University Hospitals Coventry and Warwickshire NHS Trust

## Centre for Reproductive Medicine

# PATIENT INFORMATION BOOKLET

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## Introduction

This booklet contains information about a number of different conditions and treatments that relate to infertility. Not all of the information will be relevant to your particular needs and circumstances but some will and we hope you find this useful.

This booklet is not intended to replace the information given to you during consultation or by staff at your Centre but should complement that received at consultation and other visits.

More detailed information about specific treatments, for example IVF, will be provided separately according to your specific needs.

All efforts are made to keep the information contained within this booklet up to date and accurate. However, this is a fast moving field and if new information becomes available which is material to your treatment and that is not provided here it will be issued as supplementary information.

***We would welcome your comments about this booklet and any of the information we provide to enable us to continue to improve our services.***

**Comments should be sent to:**

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# Causes, investigations and treatment of infertility

Infertility can be caused by problems affecting either the female or male or a combination of both. Approximately 25 % of patients that attend with infertility problems have more than one problem. Minor problems may only have a slight effect, for example mild endometriosis in the female, but several minor problems added together may have a more striking effect. Before we deal with the causes of infertility, there follows a brief description of the control of the female menstrual cycle, an understanding of which is important for a couple going through infertility treatment.

### Control of the Menstrual Cycle and Release of the Egg

The normal menstrual cycle is 28 days long but can vary from 21 - 35 days. The menstrual cycle can be divided into four phases:

1. **The Follicular phase** - *from the first day of bleeding to about day 12 of the cycle*. At the start of this phase the Pituitary gland produces increasing levels of FSH hormone. This stimulates several immature eggs in the ovary to develop. Over the next few days one of the follicles (containing the egg) develops at a faster rate than the others - the dominant follicle. The follicle produces Oestrogen causing the Endometrium to thicken in preparation for pregnancy.

2. **Ovulation -** *day 12 - 16 of the cycle* As the Oestrogen level from the developing follicle rises (by this time the follicle has grown to about 20 mm in diameter) the Pituitary gland produces a sudden and very sharp rise in the production of the hormone LH. This rises and falls within 48 - 72 hours. The LH stimulates the final maturing of the egg, and the follicle to rupture - so releasing the egg. After the egg is released, the follicle becomes a corpus luteum.

3. **Luteal Phase -** *from day 16 - 28 of the cycle* During this part of the cycle, the Corpus Luteum is producing Progesterone which is in turn stimulating the Endometrium to undergo certain changes to prepare for implantation. At the same time in the Fallopian Tube, the egg has hopefully been met and fertilised by the sperm. During the early Luteal Phase the fertilised egg is developing into an embryo and moving along the Fallopian Tube. It enters the cavity of the uterus on about day 4 after ovulation and implants into the Endometrium on about day 6.

4. **Menstrual bleeding -** *day 28 - 4 of the cycle* If a fertilised egg does not implant into the lining of the womb (endometrium), the Corpus Luteum stops producing Progesterone (because it needs the support of the pregnancy hormones produced by the developing embryo to continue functioning) and the endometrium weakens and is shed as a period.

## Causes of infertility

### 1. Disorders of ovulation (anovulation) - the inability to release an egg

There are many reasons why a woman may not ovulate, the most common are:

- Weight changes (up or down)
- Stress
- Increased production of a hormone called Prolactin
- Failure or disturbance in the hormones that stimulate ovulation (FSH)
- Polycystic ovaries (PCO)
- Failure of the ovaries to respond to stimulation (and menopause)

## 2. Sperm of insufficient quality or quantity to reach the fallopian tube or achieve fertilisation

There are many possible causes of this, but they broadly fall into three categories:

- **Complete absence of sperm**
    1. No sperm being produced by the testicle
    2. Blockage of the vas preventing sperm from appearing in the ejaculate

- **Sperm of reduced number and/or quality**
    1. Damage to the sperm forming cells (virus, injury, bruising, infection, mumps, drugs, smoking, alcohol).
    2. Antibodies to the sperm
    3. Temperature (occupation, varicocele)
    4. Infection in the male glands

- **Sexual difficulties** (impotence)
    1. Physical illness (e.g. diabetes, nerve damage in the lower back)
    2. Medication (e.g. some drugs used for high blood pressure)
    3. Psychological

## 3. Damage to the Fallopian tube preventing the egg and sperm coming together

The possible causes of tubal problems are:

- Infection coming up through the vagina (the most common infection to cause tubal problems is Chlamydia)
- Inflammation or adhesions due to conditions such as appendicitis or any previous pelvic operation including caesarian section
- Endometriosis, when severe, can distort and occasionally block the tubes

Damage to the end of the Fallopian tube, particularly when it causes a swelling of the fallopian tube called a hydrosalpinx is the most common and most difficult to treat. Sometimes adhesions or scar tissue can form around the tube leaving the lining of the tube itself reasonably healthy. In this case the adhesions may be treated with a reasonable chance of improving fertility. If the blockage to the tube occurs at its starting point and when then end of the tube (fimbria) are healthy then tubal surgery may be effective.

## 4. Other factors affecting fertility

These causes each account for about 20 - 25 % of couples attending for infertility investigations although their incidence will vary from one clinic to another.

- **Endometriosis**
- **Sexual problems**
- **Anti sperm antibodies**
- **Failure of implantation**
- **Fibroids**
- **Congenital abnormalities of the uterus**

Despite careful investigation there remains a frustratingly high number of couples in whom there is no definite abnormality found. These couples have ***unexplained infertility.*** The percentage of couples who fall into this category is between 10 and 20%. At least some of these cases result from ***fertilisation*** problems that may only come to light during in vitro fertilisation treatment.

## Investigation of infertility

The investigation of infertility is aimed at identifying the problems mentioned above. ***It is most important that both partners are investigated together.*** Initial investigations and assessment may be carried out by the general practitioner and include:

- **Preconception advice**
- **Physical examination**
- **Cervical smear test**
- **Rubella immunity**
- **Test to assess ovulation**
- **Sperm test (two tests may be required)**

**Ovulation**

This is normally assessed in one of two ways:
1. Measuring the Progesterone (blood specimen) on day 21 of a 28 day cycle or 7 days before the next period.
2. Ultrasound scans through the cycle (Follicle Tracking) to assess development of the follicle

**Key points: The Progesterone level can only be interpreted if the date of the following period is known. To be useful this test should be taken 7 days before the period starts. The Progesterone level should be > 30 nmol/l.**

**Semen analysis**.

- This should be tested in a laboratory with appropriate expertise.
- It may need to be done twice.
- The specimen should be no older than 30 minutes before it reaches the laboratory.
- The specimen should be produced following 2-3 days abstinence from sex.

**Key point: a normal sperm count has:**
- **more than 15 million sperm per ml of fluid**
- **more than 40 % of the sperm are moving progressively forward**
- **more than 4% of the sperm are normally formed (strict assessment)**

**Anti-sperm antibodies**

The association between antibodies to sperm found in the ejaculate and infertility is not clear. It is thought that if the level of antibodies is greater than 50% then this may impair the effectiveness of the sperm. However the recent guideline from the National Institute of Clinical Excellence has concluded that because of the uncertainty of the effect of antibodies to sperm, they should not be routinely tested for.

It is our practice at this centre to test for antibodies and if we find them in high levels to recommend some form of assisted conception.

**Assessment of the Fallopian tubes and pelvic structures**

We routinely assess the pelvic organs by undertaking an ultrasound scan to assess the ovaries and the uterus. This is normally done early in the assessment process and can detect abnormalities of the uterus and ovarian cysts. It is not in itself a test of the fallopian tubes.

The most common ways of assessing the Fallopian tubes are:

- Hystero contrast salpingography HyCoSy - involves injecting an inert solution visible to ultrasound through the cervix. An ultrasound examination of the uterus and ovaries is carried out at the same time. The ultrasound can assess if there is a blockage in the tubes.
- Laparoscopy - admission to hospital for half a day. General anaesthetic is given and a telescope is passed through a small cut at the umbilicus to enable direct inspection of the fallopian tubes, ovaries and uterus.
- Hysterosalpingogram - the passage of radio-opaque dye through the fallopian tubes, assessed by taking an X-ray picture of the abdomen.

## Treatment of infertility

Treatment is determined by the cause(s) of the infertility. Because there may be more than one cause, the treatment advised may differ from that normally advised for the treatment of a single cause. ***A more detailed explanation of the main treatments is provided in following chapters***.

**Ovulation problems**

***The purpose of ovulation induction is to develop a single follicle to maturity and to ensure that it has released an egg.***

**a) Anti-oestrogens (Clomifene)**

This is tablet therapy designed to increase the levels of the natural hormones (FSH) that stimulate the ovary to produce an egg.

**b) Gonadotrophins (e.g. Gonal F or Menopur or Bemfola)**

Gonadotrophins all have the same active ingredient, namely ***follicle stimulating hormone (FSH)*** and are given by a daily injection. Their purpose is to directly stimulate the ovary to produce an egg. The ovaries may be very sensitive to this therapy and it requires careful monitoring with ultrasound scanning.

**Male problems**

The treatment of this condition was revolutionised in 1993 by the development of ***Intra Cytoplasmic Sperm Injection (ICSI***), a form of IVF therapy where the egg is injected with a single sperm.

Treatment to improve the numbers or quality of sperm are not generally very successful in improving the likelihood of a pregnancy although they may have some beneficial effect on sperm quantity, quality or both. Such treatments that have been advocated include:

- **Surgery for a varicocele (dilated veins around the vas)**
- **Advice to reduce the temperature of the testicles**

- **Treatment of infection**
- **Steroid therapy for antisperm antibodies (this treatment is not recommended because of the risk of steroid therapy)**
- **Multi vitamins**

Treatment of blockage to the vas can be dealt with by an operation. This is most successful when the cause of blockage is vasectomy with pregnancy rates in excess of 50% in these cases. The likelihood of successful reversal of vasectomy depends on the length of time since the original vasectomy and whether there are any problems with the female partner.

An alternative to surgery for a blockage to the vas is to remove sperm from above the blockage (either from the epididymis or directly from the testicle). This procedure is known as ***TESE or PESA***. The sperm so recovered is then used to inject the female's eggs (ICSI).

Some men who have no sperm in the ejaculate (***azoospermia***) and have no blockage may have viable sperm in the testicle. It may be possible to remove the sperm by taking a ***small biopsy of the testicle*** and using this sperm to inject the female's eggs (ICSI).

An uncommon problem is ***retrograde ejaculation*** where the sperm passes into the bladder after ejaculation. In these cases sperm can be recovered from the urine passed after masturbation and used to fertilise eggs in assisted conception techniques.

Men with spinal injuries leading to paraplegia and who are unable to ejaculate can also be treated by using techniques to extract the sperm which is then used for assisted conception techniques.

The choice will be determined by the exact nature of the problem.

**Tubal problems**

Tubal blockage or damage may be treated in one of two ways:

- **In Vitro Fertilisation (IVF) to bypass the blockage**
- **Tubal surgery – this is often carried out using "key hole" surgery (laparoscopy)**

The choice is determined by the extent of the damage to the fallopian tubes. If there is scar tissue (adhesions) around the tube but the lining of the tube itself is healthy, surgery may have a good chance of working. If the tube is blocked and swollen at its end then surgery is much less likely to work and IVF offers the best chance of success. If the tube is blocked at the point at which it enters the womb and the rest of the tube is healthy it may be possible to "unblock" the tube by passing a fine catheter through the opening into the tube from the womb. So called ***selective tubal catheterisation*** may be successful in a proportion of these uncommon cases.

**Sterilisation** may be surgically reversed with a good chance of success. This depends on the method of sterilisation, the time interval since it was carried out and other factors such as the age of the female and whether there is another problem such as poor quality of the partner's sperm.

If the sterilisation has been performed using clips, the time interval is less than 10 years and barring other factors such as sperm problems, the chances of successful reversal are approximately 50%. If the sterilisation has been performed by diathermy or cut and ligation, the chances of successful reversal are low. Reversal of sterilisation is not usually funded by the NHS.

Reversal of sterilisation requires an abdominal incision and a 2-3 day stay in hospital. The recovery period is approximately 4-6 weeks. One of the problems of reversal is the relatively high risk of ectopic pregnancy. Of those pregnancies that result after reversal, 1 in 10 will be an ectopic.

## Endometriosis

Endometriosis is often found in women being investigated for infertility. It occurs when the lining of the womb implants outside the womb for reasons that are not clearly understood. It is found in different degrees of severity. Symptoms that are typically associated with endometriosis include painful periods, pain during intercourse and abdominal pain at other times of the monthly cycle. Some women with endometriosis have no symptoms and the severity of endometriosis may not relate to the severity of symptoms.

In mild cases of endometriosis the relationship between endometriosis and infertility is not clear. The presence of mild endometriosis is unlikely to have a major adverse effect on fertility. In more severe cases infertility can result from scarring around the fallopian tubes and ovaries and cyst formation in the ovaries.

Surgical treatment (laparoscopic) of mild endometriosis has been shown to improve fertility. In more severe cases fertility may also be slightly improved following surgery but IVF treatment may be more effective, although this has never been proved conclusively.

Surgical treatment of endometriosis is particularly advised if it is causing troublesome symptoms. Normally surgical treatment is carried out using “key-hole” surgery by laparoscopy. Drug treatment for endometriosis may be effective in suppressing the symptoms of endometriosis but does not improve the chances of becoming pregnant.

## Fibroids

Fibroids are benign muscular growths in the uterus (womb). They are very common and may vary greatly in size. In some cases they cause no problems. They may cause heavy periods, painful periods and pelvic pain. If they are large, they can cause pressure symptoms on the bladder or bowel.

Fibroids can arise in different positions in the uterus. If they cause significant distortion of the cavity of the uterus they may increase the risk of miscarriage. Fibroids may reduce the possibility of conception if they distort the fallopian tube as it enters the womb or if they distort the cavity of the womb thus reducing the chance of implantation.

The decision to remove a fibroid is not clear cut. Removing a fibroid is not without risks. It may require major surgery,that can lead to significant blood loss. About 1% of such operations may lead to hysterectomy (complete removal of the womb) as a consequence. The decision to remove a fibroid depends on its size and position. Fibroids situated within the cavity of the uterus may be removed through the cervix. Fibroids within the wall of the uterus are best removed through the abdomen either through an incision or by key hole surgery.

### Embolisation of Fibroids

This is a treatment for fibroids that has the attraction of avoiding drug treatment and surgery. However, at present this approach is ***not advised*** for those patients with infertility problems as there are significant complications with this approach, and the ability of the womb to carry a pregnancy successfully after this procedure is not yet proven.

## Sexual problems and impotence

Difficulties in the sexual relationship are not uncommon, particularly with the stress of trying to conceive. Sexual problems can also occur as a result of physical illness or abnormalities coincidental to the infertility problem and can affect male or female partner. Causes include:

- Psychological e.g. sexual inexperience, stress, anxiety about fertility, pressure to perform, work, relationship and domestic problems and previous sexual abuse
- Medical conditions leading to impotence e.g. diabetes and hypertension
- Spinal injuries or neurological conditions leading to impotence or inability to ejaculate
- Medication causing impotence e.g. certain anti-hypertension drugs
- Pelvic surgery in the male e.g. prostate leading to impotence
- Pelvic surgery in the female e.g. from Crohn's disease or ulcerative colitis
- Vaginal infection, scarring or injury e.g. previous childbirth injury
- Congenital abnormalities in the vagina such as a membrane dividing the vagina called a septum

The problem should be thoroughly investigated and therapy involves recognition and treatment of any physical condition. If physical conditions are excluded then treatment will involve support, counselling and possible psychosexual therapy.

## Unexplained infertility

Despite thorough investigation a proportion of all cases of infertility have no clear explanation and are deemed to be "unexplained". While a proportion of such cases will eventually conceive naturally, treatments are available. These are discussed elsewhere.

## How can you improve your chances of conception ?

There are no simple answers to this commonly asked question. However here are some helpful suggestions:

- **General health and well being** If you have any on-going medical problems, get them checked out by your doctor to be sure they are optimally controlled prior to pregnancy. Diabetes, for example, should be carefully assessed prior to planning a pregnancy to ensure its control is optimal. Medication you are taking should be reviewed to ensure it does not affect pregnancy and to ensure that the dose is appropriate.

  If you are overweight make efforts to reduce your weight through sensible eating and exercise before embarking upon a pregnancy. A body mass index of greater than 30 can impair ovulation, making it more difficult for some infertility treatments to work and making you more prone to complications in pregnancy such as hypertension, diabetes and back pain.

  If you do not normally exercise, start doing some regular aerobic exercise. Not only will it help you get fit for pregnancy, which itself places physical strain on the cardiovascular system, but it will give you more energy and raise your general feeling of well being.

- **Diet and vitamins** It is sensible to get in the habit of "healthy" eating, for example a good balance of fruit, vegetables, and protein together with plenty of water. Certain foods are not recommended in pregnancy, such as patés, soft cheeses and liver.

  You are recommended to take Folic Acid 400 mcg daily whilst trying to conceive and until the 12$^{th}$ week of pregnancy. Folic Acid is important for the development of a healthy foetus and can reduce the risk of neural tube defects such as spina bifida.

  Vitamin supplements are often recommended to couples having difficulties conceiving, particularly in the male to improve sperm quality. However, normal daily vitamin requirements are likely to be obtained through eating a balanced diet. Vitamin supplements have not been shown to improve the chances of producing a baby irrespective of the cause. Vitamin supplements are, however, generally safe and if you feel you should take them then do so.

- **Work, lifestyle, stress and relationships** The type of work you do is very unlikely to affect your fertility unless it keeps you away from your partner at the fertile time of the month!! However, stressful lives can occasionally lead to problems with ovulation while difficulty in conceiving produces its own stress and can place a strain on your relationship. It is helpful, therefore, to look at your lifestyle and ways of managing your stress levels. Look also at the time you make for each other. Many of us live busy lives that can impact on the time we spend with each other and the quality of our relationship. Make time to discuss issues and spend time with each other! The Counsellor is an important source of help to explore these issues in depth.

- **Sex life, fertility aids, predictor kits and temperature charts** Unfortunately, having difficulties with conception can get us hung up on "the fertile time of the month". All efforts are concentrated around a few days and sex can become a means to an end! Although it is difficult not to focus on fertility, you should try not to plan intercourse. In truth, if you are having regular intercourse two to three times per week, fertility aids and excess focus on the "fertile time" is not going to increase your chances of conceiving. If you are having difficulties with intercourse or sex is painful, you should seek specialist advice.

# Complementary therapies

Complementary therapies can be a useful source of support, working alongside mainstream medical treatment.

They do not offer a 'cure-all' and certainly cannot resolve physical structural causes of infertility. The role of such therapies lies more in helping you feel positive, healthy and in control of your own body. Some people find this helps them prepare for and go through the types of conventional treatment offered here at the Centre for Reproductive Medicine.

Practitioners of the various complementary therapies believe that they are useful primarily in sorting out subtle imbalances and restoring the flow of the body's natural energies. They aim to treat the person holistically (mind/body/spirit as a whole) rather than focus on one specific part.

The most commonly available forms of therapy are:

- Chiropractic/Osteopathy
- Acupuncture
- Aromatherapy, Reflexology and Massage
- Homeopathy
- Herbal Medicine and Chinese Herbal Medicine
- Reiki
- Hypnotherapy and Guided Visualisation

There is also Yoga and Tai Chi which broadly combine concentration on breathing with slow controlled movements of the body.

Listening to a relaxation tape or practising meditation can also help control breathing and heart rate, and relieve physical and mental tension.

If you are pursuing any form of complementary therapy it is vital that the therapist is qualified and has membership of a professional body with recognized standards of training and practice. You should ask about these and be satisfied for yourself that the person concerned has the appropriate knowledge and expertise to meet your needs. You may also want to ask about their experience in working with fertility problems.

The benefits of complementary therapy tend to be cumulative, with regular treatments usually being more effective.

If you feel better after consulting a complementary therapist, and it helps your sense of well-being and adds to the 'feel good' factor in your life, then it is likely to be worthwhile generally.

Complementary therapy is about self-care and self-support. It may not solve your fertility problems but it may help you manage them more positively.

**NB**

- **Certain essential oils used in aromatherapy/massage should be avoided if you are trying to conceive or are pregnant**
- **It is advisable to check with the Centre's medical or nursing staff, or your GP, about any possible indications against the use of complementary therapy in your specific case.**

# Treatment of ovulation failure – Ovulation Induction

In women who are not ovulating naturally it may be appropriate to treat this problem with ***Ovulation Induction.*** This means the stimulation of egg development by the use of drugs given either by tablet or injection.

***For ovulation induction to be successful the following conditions must exist*:**

1. **At least one of the Fallopian tubes must be working, so the egg and sperm can meet.**

2. **The sperm must be good enough to fertilise the egg (although the sperm test cannot always predict that fertilisation will take place)**

3. **The ovary must be capable of producing an egg in response to the stimulation provided**

It is important that before Ovulation Induction is carried out the above factors are considered. ***It is absolutely essential that a sperm count and a test to assess the likely response of the ovaries be carried out***. To gauge the likelihood of the ovaries responding to the stimulation we carry out a blood test to measure the FSH level on day 2 or 3 of the menstrual cycle.

If there are no indications in the medical history of any problems with the fallopian tubes e.g. history of pelvic inflammation, then a test for tubal patency may not be carried out in the initial phases of treatment.

## Treatment

### 1. If the periods come infrequently

It is common practice to ***induce a bleed*** by giving a 5 day course of Progesterone (Provera 10 mg twice a day), because to wait for a period to come naturally might mean waiting a long time!

**Key point: Ensure that the woman is not pregnant before starting treatment**

### 2. Drugs used to stimulate ovulation

There are two main types of drugs used in ovulation induction:

- **Anti - Oestrogens -** these are tablets given orally, which increase the Pituitary production of Follicle Stimulating Hormone. Examples of such drugs are: ***Clomifene and Tamoxifen.***

- **Metformin –** this is a drug used in the treatment of diabetes which is increasingly being used in women who have polycystic ovarian disease and who are not ovulating. It works by lowering resistance to insulin and may be used as a supplement to conventional therapy.

