



Module 1901

Female infertility: prevalence and management

From this pharmacy CPD module on female infertility you will learn about:

- The prevalence of female infertility
- The tests performed to try and identify the cause
- Reasons for female infertility and management options
- What pharmacy teams can do to support and advise this patient group

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According to the National Institute for health and Care Excellence (Nice), one in seven heterosexual couples will experience infertility – defined as failing to conceive within a year, despite having unprotected sex every two to three days. Although prevalence is not thought to be changing, increasing numbers of these couples are seeking medical help.

The reason for a couple not falling pregnant is not identified in around a quarter of cases, despite the myriad of tests that both partners undergo. However, in more than half of cases the issue lies with the woman, with the main causes being ovulatory disorders, tubal damage, and uterine, cervical or peritoneal issues.

Ovulatory disorders

Problems with ovulation affect around a quarter of couples accessing infertility support, and often present as menstrual disturbances. The World Health Organisation (WHO) sorts these into three categories:

Group I ovulation disorders

These result from hypothalamic-pituitary failure and are sometimes referred to as

hypogonadotrophic hypogonadism. Conditions in this category include:

- hypothalamic amenorrhoea – where



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menstruation stops for several months due to a problem involving the hypothalamus. This tends to develop as a consequence of excessive exercise or low body mass index (BMI)

- a congenital disorder such as Kallmann syndrome – a condition characterised by delayed or absent puberty.

If the patient has an absence of menstruation, either primary or secondary, then group I ovulation disorders are a likely cause. Individuals with group I ovulation disorders are also likely to have low oestrogen levels when tested.

Group II ovulation disorders

These account for the majority of women with ovulatory conditions. They involve problems with the hypothalamic-pituitary ovarian axis – the term given to the tandem action of the hypothalamus, pituitary gland and gonads. The most common disorder within this group is polycystic ovary

syndrome (PCOS).

Indicators that a group II ovulation issue is at play include: absent or infrequent periods; obesity; and symptoms of higher than usual androgen levels, such as acne and excessive body hair (hirsutism).

Group III ovulation disorders

These are the result of ovarian failure, and are characterised by: high gonadotrophin levels produced by the pituitary gland; hypogonadism (reduction or absence of hormone secretion or other physiological activity of the ovaries); low oestrogen; and accompanying symptoms, such as amenorrhoea.

Other ovulatory disorders

Some ovulatory disorders do not fall neatly into any of the above categories, usually because they stem from other diseases such as thyroid dysfunction, adrenal abnormalities, and chronic conditions such as cancer, AIDS, end-stage renal disease and uncontrolled diabetes.

Non-ovulatory causes

Tubal damage is identified as the cause of infertility for 20% of all couples who struggle to conceive, with uterine, cervical or peritoneal issues responsible for another 10%. Non-ovulatory causes may result from:

- a sexually transmitted infection, such as chlamydia or pelvic inflammatory disease
- endometriosis, which distorts the tubes as well as interfering with the fimbria on the fallopian tubes that play an important role in fertilisation
- fibroids distorting the uterine cavity and impairing implantation
- defects in or dysfunction of the cervical mucus
- previous pelvic or cervical surgery, as this brings with it the risk of scarring, damage and adhesions.

Other factors affecting fertility in women include defects in the gametes or embryo and lifestyle factors.

Medication and infertility

Medication can affect female fertility, with the most obvious culprits being contraceptives. Depending on the prescribed contraceptive and when it was last taken, normal fertility can return immediately after discontinuing a combined oral contraceptive, progestogen-only pill or removal of an intrauterine system, implant or device. However, there can be a delay of a few weeks after stopping the contraceptive patch or the vaginal ring, and it can take up to a year after the final progestogen injection.

Chemotherapy is also well recognised as having a detrimental effect on the chances of conceiving, as it can cause ovarian failure, while medicines that affect the cyclo-oxygenase pathway can impair fertility, as they can inhibit ovulation. Common examples of the latter include non-steroidal anti-inflammatory drugs (NSAIDs) and asthma medication, although the effect is reversible.

Spironolactone can cause menstrual irregularities that usually resume within two months of stopping treatment. In addition, antipsychotics, thyroid hormones, antidepressants and tranquillisers have all been shown to inhibit ovulation and therefore impair fertility.

Recreational drugs, such as cannabis and cocaine, have also been associated with reduced ovulatory and tubal function, while exposure to pesticides, metals (eg lead, cadmium and manganese), solvents and formaldehyde, can have detrimental effects.

How is female infertility assessed?

Testing is not the first step when assessing female fertility issues – unlike male infertility, which typically begins with the evaluation of a sperm sample (see Update module 1898 *Male infertility: causes and management*).

