

# Welcome

in the fertility centre



# Welcome in the **FERTILITY CENTRE**

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# Introduction

Before starting a fertility treatment in our centre, we ask that you carefully read this brochure. In it we discuss a number of important aspects of the various treatment options. The purpose of this brochure is to provide you with information about medically assisted reproduction that is as complete as possible. This way you will understand what to expect and what not to expect from such a treatment, and at the same time you will be able to assess the effects that this treatment could have on you and your life.

This brochure is a supplement to what was already discussed during your consultation. For more information or if you have any other questions that relate to your personal situation, please do not hesitate to contact us.

Before starting any treatment, you will be asked to sign a declaration of consent for the chosen therapy. Among other things, this declaration states that both partners have read and understood the information brochure. This declaration is valid throughout the entire duration of your treatment. When new developments in fertility treatments are adopted, we will inform you of them.

We hope that this information has been helpful to you, and we wholeheartedly wish you all the best.

Approximately 10% of couples remain childless longer than planned. The techniques of today often offer a solution for a fertility problem, but not in every case. Fertility treatments will never offer a guarantee for success, but will increase your chances per cycle. The gynaecologists of the Fertility Centre will inform you about the different options and your personal chances. Mostly, there will be no such thing as one single solution, but rather different options to choose from after having received adequate information.

Success rates decline with the number of failed attempts. It is rarely useful to repeat the same treatment for more than six cycles. Most frequently, it will still be possible to switch to another kind of treatment, which will offer new chances. The couple itself will decide how long a specific treatment is continued, after having been informed as accurately as possible on their success rates.

It then goes without saying that medically assisted reproduction is not purely a technical matter but that this treatment can bring about very strong emotions in all of its stages, emotions that affect not only each partner individually but also their relationship to one another and to the outside world.

Please bear in mind that the majority of the couples with fertility problems (almost 80%) will obtain a pregnancy after all. We therefore can say that the chances are high, even if sometimes the efforts required to reach this final goal might be considerable.

## Allow us to introduce ourselves

The Fertility Centre of AZ Sint-Lucas is a multidisciplinary team that was formed in order to provide the best possible help to couples with fertility problems. As a rule, the general gynaecology department performs the examinations necessary to discover the cause of the fertility problem.

When more advanced techniques are needed (e.g. ovulation induction, insemination or in vitro fertilisation, IVF) or when follow-up is needed that is too stringent, the gynaecologist may refer you to the Fertility Centre.

The Fertility Centre team consists of four **gynaecologists**: dr. Tom Coetsier, dr. Jeroen De Smet, dr. Isabelle Meire and dr. Nele Van Renterghem. All four doctors work full-time with fertility research and treatment. They each maintain ultimate responsibility for their individual patients, yet together they ensure permanency for standard procedures such as the ultrasonography of inductions, inseminations, ovarian punctures and embryo transfers. As soon as pregnancy occurs, you will be referred back to the referring gynaecologist for further follow-up of the pregnancy.

When exceptional examinations or treatments are necessary in the man, a visit to dr. Jeroen De Smet may be necessary. When tissue from the testis must be prelevated to recover sperm cells (more about this further on), then it is also dr. De Smet who will be responsible for this.

The **midwives** on our team also form a very important link in the course of the fertility treatment. In most cases, they are your first contact with our team and will guide your way through the treatment, in on-going consultation with the gynaecologists. They will see you for your first appointment, discuss with you the practical steps of the treatment, assist in inseminations or ovarian punctures and at the close of the treatment will deliver you the good or less-than-good news.

For support and guidance with the psychological and emotional impact of a fertility treatment, you can call on the **psychologists** from the Psypunt team. Experience has shown that most couples gain a great deal of support and understanding simply by expressing the intense experiences and their perceptions of these experiences during the treatment. When the fertility problem threatens to dominate all of your thoughts and your life, it is most definitely worthwhile to increase your resilience through specific sessions with a psychologist. The purpose of these services is not only to lighten the load of the treatment but also to provide purely informational support.

The preparatory fertility examinations, such as blood tests and sperm tests, occur in the **clinical biology laboratory** in the hospital (street 38).