- **Gonadotrophins** - these are drugs which are always given by injection. The active ingredient of this family of drugs is ***Follicle Stimulating Hormone*** that acts directly on the ovary. Examples of such drugs are: ***Gonal F, Menopur***

Gonadotrophins must be injected and are much more potent than Anti-Oestrogens. As a consequence, patients commenced on Gonadotrophin therapy are monitored more intensively by scans and possibly blood tests.

## 3. Side effects of ovulation induction drugs

These are detailed in the Chapter on drugs used in infertility

## 4. Risks of a multiple pregnancy

Multiple pregnancy is a risk of ovulation induction therapy. Because conception takes place "naturally" we must rely on monitoring the response to indicate how many eggs are likely to be released. Eggs may be released from follicles of 12 mm in diameter and above. In practice it is likely that only those follicles with diameters 14 mm and above will produce eggs capable of fertilising. Monitoring is important because the response in any woman is unpredictable - this is particularly so with Gonadotrophin therapy.

### a) Clomifene therapy

The risk of twins is approximately 10 % and the risk of triplets is approximately 0.1 %.

### b) Gonadotrophin therapy

The risk of twins is approximately 20 % and the risk of triplets is approximately 1 %.

***There is also a small risk of a higher order pregnancy (Quads and above) with Gonadotrophin therapy. However with close monitoring the risk of such an occurrence is very low.***

**Key point: If during the course of monitoring, the number of follicles at least 14 mm in diameter is such that the risk of a triplet pregnancy or greater is significant, your treatment will be deferred and you will be strongly advised to use contraception or avoid intercourse.**

## 5. Process of stimulating ovulation (ovulation induction)

***The purpose of ovulation induction is to develop a single follicle to maturity and to ensure that it releases an egg.***

### a) Anti-oestrogens (Clomifene)

The starting dose is 50 mg daily taken from the second day of the period for 5 days. If there has been no response, the dose is increased by 50mg daily each month up to a maximum of 150mg daily for 5 days, until there is a response.

### b) Gonadotrophins (e.g. Gonal F, Menopur)

Gonadotrophins (Follicle Stimulating Hormone, FSH) are given by a daily injection usually starting on day 2 or 3 of the cycle (if necessary having induced a bleed with Provera as described above). The starting dose is normally 75 i.u. of FSH given for 14 days and increasing thereafter in weekly increments of 75 i.u. or 37.5 i.u. until response is achieved. This dose may be altered according to response in previous treatment.

### c) Human Chorionic Gonadotrophin, HCG (Ovitrelle, Pregnyl); rLH

Once a mature follicle develops using the drugs described above (18 mm in diameter), an injection of HCG may be prescribed to ensure that the egg is released. HCG plays the same role as the LH hormone produced by the Pituitary gland. Once the HCG is given ovulation will occur approximately 40 hours later.

## 6. Monitoring the response to drugs

The response to ovulation induction is monitored in two ways:

- **Ultrasound scans (follicle tracking)** These are carried out at intervals to detect the growth of the follicle. Typically a scan will be carried out every 7 days of stimulation until the leading (largest) follicle reaches 14 mm in diameter. Thereafter a scan is carried out every 2 days. A mature follicle has a mean diameter of at least 18 mm. Once the mature follicle has developed then ovulation is likely to occur within 24-72 hours. Normally a further scan will be carried out 7 days later to ensure that the follicle has ruptured - thus confirming that the egg has been released.

- **Progesterone** This is measured by a blood test taken 7 days after ovulation is presumed to have occurred.

## 7. How often will this treatment be given?

Ovulation induction relies on ***natural conception*** after drugs have been given to initiate the production and release of an egg. As a result the chances of a pregnancy, ***provided there are no other causes for the infertility***, will be close to the rate of natural conception in a woman who ovulates normally. This is about 20 % per cycle. We will review the treatment at the end of every month and decide what the next course of action is. We may continue with this treatment for a number of cycles.

# Follicle Tracking

In the normal menstrual cycle, an egg develops each month within one of the ovaries. The egg develops within a fluid filled "sac" called a ***follicle.*** The follicle grows from day one of the cycle (first day of period) and by day 12-14 should have reached the size of about 17 - 25 mm in diameter. The follicle produces a hormone called Oestrogen which in turn causes the lining of the womb to thicken. The egg is then released - a process called ovulation. Ovulation is caused by a ***sudden surge of another hormone known as LH***, produced by the Pituitary gland.

During ovulation the follicle ruptures, sometimes causing some lower abdominal discomfort and the egg escapes and passes into the Fallopian tube where it meets sperm (hopefully). After ovulation the follicle becomes the ***Corpus Luteum*** which produces another hormone called ***Progesterone*** which causes the lining of the womb to be receptive to an embryo. All evidence of the follicle and corpus luteum normally disappears by cycle day 28.

**Purpose of follicle tracking:** To confirm that a follicle is developing at the correct time in the cycle and is releasing the egg, in other words to confirm ovulation.

**Who is follicle tracking carried out on?** Follicle tracking may be carried out for the following reasons:

- **To confirm ovulation - particularly in couples with "unexplained" infertility.**
- **Monitoring of women undergoing ovulation induction therapy.**
- **To help the timing of treatment in women undergoing artificial insemination with donor or partner's sperm.**

**How is follicle tracking carried out?** The best way of looking at the ovaries is by ultrasound carried out using a vaginal probe. This method of scanning provides the most accurate image of the ovaries. A probe is inserted into the vagina (similar to having a smear taken from the cervix but usually less uncomfortable)**.** The procedure is carried out with an empty bladder, takes no more than 10 minutes and also allows us to see the womb, its cavity and the lining of the womb.

**Who will carry out the scan?** Scans are normally carried by one of the clinic nursing staff. If there are difficulties with the scan or its interpretation, a senior doctor is normally available to assist. We have trainee doctors and nurses working in the department and as part of their training they may carry out scans for this purpose. If a trainee does carry out a scan, they will be supervised by someone who has the necessary expertise and your permission will be sought first.

## How many scans are needed?

1. The first scan is carried out between days 1-5 of the cycle.
2. At the first scan you will be given an appointment for another scan - usually close to the anticipated time of ovulation i.e. around day 10-14.
3. There may be a need for a third or fourth scan depending on the findings of the second scan.
4. Once a mature follicle has been seen a final scan will be arranged for approximately 7 days later to determine whether the follicle has released the egg.

**<u>Key point:</u> Day 1 of the cycle is the first full day of red bleeding.**

**How to arrange Follicle Tracking** You should ring the Centre (for telephone numbers see end of booklet) when your period starts and book your scan with Reception, explaining what the purpose of the scan is. i.e. "follicle tracking" .

# Multiple Pregnancy

**Most assisted conception techniques increase the possibility of a multiple pregnancy. The probability of a multiple pregnancy will vary according to the type of treatment that you are having and a number of other factors described below. Multiple pregnancies carry a higher risk of complications than do singleton pregnancies and are more likely to result in the birth of a premature baby.**

**What is a multiple pregnancy?** A multiple pregnancy means that two or more babies are being carried at the same time. Twins are the most common - that is two babies. Triplets (three babies) are less common and higher numbers (4 or more) are exceptionally rare.

**How likely am I to have a multiple pregnancy?** In naturally conceived pregnancies the incidence of twins is 1 in 80 and of triplets 1 in 6,000-8,000. In patients undergoing infertility treatment the likelihood of a multiple pregnancy depends on a number of factors, the most important being the type of treatment:

1. **Ovulation induction** Depending on the type of drug regime used - ***twins occur in between 10 and 30 % of cases; triplets between 0.1 and 3 %***. The higher numbers such as quads and above can also occur with this type of treatment but are rare.

2. **Intra uterine insemination (IUI) and Donor insemination (DI) (when drugs are used to stimulate ovulation)** The risk of ***twins is approximately 20 % and of triplets 1%***. Quads and above can also occur with this type of treatment but are rare.

3. **IVF, ICSI, Oocyte Donation and Frozen Embryo Replacement** All these treatments have one thing in common - we cannot normally replace more than two embryos in any one treatment. While it is possible for a single embryo to divide into two and result in twins, this is a rare event. The risk of ***twins (for two embryos replaced) is between 20 and 30 %.*** Because of the unlikely event of an embryo splitting, triplets and, in extremely rare cases quads, can arise from two embryo replacements. The likelihood of triplets arising from two embryos being replaced is probably less than 0.1 %.

**What other factors influence my chances of having a multiple pregnancy?**

- **The female partner's age -** increased chance with decreased age
- **The cause of infertility -** unexplained less likely, tubal disease and male factor more likely
- **Previous pregnancy -** a previous pregnancy increases the likelihood
- **Length of time trying to become pregnant -** the longer the less likely
- **Quality of embryos -** better quality embryos increase the likelihood

**What measures are taken to lessen the chance of a multiple pregnancy?** With ovulation induction and IUI and DI treatments, the two main measures are:

- ***careful scanning*** of the number of developing eggs during the treatment cycle
- the ***strict avoidance of intercourse according to advice*** from the clinic staff if a treatment cycle is cancelled because of an over response to drugs

In IVF, ICSI and related treatments national clinical guidelines recommend the replacement of a single embryo in women under 40 with optimum quality embryos. We are committed to reducing multiple pregnancy rates in line with HFEA guidance and have a single embryo replacement policy that applies to women at high risk of multiple pregnancy. Please ask about this prior to treatment. Please see www.oneatatime.org.uk for further information.

**What are the problems of a multiple pregnancy?** The risks of a multiple pregnancy are due to there being more than one baby developing simultaneously. This places greater demands on the pregnant woman and leads to more rapid expansion of the uterus. While a singleton pregnancy can have complications the chances of these arising in a multiple pregnancy are generally increased by the same factor as the number of babies being carried. The following are problems more commonly found in a multiple pregnancy:

1. **Premature birth.** Because of the increased expansion of the uterus (the womb) ***premature labour is more likely***. Almost half of all twins and all triplets will be delivered before 38 weeks. The earlier a baby is born, the greater the risks to the baby - particularly with its breathing. Very premature babies will require ***Neonatal Intensive Care*** - sometimes for several weeks.
2. **Social and practical difficulties.** Having a multiple birth, either twins and particularly triplets, creates additional work for both parents and will pose an additional financial burden. All purchases for the children have to be doubled or trebled. There are few exceptions! Child care arrangements are more problematic and educational costs will be multiplied.
3. **Miscarriage.** Multiple pregnancies are ***more likely to miscarry*** at an early stage. About 10 % of multiple pregnancies spontaneously "reduce" to singleton pregnancies at a very early stage (before eight weeks usually) - this may be manifest by some bleeding but if one of the pregnancy sacs is lost the pregnancy usually carries on normally. Multiple pregnancies are also more likely to miscarry ***during the middle stages of pregnancy - between 12 and 24 weeks***.
4. **Congenital birth defects (abnormalities).** Birth defects are more common with multiple pregnancy - because there is more than one baby the odds are increased by that factor.
5. **Complications of pregnancy.** All the common symptoms of pregnancy will be exaggerated during a multiple pregnancy - ***sickness, tiredness, swelling, excessive weight gain.*** The more serious complications of pregnancy such as ***raised blood pressure, vaginal bleeding (antepartum haemorrhage), diabetes, anaemia and slower growth rate of the babies*** are also more common in multiple pregnancies.
6. **Physical and learning disability in the baby.** Babies that are born ***very prematurely are more likely to have a permanent learning or physical disability*** although the rate is less than 10 % in babies born over 28 weeks into the pregnancy.
7. **Complications during birth.** Multiple pregnancies are ***more likely to require an "operative" birth such as Caesarean Section***. This is because one of the babies is more likely to develop distress or be in an unusual position (e.g. bottom first) during labour.

**Is the care of a multiple pregnancy any different from a single pregnancy?** The care differs in a number of respects. Your obstetrician is the best person to advice on how your particular pregnancy should be cared for. Here are some of the more likely points:

- **More frequent visits to the antenatal clinic**
- **Detailed scan for abnormalities routinely offered at 18-20 weeks**
- **Scans carried out at intervals from 26 weeks to assess growth of the babies**
- **Iron supplements routinely advised to decrease the likelihood of anaemia**
- **Rest advised to lessen the likelihood of premature labour**
- **Delivery/induction of labour more likely to be planned before due date**
- **In labour continuous monitoring and epidural analgesia**

**What about after the babies are born? Will there be any special help?** Two or more babies increases considerably the effort and expense you will have to bear to raise these children. For the first weeks following the birth the midwife and health visitor will visit more frequently. There is little additional practical help for twins other than the extra child benefit. For sources of further help and advice please refer to the "Useful numbers" page.

# Ovarian Hyperstimulation Syndrome (OHSS)

***Ovarian Hyperstimulation Syndrome is a recognised side effect of the drugs used to stimulate production of eggs in fertility treatments.***

In the majority of patients OHSS is a mild condition but less commonly it can be serious medical complication necessitating admission to hospital for specialist treatment. Rarely it can be life threatening and deaths have been recorded following development of this condition. It is therefore important to recognise the signs of OHSS in order to prevent it developing into a more serious condition.

**Who can develop OHSS?** Any woman who is given drugs to stimulate ovulation or the production of eggs. Women who are known to have ***Poly Cystic Ovaries*** are at greater risk. OHSS cannot develop in women who are not given drugs to stimulate the ovaries.

**Which drugs can cause OHSS?** Any drug used in the stimulation of ovulation has the potential to cause OHSS - even fertility tablets such as Clomifene or Clomid although OHSS is very rare in these circumstances. The drugs most likely to lead to OHSS are those commonly used in *in vitro* fertilisation and related treatments known collectively as Gonadotrophins. ***Examples of these drugs are Gonal F, Menopur.***

**How likely am I to develop OHSS?** Women receiving gonadotrophins such as those listed above for treatments such as In Vitro Fertilisation have around a **15% *chance of developing mild OHSS.***
***Moderate and severe forms*** of OHSS which will require admission to hospital and specialised treatment occur in **0.1 - 2 %** of cases undergoing IVF and related treatments.

**What are the symptoms of OHSS?** The most common symptoms are ***generalised abdominal swelling and discomfort and nausea.*** The abdominal swelling is due partly to swelling of the ovaries as a result of their stimulation but mainly to accumulation of fluid. In more serious cases the abdominal swelling becomes marked and the woman may complain of a ***reduction in the amount of urine passed and breathing difficulties.***

The ***ovaries are usually quite enlarged with multiple cysts*** (where the eggs have been removed from). These may be felt in the lower part of the abdomen and can give rise to discomfort and pain in the lower abdomen.

**Is OHSS a dangerous condition?** OHSS is uncommon and when it occurs is usually a mild condition with slight abdominal distension and discomfort that passes off after a week or so without requiring admission to hospital or special treatment. In some cases, however, it develops into a more serious condition requiring hospitalisation and specialist treatment. Even in these more severe cases the condition almost always resolves completely with no long-term complications or effects. Fatalities have occurred from OHSS but are exceptionally rare.

## What treatment will be required if I develop OHSS?

**1. Mild** This is the most common type. Admission to hospital is not necessary. The centre will monitor you more closely until the condition resolves. This may involve taking blood tests more frequently. Special treatment is not necessary.
**2. Moderate** Admission may be required for a few days' closer observation. Blood tests are taken daily and fluid replacement with a drip may be required.
**3. Severe** In these rare cases hospitalisation is always necessary. Treatment will involve a drip to replace fluid, salts (electrolytes) and protein. Fluid in the abdomen, causing distension, will be drawn off by passing a small needle through the wall of the abdomen (local anaesthetic). Other specialist treatment may be necessary and intensive monitoring is carried out. This condition usually lasts 1 - 3 weeks.

***If you are admitted to a hospital away from your fertility centre we would strongly recommend that your gynaecologist contact your infertility specialist to discuss treatment. We would strongly advise <u>against</u> any attempt to operate on the ovaries in these circumstances <u>without prior discussion with your fertility specialist</u>.***

**Are there any long term effects following OHSS?** A complete recovery will occur even when the condition is severe. The ovaries, which become quite enlarged with cysts, can take several weeks to shrink down but return completely to normal within 4 - 6 weeks. There is no evidence to suggest that this condition increases the likelihood of developing cancer of the ovaries in the future.

**What about the treatment cycle?** If there are signs of this condition developing during the stimulation part of the infertility treatment we may adjust the treatment to prevent it developing into a more serious problem. Two possible ways of reducing the likelihood of OHSS developing are:

- Reducing the dose of drug stimulation.
- "Coasting" the stimulation phase – this means stopping the stimulation drugs for several days before removing the eggs.

Unfortunately the only certain way of avoiding OHSS is to stop the treatment. If we do this further treatment will be discussed with you and how it might be altered to reduce the chances of this happening again. Treatment can usually be started again within about 2 months after the ovaries have settled down.

**Is it possible to prevent this problem?** As has already been mentioned women with polycystic ovaries are more likely to develop this problem. The ovaries are scanned at the start of treatment and if they are polycystic we would normally adjust the dose of stimulation to take this into account.
During the cycle of stimulation (*in vitro* fertilisation), one of the purposes of monitoring is to detect signs of over response and possible developing OHSS. If this is the case we may either reduce the dosage of the stimulation, "coast" the treatment – stop the drugs for several days, or even abandon the treatment.
Any women receiving Gonadotrophin drugs to stimulate the ovaries (whatever the treatment) should have monitoring specifically to detect signs of OHSS. The monitoring will be with ultrasound scans to assess the development of the follicles in the ovaries and possibly by blood tests to measure the oestradiol level in the blood. Excessively high levels of Oestradiol indicate a high risk of developing OHSS. Frequency of monitoring will be determined by the treatment you are receiving, your Centre's protocol and your response to the drugs.

**What about pregnancy with OHSS?** When a pregnancy occurs in a woman who has symptoms of OHSS, the condition is likely to be aggravated and be more prolonged. For this reason, a woman who is undergoing *in vitro* fertilisation and who is at significant risk of developing OHSS may be advised to have all embryos frozen and stored for future use rather than replace fresh embryos and run the risk of worsening the OHSS. If a woman does become pregnant and has OHSS there is no reason why the pregnancy should be any more likely to fail.

**Can OHSS develop again in a future treatment?** There is a tendency for this condition to recur. If one treatment has resulted in OHSS the dosage of drugs will be adjusted in any future treatment to take this into account and lessen the possibility of a recurrence.

***If you are receiving Gonadotrophin drugs for fertility treatment and develop the symptoms described above, call your infertility centre without delay. The contact telephone numbers for this unit are at the back of this booklet.***

# Endometriosis

Endometriosis is a commonly found condition in which tissue similar in structure to the lining of the womb (endometrium) implants into other pelvic structures. Endometriosis is found in 5 - 10 % of women attending for gynaecological problems and in 15 - 20 % of women who are being investigated for infertility. Endometriosis is a benign condition and does not predispose to cancer.

**What causes endometriosis?** The cause of endometriosis is not known. There are, however, several theories:

- Backwards flow of menstrual loss entering the abdominal cavity through the fallopian tube causing implantation of tissue from the lining of the womb.
- Altered chemical (hormonal) balance preventing the normal inhibition of the endometrial tissue that finds its way into the abdominal cavity.
- Tissue similar to that found in the lining of the womb that may have been present from birth in microscopic form in other pelvic structures.

**Where is endometriosis found?** Endometriosis is found in the following sites:

- The lining of the abdominal cavity in the pelvic area (the peritoneum)
- Ovaries
- Ligaments that run from the back of the womb to the pelvic wall (uterosacral ligaments)
- In the pouch between the bladder and the womb
- In between the rectum (back passage) and the vagina just at the back of the cervix

Endometriosis can form cysts in the ovary - known as endometriotic cysts or endometrioma in about 20 % of cases. These can be up to 15 cms in diameter and are almost always benign. Endometriotic deposits can rarely be found in other places such as in the bowel, lung, kidneys and bladder. It is not unusual to find endometriosis on the outer lining of the bowel.

**What symptoms does endometriosis cause?** Quite a number of women who are found to have endometriosis have no symptoms at all - in fact it may come as quite a surprise to be told that endometriosis has been found. However, the majority of women who have endometriosis will have symptoms, the commonest of which are:

- Painful periods (dysmenorrhoea), both before and throughout the period.
- Pain during sex - deep pain felt in the lower abdomen.

As endometriosis may be found in a variety of different sites it can lead to a number of other symptoms, their characteristic being that they occur in a cyclical pattern at around the period time. Pain in the lower abdomen at times other than during a period can result from cysts on the ovary or adhesions. Pain when the bowels are opened is quite a common symptom. The majority of women have regular menstrual cycles.

***The amount of endometriosis often bears little relation to the symptoms resulting from it.***

**What happens to the endometriosis?** In about 40 % of cases the endometriosis remains the same or reduces (without treatment). In the remaining 60% of cases the endometriosis progresses. By progression is meant the development of additional deposits or the formation of scar tissue or adhesions around the pelvic organs. Commonly the ovaries become attached to the side wall of the pelvis or the fallopian tubes become stuck to the surface of the ovary. Endometriotic cysts can develop in the ovaries.

**How is endometriosis diagnosed?** Endometriosis may be suspected from the symptoms mentioned above or from a pelvic examination if there is unusual tenderness, “thickening” of the pelvic tissues, ovarian enlargement or a womb that does not move.

There are two tests that are useful in diagnosing endometriosis:

- Vaginal ultrasound scan - can detect endometriotic cysts in the ovaries - but not adhesions or small deposits.
- Laparoscopy is the only certain method of diagnosing endometriosis.

