you make your treatment decisions.

Everyone's experience is a little different depending on the underlying cause and chosen treatment but throughout each stage of your journey, please remember the following important points:

- You are not alone. Up to one in six couples worldwide have difficulty conceiving in the first 12 months of trying.¹
- For most people, the possibility of becoming pregnant is very good. More than 80% of couples become pregnant within the first 18 months.¹
- The reasons for infertility are many and varied.
- The treatments available to assist you in becoming pregnant are simple and effective.
- It is normal to feel strong and mixed emotions about what you are experiencing. However, the support you need is readily available.



As you start looking at your treatment options and progress through the steps outlined in this booklet, it is important for you to seek support from others, including your healthcare team. If you are part of a couple, you will need to talk together and often about how you are feeling and what you can do to support and help each other. If you are experiencing this journey without a partner, it is vitally important to have the support of friends, family members and relevant organisations (listed in the back of this booklet).

STEP 1. LIFESTYLE CHANGES

Your journey starts here



Most couples believe that once they stop using birth control, pregnancy will happen soon after. In reality, three out of five couples conceive within six months of trying, while one in six take between six months to a year. For the rest, conception takes more than a year.²

At least 15% of couples, at some point in their lives, will experience some degree of infertility with all of its accompanying feelings and frustrations.²

The term 'infertility' is generally used if a couple has not conceived after 12 months of regular unprotected intercourse.² 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. The need for treatment may be due in part to an increased number of women who, for career, financial or other reasons, are waiting until they are in their mid-30s before starting a family. Fertility decreases substantially after the age of 35.

If after a year of trying, you have had trouble conceiving, you should consult your local general practitioner (GP). If the female partner is over 35, it is best to seek medical help after six to nine months. Your doctor will probably want to run some tests (see page 11), discuss your lifestyle and refer you to a fertility specialist or fertility clinic.

CONSULTING YOUR DOCTOR

Regardless of your age, see your doctor if you have not fallen pregnant within six months if you have any of the following:

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

Changing your habits – both partners

Whether you are the male or female partner, you may like to check the following list of lifestyle habits, which can impact on your ability to conceive. Consider making some changes to maximise your chances of pregnancy.

☐ **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.³

For **men**, smoking may affect the development and quality of sperm, decrease the sperm count and reduce the volume of semen. In addition, there is a higher risk of impotence (erectile dysfunction).³

For information and advice on how to stop smoking, visit Quit Now at www.quitnow.gov.au or call the Quitline on 137 848.

☐ **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 males take a conservative approach to alcohol and that females abstain from drinking alcohol while trying to become pregnant.

The Australian guidelines to reduce health risks from drinking alcohol recommend that not drinking alcohol is the safest option for women planning a pregnancy.⁴ For **men**, the recommendation is to drink no more than two standard drinks on any day.⁴

- ☐ **Say no to drugs.** Illegal drugs such as cocaine and marijuana have been known to disrupt the menstrual cycle and ovulation process.^{5,6} Marijuana can also affect sperm count.^{5,6}
- ☐ **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.
- ☐ **Exercise with caution.** Exercising heavily every day may interfere with the regularity of the menstrual cycle. For men, prolonged cycling can cause damage to the groin and there is also the risk of damage to the testicles from contact sport.⁶
- ☐ **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.⁶
- ☐ **Mind your weight.** For both men and women, being overweight can cause fertility problems, especially if your weight is influenced by another condition such as diabetes, or for women, polycystic ovary syndrome (PCOS) – see page 17. For **women**, a body fat level just 10–15% above or below normal can contribute to infertility.⁷ 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.⁶

- ☐ **Avoid using lubricants.** They often contain chemicals that can damage or kill sperm.⁸
- ☐ **Avoid toxins.** Jobs involving heavy metals, such as lead or mercury, chemicals in pesticides, or chemicals used in certain manufacturing processes (such as painting or printing) may be harmful to both male and female fertility and damage sperm.⁶
- ☐ **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.

Lifestyle advice for women

- ❑ **Increase your intake of folic acid.** 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.⁹ Many foods, such as cereals and bread have added folic acid – look for this on packaging.⁹ If you have a family history of neural tube defects, or take epilepsy medications, you may need a higher dose of folic acid.



Lifestyle advice for men

- ❑ **Keep them cool.** Raising the temperature of the testicles can decrease sperm production and motility (the quality of movement).⁶ Testicles need to be at a slightly lower temperature than the rest of the body to maximise sperm production, so opt for boxers rather than briefs and avoid extremely hot baths, showers or spas.⁶

STEP 2. TIMING

Maximising your chances



To give yourselves the best chance of falling pregnant, it is recommended that you have unprotected intercourse every two to three days.¹ In addition, timing intercourse for when you are most fertile is another way to maximise the possibility of conceiving. There are several methods that can be used to determine the best timing. In order to better understand the following methods, it may help you to familiarise yourself with the menstrual cycle and the ovulation process explained on the next page.