The Fertility Centre (street 7) has its own **laboratory for sperm processing**, which is used for the preparation of sperm for inseminations (with both partner sperm as well as donor sperm). The first preparatory steps for an IVF procedure (identification of the egg cells from ovarian punctures and sperm preparation in the context of IVF) also occur in our own laboratory.

If IVF is necessary, the **IVF laboratory of UZ Gent** is utilized for the laboratory phase of the treatment. This laboratory is the second largest IVF lab in Belgium and has extensive experience with good success rates. There is also a constant collaboration between UZ Gent and AZ Sint-Lucas via Drs. Coetsier, De Smet, Meire and Van Renterghem who are also clinical staff members of the IVF Centre of UZ Gent.

The Fertility Centre of AZ Sint-Lucas is a recognised health care programme, type A and therefore satisfies all of the relevant statutory requirements. In addition, our hospital has been accredited according to the NIAZ norms (Dutch Institute for the Accreditation of Hospitals). This means that we have successfully developed and implemented quality assurance systems in all aspects of our organisation.

### **Policy options of our Fertility Centre**

During the application of the fertility-enhancing techniques at AZ Sint-Lucas, the following elements are given maximum priority:

- A fertility problem exists when within a stable relationship between two persons attempts to become pregnant remain unsuccessful for longer than normal.
- At each step of a fertility treatment, the chances of pregnancy are weighed up individually against the physical, psychological, relational and financial burden for the couple, and a decision is made, in consultation with the couple, about further steps.
- We shall strive at all times to provide you with maximal information and personal accessibility in order to be able to guarantee the best guidance possible, with sufficient attention for both the medical and the psychosocial aspects of treatment.
- The laboratory aspects of the IVF treatment are mainly carried out by the IVF laboratory of the University Hospital (UZ) in Gent. The cooperation modalities and respective responsibilities of these institutions have been established in a written protocol in conformity with the relevant legislation.
- The goal of the Fertility Centre is to support and supervise fertility treatments, and therefore the centre is not responsible for further prenatal care once pregnancy is established. At that time, the patient is referred back to the referring gynaecologist.

The term **medically assisted reproduction** is used when the essential steps in the reproductive process, namely the development of the egg cells and the uniting of the egg cells and the sperm cells, does not occur in a natural way. In other words, ovulation induction, insemination with partner or donor sperm, in vitro fertilisation and all of the other techniques related to these comprise medically assisted reproduction.

# Ovulation induction

## The theory

In women, disturbances to ovulation are the most frequent causes of reduced fertility. In other words, the hormonal interaction between the brain and the sex organs is disrupted. As a result of these disturbances, menstruation is irregular or sometimes absent for long periods.

Ovulation induction is not the same as controlled hyper stimulation:

- in hyper stimulation (or superovulation), the development of many follicles is stimulated.
- in ovulation induction, **the hormone production is adjusted for the purpose of fully developing one follicle and attaining a predictable ovulation.**

## Polycystic ovary syndrome (POS)

The problem is usually located at the level of the ovaries, which contain a sufficient number of follicles, but which remain in a resting state instead of developing further. This condition is called polycystic ovary syndrome. The ovaries are slightly swollen and contain small cysts (these are in fact follicles that are too small). Sometimes this condition is diagnosed by way of an ultrasound in someone with no symptoms and a normal cycle, but there are various symptoms which are normally associated with POS: irregular menstrual cycle possibly ranging to a complete absence of menstruation, overweight, excessive body hair, acne and oily skin. Some of these symptoms are a result of excess testosterone. The diagnosis can be made via blood tests and vaginal ultrasound. The primary cause of POS has not yet been determined but is probably related to metabolic disturbances (insensitivity to insulin).

The preferred treatment for the irregularity of ovulation that is seen in POS is clomifene citrate, Clomid<sup>®</sup>. This is a medicine that gives the pituitary gland (hypophysis, gland in the brain that controls the ovaries) the impression that there is insufficient oestrogen (female hormone) present in the bloodstream. As a result, the pituitary gland will release more FSH and LH into the bloodstream. FSH and LH are two other hormones that directly stimulate the ovaries to develop follicles.