**Treatment of endometriosis** Not all cases of endometriosis require treatment. Treatment is advised in women who have symptoms resulting from it and in some cases when the women has difficulties conceiving. There are two types of treatment - drug treatment and surgical treatment.

a) **Drug treatment** There are two types of drug treatment:
(i) **Pain killers** - these drugs are normally taken during painful periods. E.g. Mefanamic Acid

(ii) **Hormones** - the purpose of hormone therapy is to stop or lighten the periods. There are several different types of hormones which can be used for this purpose:

- **The combined pill** (used normally or continuously without the 7 day break)
- **Danazol** - this is given in tablet form and works by stopping the periods. It has several side effects including weight gain, mood changes, unwanted hair and deepening of the voice.
- **Progesterone** - there are a variety of different preparations. Again the purpose is to stop the periods. The main side effects are fluid retention and mood changes.
- **LHRH anologues - (*Zoladex or Prostap*)** - these drugs are given as monthly injections. This is the most effective drug treatment. It has the effect of stopping the periods completely. These drugs act by stopping the Pituitary gland stimulating the ovary. Because the ovary stops working (temporarily), Oestrogen falls to low levels. The side effects of these hormones are, therefore, those of the menopause - hot flushes, sweats, vaginal dryness and mood changes.
- **LHRH anologues with Oestrogen "add back" therapy** - LHRH anologues are effective in controlling the symptoms of endometriosis but because of the low levels of Oestrogen produced, they cannot be given for more than six months because of the possible risk of osteoporosis (thinning of the bones). Oestrogen can be given simultaneously with LHRH anologues reducing these side effects while not reducing their effectiveness.

**Drug treatment can be effective at improving symptoms but will not cure the endometriosis. Symptoms usually recur within a few months of stopping the drug treatment. Drug treatment will not improve fertility.**

**b) Surgical treatment** Most commonly will involve a laparoscopy and laser or diathermy treatment to destroy areas of endometriosis. If cysts are present on the ovary they can be treated laparoscopically by removal of the cyst. Alternatively the cysts can be drained and the cyst wall treated with laser or diathermy (heat). This type of treatment has the benefit of avoiding long term hormonal treatment to stop periods - this approach may be particularly helpful in a woman who is trying to become pregnant. Surgical treatment is not without risks although serious complications are relatively uncommon.

**Laparoscopic treatment is effective in about 70 % of cases but the endometriosis is likely recur in about 40 % of cases following this treatment.**

In advanced cases in a woman who has completed her family, hysterectomy and removal of the ovaries may be recommended.

**Infertility and endometriosis** Endometriosis is often found in women being investigated for infertility. In mild cases the relationship is not clear. The presence of mild endometriosis is unlikely to have a major adverse effect on fertility. In more severe cases infertility can result from scarring around the fallopian tubes and ovaries and cause cyst formation in the ovaries (endometriotic cysts). Surgical treatment (laparoscopic) of mild endometriosis has been shown to improve fertility. In more severe cases fertility may also be improved following surgery but IVF treatment may be as effective.

If significant endometriotic cysts are present in the ovaries (4 cms or more in diameter) they should be removed before undertaking IVF treatment. This is because they can limit the number of eggs produced or become infected following the egg collection process in IVF. Such cysts can usually be removed through “key hole” surgery. Currently it is thought best to either remove the cyst or to drain it and destroy the cyst lining. If the cyst is just drained it is likely to recur in a short space of time.

Surgical treatment of endometriosis is particularly advised if it is causing troublesome symptoms. As stated above, drug treatment for endometriosis will not cure infertility related to it. Surgical treatment of endometriosis may improve fertility and this should be discussed in relation to your infertility treatment.

# Polycystic Ovaries and Polycystic Ovarian Syndrome (PCOS)

**Polycystic** is a term used to describe an ovary that has a number of tiny cysts around its perimeter. **Polycystic Ovarian Syndrome (PCOS)** is a name given to a condition in which a woman with polycystic ovaries has one or more characteristic features.

**What is a polycystic ovary?** The ovary is normal in size but has a ring of tiny cysts - between 5 and 8 mm diameter - around its edge. These cysts are not dangerous or harmful. There should be more than 12 of these tiny cysts around each ovary for it to be deemed polycystic.

**What is Polycystic Ovarian Syndrome or disease (PCOS)?** This is a collection of features found in a woman with polycystic ovaries. The characteristic features include:

- Menstrual irregularity - usually infrequent and sometimes heavy and prolonged periods; occasionally no periods.
- Excess male hormones usually manifest by increased facial or bodily hair – hirsutism, or increased tendency to acne
- Difficulties conceiving due to failure of ovulation (releasing an egg), although many women with this condition conceive normally.

**What causes polycystic ovaries?** It is not understood what causes polycystic ovaries. We do know that they appear in adolescence and perhaps even earlier. We also know that there is a possible hereditary link, although the genetics of this link have not been identified.

**Why do some women develop period irregularities and other symptoms?** In some women the polycystic ovaries produce hormones erratically and not in the correct proportion to each other. These ovarian hormones - namely oestrogen and progesterone, act on the Pituitary gland to produce abnormal amounts of LH and FSH. This results in erratic ovulation or no ovulation and hence erratic periods and sometimes no periods. The polycystic ovary also produces increased amounts of male hormone, for example testosterone, resulting in acne and unwanted hair often found with this condition.
The hormonal disturbances and other symptoms are aggravated by ***obesity*** that is often found in women with the symptoms mentioned above and in women with polycystic ovaries.

**Are polycystic ovaries dangerous - am I more likely to get cancer of the ovary?** No. The “cysts” seen around the edge of the ovary are not thought to increase the chance of the development of cancerous growths.

- The greatest danger of polycystic ovaries is the obesity often found. This will make the patient more likely to suffer from high blood pressure, heart disease and diabetes.
- Women with irregular or absent periods - particularly those who do not have children and who are overweight, are at slightly increased risk of developing cancer of the lining of the womb (endometrium) in later life.

**Metabolism, Excess weight and polycystic ovaries** Poly cystic ovarian syndrome is known to be associated with increased resistance to insulin, meaning the natural insulin may not work so effectively leading to disturbance in carbohydrate and fat metabolism. Obesity often occurs in association with polycystic ovaries. The relationship is unclear although it may be related to the effect on insulin action and we also know that excess body fat acts as a gland increasing oestrogen levels, further aggravating the hormonal imbalance. In addition, women with PCO who are overweight are at increased risk of cardiovascular disease and diabetes. Weight reduction is important to help restore the hormonal balance, natural ovulation and in addition reduce the risks of coronary artery disease and diabetes.

**Are polycystic ovaries painful?** Not in themselves, although hormonal imbalance can lead to mild swelling of the tissues due to changes in the blood flow in the pelvic organs.

**How do we diagnose polycystic ovaries or syndrome?**

- **Polycystic ovaries can only be diagnosed by ultrasound scan (the current definition is to find >/= 12 follicles 5 – 9 mm and / or a volume of > 10 mls. in the affected ovary)**

- **Blood tests can help to diagnose polycystic ovarian syndrome:**

    1. LH (usually high) in relation to FSH
    2. Testosterone and other androgens (usually raised)

**Ultrasound scanning of polycystic ovaries** The ovaries are most clearly seen by vaginal ultrasound. This is carried out by passing a small ultrasound probe into the vagina. The ovary normally rests just to the side of the womb and close to the top of the vagina and can usually be quite clearly seen using this technique. Vaginal ultrasound is no more uncomfortable than having a speculum examination for a smear test and takes a couple of minutes. No special preparation is required and there are no side effects. The bladder should be empty.

**Do polycystic ovaries need treatment?** There are three circumstances where polycystic ovaries or polycystic ovarian syndrome may require treatment:

**1. Absent or irregular ovulation leading to difficulties in conceiving.**
**2. Increased unwanted bodily or facial hair.**
**3. Irregular or infrequent periods**

***Polycystic ovaries in a woman who is not wishing to conceive and who has no symptoms related to them does not require treatment.***

**What are the possible treatments for failure of ovulation due to polycystic ovaries?** Disorders of ovulation in a woman with polycystic ovaries can be treated in two ways:

- **Drug treatment to "induce" ovulation** The most commonly used drug in this situation is Clomifene - tablet therapy. In cases where Clomifene does not work, gonadotrophins (FSH) are needed and these are given as injections. Both these drugs require monitoring to ensure that they are producing the desired response and because of the risk of multiple pregnancy.

- **Surgical treatment to the ovaries** This is reserved for cases where ovulation cannot be triggered with Clomifene tablets and may be used as an alternative to gonadotrophin (injection) therapy. The "surgery" is carried out as part of a laparoscopy ("key hole") surgery. It normally requires a day in hospital and minimal convalescence. The technique involves using electrical energy (diathermy) or laser beams to "drill" holes in the tiny cysts that surround the ovary. Approximately 60-70 % of women who have this treatment will ovulate spontaneously as a result.

**What if I do not want to become pregnant but I have some of the symptoms?** If irregular and unpredictable periods are the problem, the simplest and most effective treatment is the ***combined oral contraceptive pill.***

If unwanted hair is the problem with or without irregular periods then a combination of ***Ethinyl Oestradiol (Oestrogen) and Cyproterone (anti-testosterone)***, formulated in a preparation known as Dianette, is an effective treatment although has an increased risk of thrombosis.

Resistant cases may respond to ***surgical treatment*** as outlined above.

***Metformin*** is a glucose lowering drug normally used for the treatment of diabetes that has recently been advocated for use in PCO syndrome. The rationale for this is that PCO syndrome is associated with disturbances in insulin and glucose metabolism. As yet it is not clear from research whether Metformin is a useful drug to control the symptoms caused by PCO syndrome.

**Is it safe to take the Oral Contraceptive Pill if I have polycystic ovaries?** Yes. The pill will not alter polycystic ovaries and will not make them worse. The pill will not make the periods less likely to come, neither will the pill make you less fertile when you stop using it. The combined pill is perfectly safe in women with polycystic ovaries - in fact it is beneficial in the sense of regulating the periods.

**Will I always have polycystic ovaries?** Almost certainly yes. They are very unlikely to change in their appearance over the years.

**Is there anything I can do to help myself?** Weight control is the most important thing a woman can do who has polycystic ovarian syndrome. This is particularly so in those women who have a raised body mass index (BMI). The best measure of fat content is the Body Mass Index (BMI). The ideal BMI is between 18 and 25. The unit can give you your accurate BMI reading. Weight is best controlled by a combination of healthy eating and exercise.

# Ectopic pregnancy

**What is an ectopic pregnancy?** An ectopic pregnancy is one that implants outside the cavity of the womb (uterus).

**Where does ectopic pregnancy implant?** Ectopic pregnancy can occur in a number of different places. The following is a list but by far the most common site is the ***Fallopian tube***.

- **Fallopian tube**
- **The part of the Fallopian tube that passes through the wall of the uterus**
- **The Cornua of the uterus (entrance to the Fallopian Tube)**
- **Ovary**
- **Cervix**
- **In the abdominal cavity**

Very occasionally an ectopic pregnancy can occur simultaneously with a normally situated pregnancy (twins). This is known as a **Heterotopic pregnancy.** This is more likely to occur after **In Vitro Fertilisation** and accounts for about 3 % of ectopic pregnancies arising in this situation.

**Can an ectopic pregnancy survive?** Almost without exception no. There have been very rare cases of a pregnancy in the abdominal cavity which has survived to maturity.

**What causes ectopic pregnancy?** There are a number of possible causes of ectopic pregnancy. They are **most commonly associated with damage or scarring to the Fallopian tube**. This can result from:

- Operations carried out on the tube such as **tubal surgery or reversal of sterilisation**
- **Pelvic infection** or inflammation
- **Appendicectomy**
- **Pelvic surgery** such as removal of an ovarian cyst
- Other causes of inflammation in the abdomen e.g. Gall Bladder or Bowel inflammation

The likelihood of an ectopic pregnancy is also increased by a**ssisted conception methods such as In Vitro Fertilisation.** Other factors associated with ectopic pregnancy are:

- Certain types of contraception: Progesterone Pill, Progesterone Releasing IUCD, Sterilisation
- Congenital abnormalities of the Fallopian Tube (present from birth)

**What are the chances of having an ectopic pregnancy?**

| | |
|---|---|
| In **naturally conceived pregnancy** the risk is approximately: | **1 in 80** |
| In patients undergoing **In Vitro Fertilisation** the risk is approximately: | **1 in 50** |
| Following **tubal surgery** the risk of ectopic pregnancy is approximately: | **1 in 10** |
| If you have one **ectopic pregnancy** the risk is approximately: | **1 in 10** |

**What are the signs of an ectopic pregnancy?** The most important sign is ***pain*** in a woman who might be in the early stages of a pregnancy. Other signs are ***irregular bleeding*** - usually a watery red/brown discharge - sudden feeling of ***faintness or giddiness*** and pain in the tip of the shoulder. ***It is most important to understand that there may be no warning or signs of a pregnancy.***

**How is an ectopic pregnancy diagnosed?** The following tests are helpful ***but cannot definitely exclude*** ectopic pregnancy:

- **Examination**
- **Ultrasound scan - vaginal scan is by far the most accurate**

- **Blood test to measure the pregnancy hormone HCG**

**The most accurate way of diagnosing ectopic pregnancy is by carrying out a Laparoscopy under general anaesthetic although this can occasionally miss an ectopic pregnancy.**

**It is important to note that because of the lower than normal pregnancy hormone levels found with ectopic pregnancy, a very early urinary pregnancy test may show up as negative and therefore be misleading in making the diagnosis.**

**How is an ectopic pregnancy treated?** Ectopic pregnancy is potentially a very serious condition if undiagnosed, because it can rupture and lead to sudden and serious haemorrhage internally. This can on occasions be life threatening. It is therefore important that if ectopic pregnancy is suspected it is diagnosed and treated quickly.

- Ectopic pregnancy is normally treated by "key hole" surgery as part of a laparoscopy.
- The most common procedure is removal of the affected Fallopian tube. This is done because of the damage caused to the Fallopian tube by the ectopic.
- If the ectopic is in its very early stages, it may be possible to save the Fallopian tube by removing the ectopic through a small incision in the tube. In these cases there is a significant risk of another ectopic pregnancy in the same tube and the pregnancy is not always removed completely.
- If the ectopic pregnancy is very advanced or there is considerable scarring it may be necessary to perform an open operation through an incision across the lower abdomen.
- If the ectopic pregnancy is in its very early stages, drug treatment with ***Methotrexate*** can sometimes be used to treat the condition. This treatment is not always successful.

***It is not possible to transplant an ectopic pregnancy from the Fallopian tube back into the womb.***

**What happens to the tissue that is removed?** The tissue is sent for pathological examination to confirm the diagnosis and then is sensitively disposed of in the same way as miscarriages.

**How long does it take to recover from an ectopic pregnancy?** This depends on the type of operation carried out. If the ectopic is dealt with through "Key Hole" surgery, you should only be in hospital for a couple of days and back to work in about 4 weeks. If an open operation is required then there is a longer stay in hospital and 6 weeks' convalescence.

**What is the likelihood of a pregnancy occurring following an ectopic?** This depends on the state of the remaining tube. If this is healthy and no other infertility factors exist, there is a fair chance that you will become pregnant naturally without difficulty.

If the remaining tube is diseased, or if you have had infertility problems, then you should be referred to the infertility clinic for discussion about the best way to help you become pregnant. This may be through In Vitro Fertilisation. Following an ectopic pregnancy - particularly if the affected tube has been preserved - the risk of a further ectopic pregnancy is increased. It is very important in these circumstances that when you think you may be pregnant, you must have a scan as early as possible to determine that it is correctly situated.

**What will happen to my periods after an ectopic?** You may experience bleeding like a period for a few days after the ectopic pregnancy has been treated. The next period should come in about four weeks and the menstrual cycle should then return to normal.

**How long after an ectopic should I wait before trying for another baby?** Timing is not crucial. It really depends on you and what your body tells you. You should however at least wait until your menstrual cycle has re-established a regular pattern.

## Drugs commonly used in infertility treatment

*Please note that the side effects listed for each drug are possible reactions and are by no means certain to occur. Generally speaking the drugs listed in this section do not have dangerous side effects. It should also be noted that the lists may not include all reported adverse reactions associated with the use of these drugs. For those drugs that are used in ovarian stimulation the most common serious side effects are Ovarian Hyperstimulation Syndrome (OHSS) and multiple pregnancy.*

**Clomifene/Clomid** Used to induce ovulation (produce an egg in a woman who is not producing eggs regularly). It acts on the Pituitary gland in the brain to increase the production of the hormone known as FSH. This in turn stimulates the ovary more strongly. ***This type of treatment can lead to multiple pregnancy.***

- **Dose:** 50 to 150 mg taken daily from day 2 to day 6 of the cycle
- **Administration:** By tablet
- **Side effects:** Visual disturbances, Ovarian hyperstimulation, hot flushes, abdominal discomfort, nausea, vomiting, depression, insomnia, breast tenderness, headache, irregular bleeding, convulsions, weight gain, rashes, dizziness, hair loss, aggravation of endometriosis.
- **Duration:** Limited to maximum of 6 cycles

**Tamoxifen** This drug has a similar action to Clomifene and has very occasionally been prescribed for the same purpose. The side effect profile is similar to Clomifene.

**Human Menopausal Gonadotrophins (HMG)** Drugs falling into this category include **Menopur**. This group of drugs are derived from naturally occurring hormones secreted in the urine of women who have gone through the menopause. They stimulate the ovary to produce eggs when eggs are not released regularly. They are also used in women undergoing IVF and related treatments.

- **Dose** 75 i.u to 450 i.u sub cutaneous injections

**Follitrophin Alpha (FSH)** The commercial name of this drug is **Gonal F** or **Bemfola**. It is a synthetically produced follicle stimulating hormone that stimulates the ovaries to produce eggs.

- **Dose** 75 i.u to 450 i.u sub cutaneous injections

**Human chorionic gonadotrophin (HCG)** ***(Commercial names Ovitrelle, Pregnyl***) These drugs are used to mimic the natural LH surge and are given as part of ovulation induction regimes to cause follicular rupture; as part of the follicular stimulation protocol in IVF to cause final maturation of the oocyte prior to egg recovery; to provide luteal phase support following down regulation prior to ovarian stimulation for IVF. Side effects are very few and include tiredness, headache, mood changes and local skin reaction. The major side effect, however is that it is the trigger for potential ovarian hyperstimulation syndrome (OHSS).

- **Administration** Subcutaneous injection usually as a single injection
- **Side effects** Trigger for potential OHSS, skin reaction.

**Bromocryptine** ***(Commercial name Parlodel)*** This is a drug which inhibits the production of the hormone Prolactin from the Pituitary Gland. Some women with infrequent or absent periods have high levels of Prolactin - this requires further investigation but may be treated by Bromocryptine.

- **Dose:** 1 mg daily and up to 2.5 mg twice daily
- **Administration:** Tablet

- **Side effects:** Nausea, vomiting, constipation, headache, dizziness, low blood pressure, drowsiness. **Higher doses** can give rise to confusion, psychological disturbance, hallucinations, dry mouth and leg cramps.

**Cabergoline** ***(Commercial name Dostinex)*** This drug has similar actions and the same use as Bromocryptine.

- **Dose:** 500 micrograms to 1mg weekly
- **Administration:** Tablet
- **Side effects:** Palpitations, abdominal discomfort, fainting, nose bleeds, visual disturbances, hot flushes.

**Danazol** This drug is used to suppress periods in the treatment of endometriosis. It acts on the hypothalamic and pituitary glands to reduce the production of FSH.

- **Dose:** 200 mg to 800 mg daily continuously
- **Administration:** Tablet
- **Side effects:** Nausea, dizziness, rashes, backache, mood swings, weight gain, headache, irregular bleeding, hair loss, oily skin, acne, increased bodily hair, deepening of voice, visual disturbances, reduced breast size.

**LHRH anologues** ***This category of drug includes Buserelin, Goserelin (Zoladex), Leuprorelin Acetate (Prostap).*** All these drugs have the same active ingredient namely an analogue of LHRH. Its action is to stop production of FSH and as a result stop follicular stimulation and oestrogen production in the ovary. These drugs are used in two situations, to suppress ovarian function prior to IVF or related treatment and as a treatment for endometriosis. The side effects in all these drugs are the same and are due to decreased oestrogen.

**a) Buserelin** Dose 0.5 mls injection once a day for IVF treatment

**b) Goserelin** 3.6 mg by subcutaneous implant once monthly.

**c) Prostap** 3.75 mg by intramuscular injection once monthly.

**Side effects:** Irregular bleeding, hot flushes, palpitations, increased sweating, vaginal dryness, altered libido, headache, migraine, nausea, mood swings, abdominal pain, fatigue, weight change, drowsiness, acne, oily skin, ovarian cysts, back pain, muscle pain, rashes, constipation, vomiting, sleep disorders, blurred vision, disturbances of hearing, changes in breast size, breast tenderness, increased vaginal discharge.

**LH antagonists** This category includes *Cetrotide* and is a class of drugs which act in a similar way to the LHRH anologues. However they have important differences in that they have a much quicker onset of action, blocking the production of FSH and LH by the pituitary gland within a few hours. In addition, unlike the anologues they have no stimulatory activity. They are used in IVF and related treatments to suppress LH and prevent natural ovulation in the same way as LHRH anologues are used. There main advantage is that they avoid the menopausal side effects of LHRH anologues and also the difficulties that can arise through the initial stimulation effects of LHRH anologues.

**Dose:** 0.25 mg daily as advised.
**Administration:** Subcutaneous injection.
**Side effects:** Local skin reaction at injection site.

**Progesterone** These hormones are used to replace natural progesterone which is reduced because of the use of LHRH anologues suppressing LH production. They are necessary after embryo transfer in IVF and related treatments to create a favourable environment for implantation. The most commonly used is **Cyclogest** but **Lubion**, a subcutaneous injection, is a suitable alternative.

**Dose:** 200 – 800 mg daily – the dose schedule will be advised
**Administration:** Cyclogest is given by pessary either in the vagina or back passage. Lubion is given by injection.
**Side effects:** PMT like symptoms, mood swings, pyrexia, bloating.

