Leuven university fertility centre

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I. WHY THIS BROCHURE?

Couples consult us because they are having problems conceiving. They have hope and expectations. This brochure can offer them guidance, give them something to hold on to. It provides accurate information about fertility, fertility problems, the various tests, examinations and treatments that are possible. Here and there it also explains the limits of medical capability.

We know from statistics that approximately 85% of couples will conceive spontaneously after one year of unprotected intercourse. For the remaining 15% this is not the case. A certain amount of unease develops among these couples. Why? Often we can reassure them, since half of these couples will conceive during the next year without any medical intervention. However, there are couples who have still not conceived spontaneously after two years. In this group we often find serious fertility disorders.

In most cases there is no point in carrying out examinations before the attempts to conceive have lasted one year. There are however exceptions. Women with a very irregular menstrual cycle, or no menstrual cycle at all, women who have already undergone various surgical operations on the pelvis, women with blocked fallopian tubes, etc. would do better to have examinations carried out earlier. This also applies for women over 35 years of age. If there is a strong suspicion or certainty that the sperm quality of the man is inadequate, then he is also advised to undergo examination more quickly.

Both the length of time that an unfulfilled desire to have children lasts, and the age of the woman are important factors that contribute towards determining the nature of the examinations and treatments.

Over the past few years the medical world has made enormous progress in the field of fertility treatments. We are able to help most of the couples who consult us. As these developments often have ethical consequences, they easily arouse media interest. The first test-tube baby, Louise Brown, triggered heated debate at the time. Today, in vitro fertilisation (IVF) is very common. These days the ethical discussion tends to concern research using embryos, a subject which we will also deal with briefly in this brochure.

The rapid progress made in medical science, with all the possibilities this offers, may give rise to the idea that everything is feasible, that nothing is impossible these days. Nothing could be farther from the truth. We can insert a sperm cell into an ovum physically, but this does not form an embryo. The fertilisation of an ovum calls for more than that. We can insert an embryo into the uterus, but this does not mean that the embryo is implanted ... Fertilisation and pregnancy are extremely complex phenomena. Many areas are still not accessible to research and this may well remain the case. Even as doctors or scientists, we cannot answer all questions, we do not have a ready-made solution to every problem.
This means that, despite all your efforts and ours, we cannot guarantee that everyone we treat will actually become pregnant and have a child. We can, however, guarantee a high-quality approach to all aspects of the problem of fertility. Fertility problems throw up a host of medical, scientific, ethical, social and psychological challenges. With our team, we aim to guarantee a holistic approach to fertility problems within a stable relationship.

The Leuven university fertility centre is the first Belgian fertility centre to have received the ISO 9001 2000 certificate for ‘Multidisciplinary Evidence-Based Quality Management of Couples with Subfertility. This certificate concerns all the centre’s medical, surgical and scientific activities.

Our centre strives to provide optimal patient care and ever better quality of care. We are always open to suggestions. As a university centre, it is also our task constantly to improve patient care by actively undertaking clinical and fundamental scientific research. In this context, we are always involved in conducting studies. We greatly appreciate your interest and possible participation in these studies. This is the only way to make progress.

We realise only too well that the start of life is a very delicate area in terms of ethics. This is why we always treat it with the necessary circumspection, among other things by coming to clear understandings about what you can and should not expect. In addition, we always provide accurate medical information, using the necessary tact. If there is no point in any further treatment, we say so. In that case, we can discuss other meaningful alternatives. When it is difficult to make choices, or if you find the examinations and/or the treatment very difficult or stressful, then we see it as our duty to help you, where appropriate by providing support through our fertility consultants.

This brochure should be considered a supplement to the matters we discuss during the various consultations. If there is anything that is not clear to you or if you would like further information, we are of course always happy to listen to your questions and provide you with answers.
2. POLICY OPTIONS OF OUR CENTRE

When assisting couples experiencing fertility problems we at the Leuven university fertility centre take as much account as possible of the following elements:

1. We refer to a fertility problem when, in a stable relationship between a man and a woman, attempts to become pregnant remain unsuccessful for longer than usual.

2. Reduced fertility has major psychological implications. The problem is often due to medical problems that occur equally often in men and women.

   The diagnostic phase is essential to determine exactly what problem lies behind the reduced fertility. This is important in order to choose an appropriate treatment. Right from the outset, we also pay attention to the psychological condition: fertility problems may go hand in hand with stress, feelings of depression, relational problems, etc. Psychological support remains possible during the treatment phase as well.

3. When fertility treatment is provided, we always assume that the spontaneous chance of pregnancy is smaller than the chance after medical intervention. We always weigh the likelihood of pregnancy with a specific form of treatment against the physical, psychological, relational and financial burden that it represents for the man, the woman and the couple. Finally, in conjunction with the couple, we take a decision about the policy to be adopted. This policy may consist of a wait-and-see attitude, a surgical operation for the man and/or the woman, hormonal treatment, inserting sperm cells directly into the uterus (insemination), or replacing embryos in the uterus after fertilisation in the laboratory (in vitro fertilisation).

4. We strive to attain as much continuity as possible, so that in principle each couple always sees the same medical specialist during consultations. He/she is responsible for your dossier. It may well be that a midwife or a trainee medical specialist prepares the consultation first, but the attending medical specialist is always present at the final discussion. He/she will also be present as much as possible during the treatment (surgery, insemination, embryo transfer, etc.). However, this will not always be possible. Moreover, some division of tasks is always necessary in order to provide the best possible quality all the time at every level.

5. The Leuven university fertility centre is the academic core of an entire network of gynaecologists in Flanders with whom we cooperate on a regular basis.

   We work very closely together with a number of gynaecologists and hospitals. With others, the cooperation is more limited. You will find more information about this in Chapter 3. The gynaecologists with whom we cooperate will conduct certain tests and examinations and possibly administer treatments themselves. Of course, if a pregnancy occurs, then you will be referred back to your gynaecologist.
3. WHO ARE WE

The Leuven university fertility centre is a multidisciplinary team consisting of medical staff, a paramedical fertility team and a fertility laboratory.

The team works in four stages:

✔ Examination of the cause of the fertility problems in the man and the woman.
✔ Discussion of the results at weekly multidisciplinary staff meetings and formulation of a proposal for additional examinations and/or treatment.
✔ Discussion and further development of this proposal with the patients.
✔ Evaluation of the treatment and timetable, or additional/new treatment if necessary.

You will find the centre's organisational chart on a separate page.

Clinics of the Leuven university fertility centre and telephone numbers for appointments

<table>
<thead>
<tr>
<th>Fertility centre gynaecology</th>
<th>prof. dr. Thomas D’Hooghe</th>
<th>016 34 36 50</th>
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<tbody>
<tr>
<td></td>
<td>prof. dr. Peter De Loecker</td>
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<td></td>
<td>prof. dr. Diane De Neubourg</td>
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<tr>
<td></td>
<td>dr. Christel Meuleman</td>
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<td></td>
<td>dr. Luc Meeuwis</td>
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<td></td>
<td>dr. Karen Peeraer</td>
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<td></td>
<td>dr. Sofie Pelckmans</td>
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<td></td>
<td>dr. Carla Tomassetti</td>
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<td></td>
<td>dr. Ingrid Thijs</td>
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<tr>
<td>Andrology</td>
<td>dr. Philippe Marcq</td>
<td>016 34 36 24</td>
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<tr>
<td></td>
<td>prof. dr. Dirk Vanderschueren</td>
<td></td>
</tr>
<tr>
<td>Urology</td>
<td>prof. dr. Dirk De Ridder</td>
<td>016 34 69 30</td>
</tr>
<tr>
<td>Fertility consultants</td>
<td>Lynn Van Moppes</td>
<td>016 34 36 24</td>
</tr>
<tr>
<td></td>
<td>Uschi Van den broeck</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myriam Vervaeke</td>
<td></td>
</tr>
<tr>
<td>Consultants of the Centre for Human Genetics</td>
<td>prof. dr. Eric Legius</td>
<td>016 34 59 03</td>
</tr>
<tr>
<td></td>
<td>prof. dr. Jean-Pierre Fryns</td>
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Getting to us

Map page 94.
Directions

✗ By public transport

Leuven railway station is about four kilometres from the hospital. A bus leaves from there every 10 minutes. The bus stop is near the main entrance of the hospital.

✗ By car

Via the E 40 motorway:
Between exit 22 and 23, take the E 314 motorway. Continue as for ‘via the E 314 motorway’.

Via the E 314 motorway:
Take exit 17 and go towards Leuven as far as the ring road (Brusselsepoort). Then turn right onto the ring road and leave at the first junction, marked ‘UZ Leuven’. Follow the directions at the roundabout by the work of art ‘Het Teken’. If you want to get back onto the E 314 motorway upon leaving the hospital, follow the signs at the roundabout.

Via the ring road:
If you are on the outer side of the ring road, follow the ring road until just after Brusselsepoort, to the sign reading ‘UZ Leuven’. Follow the directions at the roundabout by the work of art ‘Het Teken’.
If you are on the inner side of the ring road, follow the ring road until just after the Tervuursepoort junction. From there, follow the signs to ‘UZ Leuven’ and then ‘UZ Gasthuisberg’.

Diest satellite centre

In order to optimise our service, the LUFC has opened a satellite centre in Diest. The consultations, examination phase and treatments are organised in the same way as at the LUFC.

Consultations in Diest take place on Tuesday afternoons from 1.00 pm to 7.00 pm.

<table>
<thead>
<tr>
<th>Diest fertility centre</th>
<th>dr. Karen Peeraer</th>
<th>dr. Ingrid Thijs</th>
<th>016 34 26 38</th>
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</thead>
<tbody>
<tr>
<td>gynaecology</td>
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</tbody>
</table>

Directions

Diest fertility centre
AZ Diest, Hasseltsestraat 27/29, 3290 Diest

✗ By public transport

From the direction of Molenstede and the station, take a no. 1 local bus (Webbekom) as far as the stop in Schotlandstraat. Follow Leuvensestraat to Kardinaal Mercierstraat. Turn right and walk as far as Hasseltsestraat (below). Turn right again and walk to no. 29 in Hasseltsestraat.
From the direction of Webbekom, take a no. 1 local bus (Molenstede). The bus stops at the hospital.
4. FERTILITY IN MEN

Formation and conveyance of sperm cells

The production of sperm cells (spermatozoa) is regulated by gonadotropins, hormones that are secreted by the hypophysis, a small gland at the base of the brain. The sperm cells are formed in narrow channels in the testicle. Ideally, the sperm is formed at a temperature that is a little lower than the average body temperature. This is why the testicles lie outside the abdominal cavity.

The newly formed sperm cells are then collected in the epididymis, the soft mass that lies above the testicles. The vasa deferentia (sperm ducts) run from the epididymis via the groin region to the abdomen behind the bladder, where they flow into the sperm vesicles.

The seminal vesicles and the prostate gland produce the semen in which the sperm cells are found upon ejaculation. The semen contains a number of products to keep the sperm cells alive for a while after ejaculation.

When the sperm is expelled, the seminal vesicles and the prostate gland contract rhythmically, thrusting the sperm cells and the semen out. The volume of sperm and semen (the ejaculate) is not always the same and usually lies between two and six millilitres. An ejaculate consists almost entirely of semen from the prostate gland and the seminal vesicles. The actual sperm cells account for barely one per cent of this. Yet microscopic examination of the semen usually reveals over 20 million sperm cells per millilitre.

When the quantity of semen falls below 1.5 mm, this is referred to as an abnormal situation. This is usually an abnormality in the sperm vesicles or the prostate gland, but there may also be other causes, such as problems collecting the sample. The sperm cells retain their capacity to fertilise for two days and remain alive for up to three days in the vagina, the uterus and the fallopian tubes. Only a small number of sperm cells manage to reach the fallopian tubes where there may be an ovum at that moment.
The sperm cell's journey

The sperm cells are largely passive during their journey from the vagina to the ovum in the fallopian tube. Agility is only of essential importance at three points during their journey: as they make their way through the cervix, as they cross between the uterus and the fallopian tube, and when they penetrate the shell around the ovum.

The cervix forms the first obstacle for the sperm cells. The cervix is blocked by a tough sputum throughout most of the woman’s cycle. Shortly before ovulation, under the influence of hormones, the mucus becomes far more flexible, less viscous, clearer, elastic and less acidic, and therefore more accessible for sperm cells. Abnormal and less agile sperm cells find it difficult to cross this barrier.

In the uterus itself, the sperm cells are driven mainly by the rhythmic contractions of the uterus. These contractions are particularly powerful when the woman has an orgasm. A second difficult point is the transition from the uterus to the fallopian tubes. This is fairly narrow and opens only periodically. Only a limited number of sperm cells, mostly just a few hundred, make it through. In the meantime, a stringent selection is made, so that the sperm cells that do manage to make it through display virtually no abnormalities.

Once past this barrier, rhythmic contractions and cilia or hair-like projections in the fallopian tube propel the sperm cells onwards towards the ovaries, until they reach the ovum. The fastest sperm cells reach the abdominal cavity about 15 minutes after intercourse.

The fate of the sperm cells

Usually only a limited number of sperm cells survive the entire journey as far as the fallopian tubes, and ultimately only one sperm cell can fertilise the ovum. The remaining sperm cells are destroyed. Those that do not make it past the cervix are destroyed by the acid environment in the vagina. The sperm cells that succeed in making their way to the cervix or higher up on the way towards the ovum are mainly cleared up by defence cells and white blood cells. It may happen that the remaining sperm cells are presented to the defence system and that a defensive reaction is set in motion. In that case, the defence system of the woman forms antibodies against her partner’s sperm cells. The defence system considers the sperm cells to be ‘dangerous invaders’ and destroys them. Fortunately this only occurs in very rare cases.
5. FERTILITY IN WOMEN

The menstrual cycle in four stages

A normal menstrual cycle can be divided into four main phases:

- **Follicular phase**: the ovum matures.
- **Ovulation**:
- **Luteal phase**: the uterus prepares for the possible implantation of the fertilised ovum.
- **Menstruation**: the uterus cleanses itself.

The follicular phase: the ovum matures

The menstrual cycle begins with the growth and maturing of a new ovum. This process takes place in a vesicle (follicle). The follicle is in turn a major hormone producer. As the follicle grows, it increasingly secretes oestrogen. The peak concentration of oestrogen in the blood in turn influences the cervix and the sputum found there. Sperm cells cannot usually pass through this mucus, but under the influence of the oestrogen, it changes and for a few days sperm cells are able to pass through it. Furthermore, the muscles around the cervix relax under the influence of the oestrogen so that the cervix opens slightly and offers the sperm cells passage.

In reaction to the peak in oestrogen production, the hypophysis suddenly begins to secrete a great many luteinising hormones. This stimulates the release of the ovum from the follicle. The follicule in the ovaries grows within a period of barely two weeks from no more than a few tenths of a millimetre in diameter at the start of the cycle to upwards of two centimetres at the end of the follicular phase. A mature follicle protrudes clearly from the ovary and is easily visible to the naked eye (for example during a laparoscopic examination). Mature follicles are also big enough to be detected by an ultrasound scan and collected (for instance when ‘harvesting ova’ for in vitro fertilisation).
Ovulation (see ‘1. Ovulation’ in figure)

Ovulation is the moment when the follicle bursts and the ovum is released. This happens about 14 days before the end of the menstrual cycle. Shortly before ovulation the fallopian tube and the fringes at the end of the tube fold themselves around the ovary containing the mature ovum ready for ovulation. When the ovum is released, it is usually caught by the fringes of the fallopian tube within a few minutes.

Rhythmic contractions of the uterus and the fallopian tubes create a wave of fluid that carries the ovum further into the fallopian tube. The ovum is carried from the ovary to the central, broader part of the fallopian tube (ampulla) in less than seven hours. After this, the ovum remains in the ampulla for about 72 hours, but can only be fertilised within 24 hours of ovulation. So fertilisation must take place at the latest here. After 72 hours the ovum, fertilised or not, starts being carried to the uterus.

The luteal phase: the uterus is prepared

The remains of the follicle undergo a change after ovulation. They are transformed into a yellow body (corpus luteum) under the influence of the luteinising hormone. Hence the name luteal phase.

The corpus luteum in turn produces progesterone, a hormone that stimulates the endometrium (mucous membrane of the uterus) to prepare itself for the implantation of the fertilised ovum. This ovum reaches the uterus five or six days after ovulation.

Menstruation

If the ovum is not fertilised after ovulation, then the corpus luteum is soon exhausted. In that case, progesterone production declines sharply around the 13th day. The stimulation of the endometrium (mucous membrane of the uterus) also ceases. The mucous membrane of the uterus dies and is rejected. This is the start of the fourth major phase in the cycle: menstruation (menses or periods). The start of menstruation also marks the beginning of a new cycle: there is no pregnancy. Everything is set for a new ovum to mature.
How long does a normal menstruation cycle last?

A typical menstruation cycle lasts an average of 28 days. In practice, however, the length of the cycle varies from one woman to another. In some women it is somewhat shorter, in others, longer. Moreover, the length of a cycle can alter in the same woman over the course of her life. Fluctuations in the length of the cycle are usually the result of fluctuations in the length of the follicular phase. These fluctuations are not, however, necessarily a cause for concern. They occur in many women and may be due to a number of factors (for instance change in habits when on holiday, a busy time at work, a poignant event in the family circle or among friends).

Fertilisation and implantation (see ‘2. Fertilisation’ and ‘3. Implantation’ in figure page 14)

If an ovum encounters a sperm cell shortly after ovulation, then fertilisation can occur in the fallopian tube. This fertilisation takes place in a number of steps. In the first phase the sperm cell lies against the wall of the ovum and the cell walls blend to form one large cell. In the next phase the nuclei of the cells also blend together. These first cell nucleus of the embryo forms within between 12 and 20 hours after fertilisation. After this, the first embryo cell divides and the embryo starts to develop. In the meantime, the fresh embryo begins its journey to the uterus. When it arrives, it makes contact with the mucous membrane of the uterus (endometrium) which will accept it fully over the course of the next few days. By the tenth day after fertilisation, the implantation process is complete. The embryo and the mucous membrane of the uterus secrete various substances as the embryo approaches, becomes attached and is accepted which are intended to ensure the successful completion of this process. One of these hormones is human chorionic gonadotropin (hCG). This pregnancy hormone stimulates the corpus luteum to continue to prepare and secrete a greater quantity of oestrogen and progesterone, which are necessary to maintain the pregnancy.

Which is the most fertile period of the cycle?

Recent research shows that the fertile period of the cycle can vary considerably, even in women whose cycle is very regular. A woman is only fertile on very few days during the cycle. For women with a regular 28-day cycle, the most fertile period is between day 11 and day 16 of the cycle. Without taking into account the day of the cycle or the moment of ovulation, the greatest likelihood of fertilisation occurs when a couple has sexual intercourse every two days, that is about two or three times a week. Couples who make love less than once a week have a far smaller likelihood of a pregnancy than couples who have sex regularly. This likelihood is estimated at approximately 16% over a six-month period. For couples who make love about three times a week this likelihood would increase to around 50%.
The following should be taken into account:

✔ Male sperm remains fertile for about two days (on average about 48 hours).

✔ The female ovum is fertile for about one day.

✔ Consequently you have the best chance of fertilisation by having sexual intercourse every two days, from four days before to two days after the expected ovulation.

Measuring temperature and planning sexual intercourse

Measuring temperature is not a suitable means of planning sexual intercourse, as the temperature only rises about two days after ovulation.

Pregnant nonetheless

Women who do not use any means of contraception and who have not had sexual intercourse for at least one week before ovulation sometimes – and totally unexpectedly – prove to be pregnant. This is indeed possible, because sperm cells can sometimes survive for quite a long time in the cervix and the fallopian tubes. Both these places secrete the fluid and nourishment that help keep the sperm cells alive. Living sperm cells are sometimes found as many as eight days after sexual intercourse.
6. CAUSES OF REDUCED FERTILITY IN MEN

It is not fully known which factors can disrupt the production of male sperm cells. For a number of men with fertility problems, no clear cause of the problem can therefore be given. We can divide the known causes of infertility in men into two main groups, i.e. disrupted sperm production and disrupted sperm conveyance.