### Premature ovarian failure (POF)

A situation that is luckily rarer is when the supply of follicles is used up more quickly than normal. This premature failure of the ovaries is also sometimes called premature menopause, and this term is used for women whose supply of egg cells stored in the ovaries is exhausted before the age of 40. Contrary to the lifelong production of sperm cells in men, the supply of egg cells in women is limited, and during the course of a woman's life, no new egg cells are produced.

Premature menopause can be purely dispositional, but the following causes must first be ruled out:

- genetic causes (abnormalities of the X chromosome). If the mother or the sister of the patient entered menopause early, this must be reported since this condition can be hereditary.
- autoimmune diseases
- radiation therapy or chemotherapy
- extensive surgery of the ovaries

Unfortunately, in these cases, egg cell donation (or adoption) is the only option.

### In practical terms

You take clomifene citrate (Clomid®) (1 to 3 pills per day) for five days starting on the third day of your cycle. Possible, yet temporary, side effects of this treatment are hot flashes, headache and mood disorders. The next step is an ultrasound and/or blood test to assess your reaction to the treatment. This examination usually occurs on day 9, 10, or 11 of the cycle. If the growth of the follicles has not progressed far enough at that time, a second ultrasound will be scheduled a few days later. When one or more egg cells are seen on the ultrasound, the moment of the impending ovulation will be determined and advice related to sexual relations will be provided.

Approximately 25% of patients do not react to Clomid® stimulation, even at its maximum dosage. For these patients and in cases where pregnancy is not achieved after 4 cycles with Clomid®, we have the option of stimulation using gonadotrophins (Menopur®).

These injections contain FSH, are effective for only a short period of time, which means they must be administered daily, and affect the ovaries directly. The follow-up for this treatment is identical to a Clomid® induction. The only difference is that the dosage can be adjusted during the cycle. Finding the optimal dosage is not always obvious and can take several weeks given the fact that a slight increase in the dose can lead to an excessive reaction. The use of gonadotrophins is more labour-intensive than using Clomid®, but these agents do have a favourable effect on the endometrium (lining of the uterus, where the embryo will implant), while Clomid® can have a rather more negative effect on the endometrium. The reimbursement for gonadotrophins is reserved for patients who are Clomid®-resistant or who do not become pregnant after 4 cycles of treatment with Clomid® (a reimbursement request for the medical advisor from the National Health Service is required). Gonadotrophins are only available in the Fertility Centre pharmacy at the hospital. Therefore, if for any reason you run short of ampoules, you must contact the Fertility Centre. These medicines should not be ordered in the public pharmacy, since any ampoules supplied by the public pharmacy will not be eligible for reimbursement.

For every cycle which results in ovulation there is a 15 to 25% chance of pregnancy on the condition that there are no other problems and that the sperm is of good quality. Of all of these pregnancies, approximately 90% are single pregnancies, 8% are twins and 2% are triplets.

### Multiple pregnancies

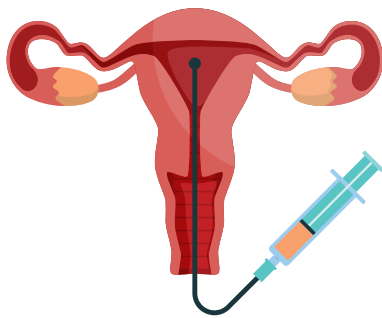
We try to prevent multiple pregnancies as much as possible, since they carry important risks for the newborns (premature birth, low birth weight). When the gynaecologist sees that too many follicles develop at the same time, he/she can advise to cancel the stimulation or to avoid intercourse around the time of ovulation. We understand this might be disappointing and frustrating, but the future children's health has to prevail at that moment. In repetitive cases of very difficult stimulation, a follicular puncture might be considered. In these cases, we can aspirate the content of the supernumerary follicles vaginally (small surgical procedure, usually without anesthesia). This allows to save the cycle and at the same time reduce the risk for multiple pregnancy. The intervention is very comparable to a follicular aspiration for IVF (see page 12).



