FEMALE INFERTILITY & ASSISTED REPRODUCTIVE TECHNOLOGY (ART)

INSIDE:

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

PART OF THE PATHWAYS TO PARENTHOOD BOOKLET SERIES

ABOUT THIS BOOKLET

Merck Healthcare 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 circumstances.

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

Medication availability and funding criteria may differ between Australia and New Zealand.

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INTRODUCTION[1-4]

If you are concerned about your fertility, the first thing to understand is that you are not alone. Up to one in six couples have difficulty conceiving.[1]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.[2]

Scientific advances over the past three decades have helped millions overcome problems with fertility. Assisted reproductive technologies (ART), including in vitro fertilisation (IVF) have assisted with more than 5 million children born worldwide[3]. 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 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.[4]

Scientific advances over the past three decades have helped millions of women overcome problems with fertility.[3]

WHAT IS INFERTILITY?[1,3,5,6]

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. The term 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.[3,5] There are two types of infertility. The first is known as primary infertility and this is where a couple has never achieved a pregnancy. Secondary infertility is where a couple is unable to conceive after they have already had a pregnancy or child.[3]

The causes of infertility are many and varied, with one in six couples have trouble conceiving. In one-third of of cases the issue is attributable to the female, while one-third of cases trace the issue back to the male. The remaining one-third of cases are caused by both male and female reproductive issues, or by unknown factors.[1,5]

Couples who have difficulty conceiving may have a specific medical condition hindering the woman's ability to become pregnant.[6] If after a year of trying, you have had trouble conceiving, you should consult your 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 18), discuss your lifestyle and refer you to a fertility specialist or fertility clinic.[1]

SIGNS AND SYMPTOMS OF FEMALE INFERTILITY[7]

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:[7]

- irregular or absent menstrual periods
- painful menstrual periods
- history of pelvic inflammatory disease
- history of endometriosis
- two or more miscarriages
- history of fertility problems
- difficulties with sexual intercourse
- history of conditions or treatments that may affect fertility, such as cancer treatments or surgery

The impact of age[5,7-10,11]

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 30's an 40's before starting a family.[5,8]

An age-related decline in the number of healthy eggs in a woman's ovaries is one of the reasons for infertility. 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.[8]

Women are born with about about 1 to 2 million eggs, which is reduced to about 3–500,000 at puberty and to about 25,000 eggs by the age of 37. By the fifth or sixth decade of life most women will have depleted the egg supply they were born with.[9] In contrast to women, male fertility can persist into old age, even though sperm counts and semen quality start to deteriorate in men from their late 40's to mid 50's.[10]

As women grow older, other changes affecting fertility include:

- menstrual cycles can become irregular and shorter[11]
- the endometrium (lining of the womb) may become thinner and less able to nurture a fertilised egg[8]
- vaginal secretions can become less fluid and more hostile to sperm[11]
- some conditions can damage the reproductive organs as time passes, or worsen if not treated properly, including endometriosis and polycystic ovary syndrome.[7,9]

If a pregnancy occurs, older women are more likely to develop medical disorders including diabetes and high blood pressure.[8] 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.[8]

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

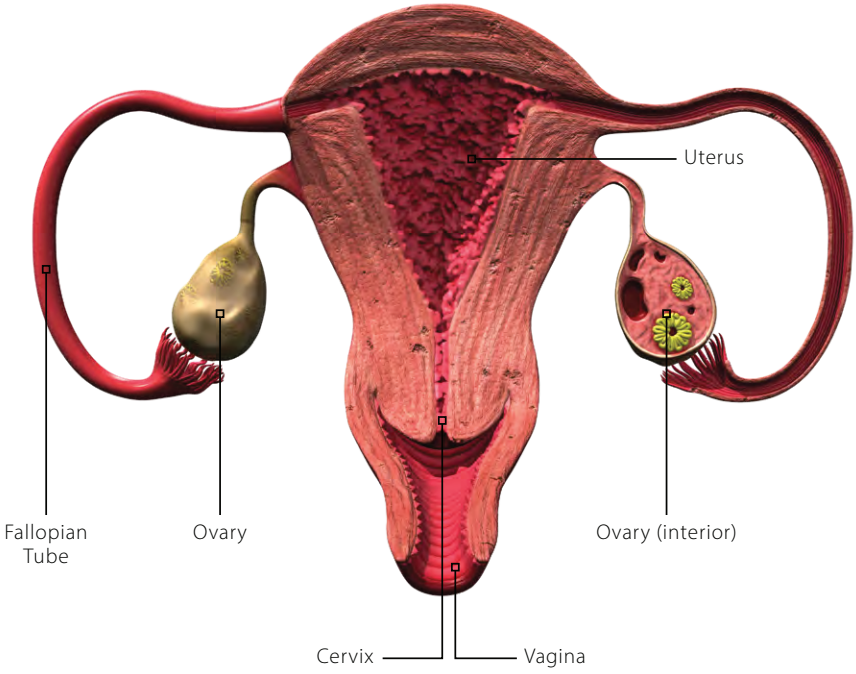
Despite the biological facts, many women aged over 35 do successfully become pregnant and have a baby without any complications. However, it is important to realise that age does matter in becoming pregnant, even if you do not look or feel your age. While keeping yourself fit with regular exercise and a healthy diet is important, your body knows exactly how old you are and there is no way to reverse the ageing of your ovaries and eggs.[7-9]