**Oestradiol valerate** ***The most commonly used commercial preparation is Progynova.*** This is a natural oestrogen which is used to provide hormonal support who is unable to produce her own oestrogen because her ovaries are not working either temporarily or permanently (menopause). It is used in infertility treatment to thicken the lining of the womb in women who been given LHRH anologues prior to frozen embryo replacement (HRT cycle) and to women who are receiving donor eggs.

- **Dose:** 1mg to 8mg dose, determined by the treatment protocol.
- **Administration:** Given daily by tablet.
- **Side effects:** Nausea and vomiting, weight changes, breast enlargement and tenderness, pre-menstrual like symptoms, fluid retention, liver upset and jaundice, rashes, mood changes, headaches, irritation of contact lens.

## Cancer risk and drugs used to induce ovulation

There have been several reports published during the 1990s of an increased risk of ovarian cancer in women who have been exposed to drugs used to induce ovulation such as Clomifene tablets and gonadotrophin injections.

The evidence is not strong, and there have been several more recent reports, for example a Scandinavian national survey, which have shown no increased risk. In the reports that demonstrated a risk, this was confined in the main to cancer with “low malignant potential” and mainly associated with the long term use of Clomifene. The reported risk showed a two fold life time risk of developing ovarian cancer in women who had received infertility treatment with these drugs. The data is further complicated by the fact that ovarian cancer occurs more commonly in women who have never been pregnant. Furthermore, women who have had treatment with these drugs and then have a baby, have the same risk of ovarian cancer as the general population.

The current position is that all the available data is reassuring and that the risk of ovarian cancer, if it exists at all, is very small and relates to the long term use (more than 1 year) of Clomifene.

There is no known increased risk of breast cancer with the use of drugs given to induce ovulation or stimulate the ovaries as part of IVF treatment

# Unexplained infertility

**Definition** Unexplained infertility is defined as 3 years' infertility in a couple who are having regular intercourse and in whom there are no clearly identifiable causes for their problem. This is a very frustrating diagnosis which is found in about 20 % of couples who present for investigation of infertility. The main features of "unexplained" infertility are:

- **Ovulation confirmed or successfully treated**
- **Fallopian tubes normal (assessed by laparoscopy or HyCoSy or Hysterosalpingogram)**
- **None or only mild endometriosis**
- **Normal sperm parameters**
- **No significant anti-sperm antibodies**

**Rationale for treatment** There are several options for a couple with "unexplained" infertility ranging from doing nothing, through Intra Uterine Insemination (IUI) to In Vitro Fertilisation.

a) **Doing nothing** Couples who have no explicable cause for their infertility may still conceive naturally - even though they may have been trying for a long time. The chances of a spontaneous pregnancy are determined by a number of factors including the age of the woman, the length of time the couple have been trying to become pregnant and whether the female partner has been pregnant before. The longer time goes on, the less chance there is of a natural pregnancy.

For example a couple who have unexplained infertility and have been trying to conceive for 2 years in whom the female partner is 32 years old and who has never been pregnant, the chances of a spontaneous pregnancy occurring, without any treatment, in the subsequent 12 months are approximately 40%.

The "do nothing" option is sometimes difficult to choose. Nevertheless, providing the couple have been properly investigated, the use of treatment, which is not without some risk, and its likelihood of producing a pregnancy, needs to be weighed against the possibility of a pregnancy occurring naturally.

**b) Intra Uterine Insemination with or without stimulation of the ovaries (IUI and Controlled Ovarian Stimulation -COS) -** the purpose of this treatment is:

1. To improve the woman's fertility by enhancing her ovulation by increasing the number of eggs which are produced to more than would have been the case naturally.

2. To time when the eggs are ripe by scanning the ovaries.

3. To prepare the sperm by wash, centrifugation and swim up into culture medium, thus improving its quality and - hopefully - its fertilisation potential.

4. To inseminate the sperm directly into the uterine cavity at a precisely determined time to ensure the sperm is as close to the egg at the time it is released, and to by-pass any possible hostile effects of the cervical mucous on the sperm.

*The current guideline from the National Institute of Clinical Excellence (CG 156 published 2013) recommends that people with unexplained infertility, who are having regular unprotected sexual intercourse should not be routinely offered intrauterine insemination, either with or without ovarian stimulation (exceptional circumstances include, for example, when people have social, cultural or religious objections to IVF). This is a change to previous recommendations and reflects the improved success rates with IVF.*

c) **Gamete Intra Fallopian Transfer (GIFT)** - This treatment is rarely carried out and is not recommended by the National Institute of Clinical Excellence because of the disadvantage of requiring a laparoscopy. *We do not carry this procedure out locally for the above reasons.*

d) **In Vitro Fertilisation (IVF)** The rationale is similar to IUI treatment. Its main difference and advantage is that we are able to witness the process of fertilisation during the IVF cycle. One of the possible diagnoses in a couple with "Unexplained Infertility" is that the egg and the sperm are incompatible when placed together. The laboratory tests we normally carry out on sperm are a relatively poor indicator of fertilising potential. IVF in these circumstances becomes a diagnostic test. IVF is now the recommended option for couples who have been trying for 2 years without success.

# Intra Uterine Insemination (IUI)

***The current guideline from the National Institute of Clinical Excellence (CG 156 published 2013) does not recommend intra uterine insemination in patients with unexplained infertility, a low sperm count or poor quality sperm or with mild endometriosis. In these circumstances you should be advised to keep trying to conceive through regular unprotected intercourse for a total of 2 years after which time you may be offered IVF.***

***You may be offered IUI treatment if:***

- **You and your partner are unable (or find it very difficult) to have sexual intercourse, for example because of a physical disability.**
- **You have a condition (such as a viral infection that can be sexually transmitted) or require sperm washing before conception can take place.**
- **You are using donor sperm and have not become pregnant after 6 cycles of artificial insemination.**

**Definition** Intra Uterine Insemination (IUI) is the artificial insertion of sperm directly into the cavity of the womb (uterus). The sperm may be either partner's or donor. The sperm is always "prepared" before insemination. The preparation involves the sperm "swimming" up from a pellet into culture medium to form a clean concentrated suspension of moving sperm (only the best swimming sperm swim up into the culture medium). Unstimulated (i.e. no fertility drugs) IUI treatment is recommended by NICE, however, in exceptional circumstances you may be offered IUI treatment with enhancement of ovulation by using ovarian stimulation drugs.

**The purpose of this treatment is:**

1. To improve the woman's fertility by enhancing her ovulation by increasing the number of eggs which are produced more than would have been the case naturally.

2. To time when the eggs are ripe by scanning the ovaries.

3. To prepare the sperm by wash, centrifugation and swim up into culture medium, thus improving the quality of the inseminated specimen and - hopefully - its fertilisation potential.

4. To inseminate the sperm directly into the uterine cavity at a precisely determined time to ensure the sperm is as close to the egg at the time it is released, and to by-pass any possible hostile effects of the cervical mucous on the sperm.

**Pre treatment information** You will be sent an appointment to attend the CRM for a detailed information session with a member of the nursing team.

The Centre is required by law (Human Fertilisation and Embryology Authority) to check the identity of patients undergoing licensed treatment. We therefore request that both partners bring photographic ID to the pre-treatment information session that they will attend prior to undertaking licensed treatments.

**How likely is this treatment to succeed?** The chances of a pregnancy resulting are between 7 and 10 % per treatment cycle. The chances will vary according to the individual circumstances of the couple. For example the chances will be increased if the couple has had a pregnancy before or if the age of the female is under 38.

**Are there any risks with this treatment?** This is relatively straight forward treatment and the risks are very small. There are, however, risks in anything that you do. The main risks with this treatment are:

**If undergoing stimulated IUI:**

- **Risk of ovarian hyperstimulation syndrome (OHSS).** When any drugs are used to stimulate development of eggs there is a risk of this condition. Because of the relatively low doses of drugs used in this treatment the risks of developing OHSS are very small. This condition is discussed in more detail elsewhere.

- **Multiple Pregnancy.** This treatment depends to some extent for its success on the increased number of eggs that are formed. We will monitor you to assess this response. Fertilisation and conception in this treatment occurs naturally in the Fallopian tube - therefore we have no control once the eggs are released and insemination is carried out. There is therefore a possibility of a multiple pregnancy. The incidence of triplets is about **1%** and of twins **20 %.**

**The treatment involves the following stages:**

1. **Clomifene** (50 mg daily from the second day of a period to day 6) **and injections of Gonadotrophins (e.g. Menopur)** on days 5,7, 9 and sometimes 11 of the cycle

2. **Monitoring** to assess the development of the follicles within the ovaries. Scans are normally carried out on days 5 and 11 of the treatment cycle and sometimes day 13. If indicated additional scans will be carried out as necessary.

3. **A further injection (HCG e.g. Pregnyl or Ovitrelle**) is given to cause the eggs to be finally matured and released at a predictable time.

4. **The Sperm** The partner or husband produces a sperm specimen on the day of the insemination.

5. **The insemination** is carried out some 40 hours after the HCG injection. This involves attending the clinic. A speculum examination is carried out to visualise the cervix. A fine catheter is passed through the cervix into the womb. The sperm specimen is inseminated.

***The procedure takes about 10 minutes. No anaesthetic is required - the procedure is similar to having a smear test carried out.***

There is no drug treatment after the insemination but a blood test is sometimes carried out on day 21 of the cycle to confirm ovulation has occurred.

**Cancellation of treatment** In this process fertilisation is taking naturally and if too many eggs develop and release there is a possibility that a number of them will fertilise. In this situation a multiple pregnancy with several babies may be produced. To avoid this consequence we have set criteria for cancelling the treatment if more than a certain number of follicles develop.

***In these circumstances we will advise you against going through treatment and - however unlikely a natural pregnancy may seem to you - advise you against having intercourse without using condoms. You will also be asked to sign a form indicating that we have advised you of this risk.***

**How many treatments will be carried out?** 3 cycles of treatment are normally carried out and then the situation reviewed. Subsequent advice will depend on a number of factors, not least of which are the age of the woman and the length of time that you have been trying to become pregnant. Normally IVF will be advised after three failed IUI treatments.

# In Vitro Fertilisation

## *In vitro* fertilisation (IVF) is the fertilisation outside the body of the egg by the sperm and the replacement of the embryo back inside the cavity of the womb (uterus).

**How long has IVF been carried out for?** IVF was first successfully performed in 1978 and resulted in the birth of Louise Brown. Professor Robert Edwards and Patrick Steptoe were the pioneers who first performed this procedure successfully. World-wide many tens of thousands of babies have now been born as a result of IVF treatment. It is estimated that 1.5% of babies born in the UK are born following IVF/ICSI treatment.

**Why is IVF necessary?** IVF may be necessary for a number of different reasons:

- Blockage, damage or absence of the fallopian tubes
- Endometriosis
- Unexplained infertility
- Male factor infertility
- Ovulation problems that are difficult to treat by conventional means
- Combination of infertility factors

**How will I know if I need IVF?** The assessment of any couple who are having difficulties conceiving will involve a number of tests. Once these tests have been completed a plan of how best to treat the infertility problem will be discussed. IVF is only one of several different treatments that may be appropriate depending on your particular circumstances.

**Are there circumstances in which IVF cannot be carried out?** There are certain circumstances in which IVF is not possible:

- If the woman does not have a womb or there is an abnormality of the womb which prevents implantation.
- If the ovaries are incapable of producing eggs unless donor eggs are to be used.
- If there are reasons in which it would be dangerous to carry out IVF, for example if the woman has medical problems which would make IVF hazardous e.g. previous pelvic abscess formation or major bowel surgery in the pelvic area.
- If it would be dangerous to embark upon a pregnancy.

**Is there an upper age limit for couples undergoing IVF?** Different units will have their own policy on the age limit of patients undergoing IVF. Generally, IVF is ***much less successful when the female partner is over 40***. We have an upper age limit of 45 years (female partner) in this centre.

**How successful is IVF?** The success of IVF treatment varies according to several factors. These include the woman's age, the duration of infertility and whether the woman has been pregnant before. The particular circumstances that affect your chance of successful treatment will be discussed with you and the most up to date results will be provided to you. If you have not been given these, please ask.

**What are the chances of a multiple pregnancy?** The incidence of triplets is no more than 1%. We aim to achieve a twin rate of no more than 10% in accordance with professional recommendations. Our policy is to replace either one or two embryos depending on factors such as patient age; attempt number and embryo quality. There may very occasionally be exceptional circumstances in which three embryos are replaced, but if three embryos are replaced the likelihood of triplets increases. Factors that increase the possibility of a multiple pregnancy include:

- Younger age of the woman
- Previous successful pregnancy
- Higher grade of embryo quality

**Is a baby resulting from IVF treatment at greater risk of an abnormality?** The risk of birth defects in the general population is low: 2% of children in Europe are born with birth defects. Although some research suggests that fertility treatment may be associated with an increased incidence of birth defects, this risk remains low.

**Will a baby resulting from IVF treatment develop normally?** The first person conceived following IVF treatment was born in 1978 and has gone on to have children herself naturally. As far as we know to date, other than problems of prematurity caused by multiple pregnancy, a baby conceived through IVF is as likely to develop normally as a child conceived naturally.

**Will a female resulting from IVF treatment have normal fertility?** There are some conditions which affect fertility that are known to have a genetic basis e.g. Poly Cystic Ovarian Syndrome. Apart from known inherited conditions, the process of IVF conception is not known to affect fertility in the offspring.

**Will a male resulting from IVF treatment have normal fertility?** Approximately 10 – 15% of severe male infertility has a genetic basis and is likely to be passed on to the male children that result from assisted conception. Apart from these cases the IVF / ICSI process itself is not know to affect fertility in the male.

**What is involved in IVF?** There are a number of steps involved:

- Preliminary tests - sperm count, blood tests for FSH level, HIV and Hepatitis B, C and Rubella, swabs from the cervix for bacteria and Chlamydia.
- Pre-treatment information session - information and implications.
- Your own hormones will be suppressed by injections.
- Stimulation of the ovaries with different drugs given by injection to cause the production of several eggs
- Monitoring the development of the eggs with ultrasound to assess the development of “follicles”
- Admission to hospital for the eggs to be removed (carried out under sedation or anaesthetic as a day case procedure)
- Fertilisation of the eggs by the sperm in the laboratory (this may require the additional assistance of ICSI – *please see information elsewhere in this booklet)*
- Replacement of the fertilised eggs - the embryos - inside the womb
- Drugs given to encourage implantation of the embryos.
- Two week wait during which the embryos may implant.
- Follow up visit for a pregnancy test.

The Centre is required by law (Human Fertilisation and Embryology Authority) to check the identity of patients undergoing licensed treatment. We therefore request that both partners bring photographic ID to the pre-treatment information session that they will attend prior to undertaking licensed treatments.

**Who will carry out the treatment?** IVF treatment to be successful involves a large number of professionals with different expertise who together form the ***Multidisciplinary Team.*** During the course of your treatment you will be seen by different members of this team at different stages. Your day to day contact will be with the nursing team, the majority of whom are experienced infertility practitioners who can answer most of your concerns. A doctor or trained senior nurse will undertake the removal of the eggs and replacement of the embryos.

**If treatment doesn’t work?** IVF / ICSI treatment is successful in only a proportion of cases but if treatment is unsuccessful it is important to gain from this as much information as we can, to inform you of your future chances and options. When you attend for a pregnancy test, if this is negative, the nurse will

have a brief chat about the treatment and provide you with the support that you need at this time. She will offer you an appointment to attend clinic to see one of the medical team to discuss this treatment and future recommendations and further treatment.

**Are there any dangers with IVF?** Generally speaking IVF is a safe procedure. There is a small risk of a pelvic infection developing after removing the eggs (0.3%). The most common complication is the ovaries over-responding to the stimulation regime (0.5%-2% of patients), so called Ovarian Hyperstimulation Syndrome. Very occasionally excessive bleeding occurs from the needle puncture sight during the removal of the eggs. Multiple pregnancy has been mentioned above. There has been some recent evidence to show that women who have received infertility drugs have a slightly increased risk of developing ovarian cancer in later life. This has not been substantiated and if the risk exists at all it is likely to be very small. This finding is further complicated by the fact that women who have not had children are at slightly higher risk also (***see elsewhere in this booklet for more details).***

**Are drugs always necessary in IVF treatment?** The purpose of the drugs used in IVF treatment is to increase the likelihood of successful treatment by potentially increasing the number of eggs available for fertilisation and replacement.

**What about freezing spare embryos?** If there are more embryos created than are necessary for the treatment i.e. one or two embryos are normally replaced, it may be possible to freeze and store the spare embryos. This is only usually offered if the quality of the spare embryos is good. Generally the success rates of replacement of frozen/thawed embryos is slightly lower than replacement of fresh embryos. *Please see further information on this elsewhere in this booklet.*

**Can donor sperm or eggs be used in IVF?** Yes. When the woman is unable to produce her own eggs, the use of donor eggs can provide the opportunity for treatment. The process is essentially the same except the patient does not have to go through the stimulation phase or the removal of the eggs. Donor sperm can also be used in circumstances when the woman requires IVF for her own particular reasons e.g. blocked fallopian tubes, and the male partner has no sperm.

**What is the difference between IVF and ICSI?** The couple undergoing Intracytoplasmic Sperm Injection (ICSI) goes through exactly the same process as they would in IVF. The key difference is that in IVF the sperm and egg are mixed together in a test tube, whereas in ICSI a single sperm is injected into the substance of the egg.

**How much does IVF cost?** This treatment may be available as NHS treatment. Eligibility for NHS treatment is determined by the Clinical Commissioning Group (the body that funds all health care in the district in which you live). Those who are not eligible for NHS treatment will have to pay for their own treatment. An up to date list of charges is available on request.

**Counselling** Independent counselling is available to all patients. Please ask any of our staff if you feel this would be beneficial. Separate information on the availability of counselling is provided. *Please see the details on counselling elsewhere in this booklet.*

# Intra Cytoplasmic Sperm Injection (ICSI)

**What is ICSI?** Intracytoplasmic Sperm Injection (ICSI) is a treatment that helps to promote fertilisation of eggs in circumstances where normal In vitro fertilisation will give a reduced chance of success. It involves the injection of a single sperm into an egg. ICSI requires all the steps that are involved in In Vitro Fertilisation (IVF) and this information should be regarded as supplementary and read in conjunction with that for IVF.

**Who is suitable for ICSI treatment?** ICSI is offered to patients who have a severe problem with sperm quality (very low numbers of sperm, a high percentage of abnormally shaped sperm or low percentage of moving sperm).

ICSI may also be offered to couples who have been through IVF treatment previously and who failed to achieve fertilisation of the eggs or had a particularly low fertilisation rate with IVF. Failure of fertilisation may occur even when the sperm looks perfectly normal. The reasons for failed fertilisation may then be due to subtle abnormalities of the sperm or possibly to problems with the egg. In most cases ICSI can overcome these problems.

In men who have no sperm in their ejaculate due to a blockage, sperm can be surgically recovered from above the block. In these cases ICSI is carried out to increase the chance of sperm recovered in this way fertilising the eggs. This is because sperm recovered surgically from the testicle or epididymis are usually in much smaller numbers than are needed for natural conception or normal IVF.

**What does ICSI involve?** The main difference between IVF and ICSI is that whereas IVF involves placing several thousand sperm together with the egg in a test tube, in ICSI a single sperm is injected into the substance of the egg. In IVF we need many thousands of sperm to achieve fertilisation, whereas in ICSI we only need one sperm per egg! As far as the woman is concerned, all steps of the treatment are identical to IVF. This is also true for the man, except in cases where sperm have to be surgically extracted from the epididymis or testicle. This latter circumstance is only applicable in a small number of men.

**How do we know if ICSI will be required?** The circumstances in which ICSI may be used have been described above. The main criteria for determining whether ICSI will be necessary are:

1. The sperm test results. Broadly, if there are fewer than 1.5 million motile sperm in the ejaculate or a combination of reduced numbers and increased percentage of abnormally shaped sperm.
2. Previous reduced or failed fertilisation in IVF treatment.

Unfortunately assessment of the sperm is not an exact science. Thus the fact that the sperm is reduced in quality or numbers does not necessarily mean that normal fertilisation cannot take place as many couples will testify to. Decisions on which treatment is best take account of a number of factors including the female circumstances, duration of infertility and previous conception.

**Will the act of injecting a sperm into the egg damage the egg?** Injecting a fine pipette into the egg can result in damage to the egg. In these cases the egg will not survive. Approximately 85 % of the eggs injected will survive.

**Are all eggs suitable for injection?** Eggs have to be at a certain stage of maturity for us to be able to inject them. Most eggs that are removed are at this stage, and it is rare not to have some eggs from a patient at the correct stage for injection.

**Does ICSI guarantee fertilisation?** No. We can never guarantee that we will achieve fertilisation. However, on average, we expect between 60 and 70 % of those eggs that are injected to fertilise. The incidence of complete failure of fertilisation with ICSI is very low.

**Is there any possibility that ICSI will increase the chances of an abnormal baby?** Because intra-cytoplasmic sperm injection (ICSI) is a fairly new treatment (it was introduced in 1992), it is not yet known whether there is any risk that injecting the sperm into an egg could damage it, with possible long-term consequences for the child.

The risks that have so far been associated with ICSI are:

- Certain genetic and developmental defects in a very small number of children born using this treatment. However, problems that have been linked with ICSI may have been caused by the underlying infertility, rather than the technique itself.

- The possibility that a boy conceived as a result of ICSI may inherit his father's infertility. It is too early to know if this is the case, as the oldest boys born from ICSI are still in their early teens.

- An increased risk of miscarriage because the technique uses sperm that would not otherwise have been able to fertilise an egg.