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 three or four days prior to, and on 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/ or www.mydr.com.au/tools/OvulationCalculation

It is recommended that you have intercourse three or four days prior to, and on your ovulation day in order to maximise your likelihood of becoming pregnant.

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.⁶

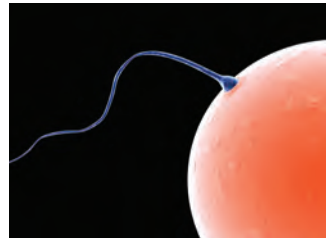
To be on the safe side, when you are close to ovulating, have intercourse at least every other day, if not every day.

Ovulation and the menstrual cycle

Ovulation is the development and release of an ovum (egg) from a woman's ovaries (the two small almond shaped sacs that contain a woman's eggs). Ovulation is the fertile period of a woman's menstrual cycle. The menstrual cycle refers to the maturation and release of an egg and to the preparation of the uterus (womb) 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 uterus is a pear-shaped organ where 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 inside 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. The two fallopian tubes are approximately 10 cm long and lead from the uterus, ending in finger-like projections called fimbriae. The fimbriae 'hover' over the ovaries but are not attached to them. The ovum (egg) remains in the fallopian tube for a few days. Fertilisation normally takes place in the fallopian tube.

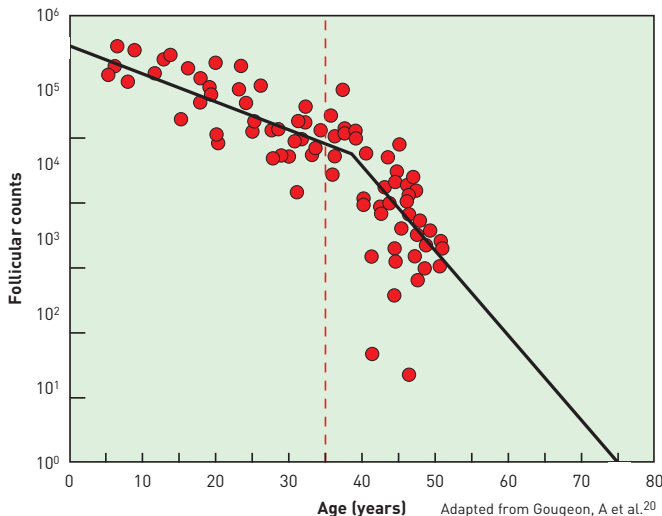


3. Luteal (Days 15–28). If the egg meets the sperm in the fallopian tube, conception may occur. The fertilised egg is swept through the tube toward the uterus where the embryo – as it is now called – will implant into the lining about six days after ovulation. It begins to produce a hormone called **human chorionic gonadotrophin (hCG)**, which tells the body it is pregnant. 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 cycle begins.

BORN WITH A LIFETIME'S SUPPLY OF EGGS

Females are born with about 400,000 immature eggs (oocytes) stored in their ovaries. Each cycle, one of your ovaries selects between 10 and 20 eggs to become possible candidates for release. However, only one egg is released each cycle.

There is a steep decline in the number of human ovarian follicles after age 35



Home ovulation kits

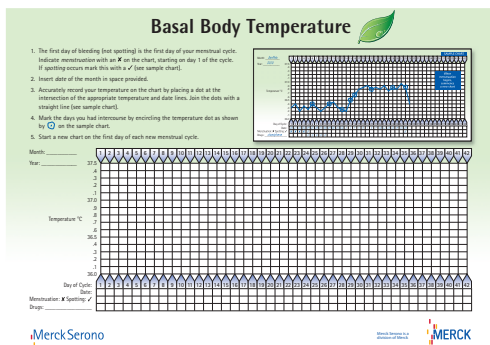
There are some different types of ovulation predictor kits available from your pharmacist, which can help you more accurately determine the times when you are most likely to become pregnant. One is a urine test that detects the amount of luteinising hormone (LH), which helps induce the release of an egg.¹⁰ Levels of LH peak in the urine 24 to 36 hours before an egg is released.¹⁰



Another type of kit involves testing and examining your saliva, which changes appearance into a distinctive 'fern-like' pattern (pictured) when your oestrogen hormone levels rise several days before ovulation. Oestrogen encourages the eggs to mature and helps prepare the uterus for pregnancy.

Monitoring your basal body temperature

Following ovulation, your temperature increases quite significantly and remains higher for the rest of the cycle. This is because your progesterone hormone level – which helps prepare the uterus for implantation and pregnancy – increases with ovulation. You will need to take your temperature every morning with a basal body temperature thermometer (available from pharmacies) as soon as you wake up and before you get out of bed, eat or drink anything. The thermometers typically come with graph paper so that you can chart your temperature. After two or three months, you will hopefully see a pattern (see example) and be able to determine your ovulation day.



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.