THE FEMALE REPRODUCTIVE SYSTEM[12]

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[12]

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; it is slowly replaced in the course of the next menstrual cycle.



Adapted from Mayo Clinic.[7]

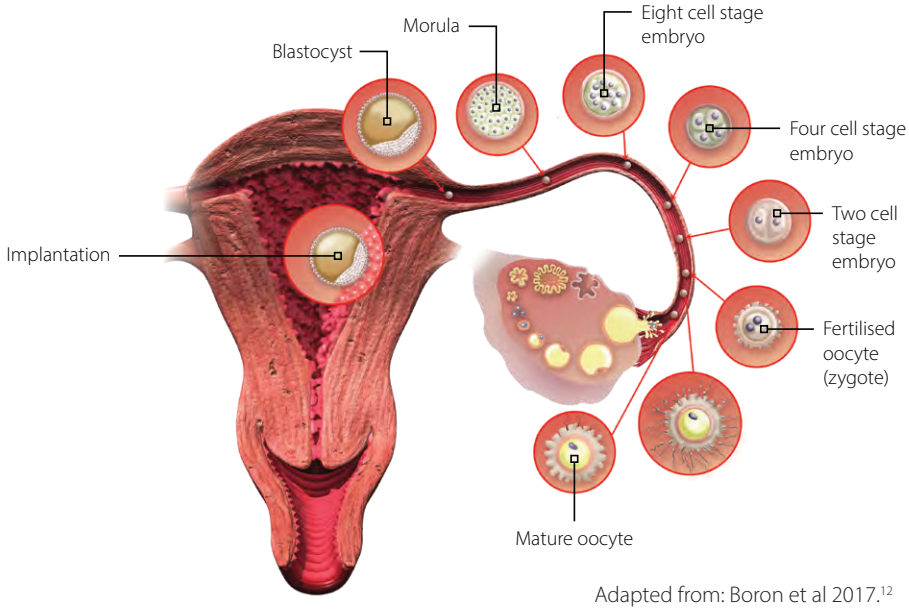
The ovaries[12]

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[12]

The fallopian tubes consist of two tubes 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.

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.



Adapted from: Boron et al 2017.[12]

Summary of the female reproductive system[12]

Structure	Description	Function
Uterus	Pear-shaped cavity containing endometrial tissue, and a lower portion called h cerix.	Site of embryo implantation and development. Provides muscular contractions to deliver the foetus during labour.
Ovaries	Two almond-shaped structures located on 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 fallopian 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 the opening to the vagina.