**Disrupted conveyance**

- **✗** Erectile dysfunction means that the sperm cannot be deposited in the vagina and carried to the cervix in a normal way. The penis is not hard enough or does not remain hard long enough for normal sexual intercourse. As a result, the likelihood that the sperm cells reach the ovum in the fallopian tubes naturally is very small.

- **✗** In the event of premature ejaculation the sperm is not taken deeply enough into the vagina. In this case, too, the likelihood of fertilisation is greatly reduced.

- **✗** In the event of retrograde ejaculation, the sperm does not follow the usual path to the outside, but is redirected to the man’s bladder. This is referred to as a “dry orgasm”. Retrograde ejaculation can occur among other things when using high blood pressure medication, if the vasa deferentia (sperm ducts) are not properly positioned, in the event of disorders such as diabetes or after prostate surgery.

- **✗** If the ejaculatory duct is obstructed, the sperm cells will not enter the ejaculate. This obstruction may be congenital (for instance in the event of mucoviscidosis), or acquired (for instance after sterilisation). The volume of the sperm sample may be normal in these cases, as most of it consists of the fluid from the sperm vesicles and the prostate gland.

**Disrupted sperm production**

One of the main reasons for reduced fertility is an inadequate number of sperm cells. This problem may be due to a whole range of factors. Some of these lead to total infertility.

- **✔** **Hormonal disorders**: inadequate stimulation of the sperm cell production by the hormones that are secreted by the hypophysis (a gland at the base of the brain) can cause a total lack of sperm production. This is often due to an acquired or congenital abnormality of the hypophysis.

- **✔** **An infection or inflammation of the testicles**, for instance the mumps virus or a sexually transmitted disease such as gonorrhoea.
Varicocele is an abnormal enlargement of the veins in the scrotum (varicose veins). This causes the veins to feel like a twisted mass. In a horizontal position they disappear. For the examination we usually ask the man to blow hard on the back of his hand for a couple of seconds. The increased pressure causes the blood to flow back to the scrotum, and the doctor can clearly feel this. An ultrasound scan is needed to provide a better and more accurate picture of the situation. Hormonal factors undoubtedly play a role in the development of a varicocele, since this only exceptionally occurs before puberty. A varicocele occurs in approximately 15% of all adolescents, almost always on the left side. Almost half of all men with fertility problems have a varicocele.

Men with a varicocele therefore have fertility problems more often than other men. Nevertheless, most of them remain fertile. The presumption is that the varicose vein slightly increases the temperature in the scrotum and that this threatens the production and maturing of sperm cells. In almost half of the cases, the sperm quality improves once the varicocele has been treated. However, it is impossible to predict whether and for whom this will be the case. Nor is it clear whether the likelihood of pregnancy increases as a result.

Scar tissue after a wound or damage to the scrotum and testicles: twisted testicles (torsion). This squeezes off the blood flow to the testicles so that they die off unless action is taken very quickly. However, torsion like this is very rare. It can occur, among other things, if an individual engages in intensive sport or physical effort, but also without any apparent reason, even when someone is just sleeping. The latter occurs mainly in children.

Undescended testicles or other abnormal positions, such as an overly high implantation. In this case, the temperature in the testicles may rise too high, causing damage to sperm production. In principle, the descending of the testicles should be followed up, primarily at a young age, as there is a risk of permanent damage to sperm production. If the testicles return easily to their abnormal position, for instance if they move back into the inguinal canal, then a minor surgical operation may be necessary to attach them in the scrotum.

Hereditary abnormalities: both abnormalities in the chromosomes, bearers of the hereditary material, and the hereditary material itself (DNA). This is why it is also important in the case of a sperm abnormality, always to have a genetic analysis carried out on a blood sample (see below).

Damage to the partition between the sperm canals and the blood. Contact between sperm cells and the blood is usually impossible because the sperm canals and the blood vessels are totally separate from one another. However, if direct contact does occur, the defensive cells are activated. This often occurs after an operation when a sterilisation procedure is reversed by means of the microsurgical repair of the vas deferens (sperm duct). During the operation
sperm cells inevitably come into contact with defensive cells from the blood. Sperm cells have characteristics that differ from the rest of the cells in the body so that the defensive cells from the blood fail to recognise the sperm cells. They consider them unwanted intruders that have to be destroyed, for instance by making antibodies against the sperm cells.

✔ Medication can disrupt fertility. Some cause a temporary decline in fertility. When the treatment with these types of medication is interrupted, then fertility gradually returns. Others may cause long-term or even permanent sterility. This is the case, among others, with anabolic steroids (muscle-building remedies) as used by bodybuilders, for example.

✔ Chemotherapy and radiotherapy in the treatment of cancer can lead to permanent sterility because they damage or kill the cells in which the sperm cells are formed. Those who have to undergo treatment for cancer are therefore usually advised to have sperm stored in a sperm bank before the start of the treatment.

✔ Pesticides and chemical substances with which people may come into contact in their profession may adversely affect sperm production. This may occur, for example, with fruit pickers after exposure to pesticides based on dibromochloropropane, painters in shipyards through exposure to solvents in the paints such as ethylene glycol or welders through breathing in the welding fumes.

Erectile dysfunction, reduced fertility or sterility?

The terms relating to male fertility and sexual performance, such as impotence, infertility and sterility, are often confused with one another and incorrectly used. In this brochure we use the terms erectile dysfunction, reduced fertility and sterility as much as possible. These terms clearly express the condition to which they refer.

• Erectile dysfunction means that the penis does not become hard enough or does not stay hard enough to have sexual intercourse. This term is far clearer than the ‘impotence’ which is all too often used in the context of all sorts of other male fertility problems.

• Reduced fertility implies that the likelihood of reproducing is significantly reduced but is not impossible. After all, most men with fertility problems are not infertile. The same applies, for that matter, to women.

In the event of sterility there are no sperm cells (for women no ova) or they are not viable. An individual who is sterile cannot reproduce. They can, however, have normal sexual intercourse.
7. CAUSES OF REDUCED FERTILITY IN WOMEN

Just as with men, a wide variety of factors may lie behind fertility problems in women. The menstrual cycle is a complex phenomenon and things can go wrong at various points. Below we provide an overview of the main problems that may arise.

Defective ovary and ovulation function

✗ Anovulation: many different hormones play a role in the course of the menstruation cycle. If something goes wrong in this hormone production chain, then it is possible that none of the ova will mature and thus no ovulation will take place. This is referred to as anovulation. A number of different causes may lie behind this, including an excessively high or low body weight, serious weight loss, psychological (stress) factors, excessive production of prolactine by the hypophysis or excessive production of male hormones (for instance in women with polycystic ovaries).

✗ Disovulation: in this case, the ovum matures, but it receives the signal to leave the ovary far too early, before it is sufficiently mature. In this case the immature ovum remains caught in the follicle. Disovulation is also referred to by the term LUF syndrome (luteinised unruptured follicle syndrome).

✗ Luteal insufficiency: here the cycle runs smoothly up to and including ovulation, but something goes wrong during the luteal phase, when the mucous membrane of the uterus (endometrium) is prepared.

Polycystic ovaries and ovarian cysts: what is the difference?

Polycystic ovaries contain a large number of small cysts (polycystic), each of which is between five and eight mm in size. Women with polycystic ovaries are often overweight and usually have an irregular menstrual cycle, often without ovulation. As a result, they do not become pregnant, or only with difficulty. The ovary also produces too many male hormones, which means that these women sometimes have a rather male type of hair growth on the arms, trunk and face. The small cysts are in fact not really cysts but rather follicles that have not grown any further. Therefore, this is a totally different situation from the case of real ovarian cysts, which may be functional (after ovulation, during the maturing of the ovum) and then disappear spontaneously. The cysts may be benign (for instance endometriosis, etc.) or in some rare cases malignant. If a cyst does not disappear spontaneously or when taking the pill, then it is best if it is surgically removed in order to improve fertility and ensure that it is not malignant.
**Disrupted conveyance**

The fallopian tube collects the mature ovum that is released when the follicle bursts open and carries it to the uterus. This requires the necessary freedom of movement and permeability as well as an intact cilia function in the fallopian tube. Deformities in the abdominal cavity can impede smooth conveyance. These deformities may be the result of earlier surgical operations in the abdominal cavity, severe endometriosis or an infection in the abdominal cavity.

**Causes of reduced fertility in women**

**HYSTEROSALPINGOGRAPHY**

1. Catheter for injecting contrast medium (contrast fluid)
2. Open fallopian tube: contrast medium flows into the abdominal cavity via the fallopian tube
3. Blocked fallopian tube: contrast medium cannot pass through the fallopian tube

**BLOCKED FALLOPIAN TUBES**

1. Fallopian tube blocked at the passage to the uterus
2. Deformity between the ovary and the fallopian tube
3. Fallopian tube blocked at the end, resulting in fluid accumulation in the fallopian tube
**STERILISATION**

1. Sterilisation by means of a ring (often reversible)
2. Sterilisation by means of coagulation (irreversible)

**PROBLEMS DUE TO DISRUPTED IMPLANTATION**

We refer to disrupted implantation if a large number of pregnancies fail right from the outset as the foetus is not successfully implanted in the mucous membrane of the uterus (endometrium). Both the shape of the uterus and the quality (for instance free of inflammation) of the mucous membrane must be intact for successful implantation. The form of the uterus may be abnormal due to the presence of small benign swellings in the mucous membrane of the uterus (known as polyps), or benign swellings of the uterus muscle (fibroids or myomas), particularly if these are near the mucous membrane of the uterus. An inflammation of the endometrium can also hamper the chances of implantation and is therefore sought during the examinations. A serious inflammation of the mucous membrane of the uterus with a rising pelvic infection, after curettage or after childbirth, can cause deformities in the uterine cavity.

**PROBLEMS IN THE CERVIX**

Finally, defects in the cervix can also jeopardise the passage of sperm cells and hence give rise to reduced fertility in the woman.
Endometriosis

When a pregnancy does not occur, the uterus no longer has to prepare for the implantation of the fertilised ovum and menstruation begins. The inner lining of the uterus (the mucous membrane or endometrium) flakes off and is expelled. Menstrual blood is thus mixed with endometrial tissue. During menstruation some blood may end up in the abdominal cavity via the fallopian tubes, with the result that the endometrial cells present may become implanted in the abdominal cavity. This is referred to as endometriosis (see also insert). Endometriosis may be mild, but it may also be moderate or severe (possible formation of cysts in the ovary with deformities in the abdominal cavity). Endometriosis may cause pain, particularly during menstruation, during sexual intercourse, and sometimes chronic abdominal pain is reported. Endometriosis can also lie behind reduced fertility (due to ovulation disorders, the impeded conveyance of ova and/or sperm cells, etc.).

Endometriosis

Endometriosis is not a malignant disease, but it often plays a part in reduced fertility. It is estimated that 30 to 40% of women struggling with infertility have endometriosis at one stage or another. The disorder affects approximately 10% of women in their fertile phase, but half of them never notice anything.

How does endometriosis occur?
There are a number of theories about the causes of endometriosis. Experts entirely agree that in the vast majority of cases the condition arises because during menstruation blood and the mucous membrane of the uterus flow to the pelvic cavity via the fallopian tubes. This is known as retrograde menstruation.

Sometimes the mucous membrane attaches itself to the surrounding organs and tissues and begins to grow there, resulting in endometriosis. In almost all women, during menstruation the blood and mucous membrane not only flow out via the vagina, but some ends up in the pelvic cavity (abdomen). Yet not every woman develops endometriosis.

Hence other factors must also be involved. Research into this is still going on, but a certain level of inflammation in the pelvic cavity probably also plays a role. Experts discovered that the condition also has a hereditary component. If someone in the family has a severe form of endometriosis, then there is a greater chance that her sister or niece will also have the disease.

How is endometriosis treated?
Endometriosis can be treated with medication, by means of an operation, or both. All treatments result in partial or total alleviation of the symptoms in 80 to 90% of women. Unfortunately, according to the experts no treatment offers the prospect of a lasting cure. Of all patients with moderate or severe endometriosis, 20% of the women suffer a relapse of endometriosis within 12 months and around 50% within five years. As long as the menstruation
cycle continues, endometriosis can reoccur. Even with the best surgical operation, recurrence remains a real problem. Researchers are continuing to look for medication that can keep this disease under control for good.

Medication

✗ Patients who suffer from painful menstruation are often prescribed prostaglandin inhibitors such as Ibuprofen®, Diclofenac® and Naproxen®. These are only taken during menstruation, when the woman experiences a lot of pain. They work best if taken before the pain begins. These medicines are usually well tolerated.

✗ Hormonal treatments aim to imitate pregnancy or menopause. During these periods women suffer little if at all from endometriosis. The treatment affects the hormones that are responsible for the build-up of the mucous membrane of the uterus (endometrium), ovulation and menstruation. All hormonal remedies have side effects, but these may vary in number and severity from one medication to another and from one woman to another.

✗ The contraceptive pill is the best-known form of hormonal medication. Many women know from experience that menstruation is often lighter and less painful if they are taking the contraceptive pill. This is usually the case with endometriosis, too. Women are often advised to take the pill continuously and not stop for a week. The mucous membrane of the uterus then remains thin and is not expelled during menstruation. Taking pills that contain the hormone progesterone on a daily basis halts menstruation. However, this does not always work, and sometimes there is interim blood loss.

✗ LHRH agonists are the most recent means of fighting endometriosis. They imitate the menopause. They are injected just beneath the skin of the abdomen or administered as a nasal spray or in the form of a small capsule. As ovulation and the growth of the mucous membrane of the uterus are no longer stimulated, these medications cause sites of endometriosis to shrink and dry up. The disadvantage is that the LHRH agonists cause a reduction in bone density, which means that there is a risk of developing osteoporosis. Talk to your doctor about this.

Operations

In principle, endometriosis is best operated by using keyhole surgery. With minimal to mild endometriosis this can be done at a one-day clinic. If the endometriosis is more extensive, then the operation is carried out by a multidisciplinary team at our centre. This means that if the intestine or the bladder is involved in the endometriosis process, a specialist in intestinal surgery or a urologist can be called in. In some cases several operations are needed to be able to remove endometriosis radically. Of course, we always try to retain and restore fertility as much as possible.
8. ENVIRONMENTAL FACTORS, AGE, LIFESTYLE AND FERTILITY

Apart from a number of specific factors that can endanger the fertility of the man or the woman, there are also more general environmental and lifestyle factors that can impact on the fertility of an individual. Below we will consider the possible impact of the use of medication, exposure to chemicals, smoking, body weight and age.

**Medication**

Taking some medications can adversely affect fertility. This applies to both men and women. In most cases fertility gradually returns once the treatment comes to an end. For some forms of medication this is not the case. The use of anabolic steroids, for instance (muscle-enhancing substances taken among others by bodybuilders) can cause long-term or even permanent sterility in men. Chemotherapy and radiotherapy used in the treatment of cancer are particularly worthy of attention. Both treatments can lead to permanent sterility. In men they can damage or kill the small group of stem cells from which new sperm cells form. Young men with cancer who may still want to have children can have sperm saved in a sperm bank before the treatment begins.

In women, the effect of chemotherapy on fertility depends on the precise composition, the dose used and the age of the woman. Whereas for men a stock of sperm can be frozen, there is currently no ideal solution for women. In the event of chemotherapy, the ovaries can be protected hormonally by means of (three-) monthly injections of hormones that shut down the ovary (LHRH agonists, see Chapter 13). It is best to start this a few weeks before the chemotherapy begins. It is also possible to freeze ovarian tissue before the chemotherapy begins. To do this, half an ovary must be removed by laparoscopy under general anaesthetic at a one-day clinic. Methods of re-implanting frozen ovarian tissue are currently being researched. Research is also being carried out into the possible use of frozen and thawed ovarian tissue for in vitro fertilisation (IVF).
**Pesticides and chemicals**

A number of pesticides and chemicals seem to affect sperm production in the event of frequent contact (for example exposure through work, which is usually far more important than accidental exposure). This may occur in fruit growers who spray pesticides based on dibromochloropropane, painters in shipyards who are exposed to certain solvents in paints (such as ethylene glycol), or welders who breathe in welding fumes.

**Smoking**

Cigarette smoke contains thousands of substances, many of which are harmful to the ovum, the sperm cell, the fertilised ovum, the embryo and the foetus developing in the uterus. There is no doubt that smoking adversely affects the fertility of the woman. The more cigarettes a woman smokes a day, the greater the harm to her fertility. Women who smoke therefore take longer to become pregnant. The effects remain for a long time: even five years after having stopped smoking, the number of women who want a child but are still unable to become pregnant is almost twice as high as among non-smokers. What is more, smoking doubles the risk of a miscarriage and low birth weight. Smoking also leads to more premature births and increased risk of death of the foetus/baby before, during and after childbirth. There is a clearly increased risk of cot death among babies whose mothers smoke, as well as indications of an increased risk of congenital abnormalities.

The effect of smoking on male fertility is less clear. The problem is that various studies contradict one another. Some studies posit that there is a risk of hereditary damage in the sperm cells. This can lead to congenital defects and there is a possibility that children whose fathers smoke may in turn pass on these abnormalities to their own children in their hereditary material. Other studies suggest that smoking can disrupt the hormonal control of the sperm cell production. Yet another study gives rise to the suspicion that cigarette smoke can endanger the survival chances of the sperm. The authors of this study compared the survival chances of sperm from smokers and non-smokers. They came to the conclusion that sperm from smokers deteriorates significantly more quickly than sperm from non-smokers. The danger apparently lies mainly in the semen. The assumption is that all sorts of toxic substances eventually end up in the semen and threaten the survival of the sperm cells of smokers.
**Alcohol**

There is no doubt that serious abuse of alcohol has a harmful effect on fertility and on the development of the foetus in the uterus. In men heavy drinking can seriously disrupt sperm production. Women who drink more often suffer from an irregular cycle and have more miscarriages. Precisely where the boundary lies remains unclear. It is possible that the effects are felt even with limited alcohol consumption. This is why couples who are experiencing problems having children would be well advised to limit their intake of alcohol during the period when they wish to have children, and to stop drinking completely during pregnancy.

**Body weight**

Body weight seems to play a greater role in women than in men in terms of fertility. Women with a normal body weight on average fall pregnant more quickly than women who are under- or overweight. A Body Mass Index (BMI) between 20 and 25 is ideal. If women are underweight, ovulation may cease, with lack of menstruation being a clear sign of this. During pregnancy, too, if the mother is underweight this is a threat for the baby and the risk of miscarriage or premature birth is increased. Women who are overweight usually find it more difficult to become pregnant. Fertility problems experienced by obese women are usually due to the lack of or irregular ovulation. This is often linked to the presence of polycystic ovaries (see Chapter 7).

Among men, excess weight does not appear to have any direct effect on fertility. However, obesity in men can cause problems during sexual intercourse.
Diet

There are no indications that special diets have a clear impact on fertility. A good, varied and balanced diet is advisable for everyone, and certainly for women who wish to have children. Particular attention should be paid to folic acid (vitamin B11). An extra daily dose of this vitamin from at least one month before until at least three months after fertilisation helps limit the risk of spina bifida. Women with a high risk of children with spina bifida (particularly women who already have a child with spina bifida, the direct relatives of such women, and women with type 1 diabetes or epilepsy (falling sickness)) are advised to take 4 mg of folic acid per day. This should reduce the risk of spina bifida by approximately 70%. For other women, a daily dose of 0.4 mg is recommended (expected risk reduction of 45%).

Age

Age is extremely important for the fertility of a couple. The age of the woman in particular has a major impact, but over the past few years it has become increasingly clear that the age of the man is also important. Women are at their most fertile between the ages of 20 and 30. After this, their fertility declines systematically while at the same time the number of spontaneous abortions increases. Both trends become even stronger once the woman is older than 35 years of age. At age 38 the likelihood of pregnancy per cycle amounts to about 10%. The chance that this pregnancy will be spontaneously terminated rises to almost 45%. At the same time, the risk of hereditary and congenital abnormalities also increases. The decline in the woman’s fertility is probably mainly to do with the deteriorating quality of the ova.