STEP 3. TESTS

Seeking medical help



If you have been trying to become pregnant for more than a year, or for six months if you are a woman over 35, it is now time to seek medical help. Your first visit should be to a general practitioner (GP) with whom you feel comfortable. 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 steps). Sometimes your GP may run some preliminary tests for both male and female partners (as outlined on page 13) or they will refer you to a gynaecologist who specialises in reproductive health. Alternatively your doctor may refer you to a fertility clinic. Please note that many of these clinics run regular information evenings or seminars, which you can attend free of charge to find out more about their services and the treatment options.

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. Concerns not shared openly by partners should be discussed privately with the doctor. The next step may be an examination of both partners.

How might you feel?

Experiencing a range of emotions

In addition to coping with the unreasonable social stigma attached to infertility, it is natural to feel a range of emotions when pregnancy doesn't happen quickly or easily. Feelings of anger, embarrassment, inadequacy, guilt and shame are all extremely common. However, this shouldn't stop you from seeking medical help. While the causes are many and varied (see page 15), the treatment options are not as daunting as most people believe and many modern treatments are simple, non-invasive and very effective.

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 for the egg to be fertilised.
5. The ability of the female body to allow for implantation of an embryo, and to maintain and nourish that embryo.

Initial examination

Female partner

Examination of the woman includes a general physical, including a breast and pelvic examination. If you haven't had one 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).



Male partner

The male examination may consist of a general physical and a more detailed examination of the testes, penis and scrotum. The doctor will also seek to determine the presence of a varicocele (swollen varicose vein of the spermatic cord), as this is a common infertility problem.

Preliminary testing

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 and endometriosis (see page 17)
- the thickness of the uterine lining and how well the uterus is responding to hormone production
- the size of your ovaries and the number of follicles present in your ovaries.

Semen analysis (also called a 'sperm count') – Semen analysis is usually performed on a sample collected following a period of at least 36 to 72 hours without sex. It can be produced at your clinic or doctor's surgery or taken from home (as long as it arrives within one hour of production). The test gives a measurement of the number, movement (motility), size and shape of the sperm, and the volume of the ejaculation. The presence of antibodies, which may cause the sperm to clump or lose their progressive motion, will also be tested. Sperm samples may be characterised as potentially fertile, sub-fertile or infertile (azoospermia).

LOW SPERM COUNT AND FERTILITY

Despite a low sperm count, many men with high-quality sperm (viable and highly motile) may still be fertile.

Preliminary testing – Semen analysis (cont.)

The table below lists the World Health Organisation (WHO) criteria for normal semen analysis, which may be helpful when your doctor discusses your results.

Normal semen analysis WHO 2010 ¹¹	
Volume of semen	≥ 1.5 mL
Sperm concentration	≥ 15 x 10 ⁶ / mL
Total motility (PR & NP)	≥ 40%
Morphological normal sperm	≥ 4%

PR: Progressive motility, NP: Non-progressive motility

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.

A special ultrasound called a HyCoSy (hystero-salpingo contrast sonography) may also be arranged to check that there are no blockages in your fallopian tubes. It is used less commonly now due to improved ultrasound techniques.

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

Depending on your medical condition, your doctor may choose to do other procedures or tests. Ask them for more information.

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.¹

STEP 4. DIAGNOSIS

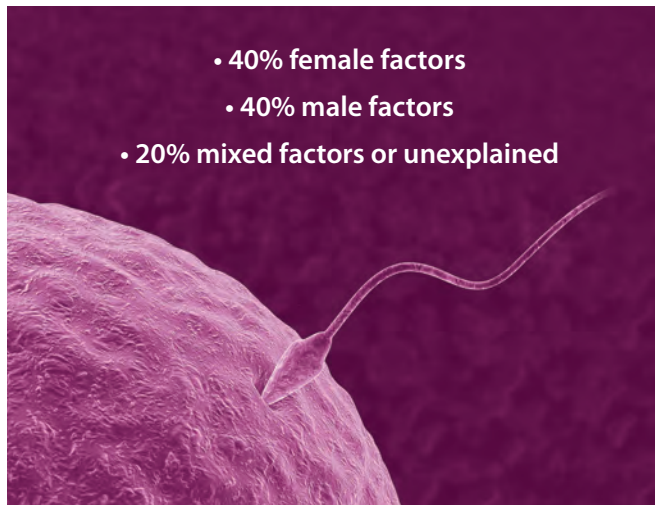
Establishing the cause



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 with medication, or recommend a procedure that may assist you in becoming pregnant. 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.^{2,12} In about 10% of cases, fertility

problems are linked to both partners. The remaining 10% of infertility is unexplained, even after exhaustive testing.^{12,13}



A woman's age is a definite factor in how easily they will become pregnant. A woman is most fertile between the ages of 15 and 24.¹⁴ There is a decrease in fertility, although not significant, for women aged between 30 to 35.¹⁵ However, between 35 and 40, the fertility rate drops by at least 30%.¹⁵

Causes of female infertility

These 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 that is capable of being fertilised by a healthy sperm. However, if your period is irregular or absent then your production and release of eggs may be affected. About 25% of women who are infertile will have problems with ovulation.^{12,18} Infrequent periods (oligomenorrhoea) or the absence of periods (amenorrhoea) are most often caused by a deficiency in one of the controlling hormones. These can be successfully treated with medication. 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.