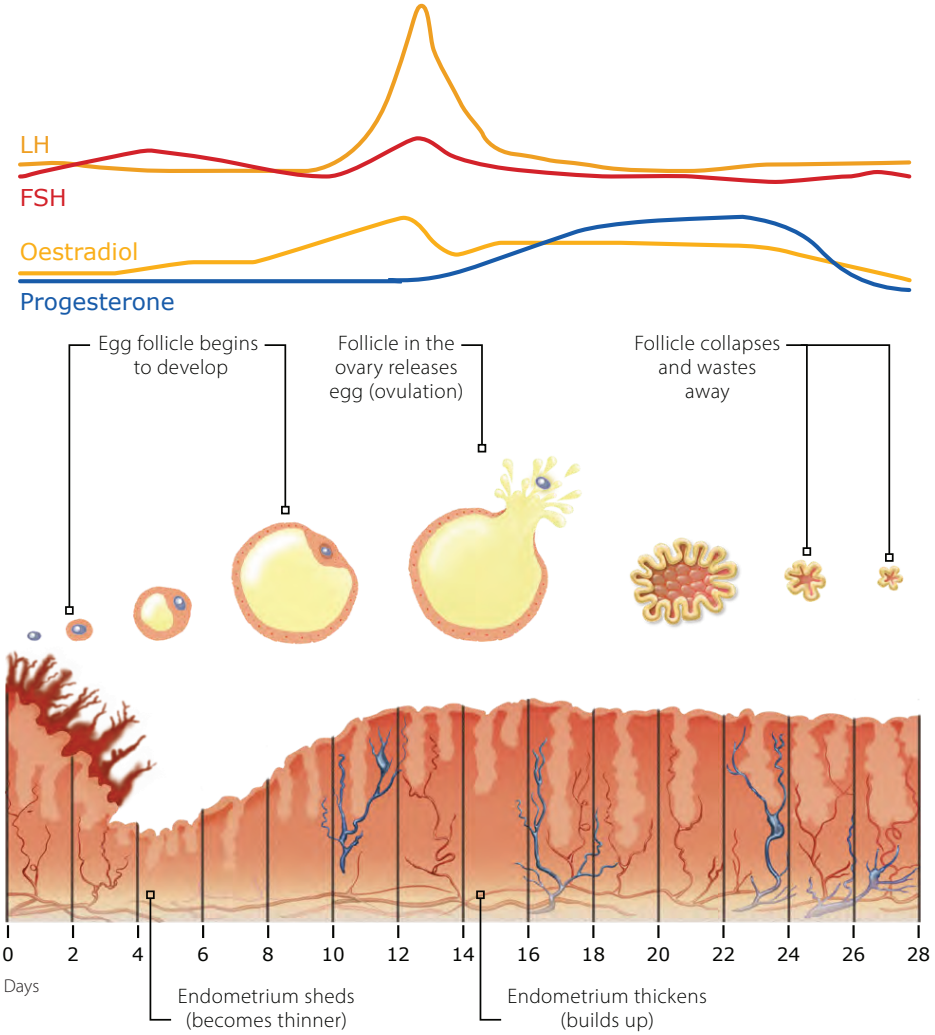
Ovulation and the menstrual cycle[12]

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 maturation and release of an egg and to the preparation of the uterus to receive and nurture an embryo. A typical cycle takes approximately 28 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 30 eggs to become possible candidates for release. The chosen eggs begin to mature in the ovary within their own sacs, called follicles. The developing follicle also secretes oestrogen, which helps develop watery mid cycle changes in cervical mucus that assist the passage of sperm into the uterus and helps thicken the endometrium in preparation for implantation.[12]

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 9.[12]

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 cycle begins.[12]

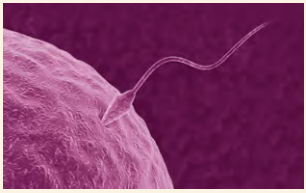


Adapted from: Boron et al 2017.[12]

Fertilisation

Stages of development[12,13]

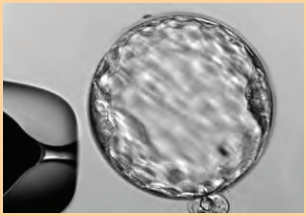
Zygote: A single sperm penetrates the mother's egg cell, and the resulting cell is called a zygote. The zygote contains all of the genetic information (DNA) necessary to become a child. Half of the genetic information comes from the mother's egg and half from the father's sperm. The zygote spends the 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.[12,13]



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.[12,13]

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.[12,13]

Embryo: The blastocyst reaches the uterus around Day 5, and implants into the uterine wall on about Day 6. 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).[12,13]



BOOSTING YOUR FERTILITY[2,7]

To give yourselves the best chance of becoming pregnant, it is recommended that you have unprotected intercourse every two to three days. 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.[2,7]

Lifestyle changes[2,7,14-20]

☐ **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.[7,14]
For men, smoking may affect the development and quality of sperm, and decrease the sperm count. In addition, there is a higher risk of impotence (erectile dysfunction).[14]

☐ **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.[7]
If you choose to drink, you should discuss this with your doctor.