- A low sperm count caused by genetic problems could be passed on to a male child, so you may want to undergo genetic tests before going ahead with ICSI. Infertile men with low sperm count or no sperm in their ejaculate may be tested for cystic fibrosis genes and for chromosome abnormalities.

**Are there any other risks with ICSI?** ICSI involves the same procedures and drug administration for the woman as does IVF. There are the risks of ovarian hyperstimulation because of the drug stimulation of the ovaries, and the risks of the collection of the eggs. These problems are discussed in greater detail elsewhere in our patient information, and before undergoing ICSI you should read this information carefully.

**Will special follow up of a pregnancy or child be necessary as a result of this treatment?** It is important for the reasons mentioned above, and so that we may learn more about male infertility, that children are followed up in the long term. This will involve maintaining a register of children conceived in this way and periodically writing to the parents and eventually the offspring themselves - when they reach adulthood. As yet no definite plans have been established as to how this follow up might be conducted. As far as a pregnancy is concerned, the usual pre-natal tests will be offered. You may also wish to discuss the possibility of amniocentesis to assess the chromosomes of the baby, but this is by no means essential and does carry with it a small risk of miscarriage.

**How likely is this treatment to be successful?** ICSI is at least as successful as normal IVF. For more up to date information on success rates for this treatment please ask the unit's staff who will be happy to provide the information.

# Freezing of embryos - cryopreservation

Treatments such as IVF, ICSI and Egg donation often generate embryos that are surplus to the immediate requirements of the treatment. If these "spare" embryos are of sufficiently good quality they can be frozen and placed in storage for your future use.

**Why are surplus embryos created?** IVF and related treatments normally involve stimulation of the ovaries to produce a number of eggs. We aim to fertilise all of the eggs removed in order to have a selection of embryos to grow because not all embryos have the potential to develop. As they are growing, we are able to select the best quality embryos for replacement. In about 25% of cases, more embryos than the one or two necessary for replacement are of good quality and have the potential to survive cryopreservation and storage and be viable once they are thawed. If we place these embryos in storage this provides another possibility of pregnancy without having to go through the process of ovarian stimulation.

**Do we have to cryopreserve spare embryos?** No, it is not necessary to cryopreserve but we normally recommend this because it provides the opportunity of a pregnancy if the fresh replacement doesn't work - without having to go through the whole treatment again.

**Can all embryos be cryopreserved?** Only good quality embryos are likely to survive the freezing and thawing process. If you have spare embryos which are not good quality but you feel strongly that you would like them placed in storage, we will happily discuss this with you.

**How are the embryos cryopreserved and is there any danger to them?** The embryos are selected, placed in "cryoprotectant" fluid and inserted into a "straw" that is labelled with your unique details (this part of the process is witnessed to avoid any error). The straw is then placed into liquid nitrogen which lowers the embryos' temperature very rapidly to the storage level of -196°C. The straws are then placed into a large storage tank filled with liquid nitrogen. The method that we usually apply is called 'vitrification' which is a very rapid process of cooling embryos that attempts to minimise ice formation.

Embryos can be cryopreserved at various stages in their development e.g. day 1 (pronuclear stage), day 2/3 (4-8 cell stage) and day 5/6 (blastocyst stage). Eggs can also be cryopreserved. Generally speaking, during early development, most cells of the embryo have the potential to develop into all structures so that even if some cells are damaged, provided sufficient numbers of cells survive, they may have the potential to develop into a normal baby.

About 70% of embryos are expected to survive cryopreservation and there is no evidence of harm to the ability of the embryo to develop into a normal baby. Replacement of embryos after thawing from the frozen state has been carried out since 1984. It is not known how many babies worldwide have been created in this way but probably many thousands of babies have been born using this technique. Vitrification is a newer cryopreservation technique but is also widely used across the world for about 10 years. As far as we know there is no known increase in abnormalities resulting from vitrification. However, as with all assisted conception treatments, it is important to collect information on the outcome of such treatments.

**How long can embryos be stored for?** Embryos can be stored for up to 10 years in the first instance. Your embryos can only be stored for more than 10 years if you or someone to whom your embryos have been allocated (including your partner) is prematurely infertile or is likely to become prematurely infertile. A medical practitioner must certify in writing that the medical criteria have been met.
Where the criteria have been met, the storage period will be extended by ten years from the date the criteria are met. The storage period can then be extended by further 10 year periods if it is shown at any time within each extended storage period that the criteria continue to be met. There is a maximum storage period of 55 years. There is no known deterioration in the health of the embryo with time.

**Will the embryos survive the thawing process?**
Approximately 70% of the embryos will survive sufficiently intact for use. We have no way of knowing until they are thawed if they are going to survive.

**How long does it take to thaw the embryo?** Only a few minutes! Normally, the embryos are taken out of storage only a short while before they are going to be replaced. Sometimes we grow the embryos for a day or more after thawing to see if they can develop further. We will do this particularly if the embryos were at an early stage when they were stored.

**How many embryos will we thaw?** If we plan to transfer embryos on day 2 or 3 after ovulation, we normally thaw two initially depending upon the stage at which they were cryopreserved and assess their viability i.e. the number of cells which have survived from the original embryo. If either one or none of the first two embryos survive we will thaw the next one or two embryos until we have two embryos available for replacement into the womb. However, occasionally, no embryos will survive for transfer. Sometimes, we will thaw more embryos and select those for transfer by culturing for a day or two.

**Extended culture after thawing (for blastocyst transfer)** Increasingly we are thawing a group of embryos and culturing them for several days until they reach the blastocyst stage. This has the advantage that we are better able to select the embryo that has, theoretically, the greatest potential for further development and implantation. The disadvantage of this technique is that fewer embryos will survive if placed in culture for several days. If we begin this process with too few embryos it is possible than none will develop further or they will deteriorate in culture, and there may be no embryos to transfer into the womb. To give it the best chance of working we normally require five or more embryos. In case more than the required number of blastocysts develops, it is possible to refreeze the embryos at the blastocyst stage, but this may not always be advisable. We would discuss this situation with you if it arose.

**Cryopreservation and transfer of blastocysts**
If your fresh treatment cycle included blastocyst culture then you may have any spare blastocysts cryopreserved. Blastocysts have historically been more difficult to cryopreserve and less likely to survive than earlier stage embryos. However, the newer method of vitrification is believed to have made blastocyst culture a much more successful option. This is a relatively new technique, but it has rapidly gained popularity worldwide. The preparation for transfer of a cryopreserved blastocyst is the same, but the transfer usually takes place 5 days after ovulation, rather than 2 or 3 days for earlier embryos.

**What process is involved in the transfer of the embryos?** Embryos can be transferred in either a natural cycle (no drugs involved) or in a cycle in which the lining of the womb is stimulated with hormonal therapy *(if you are going to undertake this process, details of the drug regime will be provided to you).*

**How likely is the replacement of cryopreserved embryos to result in a pregnancy?** Our live birth rates for replacement of cryopreserved embryos have fairly consistent over the years (please review our success rates for latest figures). This is less than some units because we tend to freeze a larger proportion of spare embryos in order to give more chances of a pregnancy and our policy for thawing has been to replace the first two embryos which have an indication of viability. As stated above, we are increasingly culturing the thawed embryos for several days and replacing them at the blastocyst stage. Although this means that there are likely to be fewer surviving embryos, those that do survive are more likely to result in a pregnancy and our early results indicate almost a doubling of the pregnancy rate using this technique. We have performed relatively few transfers of cryopreserved blastocysts so it is too early to tell whether it is a better option overall.

**Your obligations.** The storage of embryos is governed by an act of parliament and we are obliged to comply with the law as it relates to this storage. This means that the storage of embryos requires your written consent, and we need to contact you periodically to confirm your wishes. ***Therefore it is most important that you remember if you have placed embryos in storage because if you change address or your personal circumstances change we may not be able to track you down unless you have informed us. Once your embryos in storage are approaching the maximum amount of***

***time covered by your consent and the legal requirements, then if you wish to extend the storage period, you must attend the clinic again to demonstrate that you meet the criteria for extended storage. Otherwise, the embryos will have to be taken out of storage and allowed to perish, to comply with the law.***

**What if I separate from my partner?** Embryos are created from a sperm and an egg. Therefore the provider of the sperm and the egg each have to consent individually to the terms under which the embryo is stored. Both partners (unless donor eggs or sperm are being used) will be required to complete a special consent form to indicate their wishes for the use of stored material. Embryos can only be used if both partners consent to the use which is being proposed. It is also important to consent to what you want to do with the embryos in the event that one or other of you dies. While this may seem, hopefully, very unlikely,it still needs to be considered. If donor gametes are used, the donor's consent is required too.

If you and your partner disagree over the use of embryos that you had in storage for future treatment, then the law requires there to be a 12 month 'cooling off period' during which time the embryos can be kept in storage until an agreement is reached. This period cannot over-rule the expiry date. This 1 year period is intended to allow time for all parties to be informed, and for discussion and consideration of all options by those concerned, with a counsellor, if necessary. If agreement is not reached by the end of the period, then the default position is that the embryos will be destroyed, unless legal proceedings by either party prevent this.

# Risks and complications of IVF/ICSI treatment

**There are few forms of medical treatment which are entirely free from risk. In Vitro Fertilisation and other forms of assisted conception are no exception. However, while it is important to have information about these risks, it is also <u>important to appreciate that many women go through these treatments without any problems</u>.**

**This section has been written to provide general advice for patients considering assisted conception treatment. This includes the following treatments:**

- **ovulation induction in which drugs are used to treat women who are not ovulating**
- **intrauterine insemination of sperm when used with drugs to stimulate egg production**
- **in vitro fertilisation and related treatments such as intra cytoplasmic sperm injection (ICSI) and egg donation**

**The risks of these treatments can be considered in five areas:**

1. **The risks associated with the drugs used to stimulate egg production**
2. **The surgical risks associated with egg removal during IVF, ICSI and egg donation**
3. **The risks associated with pregnancy resulting from any treatment**
4. **The risks of producing an abnormal baby following IVF, ICSI or egg donation**
5. **The risk of treatment not working**

**Risks associated with drugs used to stimulate egg production**

**Excess stimulation of the ovaries -Ovarian Hyperstimulation Syndrome (OHSS)**

Stimulation of the ovaries is a deliberate consequence of IVF treatment in order to obtain more eggs than would arise in a natural cycle. When the ovaries are too strongly stimulated there is a possibility of **OHSS** developing.

The majority of cases are a mild to moderate form, occurring in up to 6% of all patients undergoing IVF treatment. This is manifest by abdominal distension, abdominal discomfort and nausea. These cases settle in a few days and require observation, possible blood tests but no specialist treatment.

Less commonly a more severe case occurs. This happens in 0.1-4% of all IVF cycles. This is manifest by more marked abdominal distension, nausea and vomiting, decreased output of urine and some difficulty with breathing. This requires admission to hospital for treatment that may include replacement of lost fluids, replacement of protein (albumin) and drainage of fluid from the abdominal cavity. This condition normally responds to treatment and resolves completely in 1 - 2 weeks. Extremely rarely OHSS can be life threatening and fatalities have been reported.

***One of the purposes of monitoring the IVF cycle is to detect early signs of OHSS and modify or cancel the treatment if there are indications that this is developing. Treatments may be modified by reducing the strength of stimulation, coasting the stimulation (continuing the treatment but stopping the stimulation for several days or going ahead with the egg collection but freezing the embryos as we know pregnancy aggravates OHSS and can prolong and worsen its course).***

***Ovarian Hyperstimulation Syndrome only rarely occurs after ovulation induction and following ovarian stimulation associated with intrauterine insemination (IUI).***

**Cancer**

a) **Ovarian cancer.** It has been suggested that the use of drugs used to stimulate ovaries may increase the risk of ovarian cancer. Two studies from North America suggested that the risk of ovarian cancer developing increased in women using the drug Clomifene. Subsequent studies have not confirmed this risk. Women who have never been pregnant are known to be at slightly increased risk of ovarian cancer. The current position is that if a risk of ovarian cancer exists it is very low and unconfirmed.

b) **Uterine cancer**. There is no association between the use of drugs to stimulate ovulation and the development of uterine cancer.

c) **Cervical Cancer.** There is no association between the use of drugs to stimulate ovulation and the development of cervical cancer.

d) **Breast cancer.** There is no association between the use of drugs to stimulate ovulation and the development of breast cancer

## The surgical risks associated with egg removal during IVF and related procedures

**General anaesthetic and intravenous sedation**

Patients undergoing IVF and related treatments will receive either intravenous sedation or general anaesthetic. This is a safe procedure, but very occasionally there will be an adverse reaction to drugs, or other complication. The risk of serious harm is very low (**0.01 %)** and is similar to that of other elective surgery.

**Egg collection and damage to internal blood vessels**

The ovaries are surrounded by important structures, including bowel, bladder, and major blood vessels. It is theoretically possible to puncture one of these structures although the likelihood is very low. The risk of a significant haemorrhage from an internal blood vessel is approximately **0.05 %.** If this occurred it would require immediate abdominal surgery to rectify the problem.

**Pelvic Infection**

Removal of eggs involves passing a needle through the vaginal wall into the ovary and it is possible to introduce infection into the ovary. This possibility is increased if there is an endometriotic cyst in the ovary at the time of treatment. This complication may cause pelvic pain and other signs of infection developing in the weeks after the procedure. It is treated with antibiotics but may rarely require abdominal surgery to drain an abscess. The risk of serious pelvic infection is approximately **0.2 %**.

## The risks associated with pregnancy resulting from any treatment

**Multiple pregnancy**

***Multiple pregnancy can result from any treatment involving the use of drugs to stimulate egg production or when more than one embryo is replaced during IVF / ICSI or egg donation treatment.***

The likelihood of a twin pregnancy resulting from Clomifene treatment is approximately 10%, following IVF when two embryos are replaced 20-30%, and following IUI treatment 10-20%.

Triplet pregnancy can also result from any of these treatments but is less likely: after Clomifene therapy less than 0.5%, and following IUI treatment 1-2%. The risk of triplets following IVF and related treatments is very low if 1 or 2 embryos are replaced although occasionally an embryo can split. If three embryos are replaced the likelihood of triplets increases.

The complications of multiple pregnancy are:

- Increased risk of miscarriage
- Increased risk of premature labour
- Increased risk of pregnancy-associated problems such as haemorrhage and high blood pressure
- Increased requirement for caesarean section and its complications
- Increased loss of a baby (still birth)
- Increased risk of a baby with physical or learning disability (as a result of premature birth)
- Increased risk of an abnormal baby

**Ectopic Pregnancy**

IVF and related treatments increases the likelihood of an ectopic pregnancy. The incidence of ectopic pregnancy is **1-3 %** of all pregnancies resulting from embryo transfer. Patients who become pregnant following these treatments should have an early scan to ensure the pregnancy is correctly positioned. Ectopic pregnancy is usually treated surgically by removing the fallopian tube.

**Heterotopic Pregnancy**

This is a twin pregnancy with one in the Fallopian tube (or other ectopic place) and one correctly situated in the uterine cavity. Although this is a rare condition its incidence increases following IVF and related treatments. This should be excluded by careful ultrasound undertaken in the early stages of pregnancy following these treatments.

**Miscarriage**

Early miscarriage is very common in naturally conceived pregnancies. IVF and related treatments neither prevent nor increase the risk of miscarriage. However the risk of miscarriage is increased in multiple pregnancy although not specifically those resulting from IVF treatment.

## Risk of an abnormal baby following IVF / ICSI and related technologies

The risk of birth defects in the general population is low: 2% of children in Europe are born with birth defects. Although some research suggests that fertility treatment may be associated with an increased incidence of birth defects, this risk remains low.

Because intra-cytoplasmic sperm injection (ICSI) is a fairly new treatment (it was introduced in 1992), it is not yet known whether there is any risk that injecting the sperm into an egg could damage it, with possible long-term consequences for the child.

The risks that have so far been associated with ICSI are:

- Certain genetic and developmental defects in a very small number of children born using this treatment. However, problems that have been linked with ICSI may have been caused by the underlying infertility, rather than the technique itself.

- The possibility that a boy conceived as a result of ICSI may inherit his father's infertility. It is too early to know if this is the case, as the oldest boys born from ICSI are still in their early teens.

- An increased risk of miscarriage because the technique uses sperm that would not otherwise have been able to fertilise an egg.

- A low sperm count caused by genetic problems could be passed on to a male child, so you may want to undergo genetic tests before going ahead with ICSI. Infertile men with low sperm count or no sperm in their ejaculate may be tested for cystic fibrosis genes and for chromosome abnormalities.

**ICSI, and other treatments which combine with ICSI e.g. PESA.** A proportion of men with severe sperm abnormalities have a genetic basis for this, usually an abnormality of the Y chromosome. This is likely to be inherited by male offspring following ICSI. There has also been reported an increase in abnormalities in the number of the X or Y chromosomes in infants conceived following this treatment also likely to have resulted as a consequence of the cause of infertility (0.6% compared to 0.2% in naturally conceived children).

**Embryo cryopreservation and thawed embryo transfer.** This technique has been carried out since 1984. The number of babies born is considerably less than by IVF. To date there has been no conclusive evidence of any increased incidence of abnormalities in babies born following replacement of thawed embryos.

## Psychological and emotional risks

Undoubtedly infertility can lead to stress. Stress can also lead to infertility in some cases. Treatment for infertility is also stressful because of the emotional "roller coaster" of expectation, disappointment and success and the marked hormonal changes that occur during the cycle of treatment. This can in turn place strain on the relationship. Support should be provided by the staff of the infertility unit during this difficult time and additionally patients may find benefit from counselling.

## Laboratory risks

The processing of sperm and eggs in the laboratory is a complex and skilled process carried out by qualified scientists. It involves a number of stages including gamete preparation, fertilization, embryo assessment and culture and replacement. Additionally there may be a requirement to freeze spare embryos and prepare them for storage.

Protocols and quality assurance are rigorous and are designed to minimise errors in laboratory procedures. While serious mistakes are rare, things can and do go wrong. There will be occasions when an unforeseen problem with equipment or the culture media may give rise to adverse conditions and lead to one of the following:

- **Lower than expected or failure of fertilisation**
- **Low percentage of embryos dividing after fertilisation**
- **Lower quality of embryos than would normally be expected**

Problems of this nature are uncommon, nevertheless all IVF laboratories will experience such problems from time to time.

Patients may also, quite reasonably, be concerned about the possibility of a "mix up" in sperm, eggs or embryos. Procedures in the UK include specific measures to minimise the likelihood of such an event. The regulatory authority, the Human Fertilisation and Embryology Authority, inspects laboratories on an annual basis to ensure these procedures are in place.

## Embryo transfer

The placement of the embryos back inside the cavity of the uterus (womb) is a relatively simple procedure. There are virtually no risks to the female in carrying this out. Occasionally, however, one or more of the embryos may be lost during the course of placement. This is because the fine catheter that is used has to be passed through the canal of the cervix which is normally very narrow and contains mucus. Despite taking great care with this procedure the catheter does not always pass through the cervix easily and sometimes the embryos get caught in the mucus.

## Risks of treatment failing

There are reasons for failure at every stage and these include:

- Failure of the ovaries to respond to drug stimulation.
- Failure of the eggs to be released or for the eggs to be released prematurely – although the stimulation cycle is managed in such a way as to minimise this risk.
- Failure to collect eggs – either for the reasons stated above or because of technical problems during egg collection such as inaccessible ovaries.
- Failed fertilisation. Although this may sometimes be anticipated it occurs despite normal egg and semen quality in a small proportion of cases.
- Failed embryo development.
- Infection in the culture media. This is very uncommon.
- Difficulty in replacement or loss of embryos during transfer. This is also very unusual.
- Despite all components of the treatment progressing normally the patient may still not become pregnant.

# Special Techniques

## Blastocyst or extended culture of embryos

During natural conception, fertilisation takes place in the fallopian tube and the embryo enters the womb 4-5 days later when implantation takes place. At the stage of implantation the embryo is termed a blastocyst. Blastocyst is the term given to an embryo which has grown normally for 5-6 days after fertilisation and normally has about 100 + cells. We can recognise a blastocyst because it has certain characteristics, for example a small central fluid filled area and the developing fetal cells to one side of the embryo. Research has shown that replacement of embryos into the uterus at the blastocyst stage of development may improve the likelihood of implantation. The possible reasons for this are firstly that the embryo is being replaced into the uterus at a more natural time, and secondly that observation of the growth of embryos to the five / six day stage allows us to select those embryos that are most likely to have the potential to continue development as it is known that embryos can stop growing at certain stages in the first few days.

The drawback of extended embryo culture is that approximately only 25% of the embryos are likely to survive to the blastocyst stage and it is not known whether this because of the artificial culture medium or the fact that the embryo would not have developed anyway.

Those patients best suited to this type of treatment are those that produce more eggs than average and have good rates of fertilisation. In these cases it is much more likely that there will be embryos reaching the blastocyst stage. If 10 eggs are fertilised there is a very good chance of having two blastocysts for replacement.

There are no proven risks to the embryo using this technique, indeed the very first IVF baby was created in this way. However some experts have raised concerns about prolonging culture outside the body longer than is absolutely necessary. The known risks of blastocyst transfer are those of the general IVF process itself (see elsewhere) except that there is likely to be an increased chance of a multiple pregnancy.

Published results from those centres (mainly in the US) using this technique routinely report very high pregnancy rates, however these results have not been repeated in the UK or Europe.

At this centre we offer blastocyst culture and replacement to selected patients and we are happy to discuss this with you. We have recently audited our results with blastocyst replacement and ongoing pregnancy rates are in excess of 35% in a relatively small number of patients.

The process of blastocyst culture relates specifically to the laboratory procedure. All aspects of the treatment for the male and female partner are the same as for normal IVF (see elsewhere) with the exception that the timing of the embryo transfer is delayed. The replacement of the embryos is also the same as in normal IVF (although the embryos are further advanced, they are still microscopic).