Every woman has a reserve of ova in her ovaries at birth. These ova are formed even before she is born. No new ones are added thereafter. A woman’s ova are consequently as old as she is herself. Shortly after birth, the reserve of ova is still very large. At that moment, each ovary contains literally thousands of ova. During the years that follow, a great many of these will be spontaneously lost. The rest of the reserve is slowly used up during the woman’s fertile years. When the reserve is exhausted, the menopause begins. When we talk about the reduced quality of the ova, we should think first of all of possible damage and less about actual aging processes. The ova do not undergo any changes during the woman’s life and they seem to withstand aging well. Presumably, however, they can be damaged during the course of the woman’s life. Although there is no hard evidence for this, we do observe that the number of children born with congenital abnormalities increases with the age of the mother (Table 1).

Down’s syndrome is a good example of this. Genetic research shows that the number of chromosome defects in the ova rises sharply after the age of 35. The assumption is that damaged ova are less easy to fertilise, do not divide optimally, develop less often into a viable embryo, etc. The number of spontaneous abortions also increases with the age of the mother. The results of ovum donation also point to declining quality of the ova with age. The likelihood of fertilisation and the occurrence of a spontaneous termination of pregnancy are linked to the age of the woman who donates the ova and not the age of the woman in whom the ova are implanted. It is not known which substances or influences can damage the ova, but the assumption is that
the older an ovum becomes, the greater the chance of damage. It is less clear whether the environment in the uterus becomes less suited with age to receiving ova and to a problem-free full-term pregnancy.

**Young couples make love more frequently**

The age of the couple plays a role in another way, as well, i.e. through the decline in the frequency of sexual intercourse. On average, younger couples have sexual intercourse more frequently than older ones, so that they have a greater chance of becoming pregnant. However, the importance of this assertion should not be overestimated. Without taking into account the day of the cycle or the moment of ovulation, the greatest likelihood of pregnancy occurs when a couple has sexual intercourse every two days, i.e. about two or three times a week.

Couples who make love less than once a week have a far smaller chance that the woman will become pregnant than couples who have sex regularly. This likelihood is estimated at around 16% over a period of six months. With couples who make love three times a week, this likelihood would increase to about 50% (see Table 2).

<table>
<thead>
<tr>
<th>Woman's age</th>
<th>Likelihood of pregnancy</th>
<th>Waiting period</th>
</tr>
</thead>
<tbody>
<tr>
<td>25 years</td>
<td>60%</td>
<td>6 months</td>
</tr>
<tr>
<td></td>
<td>85%</td>
<td>1 year</td>
</tr>
<tr>
<td>35 years</td>
<td>60%</td>
<td>1 year</td>
</tr>
<tr>
<td></td>
<td>85%</td>
<td>2 years</td>
</tr>
</tbody>
</table>

*Table 1: the likelihood for women aged between 25 and 35 years of becoming pregnant within a certain period of time.*

<table>
<thead>
<tr>
<th>sexual intercourse per week</th>
<th>pregnancy within six months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 1x</td>
<td>16%</td>
</tr>
<tr>
<td>1x</td>
<td>30%</td>
</tr>
<tr>
<td>2x</td>
<td>45%</td>
</tr>
<tr>
<td>3x</td>
<td>50%</td>
</tr>
</tbody>
</table>

*Table 2: the likelihood of a pregnancy increases significantly when a couple has sex regularly.*
9. HOW, WHERE AND WHEN TO MAKE AN APPOINTMENT

The likelihood of spontaneous pregnancy for a couple who have unprotected sexual intercourse diminishes as time passes. Generally speaking, ‘trying’ for one year is a minimum before undergoing fertility tests. There are, however, a few exceptions to this general rule, such as if the woman is somewhat older (more than 38 years of age) or if there are known factors that have a negative impact on the fertility of the man or the woman. For instance, it is normal for a woman who does not have a spontaneous menstruation cycle to ask for help earlier. Also a man who had surgery for undescended testicles as a child might perhaps come for a consultation more quickly to find out if this surgery has had any effect on his sperm production.

When couples decide to go to a fertility centre therefore depends on various factors. You can come to our centre at any time, either on your own initiative or after referral by your GP, your gynaecologist, a cooperating fertility centre or an andrologist.

Couples who come to us following referral have often already been given a great deal of information about their chances of fertility and the possibilities of increasing these chances. GPs, for instance, may already have carried out tests or had them carried out. A more thorough examination is also often carried out by a gynaecologist or an andrologist. In that case we will also check up on the data already available. In this way we avoid the needless repetition of certain examinations. In some circumstances, however, it may be useful to carry out certain examinations again. Some hospitals have their own fertility department where many tests can be carried out perfectly well and where the patients also receive information about their problem and the possible treatments.

Gynaecologists in these departments sometimes perform a great deal of the fertility treatments themselves: surgery, hormone stimulation, etc. Some centres (recognised A centres) can also carry out ovum aspiration in the hospital. For other, highly specialised treatments, such as complex surgical operations, medically assisted fertilisation with embryo transfer, pre-implantation, genetic examination or the freezing of ovarian tissue, testicle tissue, sperm cells or embryos, etc., they refer patients to a more specialised centre (B centre) such as the Leuven university fertility centre.

Where are the examinations/treatments carried out?

Most examinations and treatments at the Leuven university fertility centre (LUFC) take place at level -1 following the orange arrows, either at the gynaecology-obstetrics consultation clinic, or at the fertility centre (E 495), or in the fertility centre’s laboratory. All these locations are indicated by orange arrows or signs. You can also report to reception in the entrance hall. The staff members on duty will be pleased to help you.
If you come to the LUFC for a consultation
Please check in first at the registration desk in the reception area for the gynaecology clinic (E 499). You can also use the booth, where you can register using your SIS card. The fertility centre consultation takes place in the gynaecology and obstetrics clinic (orange arrow, level -1).

If you come to the LUFC for a blood test
Blood samples are always taken by appointment between 9 and 10 am in the fertility centre. You can make an appointment with the midwife by calling 016 34 36 24. For the fertility centre (E 495 FER) please check in first at the registration desk in the general reception area or sign in at the booth. At weekends you will always have to sign in at the booth.

If you come for a gynaecological ultrasound as part of your fertility treatment
This test is always carried out by appointment between 7.30 and 10 am at the fertility centre. For the fertility centre E 495, please check in at the registration desk in the reception area or sign in at the booth. At weekends you will always have to sign in at the booth.

If you come for ovum aspiration, embryo transfer or intra-uterine insemination
Please check in first at the registration desk in the reception area for the fertility centre (E 495 FER). At weekends you will always have to sign in at the booth. If you have an appointment for ovum aspiration, you must have an identification bracelet. To obtain one, check in at the registration desk in the hospital reception area. For intra-uterine insemination or embryo transfer you can register at the booth. Ovum aspiration, embryo transfer, high intra-uterine insemination or cyst puncture take place in the fertility centre (orange arrow, level -1).

If you come for a sperm sample test
Please check in first at the registration desk or sign in at the booth in the reception area for the fertility lab (E 497 FER). Next time, you can report directly to the fertility centre lab.
How to contact us during the fertility treatments

Monday to Friday from 9.00 am to 12 noon and from 2.00 pm to 4.00 pm
Tel. 016 34 36 24
Fax 016 34 36 07

For instructions relating to starting your treatment and for more information about this, you can contact us every weekday on 016 34 36 24, between 2.00 pm and 4.00 pm.

For instructions relating to the course of the treatment you will be contacted by the midwife during the week between 2.30 pm and 4.30 pm. At the weekend you will be contacted between 11.00 am and 3.00 pm.

For urgent matters during the weekend you can reach the midwife at the fertility centre via the exchange (Tel. 016 33 22 11).

Blood tests and ultrasound scans

You can go to the fertility centre for a blood test and an ultrasound scan:

- Monday to Friday: from 7.30 am to 9.30 am
- on Saturdays and Sundays: from 8.00 am to 9.00 am, by appointment with the midwife (no pregnancy blood tests).

If you are not in a hurry in the mornings we would ask you to come along after 9.00 am so that we can avoid long waiting times as much as possible. If you go to a gynaecologist in your area for blood tests and ultrasound scans, please have the results sent through by fax before 12 noon on 016 34 36 07.

Please also let us have a telephone number on which we can reach you between 2.30 pm and 4.30 pm.

How to make an appointment at the LUFC
You can make an appointment at our centre via the secretariat, which you can call on 016 34 36 50 from Monday to Friday between 9.00 am and 12 noon and between 2.00 pm and 4.00 pm.
To ensure that everything runs smoothly, to avoid certain tests, examinations and/or treatments being repeated unnecessarily and so that no time is wasted, we would ask you to request all the results from previous tests, examinations and treatments from your GP in advance and bring them along to the consultation, if possible with a letter of referral from your GP or specialist. However, a letter of referral from your GP or specialist is not essential. You can also make an appointment yourself. Make a note of all the questions that are of concern to you in advance and bring them with you to help you remember.

What questions do couples ask at a first consultation?

- Some couples come simply to obtain information. They first want to find out about fertility, the tests, the possible forms of treatment and the chances of success. They want to let that sink in calmly first before taking any further steps.

- Other couples only want information about their specific chances of pregnancy. They want to have the necessary examinations carried out so that they can be clear about their chances of pregnancy in the coming months or years. They mainly want a diagnosis (is there something wrong and what?), but not any treatment as yet.

- Yet other couples come only to have surgery. This can vary from reversing sterilisation in the man or the woman to a specialised laser laparoscopy by our team.

- Most couples who come to our centre, however, come requesting a diagnosis and treatment. They have already spent enough time trying for a spontaneous pregnancy and now they would prefer results as quickly as possible.

- Couples also come to us regularly requesting a second opinion of a diagnosis or proposal for treatment received elsewhere. Our centre is available for this as well.

How long do you have to wait?

Couples who make a first appointment for a consultation at our centre should expect to wait for a maximum of six weeks. We can see those receiving treatment and who want to make an appointment sooner than this. At our centre we work by appointment only and try as much as possible to keep to the appointment times. You can expect to be here for between half an hour and an hour. However, we always advise you to bring something to read, since the appointments may run over. Some problems call for more explanation and more work than expected, and we want to be able to help and speak to everyone as much as possible.
Cooperation with B centres, A centres, satellite centres and peripheral gynaecologists

The Leuven university fertility centre cooperates with a number of A centres, B centres, satellite centres and peripheral gynaecologists.

Cooperation with A and B centres
The cooperation with A centres is regulated by law. All tasks, areas of competence and responsibilities for the A centre and the LUFC (B centre) are laid down in an agreement that is valid for five years. Any supplements and/or exemptions are also laid down by contract. The list of cooperating A centres can be found in a separate appendix entitled ‘Cooperating centres and gynaecologists’.

Cooperation with satellite centres
The LUFC also cooperates with a number of satellite centres. The diagnostic phase and the medical needs assessment after consultation between the specialists at the satellite centre and the LUFC take place in these satellite centres. In addition, the medical staff at the satellite centre are responsible for hormone stimulation. Patients come to the LUFC for ovum aspiration, IVF, embryo transfer or any other fertility treatment. After-care and follow-up take place in the satellite centre again. The list of satellite centres can be found in a separate appendix entitled ‘Cooperating centres and gynaecologists’.

Cooperation with gynaecologists from peripheral hospitals
Finally, a number of gynaecologists from peripheral hospitals take responsibility during the treatment received at the LUFC for monitoring the patient and for first-line follow-up. They perform the ultrasound scans, take blood and provide follow-up after the embryo transfer by the LUFC. They send the results and data from their examinations to the LUFC by fax. This has to be done before 12 noon on the agreed days. The nursing team draws up the timetable and puts it on computer. A nurse checks daily to see that all the data to be received have come in. If this is not the case, the nurse contacts the gynaecologist concerned.

The separate appendix ‘Cooperating centres and gynaecologists’ contains a list of gynaecologists who work with our centre. This list is not in any way exhaustive: we are willing to work with any gynaecologist who is prepared to help you and cooperate with us.

Whatever the form of cooperation, after the pregnancy we refer the patient back to the primary attending gynaecologist.
10. WHAT IS THE PROCEDURE?

The following road map provides an overview of the working method that we adopt at the Leuven university fertility centre.

1. The first consultation
   This consultation with the attending gynaecologist provides an opportunity for an in-depth discussion and physical examination. During the discussion, the doctor asks targeted questions in order to form a clear idea of the problem and of the further examinations and support. To make everything run more smoothly, sometimes this discussion is prepared by a trainee doctor or by a specialised midwife or nurse. The attending gynaecologist (your gynaecologist) does, however, always go through all the data and asks additional questions where necessary. Questions asked during this initial consultation include your age, your profession (this is important to rule out exposure at work to substances that can affect fertility), any stress you may be under at work or at home, previous operations or diseases, allergic reactions, other health problems, use of medication, lifestyle, any fertility problems or hereditary problems among family members, the occurrence in the family of congenital abnormalities or of ovarian cancer. We also look in depth at the course of the menstrual cycle, specific gynaecological complaints or problems, previous contraception, sexually transmissible disorders, sexual activities, etc.

   A gynaecological examination is also usually carried out during the first consultation, including a cervical smear test (if this has not been done for over a year) and an internal examination of the uterus and ovaries. Sometimes this examination is postponed until a later consultation, for instance if you have your period or if you would prefer not to have this examination done during the first meeting or because it would be best to combine this examination with another. During this first consultation we also schedule the further course of examinations and make another appointment with the specialist to discuss the results once all the tests have been carried out and all the results are known. If a great many tests and/or courses of treatment have already been carried out, it is possible that very few if any additional tests are necessary, and that we can actually begin treatment.

2. The diagnostic phase
   During this phase, which can take between two and three months, we carry out the tests needed in the man and the woman (see Chapters 11 and 12). The woman will have to undergo various tests and examinations at specific times during the menstrual cycle. This is why this examination phase takes some time.

3. The multidisciplinary staff meeting
   Once the series of tests is complete, we discuss all the results anonymously during a multidisciplinary staff meeting. Apart from the gynaecologists and andrologists, this meeting is also attended by people from the fertility laboratory, as well as by the fertility consultants, the nursing team, the referring doctor and sometimes doctors specialising in other areas (genetics, urology, infectious diseases, etc.). In this way we bring together all the strengths...
and scientific knowledge to come to the best possible conclusions and make the best possible proposals for each individual problem. This means that it is not one doctor alone, but a whole team of people, all experts in one particular aspect of fertility, who determine what is best for each patient.

4. The discussion of the results
The consultation between the multidisciplinary staff members regarding the results of the examinations is followed by an appointment with the gynaecologist who will discuss the details with you. He will also give you an idea of your fertility, expressed as the chances of pregnancy per month or over the coming years without treatment. During this discussion, we also plan possible additional tests and propose a form of treatment, in each case setting out the advantages and disadvantages and the likelihood of pregnancy. The aim during this consultation is to reach a joint decision on a possible treatment. If you like more time to consider this information before making definite arrangements, then you can contact us again later to make further arrangements.

5. The treatment phase
If there is a very good chance of a spontaneous pregnancy, sometimes a wait-and-see attitude is adopted for six months to one year. This is the case in particular if the woman is still young and if no abnormalities have been found. Sometimes this approach is also adopted after surgery during which a major cause of infertility has been eliminated, such as an operation to remove endometriosis and/or pelvic deformities, or an operation to reverse sterilisation in the man or the woman. In other cases stimulation of ovulation, insemination, IVF or ICSI is proposed. We then discuss the stimulation plan and put together a package with all the practical arrangements. This is followed by an intake interview with the nurse. She/he talks to you about the right time to start the stimulation, who will administer the injections, who will carry out the check-ups, when you can be reached and on what telephone number, etc.
II. TESTS FOR MEN

In around half of the cases where pregnancy fails to occur, the cause lies with the man. The problem can usually be attributed to a reduction in the quantity or the quality of the sperm cells. Examining the sperm is therefore a central element in the examination of male fertility problems. It is a relatively simple examination, certainly in comparison with the far more technical tests that have to be carried out for women. This is why it is important to detect any problems in the man quickly, so as to spare the woman pointless tests.

The examination for the man consists of:

- An extensive interview discussing all of life's aspects and events that could be of importance for the man's fertility
- An examination of the genitalia
- Laboratory tests of the sperm, blood samples and possibly a urine sample

A general examination

During the interview and when investigating the medical history of the man, we check to see whether there is (or has been) any question of:

- earlier illnesses: mumps, for instance, can cause fertility problems in men
- an undescended testicle
- surgery on the genitalia
- genital or urinary infections
- problems during sexual intercourse, such as premature ejaculation, erectile dysfunction, lack of ejaculation.

An examination of the genitalia

When examining the genitalia, the andrologist will check the testicles, the epididymis, the seminal ducts, the prostate gland and the penis for any abnormalities. Specific attention will be paid to the shape, the volume and the sturdiness of the testicles, the epididymis and the seminal ducts and to any varicose veins and groin hernias. These aspects can provide valuable information about the possible cause of the abnormal sperm production. It is possible, for instance, to detect a blockage of the seminal ducts by means of a careful clinical examination.
An ultrasound scan can then be carried out. The great advantage of ultrasound examinations is that they do not cause any significant discomfort. The doctor does not have to penetrate the body, apart from – exceptionally – via the anus to check the prostate gland and seminal vesicles.

**Laboratory tests**

Examination of sperm

- **Motility**
- **Concentration**
- **Morphology**

Analysis of the sperm sample is an important element in the diagnostic assessment of the fertility of the man. When a sperm analysis like this is carried out, a number of rules are followed, such as the period of abstinence (see insert). Failing to follow the instructions correctly produces an unreliable analysis from which false conclusions could be drawn. Moreover, to ensure a reliable interpretation of the results, the sperm examination should be repeated at a later date. Sperm consists of sperm cells and seminal plasma (= the liquid that contains the sperm cells). A number of analyses are conducted on this sperm sample that give us an idea of the quality of the sample. The sperm sample provided by the man cannot be analysed immediately upon receipt. The sample is very viscous or ‘syrupy’ for the first 20 minutes. After about 20 minutes the viscosity lessens and we can look at a number of parameters.

✔ The volume of the sample. The volume of a sperm sample varies between two and six millilitres. The quantity of the sample provides no indication of its quality. However, a volume of less than two ml may be an indication that the sample has not been collected properly, and therefore a reason to repeat the analysis.

✔ The motility of the sperm cells. The sperm cells have to be motile to be able to travel from the vagina to the ovum, in the fallopian tubes. We use a spermiogram to check this parameter. Sperm cells can be classified on the basis of their motility: rapidly progressive motile sperm cells, moderately progressive motile sperm cells, sperm cells that move but do not advance and non-motile sperm cells. To fulfil the conditions of a ‘normal’ sample, at least 50% of the sperm cells must demonstrate progressive (rapid + moderate) motility.
The number of sperm cells per millilitre (concentration). A second important parameter is the number of sperm cells per millilitre of sperm sample. We can determine this number by counting the number of cells in a set volume using a special counting chamber. To be catalogued as ‘normal’ the number per millilitre must be above 20 million.

The morphology of the sperm cells. The appearance of the sperm cells, after staining, is the third parameter. Important parameters include the shape of the head or the presence of a tail. To be considered ‘normal’, the percentage of sperm cells with a normal shape must be above 10%. A large number of misshapen sperm cells does not increase the risk of abnormalities in children.

Other tests. In certain cases we check other parameters as well. One of these is the presence of white blood cells in the sample, which may point to the presence of an infection.

Sperm sample capacitation. A sperm cell from a sample that has just been taken cannot fertilise an ovum. To do this, the sperm cell first has to undergo a number of changes. All these changes together are known as ‘capacitation’. We can imitate this capacitation in the laboratory. This will be done on one of the samples supplied by the man, in order to check whether everything is progressing ‘normally’ in that area. During this capacitation, approximately 60% of the cells are lost. The number of properly motile cells that remain will be one of the factors determining what treatment is suitable for the couple: for instance, more motile sperm cells will be needed for intrauterine insemination than for in vitro fertilisation.

All these tests describe the quality of a sperm sample and provide pointers to serious abnormalities. However, these tests cannot predict whether the sperm cells will ultimately be capable of fertilising an ovum: reduced sperm quality does not necessarily mean lower fertility.