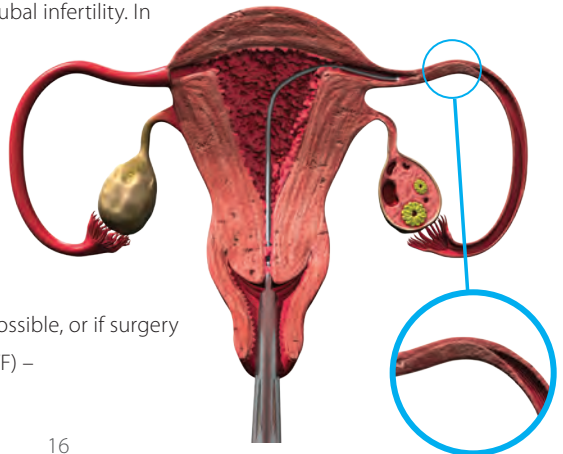
Blocked fallopian tubes

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, development of a proper embryo, 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 in 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 26 – may be the solution.



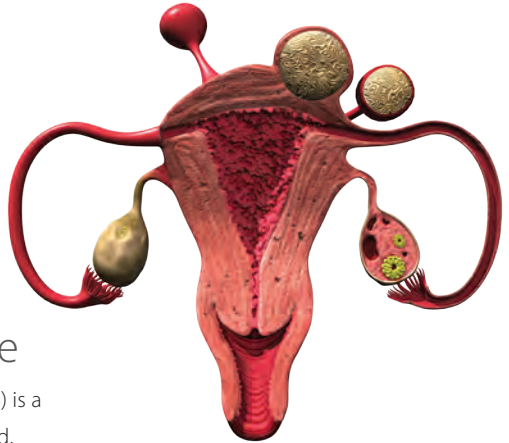
Endometriosis

This is a major cause of infertility and occurs when the 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 cycle, the tissue breaks down and bleeds, causing pain before and after your period, scarring and adhesions (organs sticking together).

A laparoscopy (see page 14) 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 50.¹⁶ A fibroid is a non-cancerous growth of the muscle in the uterus, as illustrated. 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.

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.

Causes of male infertility

For men the most common causes of infertility are:

- sperm problems
- functional problems
- hormonal problems.

Sperm problems

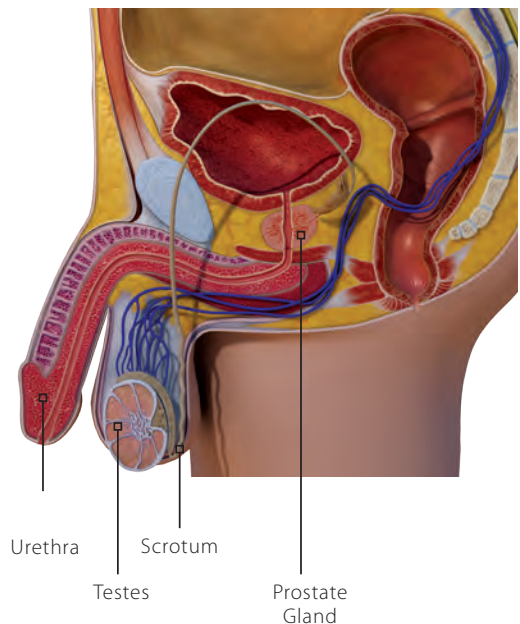
Absent sperm (azoospermia) – The testes may not be producing sperm due to genetic defects, undescended testes, physical injury to the testes or mumps occurring after puberty. This condition can also be a result of an obstruction or previous vasectomy (surgery for sterilisation).

Low sperm count (oligospermia) –

Common causes include:

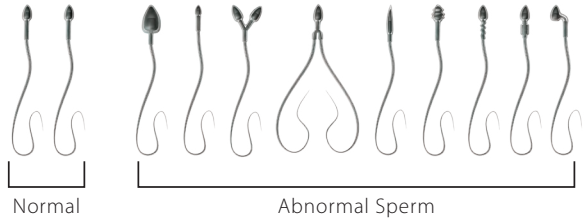
- hormonal problems
- obstruction
- side effects of medications
- environmental factors (e.g. smoking, excessive alcohol consumption, frequent hot baths or saunas)
- infection.

Poor sperm motility (ability to move) – A healthy sperm has a lashing tail that helps it swim through the woman's reproductive system. Sperm with poor motility may swim feebly or not at all.



Abnormally shaped sperm –

A healthy sperm is shaped like a streamlined tadpole. Those shaped differently may have problems penetrating the surface of the woman's egg.