It's more important to establish the woman's gynaecological history. This includes:

- any previous pregnancies (whether carried to term or not)

- menstrual cycle and symptoms
- current and previous contraceptive use
- lifestyle factors (including medicine use and any previous surgeries).

A basic physical health check is also performed, to establish BMI and to exclude any obvious issues with an examination of the abdomen.

This process is used to inform which tests are then carried out. For example, if the woman has amenorrhoea (absence of menstruation), it makes sense to check her hormone levels (see Hormone tests, right).

Someone who has very heavy periods will typically require an ultrasound scan to assess the reproductive organs for conditions such as endometriosis, fibroids and cysts. Whereas an individual who is also showing signs of thyroid

dysfunction should be put forward for thyroid function tests.

Tubal tests may be carried out as a follow up to detect whether the fallopian tubes are damaged or blocked. This test takes place after a chlamydia screening.

Hysterosalpingography involves x-raying the uterus and fallopian tubes using dye or fluid as a contrast. The procedure can show if there is an obstruction or irregularity in any of the organs. It is quick and relatively painless, although period-like pains are quite common afterwards.

Laparoscopy (a surgical procedure on the abdomen) is more complex, requiring a general anaesthetic, but enables direct and therefore much more accurate assessment of the pelvic organs.

A hysteroscopy – a procedure used to examine the inside of the womb – examines the uterus in more detail. It may be carried out if fibroids are suspected or if the woman has experienced repeated miscarriages.

Hormone tests

Infertility investigations can involve the measurement of several hormones, each of which can rule out a different potential issue. For example:

- oestrogen can help determine the reason for amenorrhoea
- progesterone gives an indication of whether the woman is ovulating
- follicle stimulating hormone and luteinising hormone are used to measure pituitary functioning; if levels are high, primary ovarian failure is likely
- anti-mullerian hormone (a hormone secreted by cells in developing egg sacs) gives an indication of whether the ovary can produce egg cells capable of fertilisation
- testosterone can help determine if the woman has PCOS
- dehydroepiandrosterone sulphate (DHEA-S) is the building block for androgens and oestrogen and may be elevated in PCOS.

Management of female infertility

There are various medical and surgical options available to women who are experiencing infertility, if an underlying problem has been identified. Examples include: surgery to remove adhesions or endometrial deposits, or to correct any tubal damage; and medicines such as clomifene or metformin to treat PCOS that is interfering with ovulation.

However, for the many women for whom no cause for infertility is unearthed, assisted conception may be appropriate. There are several techniques employed in the UK:

Intrauterine insemination (IUI) and **intracervical insemination (ICI)** involve placing the sperm directly inside the uterus or cervix



Patients have an ultrasound scan to assess the reproductive organs for endometriosis, fibroids and cysts

respectively. It may be offered to couples who find it difficult to have sex; for example, due to physical disability, or if one partner has a condition that means help is needed pre-conception – such as sperm washing for someone who has HIV.

In-vitro fertilisation (IVF) is a multistage process involving:

- down-regulation of the ovaries using gonadotrophin-releasing hormone agonists. These are used in order to make the ovaries more sensitive to stimulation – this step may be preceded by a course of progestogen to make it easier to pinpoint the right time to embark on a cycle of IVF
- ovarian stimulation using gonadotrophins followed by egg extraction, so one or two can be fertilised using a sperm sample. However, ovarian hyperstimulation syndrome is a risk (see Ovarian

hyperstimulation syndrome, below)

- the resulting embryos are incubated for a few days, then placed back in the uterus.

Intracytoplasmic sperm injection (ICSI) involves injecting a single sperm into an egg during an IVF cycle. It is particularly suitable for men who have low numbers or poor-quality sperm in their semen sample, or who require sperm extraction, as well as for couples for whom IVF has not resulted in fertilisation.

Egg donation is an option for women with no ovaries or who do not produce eggs. This may be due to chemotherapy or radiotherapy, or for those concerned they may pass on a genetic condition to their child.

What can pharmacists and their staff do?

Community pharmacy teams may be the first people turned to for information and advice by individuals experiencing infertility. General tips

Ovarian hyperstimulation syndrome (OHSS)

Stimulating the ovaries using gonadotrophins can sometimes work too well, resulting in OHSS. Around a third of women undergoing IVF or a similar treatment will develop **mild OHSS**. These patients may experience symptoms such as:

- abdominal discomfort and bloating
- nausea
- diarrhoea.

Painkillers such as paracetamol or codeine, but not an NSAID, can be recommended. In addition, you should advise patients with OHSS that staying hydrated and taking it easy are usually all that is needed.