Instructions for collecting the sperm sample

The time between the last seminal discharge and the collection of the sample for analysis is extremely important if the analysis is to be reliable. The ideal period of abstinence is two to five days. The length of time taken to transport the sample and the temperature at which it is transported are also important. A reliable analysis of motility must be conducted within 60 minutes of the sample being collected. In addition, the temperature may not drop below 20°C or rise above 37°C. For these reasons, we ask for the sample to be prepared in a special room next to the laboratory. In this way we can be certain of the ideal circumstances. If this causes problems, other circumstances can always be sought in which to collect a sperm sample. Men who have problems obtaining a sperm sample through masturbation could use a non-toxic condom which they can request from the LUFC laboratory. Never use an ordinary condom to collect a sperm sample. An ordinary condom is toxic for sperm cells and the analysis is consequently unreliable.
To obtain a reliable picture, two samples have to be analysed. In practical terms, the procedure is as follows: you are given an appointment for an initial sperm analysis (spermiogram) and a second sperm analysis in the laboratory. After this, an appointment is made with the andrologist. We then discuss the results of both analyses with the man during the consultation. It is also important that you report all possible problems in preparing and collecting the sample to the laboratory. Collection problems when obtaining the sperm sample, stressful circumstances, or a period of illness, particularly if you have a fever, should all be reported. In fact, a fever affects the quality of the sample.

The blood test
Just as with the woman, we also carry out a blood test on the man. This is done on a small quantity of blood collected in a special tube.

✗ Hormones: a regular and sufficiently high secretion of male hormones (androgens) is necessary for normal sperm cell production. A number of specific phenomena, such as very small genitalia or enlarged mammary glands, could be related to hormonal abnormalities that adversely affect the fertility of the man.

✗ Infectious diseases: we also determine antibodies to the following diseases in the blood so as to prevent possible contagion: HIV, Hepatitis B and Hepatitis C virus, syphilis. This blood test has to be repeated every six months during the fertility treatment.

✗ Investigation of heredity: male fertility problems may be the consequence of or linked to certain abnormalities in the hereditary material. Knowledge in this field has increased rapidly over the past few years. In fact, the chance of hereditary abnormalities increases as the quality of the sperm declines (although other, non-hereditary factors can also play a role here). For instance, we find a hereditary abnormality in approximately one out of five men who have fewer than one million sperm cells per millilitre of semen plasma.

Checking the fertility of the man: do not delay.

Men are far less inclined to have their fertility checked than women. Many men prefer the woman to undergo the necessary tests first, and to be involved themselves only in a second phase, for instance when it appears that all the test results are normal for the woman. Nevertheless, it is important to start checking the fertility of the man as early as possible, preferably at the same time as the tests are carried out on the woman. If major disorders are found in the man, we can usually spare the woman a number of tests.
12. TESTS FOR WOMEN

After an in-depth interview and a general physical examination (see Chapter 10), an exploratory gynaecological examination will be conducted. This gynaecological examination is the first step in a series of examinations.

It is a general check-up intended to provide an initial insight into the problem and ensure that nothing is overlooked. The findings that emerge from the gynaecological examination are then clarified by means of more specific examinations. For instance, pain during the examination may point to various possible problems. The origin of the pain often only becomes clear after targeted check-ups.

These targeted check-ups comprise:

- blood test (screening for infectious diseases, assessment of the hormonal balance, possibly determination of the blood group and Rhesus factor and a genetic examination)
- changes in body temperature
- examination of the cervical mucus (examination with the naked eye and microscopic examination)
- check-up of the fallopian tubes (hysterosalpingography, laparoscopy)
- check-up of the uterus (hysteroscopy, laparoscopy)
- check-up of the mucous membrane of the uterus (echoscopy, endometrial biopsy)
- check-up of the abdominal cavity (laparoscopy)
- check-up of the ovaries (ultrasound scan, laparoscopy).
This series of tests may seem to be a little overwhelming and that is quite understandable. It is of the utmost importance, however, to detect defective elements in the complex reproductive system of the woman as carefully as possible and remedy them as meticulously as possible. In some cases specific additional examinations are necessary.

**Blood screening for infectious diseases**

The blood analysis is useful for detecting any antibodies against a number of infectious diseases. If we find antibodies in the blood, this means that the woman is infected with this particular pathogen or has been at some point. In most cases the antibodies provide good protection against further infection with the same pathogen. Anyone who has ever had rubella or has been vaccinated against rubella has antibodies in their blood and these guarantee lifelong protection against further infection.

We check in particular for antibodies against the following diseases:

- **Toxoplasmosis**: infection during the pregnancy that can lead to serious congenital abnormalities, a miscarriage or the death of the foetus. Around one woman in two is protected against these problems because she has already had the disease (perhaps without being aware of it) and has protective antibodies against toxoplasmosis. If the woman does not have any antibodies against toxoplasmosis in her blood, this is not a problem, but in this case during the pregnancy she has to beware of infection, which usually comes via food (infected and inadequately cooked meat). The following guidelines have to be observed from the start of the pregnancy to avoid toxoplasmosis:
  - eat no raw meat (steak tartare, rare steak, barbecued meat, etc.), but only meat that has been well cooked
  - raw vegetables are allowed, but they must be thoroughly washed
  - no contact with cats (cats’ stools are infectious)
  - wear gloves when working in the garden.

- **Cytomegalovirus**: infection during the pregnancy can lead to serious congenital abnormalities such as deafness, mental retardation and problems with eyesight. Around 50% of women have already had this disease. However, this does not provide absolute protection. Re-infection is therefore possible, but without any serious danger to the foetus. There is an increased risk of infection among child care workers, nursery teachers and mothers with young children. There is no effective treatment at the moment. A few preventive measures can be taken to avoid infection, such as good hand hygiene when in contact with young children.

- **German measles (rubella)**: a woman who does not have any antibodies must be vaccinated. A rubella infection during pregnancy implies a risk of serious congenital abnormalities, miscarriage or the death of the foetus. The earlier the infection occurs in the pregnancy, the greater the risk.
✔ **HIV virus:** the HIV virus causes AIDS. There is a small but very real risk that the child may be infected during childbirth. This risk can be substantially reduced with appropriate treatment. We always request the woman’s consent to test for HIV. If one of the partners is infected, this of course implies a risk for the other partner and therefore also has consequences for the further assistance and advice provided. This raises the question of whether unprotected sexual contact is still desirable and whether it would not be best to switch to artificial fertilisation.

✔ **Hepatitis B virus:** hepatitis B is often found in women with fertility problems. The infection does not involve any immediate major risks for the child, but it is contagious and sexually transmitted. It often leads to a serious liver disorder with a clearly higher risk of liver cancer. If one of the partners is infected then the other should be vaccinated. If the woman is infected, then care must be taken during childbirth to limit the risk of infecting the baby as much as possible.

✔ **Hepatitis C virus:** hepatitis C is also a very serious liver disorder, but is less common than hepatitis B. There is a small risk (estimated at 6%) that the baby will be infected. Chronic hepatitis C is currently treated with Ribavirine, a medicine that can cause congenital abnormalities and remains in the body for a long time. For this reason, the treatment has to be stopped for at least six months before a couple can conceive. This applies to both partners, i.e. including when the male partner is receiving treatment.

✔ **Chlamydia trachomatis:** most people do not know about this pathogen, but it is a major cause of fertility disorders in women, mainly because of the resultant inflammations and the deformities in the internal sexual organs such as the uterus, fallopian tubes and ovaries.

**Blood screening for hormonal balance**

Regular and carefully adjusted secretion of hormones is necessary to ensure that the cycle follows its normal course, with the maturing of an ovum and ovulation. Checking the various hormone levels tells us something about the functioning of the various organs involved in guiding the cycle. This is another means of detecting abnormalities.

Hormones are usually checked in blood, but sometimes also in urine and saliva. The concentrations of certain hormones fluctuate considerably during the course of the cycle. For that reason it is important to measure them at various points in the cycle. This is usually done on the basis of a strict schedule. Between day two and day five of the cycle we determine the level of oestradiol 17ß, luteinising hormone, follicle stimulating hormone, androgenic hormone (androgens), prolactine and thyroid gland hormone.

About a week before menstruation is expected we determine the progesterone again, to check whether ovulation has actually occurred.
- **Oestrogens (oestradiol 17β):** the evolution of this hormone reflects the development of the follicle. Combined with an ultrasound scan, the evolution of the oestradiol level can also be used to follow the maturing of the follicles when the ovaries are artificially stimulated.

- **Progesterone:** progesterone reflects the functioning of the corpus luteum. The secretion reaches a peak during the second phase of the cycle, with the result that the mucous membrane of the uterus prepares for the implantation of the fertilised ovum.

- **Androgens (in particular testosterone):** The level of androgens only has to be measured when there is disrupted ovulation and excessive hair growth or other signs that may point to an increase in male sex characteristics.

- **Follicle stimulating hormone (FSH):**
LHRH  (luteinising hormone releasing hormone): triggers the menstruation cycle

FSH  (follicle-stimulating hormone): brings follicles in the ovaries to development

LH  (luteinising hormone): stimulates ovulation

hCG  (human chorionic gonadotropin) or pregnancy hormone: supports the further development of the embryo into a baby

HMG  (human menopausal gonadotropin): hormone mix containing LH and FSH

The hormones that play a role in the menstruation cycle and/or IVF treatment

- **Follicle stimulating hormone (FSH):** this hormone is secreted in very small quantities depending on the point in the cycle. The only reliable value for this hormone in the context of fertility tests is between day two and day five of the cycle. Increased values can give rise to the assumption that the ovaries are not reacting to this stimulus as well as they might. It is often found in women from the age of 35. Frequently there also tends to be a less effective reaction after hormonal stimulation of the ovaries in the context of fertility treatment. Because the secretion of FSH can be affected by oestradiol, these two hormones are always monitored together at the start of the menstrual cycle.

- **Luteinising hormone (LH):** the concentration of the luteinising hormone remains fairly low and stable throughout most of the cycle, but reaches a peak just before ovulation. Excessively low or high values may indicate abnormalities in the ovaries or in the pineal gland or epiphysis that stimulates the ovaries (hypophysis). If the level peaks too early ovulation may be disrupted and the ovum may be released before it has fully matured.

- **Inhibine:** this hormone provides a good picture of the quality of the follicle. The name refers to the curbing or inhibiting effect of this hormone on other hormones.

- **Prolactine:** the concentration of this hormone usually remains low and fairly stable. An increase above the normal value is not necessarily abnormal as this may be provoked by many factors, such as stress, meals, problems with the kidneys or thyroid gland, medication, etc. A really high value may indicate a tumour in the hypophysis, but this can only be confirmed if blood is taken four times an hour to determine the concentration of prolactine in the blood. If it is then confirmed that the values are too high, we always request a brain scan to rule out small tumours in the hypophysis (pineal gland (epiphysis) that regulates reproduction). If there is a tumour, this is almost always small (less than one centimetre) and benign and disappears with medication that reduces the production of prolactine.
Blood group and Rhesus factor

Determining the blood group is mainly important in order to discover the Rhesus factor. If a woman with a negative Rhesus factor is pregnant by a Rhesus positive man and the blood group of the foetus is positive, a defensive reaction may be triggered which may cause serious damage, such as retarded growth, mental handicap, miscarriage or stillbirth. Fortunately this problem is very rare and usually occurs only with the second pregnancy. However, it can also be avoided by administering the necessary protective remedies to the woman in time, i.e. an injection of protective antibodies after childbirth, after a miscarriage, after blood loss during pregnancy, or after an accident in which sudden pressure was placed upon the pregnant abdomen.

Genetic examination

We examine the chromosomes through blood tests. Special attention is paid to a number of specific genes, including that for mucoviscidosis and that for fragile X-syndrome (which causes mental retardation in boys). Someone who is not ill may be a carrier of a chromosomal abnormality or gene defect. These abnormalities can affect fertility and may be passed on to descendants. It is important to be properly informed about this.

Changes in body temperature

In most women the body temperature fluctuates sharply during the monthly cycle. A temperature graph is therefore a good means of highlighting the individual features of the cycle and any abnormalities. The better known the course of the individual cycle, the better all the tests and treatments needed to bring about fertilisation can be planned and followed up. A temperature curve with daily temperature readings over a period of three months is usually enough to gain a good idea of the cycle.

Interpreting the temperature curve

A normal temperature curve consists of two separate phases. During the first phase of the menstrual cycle, the follicular phase, the temperature is low, on average below 37°C. This phase lasts for around 12 to 16 days. At the end of the follicular phase the temperature falls to a low point. During the second phase, the luteal phase, the temperature is on average half a degree higher, around or just above 37°C. This plateau is maintained for around 12 to 14 days.

The temperature can rise sharply, over the course of 24 hours, but it may do so slowly, spread over two or three days. The speed at which the temperature rises is very probably not important. Ovulation usually occurs on the day before the first day of the high-temperature plateau. This means that by using the temperature curve the day of ovulation can usually only be established afterwards.
What is ‘normal’?

In some women, the curve deviates somewhat from the ‘typical curve’.

• Sometimes the temperature is on average abnormally low or high during the first phase, for instance around 36°C or 37°C. As long as the curve clearly shows two phases, however, there is nothing wrong.

• Similarly, a long first phase is nothing to worry about, as long as the length of the second phase remains normal. This phase lasts between 12 and 14 days. Abnormalities here may, however, point to problems.

• In some women the temperature does not rise at all. A flat curve like this usually indicates a lack of ovulation. This occurs in about one cycle in 20.

• A short first phase is a disquieting sign, particularly among women approaching the age of 40. This may be a sign that the ovaries are almost exhausted.

Take care when planning the fertile period

Following the body temperature is an appropriate means of gaining an idea of the entire menstrual cycle. The readings are not, however, a suitable way of planning the fertile period, since the body temperature only rises after ovulation. At that moment the fertile period is usually already over or is approaching the end. So this is not the ideal period to try for a child.

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**How do I make a temperature graph?**

To obtain reliable results, you have to take the body temperature every day, in the same way and at the same time. The body temperature fluctuates during the course of the day, even if you do not engage in any exertion. So you should always do as follows:

✔ Always use the same thermometer.

✔ Use the thermometer correctly, depending on the type (mercury or digital). It may be best to ask your doctor to explain how to use it beforehand.

✔ Never use an ear thermometer and do not measure the temperature in the armpit. These methods are totally unreliable for this application.

✔ Always take the temperature in the same place (under the tongue, vaginal, in the anus).

✔ Take your temperature in the morning before you get up (i.e. when you are still in bed: prepare the thermometer the evening before). Any activity, however slight, puts the temperature up, even by just a few tenths of a degree, and that is important for the curve.

✔ Always take your temperature at the same time, as far as possible. A difference of one hour can make a difference of several tenths of a degree, which can have a misleading effect on the curve. It is best to not deviate from the usual time on the chart.
Note the result on the sheet provided by the doctor for this purpose.

You should also note all important events on the chart, such as the day on which you had sexual intercourse, blood loss, brown loss, white loss, pain and anything that might influence your body temperature.

Make sure you have enough sleep, at least seven hours a night. Your temperature is affected by your general state of health (tiredness, stress, etc.).

Examination of the cervical mucus

It has already been stated earlier in this brochure that the passage across the cervix is blocked for most of the monthly cycle by a thick, viscous sputum. In this condition the cervix is impenetrable for all kinds of micro-organisms, including sperm cells. Shortly before ovulation the sputum becomes more elastic and thinner under the influence of hormones, so that sperm cells are able to pass through. The cervical mucus thus plays an important role in fertility.

The examination of the cervical mucus consists of three main steps: taking a sample of the mucus, an initial examination with the naked eye and a microscopic examination. When the cervical mucus is examined the woman lies on a conventional gynaecological examination table, usually with her legs in leg supports. The doctor aspirates a little cervical mucus using a syringe and with the naked eye immediately checks the quantity of mucus, the viscosity, clarity and elasticity of the mucus and the cervical pupil sign (dilation of the cervix). A slightly open or round cervix points to recent ovulation.

During the microscopic examination we evaluate the typical fern structure of the cervical mucus and note the presence of white blood cells. These may indicate an inflammation in the vagina or the cervix (for instance with chlamydia trachomatis). If cervical mucus is present, and is elastic and clear, then we can check at the same time under the microscope whether there are any forward-moving sperm cells in this cervical mucus. This is also known as the post-coital test (see insert). We can detect moving sperm cells in this cervical mucus up to twelve hours after sexual intercourse with ejaculation. After twelve hours, sperm cells are often still visible, but they are usually no longer moving.
The post-coital test out of date?

As the name indicates, the post-coital test takes place after coitus or sexual intercourse (six to twelve hours after sexual intercourse). The test, which is based on an examination of the cervical mucus and the sperm cells found there, seems to be on its way out. It was long assumed that the test highlighted a number of important elements regarding fertility, including the vitality of the sperm cells and the nourishing function of the cervical mucus.

We now know that the results of this test are not particularly reliable. A poor test result does not necessarily mean that the quality of the sperm and the cervical mucus is substandard. A positive result could, however, indicate that there is still a good chance of a spontaneous pregnancy, if no further abnormalities are found during the fertility examination. On the other hand, this test and in particular the need to ‘make love to order’, can put a great deal of strain on the couple. The psychological stress of the post-coital test can add an extra burden to the sexual relations which are often already under pressure with these couples. Of course, this is not at all desirable. This is a second major reason why currently this test is no longer carried out very often.

Examination of the fallopian tubes

The fallopian tubes are not simply two little tubes that connect the ovaries with the uterus. They are specialised organs in which the ovum and sperm cells can stay for a while under optimal conditions and among other things be provided with the nourishment they need. The inner surface of the fallopian tubes is covered with cilia that ensure the transport of both the ovum and the sperm cells, and of the fertilised ovum afterwards. Fertilisation takes place in the fallopian tubes. The fallopian tubes are around nine centimetres long. At the ovaries they turn into fans about two centimetres wide. These fans consist of numerous small, thin flaps whose job is to catch the ovum during ovulation.

Types of problems

We make a distinction between three main groups of problems as regards the fallopian tubes:

✔ damage to the cilia or other cells
✔ a narrowing or total blockage of the fallopian tubes
✔ deformities in the abdominal cavity which squeeze the fallopian tubes shut and cause a blockage or restrict their normal freedom of movement.
A blocked fallopian tube

If the fallopian tubes are blocked we speak of tubal infertility. In around 25% of all women with fertility disorders this is thought to lie behind the diminished fertility. Sometimes a blockage of the fallopian tubes does still permit fertilisation, but the fertilised ovum can no longer be carried to the uterus. This can be dangerous, as a fertilised ovum that becomes lodged in the fallopian tube can lead to an ectopic pregnancy. If an ectopic pregnancy is not noticed early enough, the fallopian tube can break open, resulting in severe bleeding.

Types of examination

Although the fallopian tubes play a very important role in the first stages of a pregnancy, the possibilities of examining them are limited. The only thing we can check at the moment is the permeability. This is done by means of a hysterosalpingography or laparoscopy.

Hysterosalpingography

1. Catheter for injecting the contrast medium
2. Open fallopian tube: contrast medium goes through the fallopian tube into the abdominal cavity
3. Blocked fallopian tube: contrast medium is unable to flow through the fallopian tube.

The hysterosalpingography is performed by a gynaecologist in cooperation with a radiologist. First of all, we rule out the possibility of an inflammation of the cervix during the gynaecological consultation. In the event of an inflammation we first administer antibiotics to the woman and postpone the examination for a month. For the actual examination, the woman lies on her back on an examination table with her legs in the stirrups. The gynaecologist injects a small quantity of contrast medium into the uterus. This is done using a special tube that blocks the mouth of the uterus with a sort of thickening so that the contrast dye does not flow away via the vagina. The doctor uses radiological images to follow the way the liquid flows. Normally it spreads from the uterus through the fallopian tubes to the ovaries and from there into the abdominal cavity.
If the contrast dye does not flow away as it should, this indicates abnormalities in the uterus or the fallopian tubes which may be responsible for the reduced fertility. The contrast dye also makes it possible to obtain a clear picture of the inside of the uterus and the fallopian tubes, as well as any abnormalities that may be present (myomas, polyps, an incorrectly shaped uterus, etc.). According to some researchers, injecting the contrast dye can in itself have a positive effect as the liquid may flush away slight blockages in the fallopian tubes and thus improve the passage.