About 40% of male infertility relates to the condition varicocele (swollen varicose veins of the scrotum), which affects sperm quality and quantity.¹²

While the quality of the sperm cannot be improved, modern techniques can increase the odds of conception by helping the existing quality sperm to fertilise (see pages 25–28 for more information).

Functional problems

Functional problems can cause or be due to the following:

- impotence – inability to maintain an erection sufficient for sexual intercourse
- failure to ejaculate
- presence of other diseases such as diabetes and multiple sclerosis
- antibodies – the man's immune system makes antibodies that hinder the activity of the sperm.

Hormonal problems

Although not a common cause, sometimes the pituitary gland, located at the base of the brain, does not send the right messages to the testes. This results in low testosterone levels, which means that sperm are not produced.

Unexplained infertility

Unexplained infertility (idiopathic) is defined as not being able to conceive after one year, even though the cycle is normal, semen is normal, the results of internal examinations 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.¹⁷ Emotionally, this is the most frustrating and stressful diagnosis of all because there is no cause or management plan on which to focus. 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 adoption or living child-free.

STEP 5 – TREATMENT

Starting medication or therapy



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. You and your partner should prepare yourselves for this (see page 24 for some suggested coping methods).

The treatment of female infertility can be categorised into three defined stages. These take the form of consecutive stages. In many cases the first stage 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.¹⁸

Hormonal therapy – women

Oral contraceptive pill

When taken in combination with some of the medications listed below, 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 for the female partner, medication that will help her 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. Clomiphene citrate comes in an oral tablet form and is prescribed for women whose ovaries are capable of functioning but who need a little assistance.

At the beginning of your menstrual cycle, the hypothalamus (part of the brain that controls a large number of bodily functions) releases a hormone called gonadotrophin-releasing hormone (GnRH). 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 follicle stimulating hormone (FSH) and luteinising hormone (LH). These two hormones promote growth of the fluid-filled sacs (follicles) containing the eggs. If you do not fall pregnant after three ovulatory responses to treatment, further treatment is not usually recommended.¹⁹ Your doctor will advise you on how many courses you should take. If clomiphene citrate is ineffective for you, medications containing FSH and LH, i.e. gonadotrophins (see next page) may be prescribed.

Gonadotrophins

If clomiphene citrate does not work, the next stage of treatment is usually to start administering a category of medication called gonadotrophins – synthetic forms of FSH, LH and hCG found naturally in humans. Whereas clomiphene citrate acts to stimulate the release of gonadotrophin-releasing hormone, gonadotrophins act directly on the ovary, promoting follicular development. These medications are taken by a self-administered injection under the skin, usually via an easy to use pen-like device.

The injection of high levels of FSH (and sometimes also LH) stimulates your ovaries to develop multiple follicles and eggs.

There are a variety of different treatment medications that fall under the category of gonadotrophins.

Follicle stimulating hormone (FSH) stimulates development of the fluid-filled sacs (follicles) containing the eggs.

Luteinising hormone (LH) is sometimes used together with FSH to stimulate the development of follicles.

Human chorionic gonadotrophin (hCG) causes the final maturation and release of an egg.

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, it allows for more reliable timing of egg collection and usually an increased number of eggs being available for *in vitro* fertilisation (IVF). It includes the medications nafarelin acetate and leuporelin acetate. Nafarelin acetate is given by nasal spray morning and night and leuporelin acetate is given by a daily subcutaneous (under the skin) injection.

GnRH antagonists

A newer class of injectable medication, GnRH antagonists – cetrorelix acetate and ganirelix acetate – 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. As with GnRH agonists, using this medication allows the continued stimulation of follicle growth whilst preventing the risk of premature egg release (ovulation) prior to egg collection.

Progesterone

Progesterone may be prescribed in the form of pessaries or as a vaginal 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.

BE AWARE OF OVARIAN HYPERSTIMULATION SYNDROME

Ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening medical condition which may occur 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 difficulties or problems with urinating. Contact a member of your healthcare team immediately if you believe you have any of these symptoms.



What can help?

Dealing with the demands of treatment

While taking hormonal medications, you will be closely monitored so you need to prepare yourself for frequent office visits, regular blood tests and pelvic ultrasounds. It is common to feel exhausted by the process, uncertain about the medications, as well as frustrated by the demands of therapy and the time that it takes out of your life. The following coping strategies may help:

- Read as much as you can about infertility, its causes and medications so that you feel more in control of your treatment.
- Don't dwell on the short-term ups and downs of treatment.
- Seek emotional support from a counsellor or support group.
- Communicate fears and emotions to your partner regularly.
- Acknowledge that periods of depression and anxiety may happen.
- Cut down on stressful activities and commitments.
- Allow yourself private time.
- Support one another, but understand that at times this will be difficult.
- Try sharing your problem with supportive friends or family members.