In **moderate OHSS**, the symptoms are likely to be worse; for example, pain rather than discomfort and vomiting rather than nausea. In **severe OHSS**, extreme dehydration and formation of blood clots can develop and it may be fatal. Urgent medical attention is therefore needed.

The risk of moderate or severe OHSS is greater in women who:

- have or have had PCOS
- are under 30 years old
- have experienced the condition in the past
- fall pregnant in the same IVF cycle as their symptoms, particularly if it is with twins or more.

According to the Royal College of Obstetricians and Gynaecologists, around 1% of women undergoing IVF or similar therapies develop moderate or severe OHSS. More information can be found on their website at [tinyurl.com/femaleinfertility1](https://www.rcog.org.uk/infertility).



Ensuring a patient maintains a healthy BMI is one method a pharmacist has of helping improve fertility

you can provide include:

- ensuring patients have a healthy BMI – women with PCOS who are overweight or obese are likely to be told to lose weight in the hope that doing so stimulates ovulation, or to improve the chances of the ovaries responding to medication, such as clomifene. However, being underweight is just as damaging, with low BMI associated with low oestrogen levels, which in turn impacts ovulation
- advising patients that stress and travel can have a negative effect; stress can affect the couple's relationship – often reducing libido – and travel can interrupt the frequency of intercourse – which makes conception less likely
- advising patients to avoid alcohol, smoking, caffeine and recreational drug use. Pharmacy teams can also advise on measures that women should take to try and

maximise the chance of a successful pregnancy, such as folic acid supplementation, and being up to date on 'smear' tests and vaccinations, such as rubella.

For more information

- Clinical Knowledge Summaries pull together a range of resources to provide information on conditions and their management. Infertility in both women and men is covered at cks.nice.org.uk/infertility
- The NHS website is a good source of information for patients and carers: [tinyurl.com/infertility11](https://www.nhs.uk/infertility11)
- Nice has published clinical guidelines on the assessment and treatment of female fertility problems: [nice.org.uk/guidance/cg156](https://www.nice.org.uk/guidance/cg156)
- Fertility Network UK is a charity set up to help those who want to become parents or have more children. Information can be accessed at [tinyurl.com/infertility14](https://www.fertilitynetworkuk.org/infertility14).

Female infertility – planned learning CPD

What are you planning to learn?

I want to learn more about female infertility, including its prevalence and the tests carried out to identify its causes. I also want to improve my knowledge of how female infertility is managed and what pharmacy teams can do to support and advise this patient group.

This learning is relevant to me because I recently dispensed a prescription for clomifene and realised I needed to revise and update my knowledge of the causes of female infertility and the treatments available for its management.

How are you planning to learn it?

- I plan to read the C+D Update article *Female infertility: prevalence and management* (at www.chemistanddruggist.co.uk/update-plus).
- I plan to find out more about female infertility on the NHS website at tinyurl.com/infertility11.
- I plan to improve my knowledge of intrauterine insemination (IUI) and in-vitro fertilisation (IVF) on the NHS website at tinyurl.com/infertility12 and tinyurl.com/infertility13 respectively.

Give an example of how this learning has benefited the people using your services

A young woman came into the pharmacy to purchase folic acid 400mcg tablets and then asked how long it should take to fall pregnant.

I discovered she had been trying to conceive for about 10 months and was able to signpost her to reliable sources of information and support, as well as provide lifestyle advice. She was reassured and said she would take on board the advice and information offered. Two months later she visited the pharmacy again and informed us she was now expecting a baby.

Take the 5-minute test online

1. The reason for a couple not falling pregnant is never identified in around a quarter of those seeking help.
True or false
2. Group I ovulation disorders result from ovarian failure.
True or false
3. The most common disorder within group III ovulation disorders is polycystic ovary syndrome.
True or false
4. Non-ovulatory causes of female infertility include tubal damage and uterine, cervical or peritoneal issues.
True or false
5. Normal fertility returns two to three months after discontinuing combined oral contraceptives or progestogen-only pills.
True or false
6. Medicines that can impair fertility include NSAIDs, neuroleptics, thyroid hormones and antidepressants.
True or false
7. Intracytoplasmic sperm injection involves injecting a single sperm into an egg during an IVF cycle.
True or false
8. Patients with mild ovarian hyperstimulation syndrome should be advised to take ibuprofen for pain relief.
True or false
9. Around 20% of women undergoing IVF treatment develop moderate or severe ovarian hyperstimulation syndrome.
True or false
10. Being either underweight or obese can affect ovulation and be a cause of infertility.
True or false



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