A hysterosalpingography is best carried out between the second and the fifth day after the end of the menstrual period (menses), in other words at the latest on the tenth day of a regular 28-day cycle. This means that you are a few days away from ovulation so that an incipient pregnancy is not disrupted.

A hysterosalpingography is a safe procedure that only rarely causes any problems. However, many women do find the examination painful. The injection of the contrast dye can cause the uterus to expand somewhat. Administering a good painkiller (such as Dafalgan®, Paracetamol®, Brufen®, Nurofen®, Indocid®, etc.) half an hour before the examination helps prevent pain and discomfort.

**Examination of the uterus**

To take a look into the uterus we use a hysteroscope, a kind of sight tube. During this examination we systematically check the entire uterus wall, the channel through the cervix and the openings where the fallopian tubes enter the uterus.

The doctor checks whether there are any abnormalities to be seen anywhere (congenital abnormalities of shape, deformities, polyps, fibroids (myomas), etc.), whether the walls of the uterus look normal, whether the uterus is of the normal length, whether the openings of the fallopian tubes are clear, etc. The uterus is a hollow organ, the walls of which always lie against one another, except during pregnancy. To obtain a clear picture during the hysteroscopy the uterus is filled with physiological water or with a gas mixture based on carbon dioxide.

The uterus is filled via one of the channels in the hysteroscope. A hysteroscopy is best not carried out during menstruation. The best time to detect any abnormalities in the uterus is the first week after the end of the menses. In practice, we often schedule the examination for about one
week before the start of the menstrual period. At this point it can be combined with a check of the mucous membrane of the uterus by means of an endometrial biopsy (see pages 152-153).

During the hysteroscopic examination water is introduced into the uterus, which can cause abdominal cramps (stomach cramps). This is why we advise you to take a strong painkiller about half an hour beforehand (Brufen®, Nurofen®, Dafalgan®, etc.). If the doctor thinks that the procedure may be more extensive and more complicated that usual, or if a polyp or a myoma is to be removed, then this is best done under general anaesthetic. You can request a general anaesthetic if you do not like the idea of the possible discomfort or pain or if you would prefer not to be conscious. A full bladder hampers this examination, so it is best if you empty your bladder before the examination begins. A hysteroscopy is a very safe examination which seldom gives rise to any problems.

The hysteroscope

A hysteroscope consists of a long, thin sight tube with a number of tubes running through it. The doctor can look through one of these tubes. A viewfinder is attached to the side through which he looks, and a sort of lens is fixed to the other end. The uterus is lit up by a fibreglass fascicle attached to a light source. The other tubes in the hysteroscope are used to attach small instruments, such as claws, forceps, scissors or a laser conductor needed to make a diagnosis or perform an operation.

The greater the number of instruments needed, the bigger the diameter of the hysteroscope required. A small hysteroscope of between three and five millimetres is sufficient for a diagnosis (about the thickness of a pencil). For an operation we often use wider versions of five to ten millimetres.

The narrow version passes easily and usually painlessly through the cervix. Only in very exceptional cases does the cervix have to be widened beforehand.

Examination of the endometrium (mucous membrane of the uterus)

The mucous membrane of the uterus is examined by means of an echoscopy or a endometrial biopsy. An echoscopy provides information primarily about the thickness of the mucous membrane, which is usually about fourteen millimetres around the implantation period. With an endometrial biopsy the doctor removes a small section of the mucous membrane of the uterus using a thin, flexible tube and sends it for further microscopic examination. The tube that is used for this is barely as wide as a match and thus passes relatively easily through the cervix.

However, the cervix may tense up and cause pain. Administering a good painkiller half an hour before the examination helps prevent pain and discomfort. On the basis of this examination the
doctor can check whether the mucous membrane of the uterus is normally structured and is in optimal condition in time for the implantation of the fertilised ovum. Even in women who do not have any fertility problems the mucous membrane of the uterus may not always be ready at the required time. If this is a recurrent problem, this may be a reason for the difficulty in becoming pregnant in women who otherwise have an apparently normal cycle.

The growth of the mucous membrane of the uterus is controlled by the concerted action of hormones. Any disorder in the correct timing may be an indication of an abnormality in the control and secretion mechanisms of certain hormones. An endometrial biopsy also provides an opportunity to check the mucous membrane of the uterus for possible inflammations. The pieces of tissue have to be removed at the most suitable moment in the cycle, namely during the days when a fertilised ovum should normally be settling in (the implantation period).

This period falls more or less in the middle of the second half of the menstrual cycle. In medical terms this is known as the midluteal phase: the middle of the luteal phase. In a regular cycle of 28 days this is on day 21 or 22.

**Examination of the abdominal cavity**

A laparoscopy, like a hysteroscopy, involves keyhole surgery. In this case the doctor looks into the abdominal cavity. To do this, he uses an instrument that is much like a hysteroscope, apart from a few details.

During a laparoscopy the doctor checks the position, the structure and the appearance of the ovaries, the fallopian tubes and the uterus, as well as of the other organs in the abdominal cavity (the bladder, the intestinal loops, etc.). This examination can detect possible signs of infections, deformities and any other abnormalities.

Just as with a hysteroscopy, during a laparoscopy the doctor can also perform an operation (detach and remove deformities, take cysts from the ovaries, destroy areas of endometriosis, etc.).
During the laparoscopy the doctor injects a fluid containing methylene blue (a harmless dye) carefully via the vagina and the uterus. This enables him to check whether and when this fluid flows into the abdominal cavity via the fallopian tubes and to know whether or not the fallopian tubes are blocked.

Three small incisions are usually made in the abdomen for a laparoscopy. They are less than one centimetre long. One incision is usually made just below or next to the navel and is used to insert the laparoscope into the abdominal cavity. The other two (each around five mm) are made low along the abdomen, just above the pubic bone and are used to insert auxiliary instruments into the abdominal cavity. These scars usually disappear after some time. To obtain a good view, a gas mixture based on carbon dioxide is blown into the abdominal cavity. The patient exhales this natural gas through the lungs afterwards. In some women the remainder of the gas cause some discomfort or pain after the operation, but these complaints disappear fairly quickly without the need for any additional measures. The complaints can also be avoided by remaining flat in bed after the operation and not sitting up or walking around too soon afterwards. However, a week’s incapacity for work is always scheduled, although light physical activity is permitted.

A laparoscopy is almost always performed under general anaesthetic. The patient stays in hospital for a few hours afterwards for observation, but can usually go home the same day (you will not be able to drive).

A laparoscopy is a safe procedure that seldom causes any problems. Any problems are usually mild and require only a minimum of additional care. An intestine or blood vessel is seldom touched when the laparoscope is inserted or during the procedure itself. Exceptionally this can cause serious complications involving bleeding or abdominal inflammation.

Can I become pregnant in the meantime?

The advice of the doctor not to become pregnant during the examination phase rather contradicts the wish of the couple who have come to the doctor precisely because they want a child so much. Some examinations, which are necessary to determine the exact cause of the fertility problem, may endanger an incipient pregnancy. The doctor will therefore advise you either to use condoms or not to have intercourse from the first day of your period during the examination phase. The doctor and the midwife will usually be sure to bring this subject up when the examinations are planned.

It is essential that you are not pregnant for the following examinations:

✔ Hysterosalpingography (see page 50)
✔ Hysteroscopy (see page 51)
✔ Laparoscopy (see page 53)
✔ Endometrial biopsy (see page 52-53).
13. FERTILITY TREATMENTS

Once all the tests designed to seek out the possible causes of the fertility problems have been carried out, the gynaecologist will make an appointment with you to discuss all the results and the opinion of the multidisciplinary staff meeting (see Chapter 10). Together with the doctor, you can consider what treatment is most appropriate.

We will now look at a number of specific fertility treatments, what they involve, when they are appropriate, and what chances of pregnancy they offer. We will also consider any risks. The following areas will be covered:

- Fertility surgery
- Hormonal stimulation of ovulation
- High intrauterine insemination
- In vitro fertilisation (IVF)
- Fertilisation by injection (ICSI – Intracytoplasmic Sperm Injection) as a special form of IVF
- Donor insemination, ovum reception, embryo reception (Chapter 14)
- Pre-implantation genetic examination of the embryo (Chapter 15)

**Fertility surgery**

For whom?

✔ Women with a fertility problem who require a thorough examination of the internal genitalia (internal genital organs).

✔ Women with a fertility problem due to an anatomical abnormality that can be corrected by surgery.

How?

✔ Surgery at the day centre

A day before the operation you will be told what time to come to the department. Make sure you have not eaten or drunk anything. The operation is usually performed in the morning. You will be able to leave the hospital at the earliest four hours after the surgery. A doctor will decide if you are well enough to return home. An appointment will be made with your attending physician to talk about how the operation went. You cannot drive on the day of the operation, so it would be best to arrange to be collected by a member of your family or a friend.
✔ Surgery with admission to hospital
You come to the department the day before the surgery. This day is used to prepare you for the operation. You will be given a laxative to ensure that your intestines are emptied. The operation is performed on the second day and on the third day at the earliest you can go home. Again, a doctor will assess whether you are fit to leave and an appointment will be made with the attending physician to talk about how the operation went. It is best to arrange to be collected by a member of your family or a friend the day after the operation.

Types of operation
✔ Purely diagnostic surgery
This involves first checking the inside of the uterus using a fine sight tube for the uterine cavity (hysteroscope). We examine the openings of both fallopian tubes and note any abnormalities that make it more difficult for an embryo to become implanted. We also take a piece of the mucous membrane of the uterus (biopsy). This enables us to detect any latent inflammations and check that the uterus is sufficiently well prepared hormonally for the implantation of the embryo.

After this the abdominal cavity is examined using a sight tube for the abdominal cavity (laparoscope). A small incision is made in the navel to insert this tube. A second incision is made in the pubic hair, so that no scar is visible afterwards. A tiny instrument is inserted through this incision that enables us to inspect everything thoroughly. The uterus is then filled with a blue dye via the vagina and the cervix. If the fallopian tubes are properly open, we see this dye find its way easily through the fallopian tubes and appear in the abdominal cavity. This means that we are sure that an ovum can be collected by the fallopian tube when ovulation occurs and conveyed to the uterus. The operation takes place in the surgical day centre. After a few days to a week off work you will be entirely recovered.

✔ Operative hysteroscopy
If an abnormality is observed in the uterus that can be corrected surgically, this is often possible with a very small operation. The sight tube is somewhat thicker this time and, in addition to a viewing channel, it also has a channel through which a cutting electric loop can be inserted into the cervix. This makes it possible to remove polyps, fibroids (myomas) or connective tissue septa. The operation is performed in the surgical day centre. After a few days to a week off work you will be fully recovered.

✔ Operative surgery in the abdominal cavity via laparoscopy or via open abdominal surgery
Deformity in the abdominal cavity with fallopian tubes which may or may not be blocked
Fibroids (myomas)
Ovarian cyst
Repair of the fallopian tubes after sterilisation
Minimal and mild endometriosis
Extensive endometriosis

The surgeon will usually estimate the length of the operation beforehand. Depending on this estimation, the operation will be performed in the day centre or you will be admitted to hospital.
Operations involving a laparoscopy or open abdominal surgery

In principle, surgery is performed by means of a laparoscopy wherever possible, as you will make a quicker recovery and have smaller scars. However, this technique is not always possible. For instance, if overly large tumours have to be removed, this cannot be done using a small sight tube. Sometimes the surgeon judges that it is better to operate on an open abdomen using microsurgical instruments, because this increases the chances of achieving the desired result (i.e. fertility). The result is always more important that the operating method.

Sometimes during a laparoscopy it proves necessary to switch to open abdominal surgery, maybe because the operation is proving more difficult than planned, or because a complication occurs that requires open abdominal surgery. You need to be aware of this risk and realise that it is always one of the possibilities.

Surgery for deformities with or without blocked fallopian tubes

Smaller deformities and partial blockages of one or both fallopian tubes can be remedied easily and quickly during the diagnostic operation. Only with very extensive deformities and/or if both fallopian tubes are totally blocked it is possible that an operative laparoscopy may be scheduled. This usually requires admission to the hospital and preparation of the intestine (see above). Deformities are cut through with a carbon dioxide laser. This produces the best result and the least chance that a deformity will return in the same place.

If a fallopian tube is blocked, first of all we look to see where the blockage lies. This may be on the side of the uterus or on the side of the ovary. Only the latter blockage can be corrected. In this case, the fallopian tube is opened and examined outside and in. If it is judged that it can still function normally and pick up an ovum as it should when ovulation occurs to carry it to the uterus, then the fallopian tube will be repaired.

However, if the fallopian tube proves to be irreparably damaged, it may be decided to remove it. A damaged fallopian tube is no longer capable of collecting and carrying the ovum. This increases the risk of ectopic pregnancy to such an extent that it is more sensible to remove the damaged fallopian tube.

These possibilities will, of course, be discussed with you at the pre-operative consultation. As fertility surgeons, we always endeavour to choose the best solution with a view to restoring spontaneous fertility. You may also indicate at any time that you do not wish the organ to be removed, even if in our judgement this is not the best solution. Your wishes will always be respected.

Surgery for ovarian cysts

These operations are usually scheduled through the surgical day centre. We distinguish between various types of ovarian cysts, depending on their content. We try to empty most cysts by aspiration in a single procedure and then ‘peel them away’. In some cases it is best if the contents of the cysts are not released into the abdominal cavity (dermoid cysts). In these cases the peeling is performed in a bag that is inserted into the abdominal wall for the duration of the operation. This collects any leakage from the cysts.
Sometimes it is wise to operate twice, for instance with large endometriosis cysts. During the first operation the cyst is opened and aspirated until empty. The inner wall is treated with the laser to destroy the endometriosis sites. The ovary is then ‘left in peace’ for a few months so that it can recover its usual shape. The cyst is then peeled away during a second operation. Research has shown that this method saves the most healthy ovarian tissue (in which the ova lie).

✔ Operations for fibroids outside the uterine cavity

Depending on the size, the location and the number fibroids (myomas), the operation is either performed in the day centre or the patient is admitted to the hospital. If there are several myomas, or if the myomas are sizeable, open abdominal surgery (mini-laparotomy) may yield better results than a laparoscopy.

✔ Operation to reverse sterilisation in men or women

Some men and women who have been sterilised later wish to have children after all. Sometimes this is further to the loss of a child, but usually it is because they are in a new relationship. From a technical point of view it is not that difficult to reconnect vas deferentia (sperm ducts) and fallopian tubes that have been cut through, but this does not mean that they will function properly again. The success of the reversal depends mainly on the damage done by the sterilisation.

In men

If a sterilised man wishes to engender a child, it is possible to try and reverse the operation by reconnecting the two ends of the vasa deferentia (sperm ducts). This very delicate technical operation is successful in nine out of ten cases: the passage across the vas deferens is restored.

In principle, the sperm cells should therefore be able to pass through again, but this does not always mean that fertility has been restored. Only three in ten men are able to engender a child afterwards.
The restoration of fertility depends on various factors, including:

- fertility before sterilisation
- the length of the piece of the vasa deferentia that was removed
- the number of years since the sterilisation: the chance that sperm cells will reappear in the semen declines by 4% a year
- the presence of a sperm granuloma, a small node that forms as a reaction to the material used to seal the vasa deferentia or to sperm cells that seep through
- the swelling on the vas deferens (sperm ducts) still attached to the testicle. This swelling may make a perfect reconnection difficult
- antibodies: sometimes, after sterilisation, men produce antibodies against their own sperm cells. These antibodies can affect the quality of the sperm and therefore also their fertility.

If no viable sperm cells appear in the seminal discharge, sperm cells that are not yet fully developed may be sought in the testicle or the epididymis (MESA, TESA or TESE).

In women

The man’s semen is checked before this operation is planned. A normal sperm sample is important for the chance of pregnancy after a reversal operation. We also check on the technique used to sterilise the woman.

Sterilisation by burning through or removing part of the fallopian tubes cannot be reversed. The couple is also referred to a fertility consultant for a discussion first. This ensures that you do not take any over-hasty decisions and that you are properly informed of the advantages and disadvantages of this operation.

The operation is done via microsurgery by making a low, diagonal incision in the abdomen. After the operation you will need to stay in hospital for about five days and you will then be unable to work for six weeks. However, this operation can also be performed by means of a laparoscopy either with a (short) admission to hospital or in the one-day hospital, a method that is becoming increasingly common. The damaged part of the fallopian tubes is removed and the two pieces are reconnected using microsurgery. Finally, the passage across the fallopian tubes is checked. The best chance of pregnancy occurs within the first six to twelve months after the reversal operation. After this the fallopian tubes may become fully or partially blocked again.
After the operation, maximum 60% of the women involved give birth to a child. This figure falls from the age of 38. There is a greater chance of a miscarriage then, and this increases with age. In addition, the risk of an ectopic pregnancy increases. The cause lies in the damage to the fallopian tubes and also the length of the tubes after the reversal. Since the fallopian tubes play a major role in bringing together the ova and the sperm cells, the less tissue is lost the better the chances of a pregnancy. Moreover, the shorter the length of the repaired fallopian tube, the greater the risk of an ectopic pregnancy.

The presence of scar tissue in the fallopian tubes presumably also plays a role. The inner surface of the fallopian tubes is coated with a layer of cilia that guide the ovum towards the uterus, since ova cannot actively move themselves. The scar tissue left after the reversal operation may form a barrier for the ova. This seems to be less so for sperm cells, which may explain the increased risk of an ectopic pregnancy.

Endometriosis surgery

• **Operation for minimal to mild endometriosis**
  Endometriosis is a disorder that has a great many possible symptoms. It always involves the mucous membrane of the uterus (endometrium) found in places where it should not be: in the abdominal cavity on the peritoneum, on the ovary or in ovarian cysts, on the ligaments of the uterus, the bladder or the intestine. It may consist of surface damage or a deep node that grows in towards the depths of an organ. Minimal or mild endometriosis can be removed by means of a laparoscopy using the CO2 laser. The operation is performed in the day centre.

• **Operations for extensive or severe endometriosis**
  These are often extensive operations requiring admission to hospital (for three to ten days). These operations are often performed after this extensive endometriosis has been brought to light earlier on. One of more of the following may have been observed:
  • Ovarian cysts > 4 cm.
  • Deep endometriosis sites on the bladder, the peritoneum, the rearmost ligaments of the uterus or the septum between the vagina and the intestine.
  • Adhesions of the intestine on the rear surface of the uterus and or both ovaries.

Endometriosis surgery aims to achieve the radical removal of all diseased tissue (tissue affected by endometriosis) so that only healthy tissue remains. The normal anatomic proportions between the fallopian tubes and the ovaries and their normal functioning are approximated as closely as possible. In this way we endeavour to restore fertility as much as possible with the lowest possible risk of relapse.

This type of surgery requires a number of specific skills and techniques. Our centre uses the CO2 laser so as to damage the surrounding tissue as little as possible. This can be used to
make very sharply defined incisions. The CO2 laser does not damage the surrounding cells – something which always happens to some extent if you cut using scissors (when the surrounding tissue is crushed a little), or with an electric operating knife (when the surrounding tissue is slightly burned). The laser targets a cell very precisely, so that this heats up and as it were goes up in smoke. An additional advantage of the CO2 laser is that it is easier to use from a technical point of view via the endoscope. Therefore at our centre even the most extensive endometriosis injuries can be operated on by means of endoscopy.

Endometriosis may be located near other organs: intestine, bladder, ureter, vagina. In some cases it may even grow through into these organs. When removing endometriosis in these areas we therefore sometimes have to include neighbouring organs in the operation. This is why our team is always multidisciplinary. The central figure is the gynaecologist-laser endoscopist, whose job is always to remove all lesions and restore fertility. If there are lesions on the intestine he or she is assisted by a surgeon specialising in the intestine who has been trained in the use of endoscopy, and if they are on the bladder or urinary tract by a urologist trained in the use of endoscopy. Finally, the anaesthetist is responsible for your anaesthetic during this sometimes lengthy operation. A specially equipped operating theatre and trained nursing staff complete our multidisciplinary endometriosis team.