Please remember that you are not to blame for any apparent failure to respond to therapy. There is always hope, and success may be achieved after considerable effort. A successful resolution can make it all worthwhile. See contact details at the back of this booklet for information on some of the organisations that are available to help you.

Hormonal therapy – men

Hormonal imbalances that directly affect the development of sperm may be successfully treated by gonadotrophin therapy. Gonadotrophins are sometimes chosen to treat unexplained male infertility, as seen in the cases of oligozoospermia (when sperm count is abnormally low) or asthenospermia (when less than 40% of the sperm are motile). Other types of drug treatment include antibiotics to treat infertility resulting from infections.

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.

For males, a condition called varicocele, when the veins of the scrotum become enlarged, may also be fixed surgically by tying or clipping the veins.

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

Assisted reproductive technology (ART)

"If conception has not taken place after treatment with clomiphene citrate or gonadotrophins, 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)

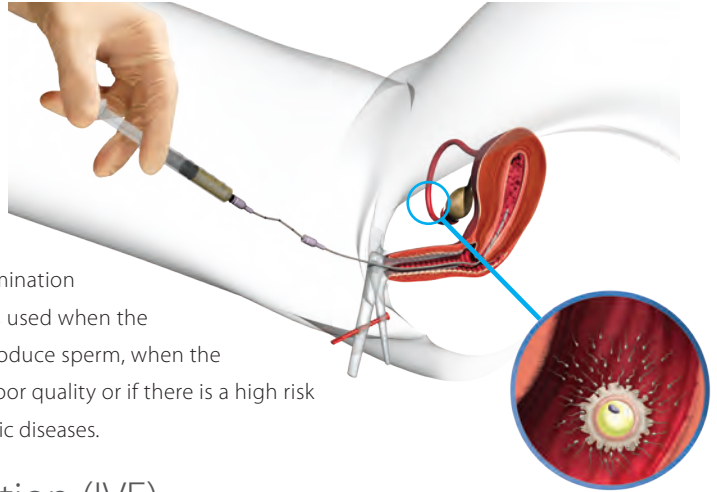
Artificial insemination (AI), is a procedure in which the sperm are placed directly into a woman's reproductive tract. A common AI procedure is **intrauterine insemination (IUI)** in which sperm are inserted directly into the uterus around the time of ovulation to assist their journey to the egg. The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

It is commonly used when there may be problems with semen volume, concentration or motility (movement). It can also be helpful when there are problems with the cervical mucus.

Artificial insemination (AI) & intrauterine insemination (IUI) (cont.)

After being 'washed' (the sperm are separated from the liquid part of the semen to remove hormones and other substances), sperm are 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). Insemination with donor sperm is used when the partner does not produce sperm, when the sperm are of very poor quality or if there is a high risk of passing on genetic diseases.



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 allow the sperm to fertilise the egg. The female partner usually takes hormonal medications to help stimulate the development of as many eggs as possible (as discussed on pages 21-23). If the eggs are successfully fertilised in the laboratory, 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. The medications also control the timing of ovulation to make it easier to retrieve the eggs.

Stage 2: Egg retrieval (Egg Pick Up [EPU])

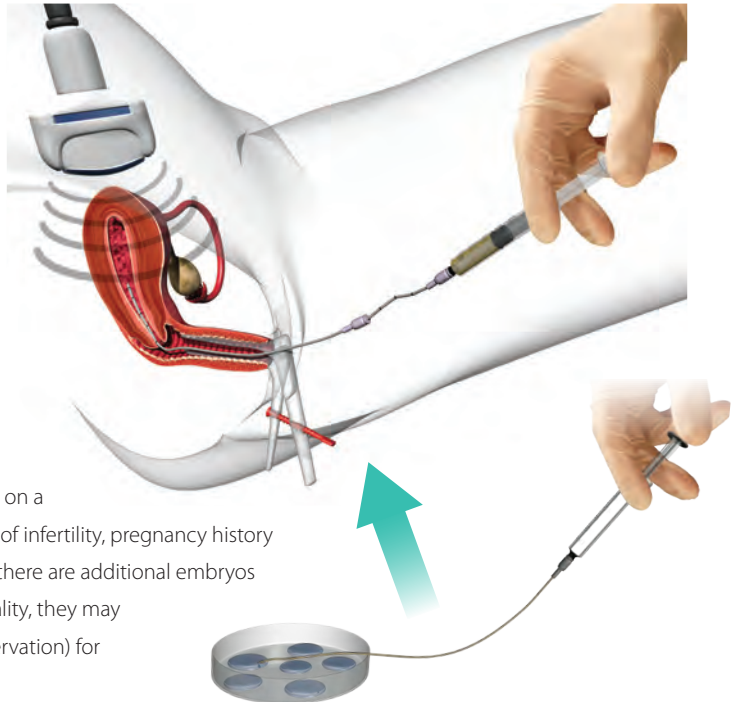
Once ovarian stimulation is complete and follicles have matured, your doctor will try to retrieve as many eggs as possible, although all the eggs may not be used in the current IVF cycle. Egg retrieval is performed under mild sedation, local anaesthesia or, in some cases, general anaesthesia. The mature 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 transfer

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. If there are additional embryos that are of good quality, they may be frozen (cryopreservation) for later use.