**Freezing of blastocysts** It is possible to freeze blastocysts in the same way as embryos at earlier stages of development. The laboratory techniques are slightly different and because of the increased complexity of the embryo the likelihood of the embryo surviving this process is less (about 50% compared to 70%). A recent audit of replacement of thawed blastocysts in this centre showed an ongoing pregnancy rate of 20% on a small number of placements.

## Assisted Hatching

This is a technique whereby the outer wall of the embryo (the zona pellucida) is deliberately weakened by artificial means.

It is believed that, before an embryo can implant into the lining of the womb, it has to “hatch” through its outer lining of cells known as the zona pellucida. Resistance to this natural process may lead to failure of implantation. Cases in which this may occur more commonly include women over 40, couples who have been through several unsuccessful attempts at IVF without any obvious reason, and cases in which the zona pellucida looks particularly thick.

The techniques that are used to undertake assisted hatching include mechanical weakening (breaking down a part of the zona with a fine pipette); laser energy (literally burning a hole in the zona using laser energy); chemical weakening (dipping the embryo into a solution containing a special substance which causes chemical thinning of the zona). There is no evidence that one technique is superior to another and in this centre we use mechanical assisted hatching. There are no known risks to the fetus using this technique, although there is insufficient data to be completely certain. The risks of this technique are therefore those of the IVF / ICSI procedure itself. It is possible to carry out assisted hatching as part of IVF, ICSI, on fresh or thawed embryos and on those which have been cultured to the blastocyst stage.

The findings from research studies have not shown conclusively that Assisted Hatching improves the chances of a pregnancy. There is, therefore, at present no evidence for its use except as part of a research study and the National Institute of Clinical Evidence in their recent infertility guidelines do not recommend its routine use.

## Surgical extraction of sperm (TESE / PESA)

Normally sperm are produced in the testes and pass through a series of tubules called the epididymis where they collect and concentrate before ejaculation through the vas. During passage from the point of formation to the epididymis the sperm mature and gain their ability to swim and fertilise the egg.

Some men produce no sperm in the ejaculate, the most obvious example of which is men who have had a vasectomy. Obstruction of the vas can also occur as a result of a congenital abnormality or due to blockage through previous surgery or infection. Another possible problem is men who are unable to ejaculate because of a spinal cord injury. In these circumstances sperm can be removed from above the point of blockage.

In some men the sperm forming cells work at such a low rate that no sperm appear in the ejaculate even though there is no blockage. There are a number of reasons for this including previously undescended testicles, certain drug therapy and mumps. In these circumstances it may be possible to remove sperm directly from the testicle.

Surgical extraction of sperm involves a small operation on the male to remove sperm from either the epididymis or testicle. The precise technique will depend on the particular problem. It is carried out with a general anaesthetic. It may result in bruising or swelling of the testicle. Infection and bleeding from the site of the extraction are other possible risks. Several small stitches may be left in the scrotal skin at the end of the procedure. After the operation you will able to go home after an hour or so. If you have had sedation or a full anaesthetic you will not be able to drive for 24 hours. It is also advisable to wear a scrotal support for a few days to limit bruising and discomfort.

It is not always possible to remove sperm in this way. In men whose sperm-forming cells are not working properly, and whose blood FSH level is raised, it may only be possible to find sperm in approximately 50% of cases. For men whose problem is a blockage in the vas, it is usually possible to obtain sperm in greater than 90% of cases.

Once the sperm is removed it is checked by the scientist, frozen and stored. Sperm removed in this way can only be used through the process of intra cytoplasmic sperm injection (ICSI). Therefore once we know there are sperm the female partner must go through the process of IVF to produce eggs which can then be fertilised by ICSI.

Sperm removed from a man whose sperm forming cells are not working (failure of spermatogenesis) are less likely to result in a pregnancy than sperm removed from a man with a blockage in his vas. Babies conceived in this way are as likely to be normal as children conceived by conventional IVF /ICSI.

## Fertility Preservation techniques including egg freezing

Fertility preservation may be called upon in a case where a man or woman are about to undergo treatment for cancer which might jeopardise their fertility, for example chemotherapy.

In such cases the patient should be offered the opportunity to discuss their future fertility with a specialist before embarking on the cancer treatment, irrespective of whether they were intending to have children in the near future.

For the man, the option is fairly straightforward. Sperm is produced, frozen and stored. This is proven and successful technology.

For the woman the issue is less straightforward. The options for the woman are as follows:

a) If she is in a relationship and had been planning to have children – to remove eggs, fertilise them with partner's sperm and freeze the resulting embryos. This is proven technology and has a reasonable chance of producing a pregnancy at some time in the future, depending on the number of embryos produced. This process is known as IVF and will typically delay the start of cancer treatment by 2-4 weeks.
b) If the woman is not in a steady relationship, or doesn't wish to create embryos there are two options. Firstly, eggs could be removed from the ovaries, frozen and stored. This requires the woman to go through stimulation of the ovary with drugs and a small operation to remove the eggs. This will typically delay the cancer treatment by 2-4 weeks. When the time comes to use the eggs, they are thawed, fertilised and replaced into the womb as embryos. The chance of these eggs resulting in a pregnancy is low - < 10% - and this treatment should still be regarded as experimental.
   Secondly, an operation could be carried out to remove a piece of the ovary which is then frozen and stored and re-implanted at a later date. This would require the woman to undergo a laparoscopy. This would delay the onset of cancer treatment by up to 2 weeks. This treatment is completely experimental and has only twice resulted in the successful birth of a human.
c) If it is not possible to preserve fertility, and the chemotherapy treatment stops the ovary working, then if pregnancy is to be achieved, donor eggs will be required. This is quite common and generally a very successful treatment.

In difficult cases such as these, careful discussion is required, part of which will inevitably have to deal with the use of stored sperm, eggs or embryos in the event of the death of the patient.

# Information and Support

The team at the Centre for Reproductive Medicine aims to provide the best possible care for every patient. This includes attending to psychological well-being as well as to physical needs. Support is provided by all clinic staff to manage not only the practicalities but also the outcomes of treatment - both positive and negative. The clinic staff are also there to provide information and support to address the implications of treatment – particularly those relating to IVF/ICSI procedures and/or the use of donor sperm, eggs or embryos.

## Contact with the clinic staff

- First of all you will have met with one of the ***medical staff*** who will have explained the nature of any fertility problem(s) and the options for treatment. They will also have discussed the nature of the treatment(s) and the likelihood of success.

- You may then see, at any time, one of the ***specialist infertility nursing staff*** who will go through with you the information covered at your medical consultation, giving you the opportunity for further discussion and clarification.

- If necessary, a further appointment will be made for you to see the medical staff.

- An appointment with one of the Centre's dedicated counsellors can be made at any stage from the beginning to end of your journey through fertility problems and treatment. The counsellors have a separate and independent role in providing support, are professionally qualified, and have specialist knowledge and skills to help you with the social, emotional and psychological experience of trying for a baby and undertaking treatment.

***Please ask at any time to see any member of the team if you would like to discuss any problem(s)/relating to your fertility and/or its treatment.***

# The Centre's Counselling Service

A professional and confidential counselling service is available free of charge to all those attending the Centre for fertility investigations, treatment, donation or storage procedures.

### Why counselling?

Having a child is a major life event for any individual and couple. When this is proving difficult to achieve, and requires medical intervention, it can feel like a major life crisis. The emotional 'ups and downs', and other pressures and uncertainties that come with needing help to have a baby, are well recognised within the field of assisted reproduction.

***We therefore regard professional counselling as an essential and integral part of the care the Centre offers you.***

### How can it help?

Whatever the nature of infertility and eventual outcome of any treatment, there are times when it may be helpful to have someone to talk to who will help you

- make sense of how you are feeling
- understand your own and others' reactions
- find ways of coping more satisfactorily
- clarify your thoughts and decide your way forward with or without treatment
- adjust to changes in how you hoped to have a child
- come to terms with not having a child
- make different plans for your life

***Counselling at the Centre provides the opportunity to talk with a specially trained person who is:***

- separate from other relationships and areas of life
- willing to listen with care and respect
- non-judgemental
- supportive without being directive or an 'expert' with advice
- informed about the processes involved in assisted reproduction and the legal, social and psychological aspects of infertility and treatment.

Having time and space to talk through whatever challenges you face can help 'lighten the load' and lessen the sense of isolation. However, counselling can also be an unsettling process as the issues and emotions involved are unsettling and often deeply felt. Addressing them takes courage and work. At the same time it is by no means an "all doom and gloom" experience.

There are times when it is important just to have some quiet space “away from it all”, and there are occasions when there is good news that needs to be shared and supported.

***Counselling respects confidentiality, individuality and people’s responsibility to make their own decisions.***

Counselling is not about ‘telling you what to do’ or ‘giving you the right answers’ but about helping you find your own answers, and regain control in a situation that often feels out of your control and disempowering.

## What kinds of issues does it cover?

### Relationships

The ‘roller coaster ride’ of investigations, treatment and results can cause tensions and affect relationships of all kinds. For a couple, the time when one partner most needs the help of the other may be the time when it is least available, as each is under pressure to cope and is not always able to give the support wanted by the other. It may be, too, that one partner holds back feelings out of concern for the other or out of fear of making things worse for them both.

Other people, even amongst family and friends, may also not react in the way you hope for. The experience of wanting and not having a baby can be difficult for you to talk about and for others to respond to , when you feel vulnerable and they feel at a loss to know what to say or do to help.

***In counselling it is possible to look at patterns of behaviour and communication in order to have more insight into your own and others’ reactions, deal with differences, and take care of your own needs.***

### Feelings of loss

Having children is what most of us expects to be able to do when we decide we want to. When this does not happen there are many different losses which each person experiences in their own way. These often include loss of self-confidence and of a sense of control over life, as well as loss of a hoped for child and family.
Along with sadness and distress there may be feelings of

- isolation
- anger
- anxiety
- envy and longing
- guilt and blame

In addition, treatment brings its own pressures and uncertainties.

***You may manage to cope successfully with all of these feelings by yourself or with the support of your partner, family or friends. Or you may consider counselling.***

## Specific procedures

There are times when counselling may be an integral part of your preparation for treatment. If you are considering

- donating eggs, sperm or embryos
- having treatment using donated eggs, sperm or embryos
- being involved in a surrogacy arrangement

***Counselling provides the opportunity, before making any final decisions, to talk through all the implications for you, your family and for any child that may be born as a result of undertaking any of these options.***

## Making decisions about the use of stored embryos

If you have remaining frozen embryos for which storage is nearing an end, and you do not wish to use them in any further treatment of your own, deciding which other option to pursue can present a difficult dilemma. Whether the chosen way forward is to donate the embryos to scientific research, training or someone else's treatment, or to allow them to perish, the ending of storage brings a finality that some people find more difficult than expected.

***In this situation counselling and embryology staff work closely to ensure that you have as much information and support as possible to make the decision that is right for you and see it through.***

## Ending treatment

Sadly not everyone who starts treatment will become pregnant, and making the decision to stop is not easy. Letting go of treatment and moving on can bring a mixture of feelings: sorrow and grief that this no longer brings hope of a child, and relief that there are no longer the pressures of each cycle to cope with.

***Counselling can support you through this process of ending, help you find ways of readjusting and, when you are ready, consider other options. Adoption is one but it is not assumed to be the automatic next step or right way forward for every person.***

## Other related issues

Infertility and treatment can give rise to many different issues that may affect you to various degrees at various times, and in various combinations. In addition to those described above, counselling may be of support in coping with

- Stress
- Depression
- Loss of interest in or difficulties with sex
- Fertility-related medical conditions
- Past events / experiences resulting in present difficulties

***If you are uncertain about whether the Centre's counselling service can offer you the kind of help you are looking for you are welcome to telephone or meet with one of the counsellors to discuss your situation.***

***If the Centre's service is does not provide the support you require the counsellors we will do their best to inform you about other possible sources.***

### When and where is counselling available?

Providing you are attending the Centre for investigations, treatment, donation or storage procedures, counselling is available at any stage of your journey, and afterwards

***Counselling can be for one session or a number of sessions – as agreed with the counsellor. The service is provided as an integral part of your care and does not involve any additional charge.***
***A counsellor is usually in the Centre three or four days during the week***

(Monday, Thursday & Friday **or** Monday, Wednesday, Thursday & Friday) Appointment times vary according to the day and may be available from 8.30am to 4.00pm. They are normally arranged in advance, with sessions taking place for an hour to an hour-and-a -half, in the counselling room in the Centre.

### Who attends?

Sessions are open to individuals, couples and others who are involved in or affected by treatment procedures or are providing immediate support.

### Who are the counsellors and how are they contacted?

The Centre's Counselling service is provided by professionally qualified counsellors who are members of the British Association for Counselling and Psychotherapy (BACP) and the British Infertility Counselling Association (BICA). They work within the BACP Ethical Framework for Good Practice in Counselling and Psychotherapy and the BICA Guidelines for Good Practice in Infertility Counselling.
The counselling service also meets the Human Fertilisation & Embryology Authority (HFEA) requirements for the provision of counselling in a clinic like the Centre for Reproductive Medicine at University Hospital, Coventry.

**Tel:** 024 **76 968879** (Reception)

Alternatively you can ask one of the Centre staff to make a referral to the counselling service on your behalf.

## For more general information about counselling

Please see: www.bica.net
www.bacp.co.uk
www.hfea.gov.uk

## Gift of a Life appeal

The Gift of a Life appeal is a ***registered charity No.702108*** set up in 1989 to raise awareness and funds to help the work of the Assisted Conception Unit (now known as the Centre for Reproductive Medicine) at University Hospitals Coventry & Warwickshire NHS Trust.

Before 1990 there was no infertility service for the people of Coventry and Warwickshire. If infertility treatment was required, patients had to travel to Oxford or London. Without the commitment, dedication and hard work of the committee and fund raisers of the Gift of a Life appeal there would be no infertility treatment available here in Coventry. Now thanks to their efforts we have one of the leading units in the UK offering a comprehensive range of treatments.

As existing equipment needs replacing, new developments and research into infertility require support so charitable funding will continue to be needed for the foreseeable future. The Gift of a Life Appeal accepts charitable donations in support of these objectives. It is run by volunteers and has no overheads so any donation contributes 100% to the support of infertility and related conditions.

# Glossary of reproductive terminology

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| **Acrosome reaction** | A test involving assessment of the capacity of the head of the sperm to undergo certain changes necessary for fertilisation. It is a test which is used for experimental purposes only. |
| **Adenomyosis** | Thickening of the wall of the uterus (womb). Cause not known. Usually occurs late thirties to mid forties. May result in heavy, painful periods. Almost invariably benign. |
| **Alpha Feto-protein test** | The so called double or triple test is a test to assess the risk of a baby having Down's syndrome or abnormalities of the spine (spina-bifida). It is a blood test carried out at 16 weeks into the pregnancy. The test is only a screening test and only detects 65 % of all babies who have Down's Syndrome. A positive result does not mean the baby has anything wrong. Indeed the vast majority of pregnancies with a positive result have normal babies. |
| **Amenorrhoea** | Absence of periods. This invariably means that there is no ovulation (egg release). There are a number of different causes depending on whether the periods existed for a number of years and then stopped or whether the women never had any periods at all. Either case requires specialist investigation. |
| **Amniocentesis** | A test carried out during the early part of the pregnancy to determine the chromosomes of the baby. It can be carried out from 11 weeks onwards. It involves passing a small needle through the abdominal wall into the fluid surrounding the baby and removing a small amount of this fluid (liquor). The fluid is sent away for analysis. The test carries a small risk of causing a miscarriage (1 in 150 tests). The test is commonly used to test for Down's syndrome. |
| **Aneuploidy** | Means abnormal number of chromosomes. Normally refers to eggs or embryos which are chromosomally abnormal. |
| **Androstenedione** | A male hormone produced by the ovary and adrenal glands in the female |
| **Anovulation** | Failure of ovulation. There are many possible causes for this. |
| **Anovulatory cycle** | A menstrual cycle in which no egg is released. About 10 % of regular menstrual cycles are "anovulatory". |
| **Anti sperm antibody** | These are antibodies found in the seminal fluid which act against the man's own sperm. It is thought they are most likely to arise after some damage to the testicle perhaps through an operation. They are frequently found after vasectomy. There are two main types - IgG and IgM. They may vary in concentration, anything less than 20 % not being significant. |
| **Artificial Insemination** | The insemination of husband's or partner's sperm close to the cervix using a fine straw or catheter. This is normally timed to ovulation using ultrasound scans and/or assessment of the mucus. |
| **Ashermann's Syndrome** | This condition results in absent or very light periods due to scarring (adhesions) affecting the lining of the womb. This can sometimes arise after repeated curettage ("scrapes" or D & C) or evacuations (performed for miscarriage). |

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| **Assisted Hatching** | A small hole is made in the outer wall of the embryo - the Zona Pellucida - just before it is replaced inside the uterine cavity. This is designed to promote the hatching of the embryo through its outer shell and its subsequent implantation in the endometrium. The treatment is the same as IVF in other aspects. |
| **Asthenospermia** | Reduced sperm movement. |
| **Azoospermia** | Complete absence of sperm. This may be due to a blockage or to failure of the sperm to develop in the testicle. |
| **Bacterial vaginal infection** | Bacteria exist normally in the vagina. Sometimes theses can cause infection around the cervix or, in susceptible individuals, in the uterus or Fallopian tubes. A common example is Group B Streptococcus. About 20 % of women carry this bacteria without problems. Infection is easily treated by Penicillin. |
| **Biochemical pregnancy** | The period is slightly delayed. The pregnancy test becomes positive but the pregnancy never establishes itself and no sac develops in the uterus. The bleeding that starts is not a miscarriage but a heavier than usual period. |
| **Blastocyst** | The name given to an embryo which is 5 - 6 days old. It is recognised because it has an inner fluid-filled area and a clump of cells to one side known as the "inner cell mass" from which the actual substance of the baby will develop. |
| **Blastomere** | A single cell of an embryo. |
| **Blighted Ovum** | This is an early pregnancy which will not continue. It is a pregnancy sac without any fetal tissue inside. Cause unknown but may be due to a chromosomal abnormality. |
| **BMI (Body Mass Index**) | An index of obesity. Calculated from body weight in kgs divided by height in metres squared. |
| **CASA - computerised sperm motion analysis** | A test in which the velocity and characteristics of sperm movement can be assessed accurately. This test is more of a research tool than having real practical value. |
| **Cervical Smear** | A test taken by scraping a fine layer of cells from the outside of the cervix to detect for early signs of cancer. It should be taken once every three years from the first age of regular sexual activity or no later than 25 till the age of 65. |
| **Cervix** | Known as the neck of the womb. It is part of the uterus. It protrudes into the top of the vagina. Cancer smear tests are taken from the surface of the cervix. It has a canal which produces mucus and through which the sperm passes to enter the womb. |
| **Chlamydia** | A common bacterial infection which is passed between sexual partners. It can cause infection of the cervix and Fallopian tubes leading to scarring, blockage and subsequent infertility. It is easily treated with antibiotics, namely Erythromycin or Tetracycline. Both sexual partners should be treated. |
| **Chorionic villus sampling** | A test carried out in the early stages of pregnancy (10 weeks onwards) to test |

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| **(CVS)** | the baby for chromosomal abnormalities such as Down's syndrome. The test involves passing a fine needle through the abdominal wall into the placental tissue lined to the inner wall of the uterus. It carries a small risk of miscarriage (1-2 %). It is able to provide a result within a few days. |
| **CIN** | The abbreviation for Cervical Intraepithelial Neoplasia. This is the term given to abnormal tissue in the cervix. It has three degrees of increasing severity. Grade 1 which is very mild and may or may not require treatment. Grade 2 which is moderate and may be early pre- cancer and does require treatment. Grade 3 which is pre-cancer and does require treatment. The treatment is usually by local excision (loop cone). |
| **Cleavage (embryo)** | The process of the cell of the fertilised egg dividing into 2 cells or more. |
| **Clitoris** | A fibro-muscular structure immediately above the entrance to the vagina. It is analogous to the penis in man. |
| **Co-culture** | A special system of culturing embryos where they are cultured in a medium which contains other types of cells such as those obtained from the Fallopian tube. |
| **Colposcopy** | Telescopic examination of the cervix. Carried out to investigate an abnormal smear. Does not normally require an anaesthetic. The procedure may also include a biopsy (specimen of tissue taken away for further tests) and treatment. The procedure takes about 15 minutes. |
| **Congenital absence of the vas** | A rare condition present from birth which results in absence of the vas deferens.This results in infertility as no sperm can appear in the ejaculate. These men can be treated by obtaining sperm from above the blockage in the vas. There is a strong association between this condition and cystic fibrosis and such men should be screened for the cystic fibrosis gene before being considered for infertility treatment. |
| **Corpus Luteum** | The follicle becomes the Corpus Luteum after release of the egg. It may persist for a week or more as an enlarged "follicle". It produces the hormone Progesterone. |
| **Culture Medium** | The substance that is used to culture the embryos in. |
| **Cryopreservation** | Sperm or embryos can be stored deep frozen for months or years and then thawed for use in treatment. |
| **Cytomegalo Virus (CMV)** | This is a micro-organism which is a cross between a bacteria and a virus. It may be acquired as a sexually transmitted disease. It is not known to cause infertility but an active infection in pregnancy can cause harm to the developing fetus. Its presence can only be detected by a blood test. Its importance in infertility is in screening prospective donors and recipients so they can be matched. |
| **Dermoid** | Is a commonly found type of ovarian cyst. It arises from "germ cells" within the ovary. It may contain structures such as hair, cartilage or occasionally teeth. It is usually a benign tumour. |
| **D & C** | The abbreviation for dilatation of the cervix and curettage (scrape) of the lining of the uterus (womb). It may be carried out to investigate abnormal bleeding patterns or to evacuate a miscarrying pregnancy. It normally requires a general anaesthetic. |
| **Donor Insemination (DI)** | The insemination of donor sperm into the uterus. A procedures similar to a smear. |

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| **Down's syndrome** | A relatively rare condition present from birth (congenital) which results from there being an additional chromosome (number 21). The chromosome complement is 47, XY, no. 21. These children are mentally handicapped and often have physical disabilities. |
| **Dysfunctional Uterine Bleeding (DUB)** | Abnormal periods. Either too heavy, irregular or too frequent. Dysfunctional Uterine Bleeding is a diagnosis arrived at after exclusion of other causes of abnormal bleeding such as fibroids or polyps. It usually results from hormonal disturbance. |
| **Dysmenorrhoea** | Painful periods. Can be Primary - they have always been painful, or Secondary - they have suddenly become painful recently. There are several possible causes e.g. endometriosis, fibroids, adenomyosis. |
| **Dyspareunia** | Pain during intercourse. May be superficial i.e. on entry, or deep i.e. deep inside, often pain in the lower abdomen. There are several possible causes e.g. scarring of the vaginal wall after child birth, infection in the vagina, endometriosis, pelvic infection, cysts. |
| **Ectopic pregnancy** | A pregnancy which is situated anywhere except the correct place. It most commonly occurs in the fallopian tube but may rarely be found in the ovary, the abdominal cavity or the cervix. An ectopic pregnancy cannot survive and must be treated/removed. They occur more commonly after IVF treatment. |
| **Egg Donation** | Eggs are donated from one woman to help another woman who is unable to produce her own eggs. Such donors may be known to the recipient (relative or friend) or may be unknown. The eggs are fertilised by the recipient's partner's sperm and the fertilised eggs replaced inside the uterine cavity of the recipient. The principles of the component parts of the treatment are the same as IVF. |
| **Embryo** | The name given to a fertilised egg. An embryo exists from day 1 after fertilisation to 4 weeks after fertilisation when it becomes a fetus. |
| **Embryo biopsy** | The removal of tissue from an embryo (usually a single cell) to carry out tests to investigate for certain diseases. |
| **Embryo Donation** | A couple may receive embryos which have been formed from donated eggs and donated sperm or which were formed during the infertility treatment of another couple who subsequently donated their "spare" embryos. These embryos have no genetic material belonging to the patient or her partner. |
| **Embryo transfer** | The placement of embryos in the cavity of the womb (uterus) carried out as part of in vitro fertilisation and related techniques. The embryos are usually replaced 2 – 7 days after the eggs are removed. We normally recommend single embryo transfer, particularly during the first cycle of treatment. |
| **Endometrioma** | This is endometriosis within the ovary which has formed into a cyst. The cyst has a characteristic appearance on ultrasound scan. The size may vary from 2 cms to 15 cms. They are almost always benign. How they are treated will depend on the particular circumstances of the individual. As a rule the larger they are, the more likely they are to require drainage or removal. |

**Endometriosis** A commonly found condition where the lining of the womb ("endometrium") implants itself outside the womb. It varies widely in the extent to which it is found and the amount of endometriosis often bears little relation to the symptoms it causes.