It is therefore not surprising that an extensive operation for endometriosis has to be thoroughly prepared. Apart from the general preparatory examinations, a colon contrast test is also carried out (IVP or intravenous pyelogram). This shows us the course of the ureter and bladder. A colon contrast test provides a radiographic view of the inside of the intestine. We can use these tests and examinations to check whether the endometriosis has already affected these organs.

During a preoperative consultation, the surgeon in charge discusses every aspect of the operation:

- The various endometriosis sites and the specific problems they present are discussed.
- The patient is asked to follow a low-fibre diet for seven days before the operation. The day before the operation the patient is given a laxative solution to drink to rinse the intestine, ensuring that the inside of the intestine is clean and not swollen, which facilitates the operation.

In the event of extensive endometriosis in the area around the ureters, a stent (thin tube) is often introduced in the ureter at the start of the operation. This will remain in place from two to six weeks and then be removed as an outpatient. The stent protects the ureter against any damage during the operation.

With endometriosis of the bladder sometimes an opening has to be made in the bladder to be able to remove all the endometriosis. After the operation a bladder catheter is left in place to allow the bladder to heal properly. Sometimes the ureter has to be opened. Here again, a bladder catheter is left in addition to the stent.

Sometimes endometriosis is found close to the top of the vagina. This can cause pain during intercourse, as well as occasional blood loss. When removing this type of endometriosis,
the top of the vagina is opened and then stitched up again afterwards. To allow the vagina to recover properly, you may not have intercourse for six weeks.

If endometriosis is found in or on the intestine, then special techniques are used to clear the intestine of endometriosis. Sometimes a small opening is made that can simply be stitched up.

Sometimes the intestine is so badly affected that part of it has to be removed. The intestinal surgeon removes the affected part of the intestine using endoscopy and attaches the healthy ends. He often uses a specially designed ‘intestine stapler’ for this. After this operation the patient is fed by a drip, and then gradually moved on to a normal diet.

Sometimes the appendix is also involved in the process, so one of the possibilities is to remove it. In exceptional circumstances this may have to involve open abdominal surgery (laparotomy).

Before the operation you are always seen by an anaesthetist who will check your fitness. During the sometimes lengthy operation, he or she may need to take additional safety precautions: adjusting the mattress on which you are lying, placing the legs in leg supports with inflatable cushions to keep the blood flow in your legs at the right level during the operation, using heated covers to prevent cooling, etc. After the operation, antibiotics are often administered to minimise the risk of inflammation.

With these measures we ensure that extensive endometriosis can be radically removed with the best possible chance that fertility will be restored and a minimal chance of relapse. However, as a relapse can never be ruled out, you may be advised to follow additional hormonal treatment after the operation or to become pregnant. As pregnancy involves a nine-month period without any menstrual periods, this can suppress endometriosis.

**Hormonal stimulation of the ovary**

Before hormonal therapy begins, with or without insemination, IVF or ICSI, you will be given another appointment with a midwife from the fertility centre. She will go through the actual course of the treatment with you. This treatment phase can be a difficult time, as well, with its ups and downs. It calls for a great deal of effort and often involves uncertainty and stress. Couples who need this and who so wish, can call upon the fertility consultants with whom we work during the treatment phase (see also Chapter 16).

A number of fertility problems can be remedied in whole or in part by hormonal stimulation of the woman’s cycle. This hormonal stimulation may be indicated in women with cycle disorders (such as no ovulation or a very irregular cycle), or with fertility disorders without any obvious cause.

The doctor may be attempting to achieve a number of aims with hormonal treatment:

- **Ovulation:** hormonal stimulation can ensure that at least one ovum matures per cycle.
• A monitored, regular cycle: careful stimulation with the aim of causing one or two ova to mature and stimulating ovulation, either in combination with sperm cell insemination or not.

• With IVF or ICSI: super-ovulation: ovulation whereby not one but eight, ten, twelve or more ova mature simultaneously. This can increase the chance of success with in vitro and injection treatments.

When several ova mature simultaneously and fertilisation occurs after spontaneous sexual intercourse or after insemination with sperm cells, this implies the risk of a multiple pregnancy. With careful monitoring and follow-up during the hormonal stimulation the number can virtually always be limited to twins or at the most triplets. Thanks to improvements in the assistance provided multiple births involving more than three babies have become a rarity in Belgium.

A second risk of hormonal stimulation is ovarian hyperstimulation syndrome (OHSS). OHSS occurs in sensitive patients, but unfortunately is also sometimes due to careless stimulation with an overly high dose of hormones. This causes the ovaries to swell badly and cysts measuring 20 to 30 mm in diameter may form. This can usually be avoided by using a sufficiently low dose and by means of good follow-up during the stimulation. Nevertheless, sensitive patients (such as those with polycystic ovaries) may react too strongly even under these circumstances. If this situation is observed in time, an attempt can be made to avoid the hyperstimulation syndrome by stopping the treatment, removing a number of follicles using ultrasound or by switching to ovum aspiration and in vitro fertilisation, possibly freezing the fertilised ova with a view to replacing them in the uterus at a later date (during a thawing cycle). (See also IVF, page 68).

Types of medication

Various hormones are used for this treatment. We list the main ones and also consider their potential side effects. This is simply for patient information and is not intended to scare patients away, since in most cases the side effects do not outweigh the advantages of the treatment.

✗ Clomiphene (Clomid®, Pergotime®) Tamoxifen (Nolvadex®, Tamizam®, Tamoplex®)

These anti-oestrogens stimulate the release of the follicle-stimulating hormone and as such are essential for the growth of the follicles. These medications are used mainly to trigger ovulation in patients with an irregular cycle without ovulation. Their effect disappears when the treatment ends.

- The treatment (tablets to be taken orally) usually lasts for two successive cycles, after which a rest cycle is scheduled. The entire treatment usually lasts for four to six cycles.

- After six months, 60 to 75% of the women treated are pregnant.

- With this medicine the likelihood of a multiple pregnancy increases by approximately 5% and can be predicted more accurately depending on the stimulation.
• These medications can lessen the quality of the mucous membrane in the cervix and disrupt the luteal phase. Enlargement of the ovaries and cyst formation in the ovaries may occur. Some women complain of hot flushes, a bloated feeling, nausea, headaches, sight disorders or insomnia. However, these complaints rarely lead to the treatment being stopped.

✗ **Pump with GnRH or gonadotropin-releasing hormone**

GnRH is used to trigger a normal cycle in women who have monthly bleeding due to the inadequate production of GnRH, LH or FSH. The hormone can also form an alternative treatment for women with polycystic ovarian syndrome, if other treatments prove unsuccessful.

• GnRH is administered continuously through a needle connected to a small pump by a tube. This is attached to the trouser belt. At first regular check-ups are needed to ensure that the dose is properly adjusted.

• Of those women who tolerate the treatment well, 25 to 30% become pregnant per cycle. This percentage may rise to 80% after six treatment cycles and to 90% after 12 cycles. The percentage of success is lower in women with polycystic syndrome.

• The likelihood of a multiple pregnancy increases by about 5% with this treatment. The risk of spontaneous abortions in pregnancies brought about in this way stands at 20%.

• Side effects are seldom experienced. There may be local skin irritation where the needle is inserted. Very exceptionally there may be over-stimulation of the ovaries causing huge numbers of ova to mature.

✗ **Gonadotropins (Menopur®, Puregon®, Gonal F®, etc.)**

These products contain a follicle-stimulating hormone (FSH), with or without luteinising hormone (LH). FSH stimulates the development of the follicles in the ovaries. These medications are used to stimulate ovulation. Apart from IVF or ICSI, they are administered for patients who do not become pregnant with other medications that stimulate ovulation, or in combination with insemination with sperm cells. In these cases, the aim is for one or a maximum of two ova to mature. The medicine is administered by injection (subcutaneously or in the muscle) by the patient herself, the GP or the home nurse.

• The treatment lasts for four to six cycles. Each cycle is usually followed by a rest cycle without treatment. After six months, 40 to 60% of the women treated are pregnant.

• One in five of the pregnancies is multiple. Three quarters of these are twins, the remainder triplets. When three or more follicles mature, we can limit the risk of a multiple pregnancy by picking up the surplus follicles using ultrasound.
• The risk of a spontaneous abortion is 15 to 20%.

• The risk of an ectopic pregnancy is 3%.

• The stimulation of the ovaries may be accompanied by a bloated feeling or pain in the abdomen. In some cases severe over-stimulation of the ovaries occurs. This risk can be limited by careful follow-up and reducing the treatment in time.

✗ Human chorionic gonadotropin or hCG (Pregnyl®, Profasi®)
This hormone prompts the luteinising hormone (LH) to peak and stimulates the start of ovulation. It is administered by injection. Apart from IVF or ICSI, hCG is administered to trigger the ovulation of the mature ovum or ova. This ovulation occurs about 38 to 40 hours after the administration of hCG. Couples are advised to have sexual intercourse or insemination with sperm cells is scheduled during this period. As part of IVF or ICSI treatment, hCG is used to prepare to pick up ova. The ova can be picked up around 35 hours after the injection.

✗ Dopamine agonists (Parlodel®, Dostinex®)
These medications are used to optimise and regulate the menstrual cycle, for instance in women with an irregular cycle with slight or no menstrual bleeding owing to an overly high concentration of prolactin in the blood (see Chapter 7). Eighty per cent of the women treated become pregnant. These medications affect the digestion and the circulation, which explains the typical complaints such as nausea, vomiting, diarrhoea, headaches, tiredness or low blood pressure. The medications are available in tablet form to be taken orally. Parlodel can also be administered through the vagina and is said to cause fewer side effects in this form.

High intrauterine insemination

With high intrauterine insemination, the sperm is prepared in the laboratory in advance (capacitated) so that it can be inserted high in the uterus at the right moment using a fine tube (catheter). In this way we activate only the most agile sperm cells and harmful components are removed from the semen.

To determine the moment of ovulation accurately, we use hormonal stimulation of the ovary. Couples who receive this treatment are asked to contact the fertility centre when menstruation begins so that the treatment can start.

Stimulation of the ovary
The ovary can be stimulated by taking pills (such as Clomid) from the third to the seventh day of the cycle inclusive. The aim is for one or a maximum of two ova to mature. We can clearly measure the size of the follicles in which the ovum is maturing by performing an ultrasound scan of the vagina. An initial ultrasound examination of the ovaries is scheduled between the tenth and twelfth day of the cycle. A blood test is also carried out.
However, the ovaries are usually stimulated by means of injections (Menopur®, Gonal-f®, Pure-gon®, etc.). These preparations are administered daily using a subcutaneous injection, by the patient herself, by the GP or by a nurse. To be able to follow up the reaction of the ovary properly, from the tenth day of the cycle we schedule an initial ultrasound follicle measurement and a blood test. These tests can be carried out at the Leuven university fertility centre between 8.00 am and 9.30 am. You do not need to fast for this blood test. The ultrasound follicle measurements and blood tests can also be carried out by a gynaecologist in your area. If you do not have your own gynaecologist in the region, you can come to the midwife at our centre. She has a list of gynaecologists who cooperate closely with our fertility centre. In this case you need to make sure that the results of the blood test and the ultrasound scan are faxed to the fertility centre before 2.00 pm on the same day.

If you have been for an ultrasound scan and blood test in the morning, the gynaecologist and the midwives discuss the treatment that same afternoon. The midwife will then contact you between 3.00 pm and 5.00 pm to discuss the next steps in the stimulation process. She will also make the next appointments for blood tests and ultrasound scans. You can assume that you will have to go to the fertility centre or to your gynaecologist in your area approximately four times for an ultrasound scan and blood tests in the morning. Stimulating the ovaries takes about two weeks. These medications usually cause little discomfort.

When we find one or two follicles on the ultrasound scan, the woman is given an hCG injection (Pregnyl). This injection ensures that the ova are released at the right moment, that is when the actual insemination is to take place. This occurs approximately 38 hours after the hCG injection. It is also possible that your body may signal the start of ovulation itself. In this case we schedule the insemination earlier.

Preventing multiple pregnancies with insemination
If there are two or more mature ova on the day of the hCG injection, we discuss the risk of a multiple pregnancy with you. One or more follicles may be picked up just before the intrauterine insemination, so that just one follicle or ovum remains. Other possibilities include ovum aspiration, IVF or stopping the treatment for this cycle.

Taking the sperm sample and insemination
On the day of the insemination, we expect the man at the fertility laboratory to provide a sperm sample between 8.00 am and 10.00 am. This is after three to five days of continence. If there are any problems then the sperm sample can also be produced at home. In this case, be sure to ask the midwife for the correct recipient. The sperm sample must be brought into the laboratory within an hour of being produced. Do not allow the sample to cool while it is being brought in.

Before the insemination we will capacitate the sperm sample. We select and isolate only the most agile sperm cells. This process takes about two hours. Two or three hours after the sperm sample is brought to the laboratory we carry out the high intrauterine insemination in the woman. A speculum or small mirror is fitted before the insemination (as is done before a cervical smear). The catheter is inserted into the uterus using ultrasound and is in principle painless.
Afterwards it is best to remain lying down for about twenty minutes.

Further procedure
Your doctor may decide to start progesterone treatment (Utrogestan®) the day after the insemination in order to keep the mucous membrane of the uterus in optimal condition during the second half of the cycle. The tablets are administered via the vagina. On the fifteenth day after the insemination, we schedule a blood sample for the pregnancy test in the morning. If the pregnancy test is positive the progesterone treatment is continued and a week later you have to come along again for another blood test. If the results of this test are good as well, we make an appointment at the clinic for an obstetrics ultrasound scan and a final appointment with the fertility doctor. After this we refer you to the obstetrician of your choice. You can of course have these final blood tests and ultrasound scans carried out by your own gynaecologist. We do, however, ask him or her to keep us informed of the progress of the pregnancy and the childbirth.

If the pregnancy test is negative, then we stop the progesterone treatment. In consultation with the midwife, you can discuss when it best to start stimulating the ovaries again. The treatment is assessed by the doctor after each attempt and if necessary he adjusts the dose. We usually advise you to include a rest cycle between each treatment cycle. During this period the secretary at our centre will provide you with the necessary documents and instructions for starting another treatment session. If you do start again without a rest cycle, it is advisable to come for an ultrasound scan when menstruation begins. The condition for starting again is that no follicles remaining from the previous stimulation can be seen in the ovaries. If you are not pregnant after three treatment cycles with high intrauterine insemination, we advise you to make an appointment with the gynaecologist at the fertility clinic. He will look into which treatment is most advisable for you.
In vitro fertilisation

Treatment involving in vitro fertilisation (IVF) comprises six successive steps:
Step 1: stimulation
Step 2: ovum aspiration and sperm processing
Step 3: fertilisation and cultivating embryos
Step 4: embryo transfer
Step 5: follow-up treatment
Step 6: freezing embryos

Step 1: stimulation

We outline a stimulation plan in accordance with the patient data. This is usually based on a long pill scheme and starts by taking a contraceptive pill for around 25 days. This will cause the ovaries to stop working. From day 21 we combine this with a daily nasal spray (Suprefact®). If the patient suffers from an allergy or has a head cold (nasal catarrh), or if the treatment is not sufficiently effective, or produces too many other side effects, this nasal spray can be replaced by a daily injection (Decapeptyl®). These medications contain a substance that will block the command centre in the brain (the hypophysis), from where the female cycle is directed, as this centre is not designed for a situation in which several ova will mature at the same time and would begin to send the wrong signals.

Once the patient stops taking the pill, menstruation follows. As long as you continue to use the nasal spray/injections, a new cycle will not start. You give the fertility centre the menstruation date. We then give you the date on which the new cycle starts.

The new cycle is now the IVF cycle. The actual stimulation is produced by subcutaneous injections of stimulating hormones. From the sixth day you will have an ultrasound scan and a blood test every two days to see whether the follicles are developing as planned. You can have these tests done at the Leuven university fertility centre between 8.00 am and 9.30 am. You do not need to fast for this blood test. The ultrasound follicle measurements can also be taken by a gynaecologist in your area. Our centre has a list of gynaecologists who work closely with our fertility centre. However, the results of the blood test and the ultrasound scan must be faxed to the fertility centre secretariat before 2.00 pm the same day. If you have been for an ultrasound scan and blood test in the morning, the gynaecologist and the midwives discuss the treatment that same afternoon. The midwife will then contact you between 3.00 pm and 5.00 pm to discuss the next steps in the stimulation process and will also make the next appointments for blood tests and ultrasound scans. If it is judged that the ova have matured sufficiently, the signal for ovulation can be given (hCG: Pregnyl®). In this case ovulation will occur between 36 and 38 hours later. Depending on your reaction in previous cycles or your medical data, we may use other stimulation plans or medications. Your nursing team (gynaecologist and nurses) will explain this in more detail.
### Step 2: ovum aspiration and sperm processing

**Ovum aspiration**

Just before spontaneous ovulation (release of ova from the ovary) we pick up the follicles one by one and aspirate the fluid containing the ovum. This is done about 35 hours after the hCG injection, using a fine needle fitted to the vaginal ultrasound probe. The ovary lies just above the vagina, so follicles can be picked up fairly easily through the vagina.

Sometimes a painkilling injection is sufficient. In some women (after an operation for instance, or if there is a great deal of stress or fear), ovum aspiration may be more problematic. In that case the procedure can be performed under light anaesthetic. The fluid (follicular fluid) is taken from the aspiration room to the laboratory, where the embryologist examines it under a microscope, looking for the ovum. The ovum is part of a whole entity known as the ovum-cumulus complex. In this complex the ovum is surrounded by a large number of cells (cumulus cells). The complex is a few millimetres in size (the ovum itself is about a tenth of a millimetre in size).

This complex is then placed in a fresh culture medium to wash away the follicular fluid and red blood cells. The final step is to transfer all ovum-cumulus complexes to small dishes containing fresh culture medium which are placed in an incubator for a few hours. This incubator creates a temperature of 37°C and ensures the right degree of acidity. At the end of the aspiration process the gynaecologist or the midwife will let you know how many ovum-cumulus complexes were found.

Bleeding and infection are known complications of ovum aspiration but these occur in less than 1% of aspiration processes.

**Sperm processing**

On the day of the ovum aspiration we expect your partner in the laboratory for a sperm sample between 8.00 am and 10.00 am. This is after three to five days of continence. If there are any problems then the sperm sample can also be produced at home, provided that you can bring the sample to the laboratory within the hour. It is important that the sperm sample is not allowed to cool while it is being brought in. Once the sample has been produced we keep it for about 20 minutes at 37°C. During this period the sample changes from a gel-like to a more fluid state. We then take a small quantity to evaluate the agility (motility) and number of sperm cells.
The next step is to separate the sperm cells from the seminal plasma, as this seminal plasma contains a number of substances that reduce the agility of the sperm cells and impedes the fertilisation of the ova. Once this step is complete we transfer the sperm cells to the same culture medium as that of the ova, and again assess the agility and number of the sperm cells. The sample is then placed in an incubator for a few hours. During the incubation the sperm cells will ‘capacitate’: they undergo a number of changes enabling them to fertilise the ova.

**Step 3: insemination and cultivating embryos**

**Insemination**

Insemination is the moment when the ova and the sperm cells are brought together. In practical terms, this means that we add a small quantity of the capacitated sperm sample to the dish containing the ova (IVF or conventional in vitro fertilisation). We then place the ova and sperm cells in the incubator until the following morning.

If there are too few agile sperm cells for a good chance that the ova will be fertilised, we can apply ICSI. ICSI stands for intra cytoplasmic sperm injection or the injection of one sperm cell into an ovum. In this process we inject a sperm cell into an ovum using an ultrafine needle. The chance that the ovum is damaged by this process and can no longer be fertilised is about 8% (ICSI). We then place the ova and the sperm cells in the incubator until the following morning.