Intra-cytoplasmic sperm injection (ICSI)

ICSI is a procedure done under a microscope using micromanipulation devices. It involves injecting a single sperm into the egg. 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 for IVF.

Other ART

The table below describes some of the other less commonly used ART procedures.

Procedure	Description	When is it used?
MESA (Microsurgical epididymal sperm aspiration)	Sperm are retrieved directly from the epididymis (area in the testes where sperm mature and are stored). Fertilisation is then attempted with ICSI.	Severe male infertility. Absence of sperm in the ejaculate (azoospermia). Congenital abnormalities (e.g. absence of vas deferens).
TESE (Testicular sperm extraction)	Biopsy of the testes is performed in order to obtain sperm directly from testicular tissue. Fertilisation is then attempted with ICSI.	Severe male infertility. Absence of sperm in epididymis. Absence of epididymis.
GIFT (Gamete intra-fallopian transfer)	Follows same procedures as IVF except that fertilisation occurs in the body (<i>in vivo</i>). Sperm and eggs are placed directly into the fallopian tubes where fertilisation can occur.	Infertility due to endometriosis and cervical mucus disorders. Religious reasons. Unexplained infertility. Some cases of male infertility.
ZIFT (Zygote intra-fallopian transfer)	Same procedures as IVF except that fertilised eggs are placed in the fallopian tubes at a certain stage of embryo development (zygote).	Same as for GIFT.

IN CONCLUSION

We hope that this booklet has given you an insight into the steps involved in treating infertility. Although at times the journey towards parenthood may seem long, every year thousands of couples become parents using the procedures and medications described in this booklet.



SUPPORT ORGANISATIONS

AUSTRALIA

AccessAustralia

www.access.org.au

Ph: 1800 888 896; Email: 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.

Andrology Australia

www.andrologyaustralia.org

Ph: 1300 303 878;

Email: info@andrologyaustralia.org Andrology Australia provides factsheets, journal articles and the latest news on male reproductive health.

Donor Conception Support Group

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

Email: 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.

Endometriosis Care Centre of Australia

www.ecca.com.au

Formed by a group of health specialists, this organisation provides patient information and a state by state 'find a specialist' search engine on its website.

Endometriosis Australia

admin@endoaustralia.org

www.endometriosisaustralia.org/#!/links/c1bfb provides information on state contacts.

Endometriosis Australia endeavours to increase recognition of endometriosis, provide endometriosis education programs, and help fund endometriosis research. They strive to build strong relationships with existing endometriosis support networks throughout the country.

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

Ph: (03) 9899 0218 (support) or (03) 9899 0217 (admin); Email: info@sandsvic.org.au

Qld

www.sandsqld.com

Ph: 1300 072 637 (support) or (07) 3254 3422; Email: admin@sandsqld.com

SA

www.sandssa.org

Ph: 0417 681 642;

Email: support@sandssa.org (quick response) or info@sandssa.org (general query)

NEW ZEALAND

FertilityNZ

www.fertilitynz.org.nz

Ph: 0800 333 306;

Email: 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/

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

Email: info@nzendo.org.nz

Endometriosis New Zealand promotes awareness of endometriosis, provides 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

Ph: 0800 726 374;

Email: contact@sands.org.nz

The website 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.

GLOSSARY

Assisted reproductive technology (ART):

A general term referring to methods used to achieve pregnancy by artificial or partially artificial means.

Amenorrhoea: Absence of periods (menstruation).

Azoospermia: The complete absence of sperm during ejaculation.

Cervix: The lower and narrow end of the uterus which connects the uterus to the vagina.

Endometrium: Lining of the uterus, which thins and thickens during the menstrual cycle.

Embryo: Term used to describe the early stages of foetal growth from conception to the eighth week of pregnancy.

Follicle: Fluid-filled sac in the ovary that holds, nurtures and during ovulation releases the developing egg.

Follicle-stimulating hormone (FSH):

A hormone that stimulates the ovary to develop a follicle for ovulation in women and stimulates the production of sperm in the testicles of the male.

Fallopian tubes: A pair of tubes that link the ovaries to the uterus. It is also where fertilisation of the egg with the sperm occurs.

Gamete: Male or female reproductive cell – the sperm or egg.

Gonadotrophin releasing hormone

(GnRH): A hormone that regulates production and release of the FSH and LH. Can be administered to induce ovulation.

Human chorionic gonadotrophin (hCG):

A hormone secreted by the placenta, which stimulates ovarian secretion of oestrogen and progesterone.

Luteinising hormone (LH): A hormone that is made by the pituitary gland at the base of the brain, which helps with ovulation in women and sperm production in men.