# Intrauterine insemination (IUI)

## The theory

In some cases, the natural fertilisation process can be helped along both literally and figuratively, by introducing the **sperm, which was prepared beforehand in the laboratory, directly into the uterus at precisely the right moment. This is done using a fine tube** (a small catheter). By first processing the sperm, the most active sperm cells can be selected and the adverse substances can be removed from the semen.



This treatment is frequently used when the couple's reduced fertility is caused by moderate abnormalities of the sperm or when the passage of the sperm into the woman's body is obstructed by antibodies present in the mucous plug of the cervix. It is also utilized for fertility problems of unknown origin or when using donor sperm (the quality of the sperm is reduced in that case since the donor sperm has been frozen).

In order to be able to accurately determine the time of ovulation, egg cell maturation is artificially induced (usually with Clomid®; see page 7). This treatment often results in the development of more than one egg cell, which increases the chance of fertilisation. Of course,

when various egg cells are 'presented' to the sperm cells, each of these egg cells has the chance of being fertilised. However, the disadvantage of this is that multiple pregnancy may result. The number of egg cells that develop and that can be fertilised can be determined using hormonal tests and ultrasonography. In the event that three or more egg cells become ready for ovulation, the treatment is cancelled. In exceptional cases, a follicular puncture can be considered (see page 7).

## Pregnancy rate

The chance of pregnancy with this method is approximately 10 to 15% per cycle. Of all of these pregnancies, approximately 90% are single pregnancies, 9% are twins and <1% are triplets. Experience shows that the chance of pregnancy during the first three cycles remains approximately equal and then gradually declines over the following three cycles. As already mentioned above, the chance is low that after six failed cycles a pregnancy will be achieved using the same technique. It is for that reason that IUI is usually only utilised for three to six cycles. Inseminations can be performed month after month without interruption and the patient remains completely ambulatory throughout the entire procedure (no hospital admission necessary).

A rare risk associated with the introduction of sperm through the cervix is the chance of also introducing bacteria into the normally sterile uterine cavity. The woman's immune system will usually eliminate these bacteria, but a small risk of infection of the uterine cavity does still remain (<1/100). This infection is usually quickly healed with antibiotics. When serious pain and/or fever persists for more than 24 hours after an insemination, the patient must contact the doctor.



## In practical terms

As a rule, when starting an insemination cycle, the Fertility Centre must be contacted to make an appointment for the first ultrasound examination. This examination usually occurs on day 9, 10, or 11 of the cycle. If the growth of the follicles has not progressed far enough at that time, then a second ultrasound will be scheduled a few days later. When one or more mature egg cells are seen on the ultrasound, an injection is administered to the woman to ensure that the egg cells are released at the right moment. The actual insemination occurs 24 to 42 hours after this injection.

The day of the insemination can fall during the week or in the weekend and depends on the reaction of the ovaries, which cannot be precisely predicted. The sperm sample is generated at home in the morning via masturbation and is collected in a sterile plastic cup and brought in to street 7 within one hour of its collection. **Moreover, it is important not to allow the sperm sample to cool off during transport to the lab (keep inside the clothing or in an inside pocket, body temperature is ideal).** In order to ensure the best possible sperm quality, it is also best to respect a period of three to five days of sexual abstinence prior to collecting the sample. It goes without saying that **the cup must be labelled, using the pre-printed sticker that you will receive from us.** You will also receive the instructions related to collection and transport of the sperm sample as well as a collection cup when you make the insemination appointment.

The best sperm cells are then isolated from this sperm sample during processing in the lab, which takes approximately one hour and a half. After this processing, the prepared sample is introduced into the uterine cavity.

This procedure is usually performed between 10h30 and 12h00 in the Fertility Centre in street 7. The insertion of the catheter through the cervix is painless and occurs during a short gynaecological examination (comparable to taking a cervical smear). After the insemination, you must remain lying down for fifteen minutes. After that, you do not need any special rest, and therefore you may return to work as normal.