**The fertilisation test**

Between 12 and 20 hours after insemination, the pronuclei in the ovum are visible under the microscope if the ovum is fertilised. One of the pronuclei comes from the ovum, the other from the sperm cell that has produced the fertilisation. These pronuclei lie next to one another. They have therefore not yet fused to form one new nucleus. When the fertilisation test is carried out we also examine the maturing phase of the ova, as sperm cells can only fertilise ova in the right maturing phase (ova in metaphase II).

With good stimulation, approximately 80% of the ova will be mature. On average about 60% of the mature ova are fertilised (both with IVF and with IVF combined with ICSI). The fertilised ova are transferred to a fresh culture medium and the whole thing is then placed in the incubator again for about 24 hours. The day after the ovum aspiration the nursing coordinator at the fertility centre will contact you by telephone to inform you of the result of the fertilisation process. She will also arrange the time when we expect you for the embryo or embryos to be re-implanted.

**The embryo culture**

From the moment of fertilisation we talk about embryos. These embryos undergo several divisions. On day two most embryos will be at the two to four-cell stage.
It is also possible to opt for a longer cultivation period, lasting until day three or day five. In the meantime the embryos have developed further. The advantage of longer cultivation is that we can make a better choice. The chance of a pregnancy after the transfer of a blastocyst on day five is higher than after the transfer of an embryo on day two. Only 35% of all embryos will develop into a blastocyst on day five.

Step 4: inserting the embryos or embryo transfer

The embryos are inserted on day two, day three or day five after the ova have been picked up. The stage at which and therefore the day on which the embryos are re-inserted is decided before the stimulation begins in consultation with the gynaecologist and depends on the number and quality of the embryos.

The woman comes to the fertility centre for a few hours to have the embryos transferred. The insertion process is usually not painful, and may be compared to the technique used for insemination. In exceptional cases it may cause some cramps and pain which in some women may be compared to the discomfort felt during their period. A sedative may be administered if necessary.

When selecting the embryos for transfer we look at the number of cells in the embryo and the appearance of the embryo. The embryo with the best quality is replaced. We then aspirate the embryos in a catheter. They are then pushed through the vagina and cervix to a position high in the uterus using ultrasound assistance.
The embryos are placed in the uterus using a syringe on the catheter. To obtain a clearer ultrasound picture and facilitate the procedure we ask you to have a full bladder when the embryo transfer is performed. The transfer process usually only takes five to ten minutes. Once the embryo has been inserted the woman usually remains in bed for about 30 minutes to be certain.

We usually insert one or two embryos, depending on the age and medical condition of the woman. It is not advisable to insert more than two embryos, as the risk of a triplet or multiple pregnancy is too great. Some women also worry afterwards that the embryos can ‘fall out of the uterus’. This is not correct. The mucous membrane of the uterus is far too sticky, so the embryos inserted stay in place without difficulty. The embryos develop in the uterus for a few days before the implantation takes place.

**Step 5: follow-up treatment, or what happens after the embryo transfer**

After the procedure the woman can resume her usual activities. However, we do advise against strenuous physical effort or sports for the first few days. Later on this is possible if you are accustomed to such activities. Steam baths and very hot saunas are also unadvisable as they have a negative effect on the pregnancy.

Progesterone treatment (Utrogestan®, vaginal tablets) begins the evening after the ovum aspiration. This is necessary to keep the mucous membrane of the uterus (endometrium) in optimal condition during the second half of the cycle. Fifteen days after the ovum aspiration we can check using a pregnancy test whether the embryos have implanted. These two weeks are a tense period for many couples. Expectations are high and at the same time there is the fear that something may still go wrong. However, there is little that you can do but wait.

If the pregnancy test is positive then the follow-up treatment is continued and we ask you to come along a week later for another blood test. If the results of this test are good as well, we make an appointment in the clinic for an obstetrics ultrasound scan and a final appointment with the fertility doctor. After this we refer you to the obstetrician of your choice.

You can of course have these final blood tests and ultrasound scans also carried out by your own gynaecologist. We do, however, ask him or her to keep us informed of the progress of the pregnancy and the childbirth.

If the pregnancy test is negative, then the follow-up treatment is stopped. You can discuss with the midwife when it is best for you to start ovary stimulation again. The treatment is assessed by the doctor after each session and he adjusts the dose if necessary.

**Step 6: freezing surplus embryos?**

To have as great a chance of success as possible, we inseminate all ova. All fertilised ova are placed in a culture medium. Almost all fertilised ova develop into embryos, with the result that there are often more embryos available than the one or two that we insert afterwards. This means that we have a number of embryos left over. We usually freeze the surplus embryos for possible use in a subsequent cycle.
Only good-quality embryos are eligible for freezing. Freezing is a burdensome procedure that even good-quality embryos do not always survive. The advantage of freezing embryos, however, is that there are always embryos available for a possible subsequent embryo transfer.

If one or more embryos are frozen, they first have to be thawed before another IVF cycle can be started. You have to allow for the fact that the embryos have about a 50% chance of surviving the freezing and thawing process. These embryos can be replaced in a natural cycle if this is regular. If your cycle is irregular your doctor will draw up a suitable stimulation plan.

How safe is ICSI?

With fertilisation by injection we insert one sperm cell into an ovum using an ultrafine needle. This technique is recommended as a last option when other treatments, such as in vitro fertilisation, fail. ICSI offers a solution for serious male fertility problems. Even men who have (virtually) no sperm cells in their ejaculate can become a father using this technical detour. If there are no sperm cells in the semen, it is still possible to take them directly from the testicles using microsurgery.

At the same time, however, the remarkable possibilities of ICSI are also a source of concern about the safety of this technique. In the laboratory the embryologist selects one sperm cell from among those available more or less at random. This may be a good or a bad sperm cell, for instance one that is carrying hereditary abnormalities, since abnormalities in the hereditary material cannot be seen by the naked eye.

It is assumed that with normal fertilisation bad or imperfect sperm cells are not given a chance to fertilise an ovum. How this happens is not known, but with ICSI such selections mechanisms are partially excluded. There is currently no means of detecting and excluding 'bad' sperm cells.

The ICSI technique has been used since 1992. As this is a relatively short period of time, and to date only limited data are available on the follow-up of the children, caution is needed. According to the current state of scientific knowledge there is a slightly increased risk of chromosomal abnormalities and possibly an increased risk of congenital abnormalities. In practical terms
this means that close follow-up is needed from the moment of fertilisation up to and including the birth and the development of any child.

There is a possibility that the cause of the infertility lies in a hereditary defect. This hereditary defect may be passed on to any children through the ICSI technique.

Couples with fertility problems who may opt for ICSI have to realise that the risks involved are not yet always fully known. It is perhaps still too soon to label this technique extremely reliable and safe and recommend it as a first-choice treatment. In particular, there is also uncertainty about the possibility of passing on fertility problems to children born further to ICSI.

For all these reasons, in principle IVF is used at the LUFC where possible and ICSI if necessary, if IVF proves impossible due to inadequate numbers of agile and normal sperm cells.

**In search of sperm cells**

Some men’s semen contains too few if any sperm cells. As a result, even ICSI may be difficult or impossible, despite the fact that in principle this technique requires just one sperm cell. In cases like this, however, it is possible to look for sperm cells surgically, for instance in the epididymis or the testicle itself. This technique is known as TESE: testicular sperm extraction. A small piece of tissue is removed through a small incision and the sperm cells are separated from this later on.

Research has shown that a sperm cell does not have to be completely developed to be able to fertilise an ovum. It simply has to contain the necessary hereditary material.

The calculated chance of a live child being born in the four IVF or IVF/ICSI cycles (with any corresponding thawing cycles of frozen embryos) is more than 85%. This means that out of 100 women who each follow four cycles, 85 will give birth to a live child.

In practice, however, this figure is substantially lower, as not all women follow four cycles. A number of women pull out earlier for various reasons, not all of which are medical (for some the combination of the treatment and their work situation is too stressful, for others the cost is too high, etc.).

The chances of success diminish with age, especially as of 38 and sharply as of 40. Very few women successfully become pregnant after the age of 42, partly due to the very high risk of a miscarriage. Belgian legislation states that no IVF treatment may be started after the age of 45. Reimbursement by the health insurance fund is provided for until the age of 43.
Discussion of the results after IVF/ICSI

After each IVF or ICSI treatment in principle we schedule a consultation to discuss the progress of the treatment. We look to see if any further adjustments can be made in terms of the hormonal stimulation, and whether it is advisable to continue. We also consider the psychological aspects of the treatment. If necessary, the embryologists are consulted to adjust the policy for the following cycle. As long as good-quality embryos are produced, we will encourage the couple to continue the treatment. If the quality of the embryos is consistently poor, we usually advise to stop the treatment and to consider alternatives, such as ovum reception or embryo reception.

Complications of fertility treatment: hyperstimulation of the ovaries

Most women temporarily have a heavy feeling in the abdomen and feel rather bloated. The number of ova that mature in the woman may vary significantly from one person to another. In some cases the ovaries do not react adequately and the ovum pick-up has to be postponed.

In other cases, the ovaries can sometimes react unexpectedly intensely and a large number of ova develop. As a result the ovaries may swell considerably and produce fluid that can accumulate in the abdominal cavity. These symptoms usually occur around a week after the embryo transfer. In rare cases a huge shift may occur in the water balance of the body. This is known as the ovarian hyperstimulation syndrome. The symptoms are a severe, painful distension of the abdomen, a weight gain of more than five kilograms, shortness of breath, stomach problems, dizziness and nausea. Contact the fertility centre if you suffer from any of these symptoms. With a blood analysis and an ultrasound scan we can assess the gravity of the situation. In most cases we prescribe rest for the woman. In more serious cases admission to hospital is necessary. The length of the hospitalisation depends on the gravity of the hyperstimulation syndrome. If the patient is pregnant, the symptoms may last longer. With medical supervision, however, a hyperstimulation syndrome does not have any adverse consequences for the health of the woman or for the pregnancy.
14. WHAT HAPPENS IF THERE IS NO SUCCESS WITH YOUR OWN SPERM CELLS OR YOUR OWN OVA?

Of course, with fertility treatments such as in vitro fertilisation and ICSI we always try to use the couple’s own ova and sperm cells. However, there are exceptions: in a number of cases there are medical reasons for using ova or sperm cells from a donor.

Sperm donation

Sperm donation is entirely voluntary. The maximum age for sperm donors is 45 years, the minimum age 25 years. A thorough examination to determine the quality of the sperm is carried out prior to the donation. The donor undergoes a thorough medical examination (physical examination, blood test and urine test) to check his state of health. Special attention is paid here to the possible presence of transmissible hereditary or contagious diseases which could be passed on via donation.

During the tests the donor is seen by an andrologist (a specialist in male fertility) and a geneticist (specialist in human genetics). The donor is also seen at least once by a fertility consultant to discuss the psychological aspects of sperm donation.

If the sperm quality is approved and the donor is free of contagious disorders, transmissible hereditary diseases and psychological problems, the donor can be accepted once he has signed an agreement. The donor then submits a number of sperm samples to the laboratory at the fertility centre. The donor will also have to undergo a blood test at every sperm donation to confirm that there are still no contagious diseases.

Only once all these conditions have been fulfilled can frozen sperm be used after a certain period of time for artificial fertilisation in a couple with a medical indication for sperm reception. Sperm donation does not involve any risks. The costs of the preparatory tests are of course not charged to the donor in person. The donor receives an allowance to cover expenses per sample.

The sperm is relinquished unconditionally and irrevocably. This means, among other things, that the sperm donor waives all his rights to the sperm he has relinquished and has no claim to children engendered using his sperm. The anonymity of the donor and of the receptor of the sperm is strictly guaranteed. The sperm donor therefore undertakes not to trace the identity of the receptors.

Similarly, the receptors do not receive any information whatsoever about the sperm donor. Sperm donation is restricted by law for each donor: one or more children may only be born to a maximum of six different women using sperm from the same donor. This restriction is essential as an unlimited number of births increases the risk of consanguinity in the future.
Sperm reception

The sperm reception is anonymous. Frozen donor sperm can be used in treatment involving insemination (IUI) or for in vitro fertilisation (IVF) with transfer. With IUI treatment, the frozen donor sperm is placed in the uterus of the woman (receptor). With IVF treatment the ova of the woman (receptor) are fertilised within six hours of aspiration using the frozen sperm from an anonymous donor. The embryos produced as a result may be inserted either in the same cycle or after freezing/thawing.

Risks

As with any medical fertility treatment, treatment using frozen donor sperm never offers an ultimate guarantee of pregnancy. Twenty percent of 'normal' pregnancies end in a miscarriage and complications can occur in any pregnancy, including those resulting from treatment with frozen donor sperm. In comparison with other pregnancies after medically assisted fertilisation, a pregnancy after treatment with frozen donor sperm does not involve any noticeably higher risks, provided it is a single pregnancy. Transferring more than one embryo can give rise to a multiple pregnancy, which involves a greater risk of premature contractions and birth, raised blood pressure, lower birth weight, etc. The number of embryos replaced in the uterus is determined in mutual consultation between the couple, the embryologist and the doctor.

Just as with a normal pregnancy, after treatment using frozen donor sperm a certain percentage of children may be born with a physical or mental abnormality.

All sperm donors are tested for infectious diseases such as the HIV virus, cytomegalovirus, hepatitis, Chlamydia and syphilis. Despite these precautions, the procedure using frozen donor sperm always involves a slight risk of sexually transmitted diseases.

Financial aspects

A flat rate is charged per cycle for the donor sample and to cover administrative costs.
Ovum donation

Ovum donation is entirely voluntary. The ovum donor must be at least 21 years old and at the most 37 years old. Prior to ovum donation the donor undergoes a thorough medical examination (physical examination, blood test). Particular attention is paid here to any transmissible hereditary diseases or contagious diseases that may be present and could be passed on by donation. The donor is seen by a gynaecologist, a geneticist and twice by a fertility consultant to discuss the psychological aspects of donation.

Ovum donation is anonymous. The ovum donor undergoes hormonal treatment and ovum aspiration. The ova obtained are fertilised with sperm from the receptor’s partner within six hours. The donor cannot therefore demand to have these ova returned for her own use.

Risks
Picking up the follicles that contain ova involves a possible but slight risk of bleeding and/or infection, or oversensitivity after local anaesthetic or after taking the medication used for stimulation. Hormonal stimulation can sometimes lead to over-stimulation, which may occasionally require hospitalisation. Individually adapted precautions are taken to limit these risks as much as possible.

During the hormonal stimulation, up to and until the time when the ovum aspiration takes place, the donor is asked to come to the hospital regularly for blood tests and ultrasound scans to follow up the treatment. This may involve time off work with possible financial consequences.

Financial aspects
The ovum donor is reimbursed for the costs of the preparatory tests and of the hormonal treatment including ovum aspiration. An allowance is provided to cover expenses.

Ovum donation is restricted by law for each donor: one or more children may only be born to a maximum of six different women using ova from the same donor. This restriction is essential as an unlimited number of births increases the risk of consanguinity in the future.

Ovum reception

For some couples, the use of ova from a donor is indicated. Such treatment is only provided for women under 45 years of age.
The main medical indications may be summarised as follows:

- **Women without ovaries** (congenital or after surgery).
- **Women with fertility problems** whose ovaries are not accessible for ovum pick-up.
- **Women with premature ovarian failure** (premature menopause).
- **Women with a proven genetic defect in their own ova**.
- **Women with no or a very low response to ovarian stimulation with IVF**.

**Anonymous ‘cross-donation’**

To guarantee anonymity with fertilisation after ovum donation, we work with two couples where the woman has a medical indication for ovum donation. Both couples seek a donor through family or friends separately from one another, or sometimes on the internet or via an anonymous advertisement in a newspaper or magazine. Eventually, the first couple will receive ova from the second donor and the second couple will receive ova from the first donor.

**Ovum receptor screening**

The ovum receptor undergoes genetic screening and extensive counselling with the fertility consultants and the gynaecologist. During this counselling the psychological and social aspects involved in receiving donated ova are looked at in detail (medical assessment, discussion of the chances of success and any risks, the anonymity of the procedure, the cost, etc.).

**Nature of the ovum reception and procedure**

Donated ova are fertilised using the sperm from the partner of the woman receiving the ovum or ova (the receptor) within six hours of aspiration. The embryos produced as a result can be inserted in the same cycle or after freezing and thawing.

**Risks**

As with any medical fertility treatment, treatment using ovum reception never offers an ultimate guarantee of pregnancy. Twenty percent of ‘normal’ pregnancies end in a miscarriage and complications can occur in any pregnancy, including those resulting from ovum reception. In comparison with other pregnancies after medically assisted fertilisation, a pregnancy after ovum reception does not involve any noticeably higher risks, provided it is a single pregnancy. Transferring more than one embryo can give rise to a multiple pregnancy, which involves a greater risk of premature contractions and birth, raised blood pressure, lower birth weight, etc. The number of embryos replaced in the uterus is determined in mutual consultation between the couple, the embryologist and the doctor.

Just as with a normal pregnancy, with pregnancies achieved using ovum reception a certain percentage of children may be born with a physical or mental abnormality.
All ovum donors are tested for infectious diseases such as the HIV virus, cytomegalovirus, hepatitis, Chlamydia and syphilis. The use of fresh ova means that there can be no absolute certainty that such infectious diseases are not present, as a certain period of time may elapse between the contamination and the possibility of detecting the virus in the blood. If you receive ova from an anonymous donor, you should therefore be aware that the ovum reception procedure always involves a slight risk of sexually transmitted diseases, despite all the precautions taken to prevent this.

Ovum donors must be aged under 37. If the ovum donor was between 35 and 37 years old when the ova were donated, there is a slightly higher risk of chromosomal abnormalities because of the age. This is why we advise you to have the necessary tests conducted during the pregnancy (prenatal blood test and ultrasound scan during early pregnancy) to check whether there is indeed an increased risk of chromosomal abnormalities in your foetus. In that case it is best to undergo chorionic villus sampling or amniocentesis.

Financial aspects
The costs of the medication, cultivating the ova, the in vitro fertilisation and the embryo transfer will be charged to the ovum receptor. These are largely reimbursed by the Belgian national health insurance institute (Riziv), provided that the ovum receptor fulfils the conditions imposed by this institute. In addition, a flat rate is charged per cycle to cover the expenses of the ovum donor (hospital costs, travel expenses, time off work, etc.).

Embryo donation

Surplus frozen embryos which a couple no longer wishes to use to fulfil their own desire for children can be anonymously donated to other couples with fertility problems. Embryo donation is of course entirely voluntary. Embryos may be donated if the female partner in the donor couple is younger than 37 years of age when these embryos are frozen. If a couple wishes to donate their embryos, both partners have to undergo a thorough medical examination (physical examination, blood test) to check their state of health. Particular attention is paid here to the possibility of transmissible hereditary or contagious diseases which could be passed on via donation. The donors are therefore obliged to report all known hereditary disorders in the family. During these tests the donors are seen by a gynaecologist (specialist in female fertility) and a geneticist. The donors are also seen at least once by a fertility consultant to discuss the psychological aspects of donation.

Financial aspects
The costs of the examinations and tests needed for anonymous embryo donation are reimbursed. The embryo donors receive a flat rate to cover these expenses.
Consequences
Relinquishing frozen surplus embryos is unconditional and irrevocable. This means among other things that the embryo donors waive all their rights to the embryo they have relinquished and can make no claim to the child or children born further to the donation of the embryos.

The anonymity of both the donors and the receptor(s) of the embryo is strictly guaranteed. The embryo donors undertake not to trace the identity of the receptors. The receptors do not receive any information at all about the embryo donors. Embryo donation is restricted by law for each donor: one or more children may only be born to a maximum of six different women using embryos from the same donor. This restriction is essential as an unlimited number of births increases the risk of consanguinity in the future.

Embryo reception

This treatment can offer a solution for couples in which the female partner has one of the medical indications for ovum reception and where the male partner has one of the medical indications for the use of donor sperm.

Risks
As with any medical fertility treatment, embryo reception never offers an ultimate guarantee of pregnancy. Twenty percent of ‘normal’ pregnancies end in a miscarriage and complications can occur in any pregnancy, including those resulting from embryo reception. In comparison with pregnancies without medical assistance, a pregnancy after embryo reception does not involve any noticeably higher risks. With a normal pregnancy, a certain percentage of children may be born with a physical or mental abnormality and the same applies after embryo reception. In addition, it is possible that the risk of fertility problems is higher among children born after embryo reception than among children born further to spontaneous fertilisation and pregnancy.