☐ **Say no to drugs.** Illegal drugs such as cocaine and marijuana have been known to disrupt the menstrual cycle and ovulation process. Marijuana can also affect sperm count.[15]

☐ **Exercise with caution.** Whilst moderate regular exercise can improve fertility, exercising heavily every day may interfere with the regularity of the menstrual cycle. For men, prolonged heavy exercise may be detrimental for sperm quality and should be avoided while trying to concieve.[16]

☐ **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.[17]

☐ **Cut back on caffeine.** Whilst not clear, it is thought that caffeine may interfere with the ability to conceive.[18]

☐ **Mind your weight.** For both men and women, being overweight, or underweight can cause fertility problems. For women, excessive or very low body fat can contribute to infertility due to homonal imbalances affecting ovulation.[19] For overweight men, losing weight may help increase their sperm count.[7]
It's important to aim for a healthy weight range before attempting pregnancy.
For women with diabetes or polycystic ovarian syndrome (PCOS) - (see page 22), achieving a healthy weight may be challenging. Seeking the advice of a dietician with expertise and experience in managing this condition may be helpful.

☐ **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. Many foods, such as cereals and bread have added folic acid – look for this on packaging. If you have a family history of neural tube defects, or take epilepsy medications, you may need a higher dose of folic acid.[2,20]

☐ **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.[2]

Getting the timing right[2,21-23]

You are more likely to conceive during your 'fertile window'. The 'fertile window' refers to the timeframe during a woman's menstrual cycle when she can conceive. It is determined by the length of the menstrual cycle which can vary among women. This window typically spans the day when ovulation occurs, when an egg is released from the ovary, as well as the five days leading up to it. Having intercourse during this time offers the greatest likelihood of achieving pregnancy. 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 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.[2,21]

HOW OFTEN IS ENOUGH?

To give yourselves the best chance of having a baby you should be having unprotected vaginal intercourse approximately every 2 to 3 days.[22]

You have a much better chance of achieving pregnancy by having sexual relations during the female partner's fertile phase, at the time of or just prior to ovulation.[22]

Home ovulation kits[22]

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. Levels of LH peak in the urine 24 to 36 hours before an egg is released.[22]

Another type of kit involves testing and examining your saliva, which changes appearance when your oestrogen hormone levels rise several days before ovulation. Oestrogen encourages the eggs to mature and helps prepare the uterus for pregnancy.
These kits may not be accurate for some women, such as those who may have a high level of LH due to polycystic ovaries, or ovarian failure. Ask your doctor for more information.[22]

Monitoring your basal body temperature[22,23]

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.[22,23]

WHERE'S THE FUN?[13]

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. 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.[13]

Changes in cervical mucus[22,23]

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[24]

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.

DIAGNOSING FEMALE INFERTILITY[1,4]

When you decide to seek medical advice about trying to conceive, your first visit should be to a 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 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.[1,4]

What are we testing for?[4,25]

When evaluating a couple, a specialist is trying to determine which of the following essential conditions required for pregnancy may not be functioning correctly.
Your doctor will check for:[4,25]

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.

Common tests[1,4,13]

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. [1,13]

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:[13]

- anything that may be affecting your cycles, such as the presence of ovarian cysts or endometriosis (see page 21)
- 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.[4]

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.[4]

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.[13]

CAUSES OF FEMALE INFERTILITY[7]

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:[7]

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

Problems with ovulation[1,7,]

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. The most common cause of female infertility is the result of ovulation disorders.[1] Infrequent periods or the absence of periods are most often caused by deficiency in one of the controlling hormones. 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.[7]

Blocked fallopian tubes[13,25,27]

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).[26]

Tubal infertility can sometimes be treated by surgery[27], but if this is not possible, or if surgery is unsuccessful, in vitro fertilisation (IVF) – see page 30 – may be the solution.