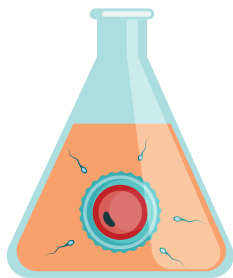
Approximately 14 days after the insemination, the result of the treatment can be determined. The most conclusive way will be to perform a pregnancy test (urinary or blood test) on the scheduled date, even if a bleeding starts. Indeed, a bleeding is not a 100% proof of not being pregnant, especially when the bleeding is minimal or if it is accompanied by more pain than normal. In particular, the possibility of an ectopic (extrauterine) pregnancy must always be kept in mind.

When it is clear that an actual menstrual period has begun and a pregnancy test is negative, this attempt has not succeeded unfortunately. A new attempt can be considered. The condition for this is that no residual follicles can be seen in the ovaries before starting hormonal stimulation. This is determined by a vaginal ultrasound. A residual follicle is nothing more than a follicle from which an egg cell has been released. When this (these) residual follicle(s) take(s) up too much space in the ovary, there is insufficient space for new follicles to grow, and you must wait for several days up to a whole cycle before restarting the procedure. This so-called 'start ultrasound' is only necessary when several follicles from the previous cycle matured simultaneously.



# In vitro fertilisation (IVF)

When intrauterine insemination fails to result in pregnancy or when the fertility problem is such that insemination has no chance of success, in vitro fertilisation can be the next step. In this treatment, sperm cells and egg cells are brought together outside of the body and the fertilised egg cells (embryos) are then transferred back into the uterus. Below you will find a short description of the most important steps in this procedure.



## 1. Stimulation of the ovaries

### The theory

The chance of success of an IVF treatment is determined in part by the number of egg cells that are obtained per treatment. To bring about the development of more than one egg cell (an average of ten), the ovaries must be stimulated. This occurs with the use of hormones (gonadotrophins), which have only a temporary effect on the body and which must be administered in the form of daily injections for a period of fourteen days. Adverse effects in the long-term are unlikely and, in any case, have not yet been determined. Usually this stimulation is combined with another type of injection which ensures that the growth of the egg cells is no longer controlled by feedback mechanisms in the body. Without the uncoupling of these mechanisms, the body would initiate ovulation at a certain moment before the ovarian punctures could be performed.

A (contraceptive) pill is usually taken for a period of fourteen days before the actual stimulation. The purpose of this is to ensure that the ovaries come to a basal state. The consequence of this is that a more even growth of the follicles (fluid-filled vesicles in the ovary which contain the egg cells) occurs. There is also another practical benefit to this method: the number of days that the pill is taken can be lengthened or shortened thereby shifting the estimated date of the ovarian puncture. This can be handy, for example, when one of the partners must travel abroad, to avoid family celebrations, to account for days when the lab is not open, to avoid excessive work load in the lab etc.

The stimulation process is followed by means of ultrasonography and with blood tests, if required. This is necessary in order to be able to monitor how many egg cells develop and, more importantly, to determine the moment of their maturity and fertility. Once the follicles have reached a diameter of approximately 20 mm, the final steps of egg cell maturation are initiated by means of a final hormone injection which also serves the purpose of preparing the uterine lining for implantation. This must occur at a specific, pre-scheduled time, because the ovarian puncture must occur between 35 and 40 hours after the injection. The injection is usually administered in the evening between 8 pm and midnight so that the ovarian puncture can be performed one day and a half later in the morning.

### In practical terms

When planning the treatment, the gynaecologist from the Fertility Centre will give you a request for reimbursement for six IVF cycles. You must submit this request to your Health Insurance Fund (mutualiteit), so that you can receive approval from the Health Insurance Fund (usually within 14 days) per post. You must bring the approval with you at the start of the treatment, since it is required for delivery of the medication. Before the beginning of the procedure, you will also receive a detailed stimulation schedule which includes all of the instructions you need



Vaginal ultrasound: Image of several mature follicles

to ensure that the stimulation goes smoothly. You will also receive the medication from the Fertility Centre. In principle, you should be prescribed sufficient doses of medication to ensure that you have enough to bridge any weekends.

Usually, the injections are started approximately five days after you stop taking the pill. You are free to choose who will administer the injections. You can do the injections yourself or you can call on an independent nurse, your general practitioner or a home nursing service via the Health Insurance Fund. It is best to have these injections in the evening. The exact time is somewhat less important (somewhere between 16:00 and 24:00). Only the final injection must be given at an exact time, since the scheduling of the ovarian puncture depends on the timing of this injection. Before the start of treatment, our midwives will provide you with the necessary explanation and instruction for providing yourself with subcutaneous injections.