**Endometrium** This is the lining of the womb. It can be up to 2 cms thick. It sheds each month as a period and then regenerates. It is very responsive to the Oestrogen and Progesterone hormone produced by the ovary.

**Epididymis** A collection of tubules or collecting ducts situated at the top of each testicle. The sperm are stored here before ejaculation. This is a common site for sperm recovery in men who have blocked vas.

**Erosion/ Ectropion** A raw area on the outside of the cervix. It is often found in women who have been taking the Oral Contraceptive Pill for a while. They are harmless but may lead to an increase in vaginal discharge or post coital bleeding.

**Fallopian tube** This is a tube (there are two) which arises from each side of top of the womb. It is narrow at the point at which it arises from the uterus and broadens out into an opening known as the fimbria. The sperm has to pass along the tube to meet the egg.

**Fecundity** The rate of conception per monthly cycle.

**Fenton's operation** This is a small operation which is sometimes used to enlarge the opening to the vagina (if the entrance is too tight, for example after childbirth).

**Fertilisation** The joining together of egg and sperm to form an embryo. This may occur naturally or artificially when it becomes "In Vitro Fertilisation".

**Fibroid** A muscular swelling arising from the wall of the uterus. They are almost invariably benign and can vary in size from a few millimetres to 20 cms or more. There may be many fibroids in the womb.

**Fimbria** Feathery like structures at the end of each fallopian tube which help to waft the egg from the ovary into the entrance of the fallopian tube.

**Folic Acid** A vitamin which is given to lessen the risk of spina bifida or neural tube defects. 400 mcg is the recommended supplement for all women who are trying to conceive.

**Follicle** A small fluid filled cyst which grows around a developing egg during the first half of the menstrual cycle. It may vary in size from 7 mm to 24 mm. A mature follicle is greater than 18 mm in mean diameter.

**Follicle Stimulating Hormone (FSH)** A hormone produced by the Pituitary gland. It stimulates the ovary to produce a mature egg - a tiny cell - within a fluid filled structure called a follicle.

**Follicular phase** The term normally given to that part of the menstrual cycle which precedes ovulation.

**Frozen Embryo Replacement (FER)** Thawing of embryos which resulted from a previous IVF or related treatment and were frozen and stored. These embryos are replaced into the uterine cavity after thawing. They may be replaced in a natural cycle or a cycle controlled by hormonal replacement drugs.

**Gamete** A sperm or an egg.

**Gametogenesis** The formation of a sperm (spermatogenesis) or an egg (oogenesis).

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| **Gamete Intra Fallopian Transfer -GIFT** | The insertion of a mixture of eggs and prepared sperm, directly into the Fallopian tube. This is normally carried out laparoscopically although it can be carried out via the cervix. |
| **Gardinella** | A mild infection in the vagina. It causes vaginal discharge but does not affect the fallopian tubes or fertility. It is readily treated by antibiotics. |
| **Gonadotrophins** | The collective term for drugs which contain Follicle Stimulating Hormone as the active ingredient and stimulate the ovaries to produce eggs. |
| **Gonococcus** | A bacterial infection which is passed between sexual partners. It can cause serious pelvic infection resulting in severe damage to the Fallopian tubes resulting in infertility. |
| **Gravida** | The terminology used to state the number of pregnancies a women has had including the current one if she is pregnant. Therefore a woman who has had two babies and two miscarriages and is currently pregnant is Gravida 5. |
| **Haematocoplos** | A collection of blood in the vagina. This is a rare condition most commonly caused by closure of the entrance to the vagina either through the labia sticking together (this can happen after surgery e.g. childbirth) or because the hymen never breaks down, or because of rare abnormalities of the vagina present from birth. This condition has the symptoms of absent periods and menstrual cramps or discomfort in the lower abdomen at around the time of the expected period. |
| **Haemocytospermia** | The presence of red blood cells in the ejaculate. This requires further investigation. |
| **Hamster zona-free penetration test** | A test of sperm function which assesses the ability of the sperm to attach to the hamster egg which has been cleared of its outer lining. |
| **Heterotopic pregnancy** | A rare complication with one pregnancy ectopically situated (usually in the tube) and one correctly situated in the womb. The ectopic pregnancy needs to be removed and the normal pregnancy will usually survive. |
| **Hormonal Replacement Therapy (HRT)** | Hormones which are given to women whose ovaries have stopped working and who are suffering symptoms such as hot flushes, vaginal dryness and night sweats. Women who have still got their uterus (womb) must have combination therapy (including progesterone) and should have a regular withdrawal bleed. HRT may very slightly increase the risk of breast cancer in long term users. |
| **Hormone** | A chemical “messenger” , there are several hormones produced in the human which are produced in and released from the endocrine glands, the Thyroid, Pituitary, Hypothalamus, Pancreas, Parathyroid, Adrenal, Ovary and Testis. |
| **Human Fertilisation and Embryology Authority (HFEA)** | The statutory (government) body which licences all hospitals and clinics carrying specialised infertility treatments such as In Vitro Fertilisation. |
| **Human Chorionic Gonadotrophin (HCG)** | This is a hormone which is almost identical to LH. It is produced by the pregnancy from the very earliest stages of development. It is detectable in the blood and urine about 10 days after conception or replacement of embryos. It can be synthesised and is used in drug form to initiate ovulation because of its similarity to LH (the hormone that sparks off ovulation naturally). |

**Hydrosalpinx** — A fallopian tube which is swollen, blocked at its end furthest away from the uterus and which is filled with a clear fluid. This is usually the end stage of pelvic or tubal infection.

**Hypothalamus** — A gland in the middle of the brain. It produces releasing hormones which stimulate the Pituitary gland to produce hormones. Many factors affect the function of the Hypothalamus - particularly weight fluctuations and stress.

**Hysterocontrast sonography (HyCoSy)** — A procedure for investigating the patency of the Fallopian tubes. Dye opaque to ultrasound is passed through a small catheter passed through the cervix into the cavity of the womb. As the dye is injected an ultrasound scan is carried out of the pelvic area.

**Hysterosalpingogram** — A procedure for investigating the patency of the Fallopian tubes. Dye opaque to X-rays is passed through a small tube fixed to the cervix. As the dye is injected an X-ray picture is taken of the pelvic area.

**Hysteroscopy** — The telescopic examination of the inside of the uterine cavity (the womb). Used to investigate abnormal uterine bleeding or infertility. Normally carried out under general anaesthetic but can, in certain circumstances, be carried out without.

**Hysterectomy** — This is an operation to remove the womb (uterus). There are many reasons why this may be advised. The most common reason is difficult or intolerable periods. Hysterectomy may be carried out in one of several different ways. It may or may not involve removing one or both ovaries. It may be carried out through the vagina (often this is done when a prolapse is being repaired) or through an incision in the lower abdomen. Sometimes a hysterectomy is carried out by “key hole” surgery (laparoscopy).

**Infertility** — The inability to conceive a pregnancy despite regular unprotected sexual intercourse over a period of a year.

**Intra Cytoplasmic Sperm Injection (ICSI)** — This treatment is identical to IVF except (most important) a single sperm is injected into each egg to overcome fertilisation difficulties.

**Intra Uterine Insemination (IUI)** — The insemination of washed or prepared sperm into the cavity of the uterus using a fine catheter. It can be carried out with partner’s sperm or donor sperm. It is normally timed to ovulation by ultrasound scans.

**In Vitro Fertilisation(IVF)** — The removal of eggs from the ovary and their fertilisation with sperm outside the body - in a test tube or dish in the laboratory. The fertilised eggs, known as embryos, are replaced inside the cavity of the uterus (womb) using a fine catheter. IVF may be carried out using partner’s or donor sperm.

**IUCD** — The abbreviation for intra uterine contraceptive device. This is an artificial device that is inserted into the cavity of the womb for contraceptive purposes.

**Karyotype** — The chromosomal characteristics of a person. Investigated by a blood test.

**Key hole surgery** — Surgery or operations which are carried out using a telescope and instruments passed through small (1cm) incisions in the abdomen. There are now many gynaecological operations which can be carried out in this way.

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| **Klinefelter's syndrome** | A rare condition of the male in which he has an extra X chromosome. Thus his chromosome complement is 47 XXY. Such men are usually tall, and they are all infertile with no sperm. The testicles are normally small. Men with this condition are intellectually normal. Fertility in these men cannot be treated. |
| **Laparoscopy** | The direct examination of the fallopian tubes, ovaries and other pelvic tissues by a telescope passed through a small (1cm) incision at the umbilicus. This procedure is carried out under general anaesthetic and normally only requires admission for half a day. |
| **Leuco cytospermia** | Increased numbers of white blood cells in the ejaculate fluid. This may indicate the presence of infection in one of the male glands such as the Prostate. |
| **LHRH** | A hormone produced by the Hypothalamus which stimulates the Pituitary gland to produce FSH and LH. |
| **LHRH pump** | This is a method of injecting LHRH hormone into a female over a prolonged period of time to stimulate ovulation which fails because of low levels of FSH and LH from the Pituitary gland. |
| **LMP** | The abbreviation to indicate the date of the first day of the last menstrual period. |
| **Loop Cone Biopsy (LLETZ)** | A cone shaped biopsy of the cervix usually carried out to treat an abnormal smear test. It is normally carried out using a local anaesthetic and takes about 10 minutes. |
| **Luteinising Hormone (LH)** | A hormone produced by the Pituitary gland. Its levels rise sharply at the mid point of the menstrual cycle and cause the release of the egg. |
| **Menarche** | The onset of the periods. Can range from 8 to 18 years. Outside these limits is abnormal and requires investigation. |
| **Menopause** | When the periods stop. Normally from 45 to 55. It is not uncommon for women in their late 30s to go through the menopause. It is also used to describe the time in a woman's life when the ovaries are reducing in function and there are signs of oestrogen deficiency such as hot flushes and night sweats. |
| **Menorrhagia** | Heavy regular periods. |
| **Menstrual cycle** | The time from the first day of a period to the first day of the next period. Normally varies from 21 to 35 days. |
| **Micro Epididymal sperm aspiration (MESA)** | The aspiration of sperm from the Epididymis through an operation to open up the skin over the epididymal tubules. The sperm recovered are then used to carry out ICSI. |
| **Mirena Coil (IUCD)** | A new type of intra uterine contraceptive device that releases a hormone known as Levo-Norgestral which causes the lining of the womb to thin and which may lessen the menstrual flow or stop it completely. |
| **Miscarriage** | The pregnancy is expelled from the uterus before the baby has reached a stage in its development when it is able to survive. Usually accompanied by severe period like cramps and vaginal bleeding. |

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| **Myomectomy** | An operation to remove fibroids from the womb. This usually involves an incision across the lower part of the abdomen although some fibroids can be removed through "key hole" surgery (laparoscopy). Myomectomy is a major operation and can very occasionally necessitate a hysterectomy being carried out at the same time. |
| **Necrospermia** | Dead sperm. |
| **Norethisterone** | A synthetic progesterone drug which acts on the lining of the womb (endometrium) and is used to stop menstrual bleeding or delay the onset of a period. |
| **Nuchal Fold Translucency test** | A test aimed at detecting those babies more at risk of having Down's Syndrome. It is carried out by ultrasound scan and simply measures the thickness of the pad of tissue behind the neck of the baby. This test is only a screening test. It carries no risk to the baby. It is carried out at about 11 weeks into the pregnancy. It is normally coupled with a serum test to provide a risk calculation of Down's syndrome. |
| **Oestrogen** | The female hormone produced by the ovary. It stimulates the lining of the womb (the endometrium) to thicken. |
| **Oligomenorrhoea** | Infrequent periods. Cycle length longer than 6 weeks. Usually associated with failure of ovulation. It has many different causes. The commonest are weight fluctuations, stress and polycystic ovaries. |
| **Oligozoospermia** | Reduced numbers of sperm. Sperm density (number of sperm per millilitre of ejaculate) should be greater than 20 million per ml. |
| **Oocyte** | The egg. The ovary starts its life with several hundred thousand eggs. After starting your periods around 12-13 years' old, several eggs mature each month, one or sometimes two of which are released at the time of ovulation. |
| **Oocyte recovery** | The process by which eggs (oocytes) are removed from the ovaries for the purposes of in vitro fertilisation. It is normally carried out under sedation or general anaesthetic and normally requires a few hours in hospital. It is variously called Vaginal egg collection, Egg retrieval, Egg collection, Oocyte retrieval. |
| **Oolemma** | The lining or (inner) wall of the egg. |
| **Oophorectomy** | Removal of one or both ovaries. May be possible to carry this out through key hole surgery (laparoscopy). |
| **Ovulation** | The process by which the egg is released from the ovary. |
| **Ovary** | There are two, one on each side, but separate from the uterus. They are normally about 2 x 3 cms. They contain the eggs and produce hormones, namely Oestrogen and Progesterone. |
| **Ovarian Cancer** | Cancer affecting the ovary is relatively uncommon but is a serious condition. There may be a slight familial predisposition. There is no reliable way of detecting it in its early stages. Drugs used to initiate ovulation do not cause ovarian cancer. Although there have been some concerns expressed about this recently, these have not been proven. |
| **Ovarian drilling** | This is a treatment that is sometimes used for the treatment of failure of ovulation in women with polycystic ovaries. It involves a laparoscopy and "drilling" several holes in each ovary using either a laser beam or diathermy heat. It is effective at restoring ovulation in about 60 % of cases. |

**Ovarian Hyperstimulation syndrome (OHSS)**

A condition which is a complication of stimulation of the ovaries by Gonadotrophin drugs (usually in IVF or related treatments). The signs of this are abdominal swelling and discomfort, nausea or vomiting, difficulty in breathing and decreased urine production. It is most likely in women who have produced a lot of eggs during IVF treatment.

**Ovariolysis**

Freeing of adhesions or scarring around the ovaries.

**Ovulation**

The process by which the egg is released from the ovary.

**Ovulation induction**

Drugs are used to stimulate the development of an egg in the ovary and encourage its release. Used to treat women who do not ovulate naturally. Requires monitoring either with blood tests or ultrasound scans or both to check the level of response.

**Ovulation predictor kit**

A commercially available kit which enables the patient to test her urine each morning for five days to detect signs of ovulation. The kit tests for the hormone known as LH. When this hormone appears in the urine (the LH surge) the egg will normally be released within 24 hours. The kit costs about £ 20 for one month.

**Parity**

The terminology used for a woman who has given birth to a live baby or baby who was born weighing more than 500 gms. Thus a women who has had 2 live born babies would be Para 2.

**Pelvic Inflammatory Disease/ Pelvic Infection**

A collective term for any infection which affects the uterus, Fallopian tubes or ovaries. It may well result in damage to the tubes and result in infertility.

**Per-cutaneous sperm aspiration through (PESA)**

The aspiration of sperm from the Epididymis by passing a fine needle through the skin (scrotal sac) overlying the Epididymis. The sperm are then used to carry out ICSI.

**Pill**

Normally used to refer to the combined oral contraceptive pill. There are many different preparations. All contain both oestrogen and progesterone.

**Pituitary**

A gland in the middle of the brain just behind the back of the nose. It produces hormones important in the regulation of ovulation - namely Prolactin, Follicle Stimulating Hormone and Luteinising Hormone.

**Polycystic Ovaries**

A term used to describe ovaries which have a characteristic appearance of having a ring of tiny cysts around the ovary; typically more than 10 with a size of between 4 and 8 mm. These ovaries occur in about 25 % of all women. They are not dangerous or pre-cancerous. They may be associated with irregular periods and other symptoms.

**Polycystic Ovarian Disease or syndrome**

This is a condition characterised by ovaries which are poly cystic in appearance irregular periods, failure to ovulate, increased or unwanted bodily and facial hair. Women with this condition are often, but not always, overweight.

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| **Polyp** | Small mucus filled or fibrous swelling which may be found at the cervix or arising from the cavity of the womb (uterus). They are almost invariably benign. They may cause irregular bleeding (between periods) or bleeding after intercourse. They are usually easily treated by a small surgical procedure. |
| **Post-coital bleeding** | Bleeding after intercourse. Usually due to an abnormality on the cervix. |
| **Posterior repair** | Repair of the back wall of the vagina, close to the back passage (rectum). |
| **Pre Implantation Genetic diagnosis (PGD)** | Tissue is removed from the embryo (at 4 or 8 cell stage) and is analysed. Specifically it is used for sexing the embryo, to detect chromosomal abnormalities and to detect certain rare but serious genetic defects such as Duchenne Muscular Dystrophy. The treatment is the same as IVF in other aspects. |
| **Premature ovarian failure** | Premature menopause when the periods stop before 45. There may be several different causes. Women who have premature ovarian failure will benefit from Hormone Replacement Therapy. |
| **Prenatal diagnosis** | Diagnosis of abnormalities in the baby once the pregnancy is established. The tests are of two types. One type is ultrasound scanning to detect major structural abnormalities in the baby. The other type is tests on either the amniotic fluid to test for chromosomal abnormalities or rarely the baby's blood to test for metabolic errors or single gene defects. |
| **Primary infertility** | Infertility in a woman, man or couple who have not previously conceived a pregnancy. |
| **Progesterone** | A hormone produced by the ovary. It is only produced after ovulation has occurred. It causes the lining of the womb (the endometrium) to be receptive to an implanting embryo. |
| **Prolactin** | A hormone produced by the front (anterior) part of the Pituitary gland. Its levels rise during pregnancy, lactation, when certain drugs are taken (such as the "pill") and during times of stress. It can also rise to high levels when there is an enlargement or small growth in the Pituitary gland (Adenoma). Raised levels of Prolactin can impair ovulation or cause absence of periods. |
| **Pronuclear stage** | The name given to an egg which has just undergone fertilisation. The egg is still a single cell at this stage but the nucleus has divided into two. This stage is recognised some 18 hours after the eggs have been placed with the sperm. |
| **Prostate** | A male gland at the base of the bladder into which drains the vas. The gland produces fluid which appears as the ejaculate. |
| **Recurrent miscarriage** | Three or more consecutive miscarriages. This requires investigation, although only in about 30 % of cases is a cause found. Investigations will include tests on the female partners blood to identify if there is any underlying disease that causes miscarriage and on both partners for chromosomal abnormalities which can affect the development of a baby. |