Endometriosis[13,25]

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 cycle, the tissue breaks down and bleeds, causing pain before and after your period, scarring and adhesions (organs sticking together).[13,25]

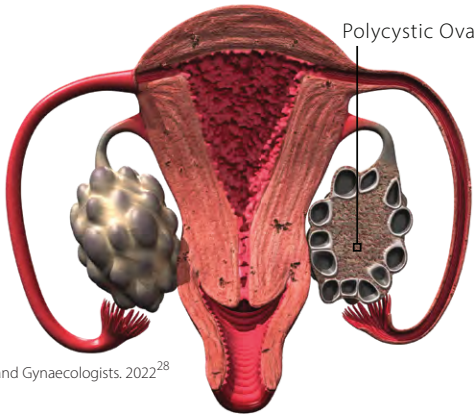
A laparoscopy (see page 19) is used to identify endometriosis and there are several forms of treatment available, involving both medications and surgery.[27]

Fibroids[26]

The uterus is commonly affected by benign growths such as polyps or tumors, including fibroids or myomas. These may require treatment if they are causing problems with fertility.[26]

Polycystic ovary syndrome[28]

A common hormonal disorder affecting many women between puberty and menopause. Symptoms are variable, but can include hormonal imbalance causing excess hair growth, acne, lack of regular ovulation or a characteristic 'polycystic' appearance of the ovaries on ultrasound.[28]



Adapted from: Royal College of Obstetricians and Gynaecologists. 2022[28]

Cervical problems[26]

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.[26]

Unexplained infertility[26]

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.[26] Emotionally, this may be the most frustrating and stressful diagnosis of all because there is no cause to focus on. Depending on a woman's age, couples might continue to try to fall pregnant naturally, discuss assisted reproductive technologies with their Doctor or consider other options, such as adoption or living child-free.

For more detailed information on endometriosis or polycystic ovary syndrome, access *Pathways to Parenthood* booklets on these topics at www.fertilityportal.com.au/merck

How might you feel?[6,27]

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:[6]

- 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:[27]

- 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[25,27]

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.[25]

The treatment of female infertility can take the form of:[27]

1. **Hormonal therapy**
2. **Surgical procedures**
3. **ART**

HORMONAL THERAPY [27,29]

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.[29]

Fertility medications that regulate or stimulate ovulation are the main treatment for women with ovulation disorders who are trying to conceive. These drugs work like natural hormones to trigger ovulation. They are also used in women who already ovulate to stimulate the production of a better egg or additional eggs[27].

Taking fertility medications[13]

Clomiphene citrate. Taken orally, this medication induces ovulation by prompting the pituitary gland to produce increased amounts of FSH and LH. These hormones then stimulate the growth of an ovarian follicle that contains an egg.[13]

Gonadotrophins: (also spelt as 'gonadotropins') act directly on the ovary, promoting follicular development. Gonadotrophins are available as a synthetic form of the naturally occurring hormones. They are given as an injection under the skin (subcutaneous), of the tummy or thigh. [13]

Follicle stimulating hormone (FSH): Given as an injection to stimulate the ovary to develop more than one egg at a time.[13]

Luteinising hormone (LH): Given as an injection for the treatment of women who have been shown to produce very low levels of some of the hormones involved in the natural reproductive cycle. It is used together with an FSH to help develop more than one egg at a time.[13]

Human chorionic gonadotrophin (hCG): Given as an injection one to two days after the last dose of FSH, it helps the egg/s mature and then release.[13]

Medications to prevent premature ovulation[13]

Gonadotrophin-releasing hormone (GnRH) antagonists: given to prevent premature ovulation (egg release). It drops the levels of FSH and LH without causing an increase in these levels (as do the GnRH agonists). This means they can be given for a shorter period of time.[13]

Gonadotrophin-releasing hormone (GnRH) agonists: given to prevent premature ovulation (egg release). 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 to control premature ovulation (egg release).[13]

Medications to prepare the lining of your uterus[30]

Your doctor might recommend that you begin taking **progesterone supplements** in the form of injections or a vaginal suppository to make the lining of your uterus more receptive to implantation.[30]

The length of treatment varies for each patient. Your doctor will advise the length of your treatment and your dose. For further information about these medications, including side effects, please speak with your Fertility Clinic.

What can help?[30]

Getting used to injections

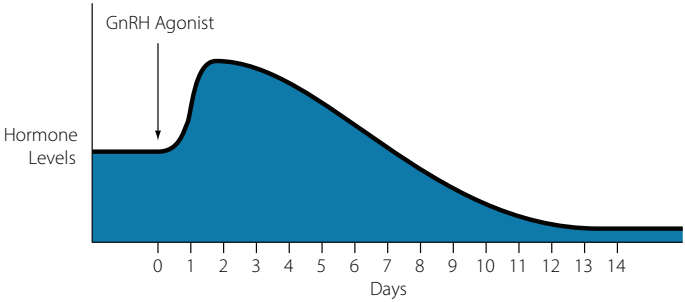
Some women find the thought of giving themselves a regular injection quite daunting but most people find it easy to do once they get used to it.