All embryo donors are tested for infectious diseases such as the HIV virus, cytomegalovirus, hepatitis, Chlamydia and syphilis.

Financial aspects
The costs of the preparatory tests and the hormonal treatment including embryo transfer are charged to the embryo receptors and are largely reimbursed by the Belgian national health insurance institute (Riziv). In addition, a flat rate is charged per cycle for laboratory and administrative costs.
15. PRE-IMPLANTATION GENETIC DIAGNOSIS AND SCREENING

Pre-implantation genetic diagnosis (PGD) is a very early form of prenatal diagnosis that takes place during in vitro fertilisation treatment (IVF). The embryos produced during the IVF treatment are checked in the laboratory after fertilisation to detect any abnormalities before they are implanted or replaced in the uterus.

Embryo biopsy and genetic examination

The technique used with PGD consists of two parts: an embryo biopsy, followed by a genetic examination. An embryo biopsy is carried out on all embryos (at the six to ten-cell stage) on day three after fertilisation. To do this, an opening is first made in the strong membrane surrounding the embryo (zona pellucida). One or two cells are then carefully removed from the embryo. These cells are examined in the genetic laboratory for possible abnormalities in the structure or number of chromosomes. The result of the genetic examination is known on day four or day five after fertilisation. After the examination, only those embryos that display a normal pattern for the abnormalities checked are replaced in the uterus. If there are any surplus embryos with a normal pattern, these can be frozen. Abnormal embryos can no longer be used, except for scientific research.

Applications of PGD

PGD can be applied in patients with a serious hereditary disease. With the help of PGD it is possible to become pregnant with a child that will not inherit this disease, as the embryos that display the abnormality are not replaced in the uterus. At the LUFC PGD is used mainly for patients who display certain structural abnormalities in their chromosomes (such as translocations, deletions, etc.). Thanks to the work carried out by the centre for human genetics at UZ Leuven, these abnormalities can be sought specifically for each individual couple in their embryos. Patients with an increased hereditary risk of children with other disorders (such as Huntington’s disease, mucoviscidosis, etc.) can also come to our centre for PGD, as the LUFC has a cooperation agreement with the centre for human genetics at UZ Brussels for these disorders.

In addition, with the help of PGD the sex of the embryos can also be determined and used with regard to gender-related diseases or breast cancer. It is possible, for instance, only to replace
female embryos in the event of a serious hereditary disease that only affects boys or men (X-related abnormalities such as Duchenne muscular dystrophy).

**Other applications of PGD: pre-implantation genetic screening**

Using the same technique, an embryo biopsy followed by a genetic analysis, it is also possible to systematically screen embryos for the most common chromosomal abnormalities.

Is this useful in the context of treatment with medically assisted fertilisation?

Recent studies indicate that 30 to 50% of the embryos that are replaced in the uterus after IVF have an abnormal hereditary pattern (abnormal chromosomes). This is probably mainly to do with abnormalities of the ova. It means that a third to half of all embryos that are replaced are genetically abnormal. The majority of these genetically abnormal embryos will not implant in the uterus or will give rise to premature termination of pregnancy (miscarriage). Some of these embryos, however, develop to become children with chromosomal abnormalities (such as Down’s syndrome). To prevent this, it is possible to screen embryos for the main chromosomal abnormalities before they are replaced in the uterus. In this way, we could increase the chances of pregnancy and reduce the risk of the birth of a genetically abnormal child.

For which patients may this be useful?

- ✔ **Women aged 35 years and over**
  The likelihood of genetically abnormal ova increases with the age of the woman. The age effect begins to make itself felt from the age of 32, and increases in importance from the age of 35. It is also known that the likelihood of pregnancy after in vitro fertilisation falls as age increases, for the same reason. This is thought to apply in particular to women from the age of 35, as in this group the risk of chromosomal abnormalities further to a spontaneous pregnancy is also significantly higher. For this reason many women from the age of 35 opt in favour of amniocentesis during the pregnancy.

- ✔ **Patients with repeated miscarriage**
  For women who have suffered a number of successive miscarriages. These miscarriages may have been caused by embryos with chromosomal abnormalities.

- ✔ **Patients with repeated implantation failures**
  For patients who have already undergone a number of attempts at IVF in which good-quality embryos could be replaced during the transfer, but which did not result in pregnancy. The chromosome content of these embryos may not be normal.

- ✔ **Patients with substantially reduced sperm quality**
  For couples where the man has problems producing sperm cells. The few sperm cells that are found may have chromosomal abnormalities. The embryos that are formed using these sperm cells may therefore be abnormal.
Which chromosomes can be examined?
At the moment it is possible to examine between seven and ten chromosomes at the same time. Usually chromosomes 13, 16, 18, 21, 22 and the sex chromosomes X and Y are examined, as we know that abnormalities in these chromosomes can lead to embryos that do not implant, to embryos that implant but that end in a miscarriage or to a live child born with a chromosomal abnormality (for instance Down's syndrome).

Aim of PGS: added value?
The aim of the screening is, of course, to replace only embryos in which the chromosomes examined are normal. So far research conducted in our centre and in other centres has not shown that PGS can provide real added value for these patients. The PGS technique is limited at the moment as only a certain number of chromosomes can be examined. This means that nothing is known of the chromosome pattern of the remaining chromosomes. The LUF C is currently researching the possibility of examining all the chromosomes in an embryo together.

Risks
The pre-implantation genetic diagnosis technique is very recent. It is possible that the embryo biopsy disrupts the development of the embryo. So far hundreds of children around the world have been born after the application of this technique. Follow-up of these children has not so far revealed any additional abnormality that may be connected with the biopsy of the embryos. However, circumspection remains necessary, as the technique is experimental and more data are still needed about the follow-up of children born after PGD treatment.

In practical terms this means that careful follow-up is needed from the moment of fertilisation up to an including the birth and development of any child that may result from this treatment. This involves, among other things, regular ultrasound scans during the pregnancy and the possibility of a prenatal biopsy after chorionic villus sampling or amniocentesis. After the birth of a child using this technique, the further development of the child can be followed up by means of questionnaires.

Patients who are treated with PGD at the LUF C are asked to cooperate with this follow-up as part of an ongoing European project.
A relationship, a good job, a house and then waiting for the arrival of a baby. It all seems so matter-of-course, that if there is no pregnancy, the disappointment can be huge. After a time, the disquiet increases, too. The emotional reactions to the lack of a longed-for pregnancy differ greatly from one person to another.

It may be that the fertility problems do not weigh all that heavily on you at the moment, but many people feel the impact of this to be far-reaching in various aspects of their life (their relationship, work, social contacts, family, etc.).

In our society, where we think we are in control of almost everything we undertake – including planning children – it is particularly stressful when things do not go as expected. Most couples assume that they can start a family when they plan to do so and in the intimacy of their relationship. This first period of ‘trying spontaneously’ to become pregnant can in itself cause a fair amount of stress. Sometimes there is no longer much talk of spontaneity in the midst of the calendars and temperature curves. Some couples experience this as a burden on their sexual relationship (‘making love to order’, for instance). Every month that the attempts fail, there is more disappointment and the tension rises. The questions and the anxiety increase (‘Will it ever work?’ or ‘Is there something wrong with us?’).

Eventually, you decide to ask for help, to go to a fertility centre in the hope that there they will be able to find the cause of the problem and a solution. This is a big step. Gradually, as a couple, you have the feeling that you have handed over your desire to have children to the medical world. You feel increasingly dependent on what the doctors say. Then come a whole host of tests. Some people will deal with this more easily than others. In any case, it remains quite a task to cope with all this and combine it with your professional activities. The treatment phase that follows also demands an effort from the couple. The expectations are high. For some, success comes quickly.

For others, the long-awaited pregnancy comes only after a number of disappointments and for others still – fortunately the minority – pregnancy quite simply never materialises. So this is a long and demanding process. Some people deal with stress more easily than others. Some people have more questions about the way fertility tests and treatment are perceived than others: why should this happen to us? Do I have to tell my parents? The people at work! etc. Will I ever tell my child how it was done? Are we taking the right decision? Are we ready for it? etc.
Why is fertility counselling useful?

Being confronted with fertility problems and a possible medical diagnosis can have a huge impact on people’s psychological and relational well-being (Daniluk, 1997). Moreover, existing psychological or psychiatric problems (such as fear, depression, sleeping problems, relational or family problems, stress at work, etc.) can worsen or be affected by the medical diagnosis. Fertility problems can raise unresolved emotional issues again. It may be a huge blow to your feeling of self-esteem and identity. Couples find themselves in a stressful situation, in which a whole host of uncertainties and doubts emerge. Both physically and emotionally, patients may become exhausted or confused.

We have opted not to limit the task of the fertility consultant to assisting couples or individuals who are already showing signs of psychological difficulties. The psycho-social aspects of fertility treatments are omnipresent. This is why at the LUCF psychological counselling forms an integral part of the medical process. Even during the first consultation with the gynaecologist, a discussion with the fertility consultant is suggested. In most cases this is offered without any obligation, although strongly recommended by the gynaecologists, and in specific situations it is mandatory. Each couple reacts in their own way. Although you may not have an explicit need for psychological assistance, being scared or suffering emotionally when faced with fertility problems is quite normal. The discussion with the psychologist aims to consider all aspects of the fertility issue carefully. We want to make time and space to exchange ideas, pay attention to the individual and relational decision-making process and promote open communication between the man and the woman. Receiving information about the ‘normality’ of feelings and emotions and about how to deal with them can prove a huge relief. Fertility counselling can give couples the support they need and help them make their journey to fertility on a healthy basis. It can help prevent a number of negative emotions, such as fear and depression. Moreover, it can help you deal with emotional pressure and failure. Finally, it can reassure and strengthen you in your capacity as parents (Ponjaert-Kristoffersen & Baetens, P; 1999).

What?

The fertility consultant is a psychologist who works specifically with the gynaecological department and the fertility centre. You can call upon the fertility consultant as a couple or individually. The fertility consultant will adapt the discussion to the time when and the reason why you are seeking fertility counselling.

When?

Introductory consultation
At the LUCF we advise all patients to have an introductory consultation with the fertility consultant. The aim of this interview is to consider all aspects of the fertility issue. We discuss a number of topics so as to map out your psycho-social, relational and sexual functioning and trace any possible risk factors and/or contraindications relating to further fertility treatments.
After drawing up a thorough personal and relational case history (including sexual aspects), first of all the (significance of) the desire to have children is considered, with the implications for the three above areas of the failure to fulfil this desire to have children. The individual way of dealing with difficult events is considered, as well as communication on this subject within the couple and with those (immediately) around them (social functioning). A number of lifestyle aspects are also examined that are increasingly being linked to fertility problems: smoking, alcohol consumption, sport, general stress level, etc. Finally, the general psycho-social functioning of the individual is assessed along with the presence of current psychiatric clinical pictures and the occurrence in the family of psychopathology or physical/mental handicaps is studied. All these elements can help gain a better insight into the course of the fertility treatment you are following. Together with the psychologist, you may decide to look at a number of these aspects in more detail.

With all your concerns, hesitations, ideas, wishes, etc., which are expressed during this introductory consultation (and any subsequent discussions), the fertility consultant takes part in the multidisciplinary staff meeting where all the test results are discussed. The fertility consultant discusses the psycho-social aspects of your situation at this staff meeting, which is important in the quest for the best possible medical and psychological treatment.

The unique story of each couple is set out orally at the staff meeting and a written report is added to the electronic file.

**Mandatory consultation**

In a number of specific cases relating to the course of the treatment, a discussion with the fertility consultant is obligatory:

- [✗] Concerns about the relationship between the partners
- [✗] Newly constituted family with children from former relationship(s)
- [✗] Current psychiatric or psychological problem in the previous history of either of the partners
- [✗] Doubts about the couple's ability to raise children
- [✗] Request for reversal operation after sterilisation of the woman
- [✗] Stress situation or difficulties in dealing with the fertility issue (see also stress management and relaxation therapy)
- [✗] Donation or reception of ova, sperm cells and embryos
This mandatory consultation is largely comparable to an introductory consultation, except that there is a specific situation that requires additional attention. As more complex factors are involved, the psychological impact of fertility problems is considered against the specific background of the couple. The emphasis in these discussions lies on exploring the complex situation and not on evaluating it, since the psychologist cannot predict human behaviour. It is, however, possible to mention and identify risk situations and to formulate worries and concerns about the psychological well-being of couples.

If the discussion with the psychologist is mandatory, the fertility consultant expresses a psychological opinion for this couple relating to fertility treatments. At the multidisciplinary staff meeting a final decision is then taken as to whether to follow up on this advice or not (ISO -9001-2000, fertility counselling).

Support consultation
During the course of the fertility treatment (both before it starts, during the treatment, and after it has ended) psychological support may prove necessary. This need may be recognised by the couple themselves or by a social worker at the fertility centre.

A fertility problem is an experience that constantly changes in intensity and direction, so that you experience different needs and emotions at different times. Many people compare it with a roller coaster where at one moment you are really high and the next right down. What is more, this experience is unique for everyone.

The need to talk may arise both in the diagnosis phase and in the treatment phase, or even once contact with the LUFC is over and the treatment has ended.

There may be certain decision-making moments along the path that couples follow in the fertility centre when a discussion is meaningful, for instance when making a choice between alternatives in the treatment, exploring other options of building a family (adoption, acting as foster parents, childlessness, etc.), thinking about using donor material (sperm donor, ovum donor, embryo donor), ending the treatment and what to do next.

In a discussion further to a decision-making moment, time and space are made to explore the various possibilities, alternatives and feelings. This gives you a clearer picture of your situation and you can pay sufficient attention to the possible differences that may exist between the partners and which could impact on your decision. We know from experience that fertility problems often lead to a great many tensions and difficulty coming to terms with the situation. These may be so intense that they determine your entire life. The treatment phase, too, can prove very difficult and raise a host of questions: is this really what I want? How far can and will we go? Are we as a couple in agreement about the strategy to follow? How do we tell our family and friends? How do we combine the treatments with our work situation, which is already stressful? How can I find peace? etc.
Certain situations and feelings may lead to the need for psychological support.

For example:

✗ differing ideas between the man and the woman about the direction to be taken or the perception of their experience of the process at this moment
✗ discussion of the desire to have children
✗ expectations with regard to the treatment
✗ support with the emotional impact of fertility problems: grief, stress, fear, anger, feelings of loss, social problems, etc.
✗ miscarriage and repeated miscarriage
✗ problems and loss during pregnancy and around the period of delivery
✗ sexual problems in the context of fertility problems (for which we are also pleased to refer you to the female sexuality clinic at UZ Leuven)
✗ relational problems in the context of fertility problems
✗ etc.

More information

For more information or to make an appointment, please contact the psychologists at the fertility centre:
Uschi Van den Broeck and Lynn Van Moppes
Tel. 016 34 28 60
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17. RELAXATION THERAPY AND STRESS MANAGEMENT

Individual counselling for woman, man or couple

Our counselling system involves first of all examining what are the stress factors within the fertility problem. Together we look at the negative thought circles that you may be experiencing. We consider which situations maintain these negative thoughts. By talking about them we try to find solutions to deal better with stress. Infertility creates stress and stress worsens the infertility problem. Together we seek ways of leaving this vicious circle. Many of these techniques are also practised to be able to cope more effectively with any painful fertility treatments. Most stress is expressed mainly through the body, because of excessive tension in the muscles, constant physical unrest, breathing problems, etc. Stress can also reveal itself in the form of recurrent negative thoughts that cannot be controlled. With various body control and stress reduction techniques such as yoga, relaxation, meditation, etc., we can help you to develop better feelings about your body and hence deal better with stress.

Group sessions for couples with fertility problems

Some people feel the need to share their problems with others in the same situation. This is why we organise annual group sessions for couples. We organise six evening sessions on various topics. In the first session the thoughts, problems and questions are collected for discussion in more depth in the subsequent sessions. The following topics in particular come up:

- differences and similarities in the way in which men and women perceive the fertility problem
- dealing with the thoughts and feelings of others (family, acquaintances, colleagues, etc.)
- perception of your body, thoughts and feelings about fertility problems
- boundaries of the treatment
- life projects

These topics are worked through in a ‘discussion/work group’. Stress-reducing techniques based on various relaxation techniques are also taught.
More information

For more information please contact via e-mail fertiliteitscentrum@uzleuven.be.

References

ISO 9001-2000: Kwaliteitshandboek; Primair Proces; Fertiliteitscounselling.
18. Patient Organisation

Since it was founded on 25 October 2002, the Endometriosis Foundation has worked very successfully on the issue of endometriosis. The various regional meetings are enthusiastically attended by an average of 170 people.

The Endometriosis Foundation works hard in the interests of all endometriosis patients. The foundation does this through:

✔ organising contact between people in similar situations
✔ organising information days for both doctors and patients
✔ promoting scientific examination
✔ offering telephone consultations where people can ask questions and request information and support about endometriosis
✔ sending a quarterly newsletter to financial supporters
✔ maintaining international cooperation and contacts

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Appendices
Cooperating A centres

✗ AZ St. Augustinus Antwerp
   Gynaecologists: dr. L. Segal (in charge), prof. dr. P. De Loecker, dr. L. Meeuwis
   Tel. 03 443 36 63

✗ AZ Imelda, Bonheiden
   Gynaecologist: dr. J. Bosteels, dr. S. Pelckmans
   Tel. 015 50 50 10

✗ Europe Hospital Site St. Elisabeth, Uccle
   Gynaecologist: dr. B. Schrurs
   Tel. 02 373 17 30

Satellite centres

✗ St. Jan Clinic, Brussels
   Gynaecologist: dr. L. Meeuwis
   Tel. 02 221 91 11

✗ AZ Diest, Diest
   Gynaecologists: dr. I. Thijs, dr. K. Peeraer
   Tel. 013 35 40 11

✗ St. Jozef Clinic, Bornem
   Gynaecologist: dr. A. Spaepen
   Tel. 03 890 16 49

✗ Monica Campus O.L.V. Middelares, Deurne
   Gynaecologist: dr. L. Meeuwis
   Tel. 03 320 50 00

✗ AZ St. Jozef, Turnhout
   dr. A. Pecceu
   Tel. 014 44 41 11

✗ AZ St. Maarten Campus Leopoldstraat, Mechelen
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Cooperating gynaecologists

Flemish Brabant

Halle: dr. N. Vandersteen
Tienen: dr. G. Donders, dr. I. Riphagen, dr. T. Van den Bosch

Antwerp

Brasschaat(Klina Brasschaat): dr. D. Coeman, dr. P. Debois
Duffel: dr. F. Vankelecom, dr. I. Wittevronghel
Geel: dr. E. Vercammen, dr. H. Coppens, dr. L. Verguts,
      dr. J. Vervliet
Herentals: dr. M. Vansteenkiste
Lier: dr. S. Dobbelaere, dr. K. Wuyts
Turnhout (Municipal Hospital): dr. B. Van Rompaey, dr. J. Berben

Limburg

Bilzen: dr. N. Minten
Bree: dr. D. Lauwagie
Herk-De-Stad: dr. P. Duivivier
Hasselt
      (Virga Jesse Hospital): dr. A. Wisanto, dr. M. Muyltermans, dr. A. Dupon,
      dr. A. Scheurs, dr. F. Jadoul, dr. J.P. Nolens
      (CAZ Midden Limburg, Salvator): dr. L. Vansteelandt
Heusden-Zolder: dr. L. Buekenhout, dr. S. Schepers
Lommel: dr. B. Bollen, dr. R. Hendrickx, dr. F. Ulens
Maaseik: dr. M. Depiere
Sint-Truiden: dr. L. De Sonnaville, dr. U. Verboven, dr. J. Michiels

East Flanders

Lokeren: dr. J. Bulthé
Sint-Niklaas: dr. M. Coenen
Zottegem: dr. A-M. Waterschoot

West Flanders

Roeselare (Municipal Hospital): dr. L. Danneels, dr. K. Watty, dr. F. Laverge
Ostend: dr. B. Timmermans