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| **Retrograde ejaculation** | When ejaculation occurs the sperm and ejaculate fluid pass into the bladder instead of coming out through the penis. This is a relatively rare condition which may arise from neurological problems or diabetes. It is a difficult condition to treat. It may be possible to recover healthy sperm from a urine specimen passed immediately after orgasm. |
| **Rubella** | A virus infection which causes "German Measles". A mild infection which can, however, give rise to serious abnormalities in a baby if the mother contracts it during the early stages of pregnancy. Immunity to this injection is checked prior to treatment. |
| **Salpingectomy** | Removal of a Fallopian tube. Usually carried out by key hole surgery (laparoscopy) |
| **Salpingolysis** | Freeing adhesions or scar tissue which surrounds the fallopian tube. This can usually be carried out by key hole surgery under general anaesthetic with a 1 or 2 day stay in hospital. |
| **Salpingostomy** | Opening a blockage in the end of a fallopian tube. This can usually be carried out by key hole surgery under general anaesthetic with 1 - 2 nights in hospital. |
| **Salpingo-oophorectomy** | Removal of Fallopian tube and ovary, on one or both |
| **Secondary infertility** | This is defined as difficulty in conceiving after becoming pregnant at least once, irrespective of whether the pregnancy resulted in the birth of a child. |
| **Seminal analysis (SFA)** | Commonly known as the sperm count. This is the basic test of male fertility. It involves the man producing a semen specimen by masturbation. This is analysed for four main factors, namely numbers (should be greater than 20 million per ml), movement (should be more than 50 % of the sperm with forward movement), shape (should be more than 10 % of the sperm normally formed), and antibodies to the sperm. |
| **Seminal vesicles** | A male gland of which there are two situated close to the base of the bladder which drain into the vas. They produce fluid which makes up the ejaculate. |
| **Sperm antibodies** | Antibodies are substances which exist in the bloodstream which attack other tissues, usually foreign tissues like bacteria. In the male, antibodies to sperm are sometimes found. Their significance is questionable, but when they occur in large amounts (high titres) they can interfere with sperm function and prevent fertilisation. They may be IgG or IgM antibodies and may attach to the head or tail of the sperm. |
| **Spermatids** | Very immature sperm - usually only obtained from the testicle. |
| **Spermatozoon** | Otherwise known as sperm (pleural spermatozoa). These are tadpole shaped cells with a head capped by an acrosome, a body or mid-piece and a tail. They exist in immature form in the testicle known as spermatogonia. Once mature they are stored in the epididymis. Between 20 million and 300 million appear in each millilitre of ejaculate. |
| **Sperm preparation** | The preparation of sperm prior to in vitro fertilisation or intra uterine insemination. |

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| **Superovulation** | The stimulation of the ovaries by drugs - usually injections - to produce the simultaneous development of a number of eggs. Used in conjunction with IUI, IVF or a related technique. Requires monitoring with ultrasound. |
| **Surrogacy** | Embryos are created using eggs obtained from the patient and sperm from her partner (the commissioning parents). These embryos are then replaced inside the uterine cavity of another woman (the surrogate) who carries the baby. The commissioning parents then adopt the child after birth. The child is genetically that of the patient and her partner. The principles of the medical aspects of the treatment are the same as IVF. |
| **Swim-up** | A method used to prepare the sperm prior to various treatments such as IUI or IVF. It simply describes a technique where the sperm are centrifuged down into a pellet and allowed to "swim - up" into clean culture medium. |
| **Teratozoospermia** | Increased numbers of abnormal sperm. Abnormal sperm are found in every man's sperm and they do not result in the formation of an abnormal baby. |
| **Testicle** | The male gland which lies in a sac called the scrotum. There are two, one on either side of the base of the penis. The testicle produces the male hormone, Testosterone, and contains and matures the sperm-forming cells. |
| **Testicular Sperm Aspiration (TESA)** | The collection of sperm from the tissue of the testicle by passing a needle through the scrotal skin. The sperm recovered are then used for ICSI. |
| **Testicular Sperm Extraction (TESE)** | The collection of sperm from a biopsy of testicular tissue through a small operation. The sperm recovered in this way are then used to carry out ICSI. |
| **Testosterone** | A male hormone produced by the cells in the Testicle but also produced by the ovary and adrenal glands in the female. |
| **Thrush / Candida** | A fungal infection which is commonly found in the vagina. It usually causes a cheesy white, thick, itchy vaginal discharge. It passes between sexual partners. It does not cause damage to the Fallopian tubes. It is readily treated with anti-fungal preparations. Both partners should be treated at the same time. |
| **Trichomonas** | A non bacterial infection of the cervix which leads to abnormal discharge. It is passed between sexual partners. It is easily treated with Metronidazole (tablet). |
| **Triple test** | A blood test carried out at about 16 weeks into a pregnancy which detects those women who are at higher risk of having a baby with Down's syndrome. It involves measuring three chemicals in the blood - HCG, Alpha Feto Protein and Oestradiol. It will detect about 70 % of Down's babies. |
| **Tubal surgery** | Operations to repair a blockage or damage to the fallopian tube. This can usually be carried out by key hole surgery under general anaesthetic with a 1 or 2 day stay in hospital. |

**Turner's syndrome**

This is a rare condition present from birth (congenital) which results from a missing X chromosome. The chromosome complement is 45, X. These women have certain physical characteristics, absent periods, no ovaries or very tiny ovaries, short stature, web shaped neck. They have a normal uterus and, although they are infertile, they can carry a baby following treatment with donor eggs. These women are intellectually normal.

**Unexplained infertility**

Infertility in a couple where there is no identifiable cause. That is confirmation of ovulation, normal fallopian tubes, no significant endometriosis and normal sperm parameters. Unexplained infertility is normally diagnosed after 3 years of regular unprotected intercourse.

**Uterus**

Otherwise known as the womb. It lies at the top of the vagina. Is normally about 9 cms by 3 cms and is pear-shaped. It has a lining from which arises the period. It produces no hormones.

**Vagina**

A muscular tube leading from the vulva to the cervix. It has the bladder immediately in front and the rectum immediately behind. The ovaries lie close to the top of the vagina and the uterus at the top of the vagina. The vagina varies in length up to about 15 cms and upwards and slightly backwards.

**Vaginismus**

Abnormal spasm of the vagina causing pain or discomfort during sexual intercourse. This may result from infection, previous surgery or childbirth or have a psychological basis.

**Varicocele**

A condition of the male in which distended or engorged veins appear close to the vas just above the testicle. They may be felt as a small swelling and may cause some discomfort. They may result in a slight reduction in the number or quality of sperm. Treatment of varicocele for reasons relating to infertility is controversial. Treatment involves a small operation carried out under general anaesthetic.

**Vas Deferens**

The fine tube which passes from the testicle to the penis and transports the sperm and seminal fluid. There are two, one leading from each testicle.

**X- chromosome**

This is the chromosome that determines female characteristics (sex chromosome). There are normally two X chromosomes in the female. In the male there is one X chromosome.

**Y- chromosome**

The chromosome that determines male characteristics (sex chromosome). There is normally only one Y chromosome partnered by an X chromosome. If a person has a Y chromosome they will invariably be male. Minor abnormalities of the Y chromosome occur in 0.3 % of the male population and may cause infertility . Additional Y chromosomes also occur.

**Y-chromosome deletion**

A minor abnormality of the Y chromosome only detectable by special testing and not generally available. Can cause male infertility.

**Yolk sac**

A tiny sac that is seen on ultrasound scanning of a very early pregnancy. It is seen from 6 weeks to about 9 weeks. Its function is to provide nourishment to the growing embryo.

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| **Zoladex** | The commercial brand name for a drug containing LHRH anologue. This drug acts on the Pituitary gland to stop the production of FSH and LH. As a result it causes the ovary to stop functioning and stops the periods. It induces a temporary menopause. It is administered as a monthly injection (implant). It is used to suppress the ovaries prior to IVF and related treatments and also in the treatment of Endometriosis. |
| **Zygote** | A fertilised egg. |
| **Zygote Intra Fallopian Transfer (ZIFT)** | The transfer of fertilised eggs (embryos) directly into the Fallopian tube as in GIFT. |
| **Zona Drilling** | The making of a small hole in the outer wall of the embryo (the Zona Pellucida), this is used for Assisted Hatching. The “hole” may be made by delicate laser beams, by a chemical enzyme or mechanically. |
| **Zona Pellucida** | This is the thickened outer layer of the egg (oocyte). It completely surrounds the outside of the egg. |

## Document History

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## Useful Contacts

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| **Human Fertilisation and Embryology Authority** | Finsbury Tower, 103-105 Bunhill Row, London, EC1Y 8HF<br>www.hfea.gov.uk<br>E-mail – enquiriesteam@hfea.gov.uk<br>Tel: 020 7291 8200<br>Fax: 020 7291 8201 |
| **Endometriosis UK** | Suites 1 & 2, 46 Manchester Street, London, W1U 7LS<br>www.endometriosis-uk.org<br>E-mail – admin@endometriosis-uk.org<br>Helpline – 0808 808 2227 |
| **Twins and Multiple Birth Association (TAMBA)** | Manor House, Chill Hill, Aldershot, Hants, GU12 4JY<br>www.tamba.org.uk<br>E-mail – enquiries@tamba.org.uk<br>Tel: 01252 332344 |
| **Adoption – British Association Of Adoption and Fostering (BAAF)** | BAAF Birmingham Office, Dolphin House, 54 Coventry Road, Birmingham, B10 0RX<br>www.baaf.org.uk<br>E-mail – adviceengland@baaf.org.uk<br>Advice Line: 020 3597 6116<br>Fax: 0121 753 7799 |
| **Adoption UK** | Linden House, 55 The Green, south Bar Street, Banbury, OX16 9AB<br>www.adoption.org.uk<br>Tel: 01295 752240<br>Fax: 01295 752241 |
| **AceBabes** | AceBabes, Chrater House, 43 St Leonards Road, Bexhill on Sea, East Sussex, TN40 1JA<br>www.acebabes.co.uk<br>E-mail – admin@acebabes.co.uk<br>Tel: 0800 008 7464 |
| **Donor Conception Network (DC Network)** | 154 Caledonian Road, London, N1 9RD<br>Tel: 0207 278 2608<br>www.dcnetwork.org<br>E-mail – enquiries@dcnetwork.org |
| **National Gamete Donation Trust (NGDT)** | Tel: 0845 226 9193 (Helpline)<br>www.ngdt.co.uk<br>E-mail – info@ngdt.co.uk |
| **COTS (Childlessness Overcome Through Surrogacy)** | Moss Bank, Manse Road, Lairg, Sutherland, IV27 4EF<br>Tel/Fax: 01549 402777<br>www.surrogacy.org.uk<br>E-mail – info@surrogacy.org.uk |
| **Surrogacy UK** | PO Box 323, Hitchin, Hertfordshire, SG5 9AX<br>www.surrogacyuk.org<br>E-mail – membership.secretary@surrogacyuk.org<br>Tel: 0845 5577 319 |
| **The Ectopic Pregnancy Trust** | 3rd Floor, 28 Portland Place, London, W1B 1LY<br>www.ectopic.org.uk<br>Tel: 0207 733 2653<br>E-mail: ept@ectopic.org.uk |

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| **Infertility Network UK (INUK)** | Charter House, 43 St Leonards Rd, Bexhill on Sea, East Sussex, TN40 1JA<br>Tel: 0800 008 7464<br>www.infertilitynetworkuk.com |
| **Complaints** | Complaints Service, 3rd Floor Central Quality Dept, UHCW NHS Trust, Clifford Bridge Road, Coventry, CV2 2DX<br>E-mail – feedback@uhcw.nhs.uk (start subject line with "complaint")<br>Tel: 024 76 965198 |
| **More to Life** | Providing support to people exploring what life without children has to offer. Tel: 0800 008 7464<br>Or from a mobile – 01424 732 361<br>www.infertilitynetworkuk.com/more_to_life |
| **Patient Advisory Liason Services (PALS)** | **c/o** UHCW NHS Trust, Clifford Bridge Road, Coventry CV2 2DX Tel: 0800 028 4203 feedback@uhcw.nhs.uk |
| **Coventry & Rugby Clinical Commissioning Group (CCG)** | Christchurch House, Greyfriars Lane, Coventry, CV1 2GQ<br>www.coventryrugbyccg.nhs.uk<br>E-mail – contact@coventryrugbyccg.nhs.uk<br>Tel: 024 76 553344<br>Fax: 024 76 226280 |
| **Warwickshire North Clinical Commissioning Group (CCG)** | Room 1, Lewes House, Nuneaton, CV10 7DJ<br>www.warwickshirenorthccg.nhs.uk<br>E-mail – contactus@warwickshirenorthccg.nhs.uk<br>Tel: 024 76 324399 |
| **Warwickshire South Clinical Commissioning Group (CCG)** | Westgate House, Market Street, Warwick, CV34 4DE<br>www.southwarwickshireccg.nhs.uk<br>E-mail – contactus@southwarwickshireccg.nhs.uk<br>Tel: 01926 353 700 |
| **The Miscarriage Association** | 17 Wentworth Terrace, Wakefield, WF1 3QW<br>www.miscarriageassociation.org.uk<br>E-mail – info@miscarriageassociation.org.uk<br>Tel: 01924 200799 |
| **RELATE** | New House, Hertford Place, Coventry, CV1 3JZ<br>Tel: 024 76 225863<br>www.relatecoventry.org<br>E-mail – info@relatecoventry.org |
| **British Acupuncture Council** | 63 Jeddo Road, London, W12 9HQ.<br>Tel: 020 8735 0400<br>www.acupuncture.org.uk<br>Fax: 020 8735 0404<br>E-mail – info@acupuncture.org.uk |
| **British Complementary Medicine Association** | P O Box 5122 Bournemouth Dorset BH8 0WG<br>Tel: 0845 345 5977<br>www.bcma.co.uk<br>E-mail – office@bcma.co.uk |
| **British Herbal Medicine Association** | PO Box 5831, Exeter, EX1 9GX<br>www.bhma.info<br>E-mail – secretary@bhma.info<br>Tel: 0845 680 1134<br>Fax: 0845 680 1136 |
| **British Association for Counselling and Psychotherapy** | BACP House, 15 St John's Business Park, Lutterworth, LE17 4HB<br>Tel: 01455 883300 Fax: 01455 550243<br>www.bacp.co.uk<br>E-mail – bacp@bacp.co.uk<br>Text – 01455 560606 |

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| **Verity (PCOS Self Help Group)** | Verity, New Bond House, 124 New Bond Street, London, W15 1DX<br>www.verity-pcos.org.uk<br>E-mail – office@verity-pcos.org.uk |
| **British Infertility Counselling Association (BICA)** | Tel: 01372 451 626<br>www.bica.net<br>E-mail – info@bica.net |
| **Daisy Network Premature Menopause Support Group** | The Daisy Network, PO Box 183, Rossendale, BB4 6WZ<br>www.daisynetwork.org.uk<br>E-mail – daisy@daisynetwork.org.uk |
| **Multiple Births Foundation** | Hammersmith House, Level 14, Queen Charlottes and Chelsea Hospital, Du Cane Road, London, W12 0HS<br>Tel: 020 3313 3519 Fax: 0208 383 3041<br>www.multiplebirths.org.uk<br>E-mail – mbf@imperial.nhs.uk |
| **National Institute for Clinical Excellence (NICE)** | 10 Spring Gardens, London, SW1A 2BU<br>www.nice.org.uk<br>Tel: 0300 323 0140 Fax: 0300 323 0148<br>E-mail – nice@nice.org.uk |
| **Pink Parents UK** | 08701 273 274<br>www.pinkparents.org.uk<br>E-mail – info@pinkparents.org.uk |
| **UK Donorlink** | www.ukdonorlink.org.uk |
| **Fertility Friends** | www.fertilityfriends.co.uk |
| **SANDS (Stillbirth and Neonatal Death Society)** | 28 Portland Place, London, W1B 1LY<br>Tel: 020 7436 5881 www.uk-sands.org |

## How to contact us

Centre for Reproductive Medicine
University Hospitals Coventry & Warwickshire NHS Trust
Clifford Bridge Road
Coventry
CV2 2DX

Email: crm@uhcw.nhs.uk

Website: www.ivf-midland.co.uk

Telephone for appointments and general enquiries:

Monday – Friday 09.00 – 16.00
**Direct line: 024 76 968879***

* Please note that this is a very busy line, if you leave a message staff will return your call as soon as they possibly can. The answer phone is checked first thing in the morning and at regular intervals throughout the day for messages. Messages left on a Saturday and Sunday will be dealt with first thing Monday morning.

or ring main switchboard 024 76 964000 and ask for CRM, ext 28879
In the event of difficulties ring: 024 76 96 7381 (secretaries)

Semen analysis test appointments: 024 76 96 8873

Embryology Queries: 024 76 96 8874

Fax: 024 76 96 8880

Nurse Helpline: 024 76 96 8856

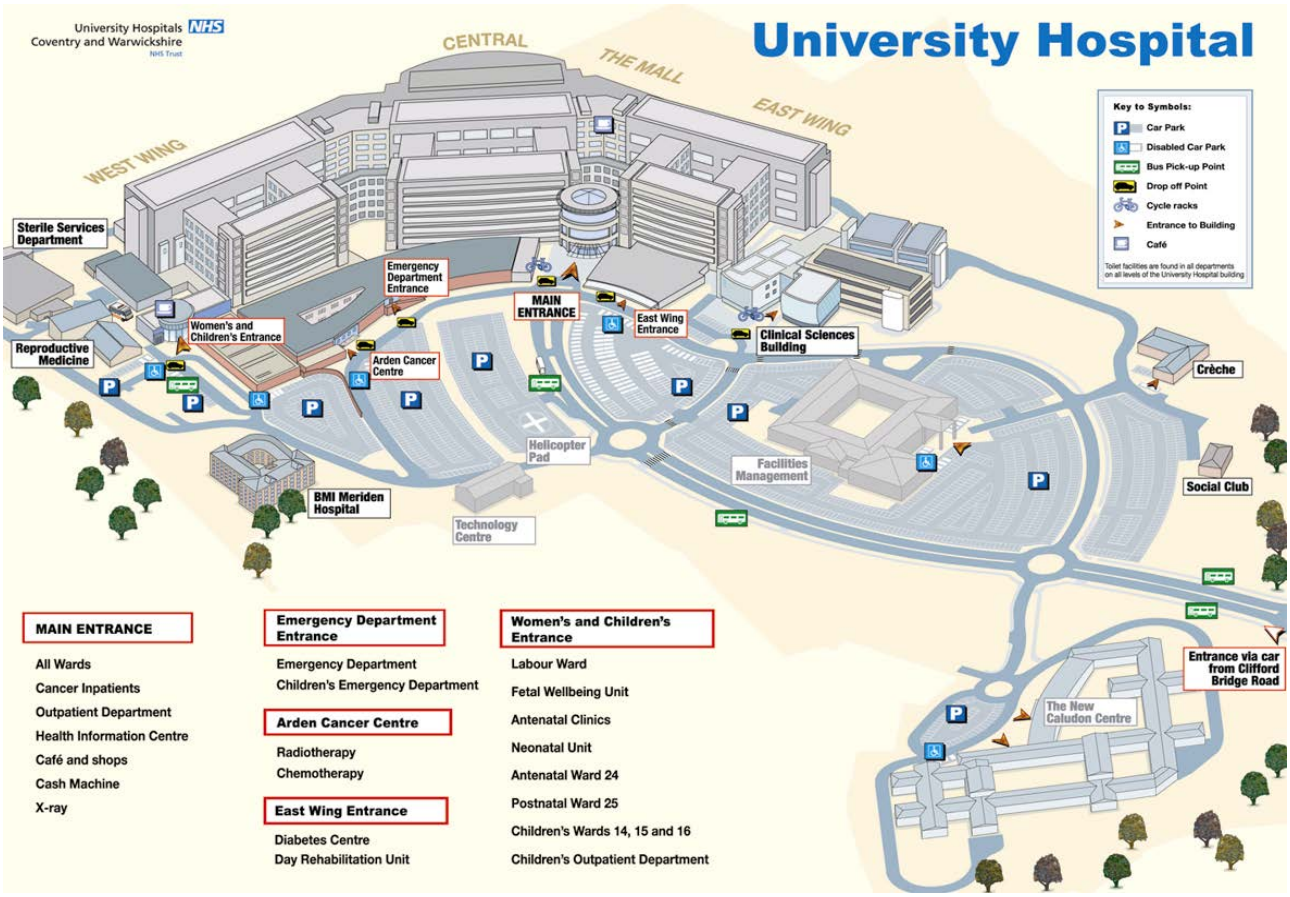
Counselling:

024 76 96 8886

Urgent calls and Emergencies:
Saturday 09.00 - 11.00 am (nurse only on duty – please keep trying as we may be with a patient)

Nurse Helpline – 024 76 96 8856
Any time out of hours 024 76 96 7000 (Gynaecology Unit)

Please be advised that the Direct Line and the Emergencies line are manned at the stated times. However the other numbers access working areas of the clinic and staff may not always be available to answer the telephone due to clinical activities. Please accept our apologies if your call is not immediately answered.




## Directions

**By car from the Coventry city centre**
Follow the A4600 towards the M6 and M69. Turn right at the first roundabout after the dual carriageway (by Homebase) onto Clifford Bridge Road. The entrance is on the left-hand side of Clifford Bridge Road.

**By car from the North, M6 & M69**
From the M6 & M69 leave at junction 2 and follow the A4600 towards Coventry City Centre. Turn left at the third roundabout (situated approximately a quarter of a mile past Walsgrave Church) onto Clifford Bridge Road (A4082). The entrance to Walsgrave Hospital is on the left hand side of Clifford Bridge Road.

**By car from the South, M40**
From the M40 leave at junction 15 and take the A46 (Warwick by-pass) then follow signs towards the M69. Continue along the A46 to the second roundabout on the Eastern by-pass and turn left onto the A4082. Continue along the A4082 and turn right onto Clifford Bridge Road. Follow this road for three-quarters of a mile. Walsgrave Hospital is situated on the right-hand side and can be accessed by a sign-posted slip road.

**By bus from Coventry city centre**
Travel West Midlands bus services, numbers 17 and 27 run regular services from Broadgate in the city centre, directly to Walsgrave Hospital. The journey takes about 20/25 minutes and the services runs at frequent intervals. All Travel West Midlands buses are pay as you enter and do not give change. A timetable is available on the Travel Coventry Internet site.

**By bus from Coventry railway station**
Outside Coventry railway station, Travel West Midlands buses 17 and 27 operate regular services from the station to Walsgrave Hospital, passing through the city centre. The journey takes around 30 minutes and runs at frequent intervals. All Travel West Midlands buses are pay as you enter and do not give change. A timetable is available on the Travel Coventry Internet site.