You will be sent home with clear step-by-step instructions and may be directed to websites that provide further information 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.[30]

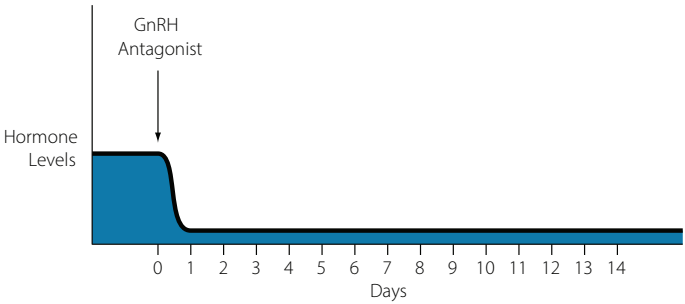
Treatment Protocols[31]

Your treatment protocol will usually include the medications you will be taking, instructions on how to take them, when you will need to have ultrasounds and blood tests and the procedures you need to follow throughout the cycle. There are a few standard protocols used and your doctor will choose the one that is right for you. The two most common ones are:

Long down regulation: During ovulation, the release of the egg is triggered by a sudden surge of the hormone LH at mid-cycle. During an IVF cycle, we do not want an LH surge to trigger an early release of these eggs. A **GnRH agonist** is used to temporarily turn off your own LH and FSH secretion in what is known as 'pituitary suppression' or 'down regulation'.



Antagonist treatment cycle: The length of **GnRH antagonist** administration is generally shorter than the GnRH agonist because it is usually given shortly after commencement of FSH injections, compared to GnRH agonist which has to start prior to FSH injections. With this protocol, a daily injection is used to suppress the LH surge, commencing five or six days after starting the FSH injections, or up to the day that sufficient follicles of adequate size are present (as measured by your doctor). In both cases, daily injections of FSH and GnRH antagonists are continued until the timing of egg pick up is determined.



BE AWARE OF OVARIAN HYPERSTIMULATION SYNDROME[25]

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 problems with breathing or urination. Contact a member of your healthcare team immediately if you believe you have any of these symptoms.[25]

Monitoring ovulation[13,29]

Throughout this first stage, your response to treatment will be carefully monitored to gain a clearer picture of what is happening to the follicles so the right timing and dose can be determined.

Ultrasound: Your clinic (doctor, nurse or sonographer) will often use one or more ultrasound scans to obtain an actual image of the ovaries and to regularly monitor follicle growth in the ovary beginning on or before day eight of the cycle. As follicles mature, they grow larger. Through ultrasound, your doctor can observe the effects of treatment on follicle growth and size, and decide when to give hCG to assist with egg release. Ultrasound may be performed abdominally or, more commonly, vaginally, using a slender probe a little thicker than a tampon. The procedure is usually painless.

Blood tests: Testing the blood every few days for oestrogen levels can monitor the response to treatment. Developing follicles secrete increasing amounts of the oestrogen hormones, in particular oestradiol (E2) – one of the main types of oestrogen. Together with ultrasound, this can help determine the best timing for giving the hCG injection to stimulate ovulation.

SURGERY[27]

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.

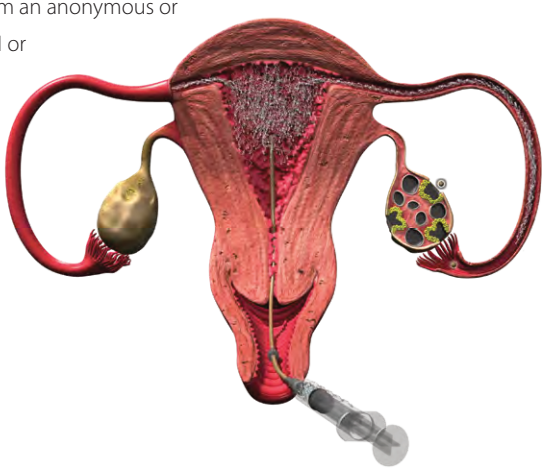
Microsurgery can be used to reverse sterilisation procedures (e.g. tubal ligation). These days, laparoscopic surgery, also called keyhole surgery, in which operations in the abdominal wall are performed through small incisions in the navel or abdominal wall, is usually preferred.