Motility: The quality of movement of the sperm, especially the forward propulsion that is caused by the effective beating of the tail.

Oestrogen: A female hormone produced mainly by the ovaries from the onset of puberty until menopause.

Oligomenorrhoea: Infrequent periods.

Ovulation: Release of a mature egg from an ovarian follicle usually at about midpoint in the menstrual cycle.

Ovulation induction or stimulation: The use of hormonal medication to promote ovulation.

Ovaries: The two small almond shaped sacs that contain the woman's eggs.

Ovum: Egg ready to be released for ovulation.

Oocyte: Immature egg.

Progesterone: Hormone secreted by a special gland in the ovary after ovulation has occurred. It prepares the uterus for pregnancy and maintains the placenta during early pregnancy.

Uterus: Pear shaped organ (the womb) that provides a safe environment for implantation of the fertilised egg.

REFERENCES

- 1 Assisted Conception Taskforce (ACT). *Trying to have a baby. Your step-by-step guide to assisted conception*. Available online: http://www.assistedconception.net/resources/ACT_Ratgeber.pdf downloaded 20/12/13
- 2 AccessAustralia. *Have you been trying to get pregnant fact sheet*. Available online: <http://www.access.org.au/wp-content/uploads/2010/01/14.pdf> downloaded 20/12/13
- 3 Smoking and reproductive health. <http://www.quitnow.gov.au/internet/quitnow/publishing.nsf/Content/malereprod> Accessed 1/6/2015.
- 4 Australian Guidelines to reduce health risks from Drinking Alcohol, 2009, NHMRC. Available at: <http://www.nhmrc.gov.au/health-topics/alcohol-guidelines>
- 5 Prof. Robert Jansen. *Getting pregnant*. Allen & Unwin. 2003
- 6 Perkins S, Meyers-Thompson. *Infertility For Dummies*. Wiley Publishing Inc. 2007
- 7 Resolve – The National Infertility Association (US). *Risk Factors*. Available online <http://www.resolve.org/about-infertility/optimizing-fertility/risk-factors.html> downloaded 20/12/13
- 8 Andrology Australia. Male infertility: A child of my own. Booklet available from <https://www.andrologyaustralia.org/wp-content/uploads/Male-Infertility-Guide-WEB.pdf>. Downloaded 1/6/2015.
- 9 MyDr website. *Folic acid and your pregnancy*. Available online: www.mydr.com.au/babies-pregnancy/folic-acid-and-your-pregnancy downloaded 20/12/13
- 10 MyDr website. *Getting pregnant*. Available online: www.mydr.com.au/babies-pregnancy/getting-pregnant downloaded 20/12/13
- 11 WHO laboratory manual for the Examination and processing of human semen. 2010, Fifth Edition, World Health Organisation
- 12 American Society of Reproductive Medicine Fact Sheets and Info Booklets. See Infertility: An Overview and Varicocele. Available online: https://www.asrm.org/FACTSHEET_Varicocele/ downloaded 1/6/2015.
- 13 Cardone BRS, Harrington N. *Treatment of the Infertile Couple in My OB/GYN Practice: Is it Feasible?* Norwell, MA: Seroon Symposia, USA; 1992.
- 14 Cohen BM. *Management of Infertility: A Clinician's Manual*. 2nd ed. Durant OK: Essential Medical Information Systems; 1991.
- 15 AccessAustralia. *Pregnancy and the Older Women* fact sheet. Available online: <http://www.access.org.au/wp-content/uploads/2010/01/35.pdf> downloaded 23/12/13
- 16 Medical Observer. *Facts on Fibroids* by Dr Elizabeth Farrell. Available online: <http://www.medicalobserver.com.au/news/facts-on-fibroids> downloaded 1/6/2015
- 17 Aboulghar M. et al. *Diagnosis and management of unexplained infertility: an update*. Obstet 2003; 267:177-188.
- 18 American Society of Reproductive Medicine. *Quick facts about infertility*. Available online: [http://www.asrm.org/detail.aspx?id=2322&terms=\(+%40Publish_To+Both+Sites+or+%40Publish_To+ASRM+Only+\)+and+85-90%25+of+infertility+treated+with+surgery+or+medication](http://www.asrm.org/detail.aspx?id=2322&terms=(+%40Publish_To+Both+Sites+or+%40Publish_To+ASRM+Only+)+and+85-90%25+of+infertility+treated+with+surgery+or+medication) downloaded 23/12/13
- 19 Serophene Consumer Medicine Information. Available from www.ebs.tga.gov.au
- 20 Gougeon A, Ecochard R, Thalabard JC. Age-related changes of the population of human ovarian follicles: increase in the disappearance rate of non-growing and early-growing follicles in aging women. *Biology of Reproduction* 1994; 50:653-663.



Looking for more information?

Other booklets in the *Pathways to Parenthood* series are available at merckserono.fertilityportal.com.au:

- Overcoming male infertility
- Female infertility & assisted reproductive technology (ART)
- 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