ASSISTED REPRODUCTIVE TECHNOLOGY (ART) [32,33]

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).**[32,33]

Artificial insemination & intrauterine insemination[7,32]

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 undergoing ovulation induction. This procedure 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 are separated from the liquid part of the semen to remove hormones and other substances – and then inserted into the cervix (neck of the uterus). When sperm quality is lower, sperm are inserted higher up the reproductive tract 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).[32]



Adapted from Mayo Clinc, 2023[7,32]

In vitro fertilisation[33]

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 laboratory, they are transferred into the woman's uterus. Ideally, one of the fertilised eggs will implant and develop into a pregnancy.

IVF is a four-stage process:[33]

Stage 1: Ovarian stimulation, monitoring, and ovulation triggering

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 as many eggs as is safe to do so (see page 24).[33]

Stage 2: Egg retrieval

Once ovarian stimulation is complete and follicles have matured, your doctor will try to retrieve as many eggs as possible. Egg retrieval (also known as egg pick up [EPU] or oocyte pick up [OPU]) is performed under light sedation, a 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.[33]

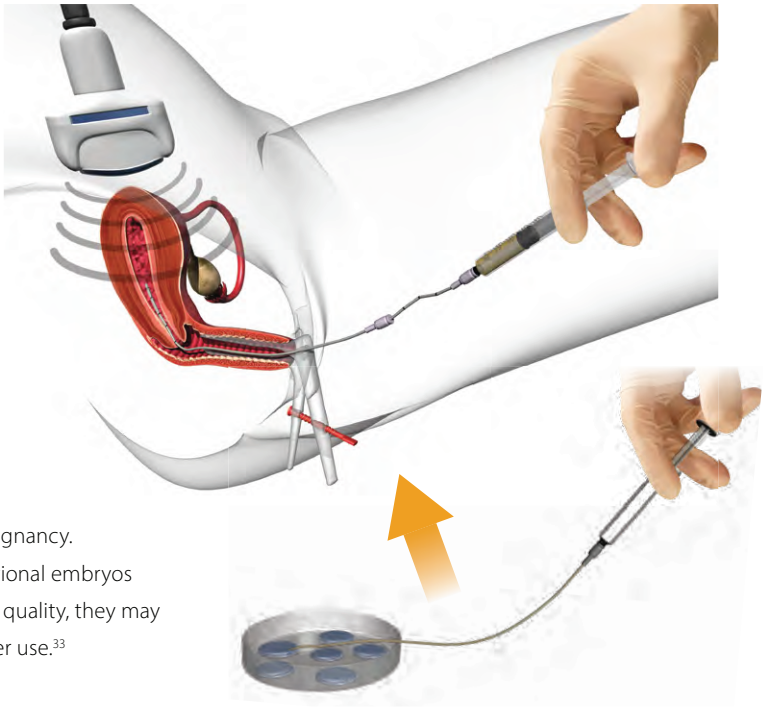
Stage 3: Fertilisation

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.[33]

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 2 (2–4 cell stage) and Day 5 (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 for later use.[33]



Adapted from American Society Reproductive Medicine, 2018[33]

Intra-cytoplasmic sperm injection (ICSI)[33]

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, as described previously for IVF.[33]

Using donor sperm and eggs[13,33]

Donor sperm

Insemination with donor sperm is used when the male 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. Donor sperm is used less frequently these days because of the improvement in techniques which can retrieve viable sperm, e.g. sperm extraction techniques.

The semen selected for a couple closely matches, as much as possible, the male partner's characteristics, e.g. eye and hair colour, height and build. 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.[13,33]

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 donor undergoes ovarian stimulation to help the recipient. A comprehensive medical and counselling process is undertaken prior to the initiation of such treatment cycles.[13,33]

CRYOPRESERVATION[25]

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. 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[25,29]

Success rates are influenced by a number of factors including (but not limited to):

- woman's age
- cause of infertility
- response to medications and treatment
- sperm quality
- number of embryos transferred
- transfer and use of cryopreserved (frozen) embryos.

You should discuss success rates with your doctor.

How might you feel?[34]

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 symptoms of pregnancy** – feeling pregnant does not always mean that you are. Some of the medications can have side effects that resemble symptoms of pregnancy
- **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** – breathing exercises or meditation can be helpful.
- **Avoid pregnancy tests** – the chance of getting a positive result before your period is late is very slim. The medications may also cause a false positive result.

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- 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)
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