The first ultrasound examination will occur after approximately one week of injections and will be scheduled when the stimulation schedule is made up. As you probably already know, the ultrasound is a painless, vaginal examination that only takes about five minutes to complete. On average, this examination must be performed two to three times during the two-week-long stimulation.



Take into account the fact that the non-refundable portion of the costs for the complete course of medication is approximately 55 euros (for patients covered by Belgian health insurance). You will receive an invoice at home from the hospital for this amount.

### In-vitro fertilisation:

Stimulation of the ovaries



Ovarian puncture



Processing of the sperm sample



Fertilisation in the lab



Transfer of the embryo

## 2. The ovarian puncture (follicular aspiration, pick-up)

### The theory

The ovarian puncture is the only step in the IVF treatment that requires a short hospital admission of a half day. During this procedure, a fine needle is inserted by way of ultrasound control through the wall of the vagina and into the follicles. The follicular fluid containing the egg cell is then aspirated into the needle. As a rule, this occurs under a type of anaesthesia called 'conscious sedation'. This means that you will receive an anaesthetic product via a drip that is a strong pain reliever and that may make you sleepy but is not a true anaesthetic (you will still be able to react when spoken to). General anaesthesia may be necessary in exceptional cases (for example, with difficult to reach ovaries). In these cases, the anaesthesia consists of a powerful, but short-acting narcotic administered under the supervision of an anaesthetist.

After the puncture, you will remain under medical supervision in our department for at least one hour to rule out any acute complications. The chance of complications however is very small. A small amount of blood from the follicle that is punctured is released into the abdominal cavity, which, by the way, also happens during natural ovulation. This small amount of bleeding however almost always stops by itself after the puncture. The point where the needle was inserted through the wall of the vagina may also bleed somewhat after the procedure. It is very rare (risk of less than 1/1000) that an infection occurs due to the puncture procedure. If fever occurs during the days following the puncture, this must be reported to the doctor.

### In practical terms

When the timing of egg cell maturation has been determined by way of ultrasound, the scheduling of the final injection is planned as is the scheduling of the ovarian puncture. The ovarian puncture is always performed in the morning, during the week starting from 8:00 and in the weekend usually a little later. **You and your partner must report to the central hospital admission 45 minutes before the scheduled time of the ovarian puncture. You may not have had anything to eat or drink since midnight of the previous night. On the day of the puncture, you must bring all of the completed and signed consent declarations and the reimbursement form with you to the Centre.**

The puncture procedure takes approximately one half hour. The partner may be present during the puncture, if you so choose. Before the puncture, the partner must generate a sperm sample. Depending on the time of the puncture, the place of residence of the patient and the preferences of the man, this sample can be generated in a room equipped for this purpose in street 7 (room 7) or at home.

After the identification of the egg cells and the preparation of the sperm, the egg cells and the sperm cells, together with the reimbursement form and the signed declaration of consent, are brought to the University Hospital in a sealed transport box. This transport box is a sealed case which is kept at a constant temperature by means of a heating element.





If you are in doubt about whether something is normal or not, it is best that you call the **Fertifoon: +32 (0)9 224 64 39**. This is a telephone number that you can use to contact the fertility team. In any case, your calling will never be held against you. The fact that you are concerned is sufficient reason to call, even if it just to hear a team member give you some assurance about your condition.

After the puncture, you must stay in the recovery ward in street 7 of the day clinic for one hour for observation before you are released to go home. The gynaecologist will come to see you to make sure there are no problems, to tell you the number of oocytes that have been recovered and to confirm that you may go home. Please note: because you have been given a form of anaesthetic, you may not drive a car for the rest of that day.

The day after the puncture, you will be contacted by the University IVF-lab to inform you about the fertilisation and to give you the appointment for the embryo transfer.

You may experience some vaginal bleeding during the first few days after the ovarian puncture. This is normal and usually stops by itself. This blood is coming from the points where the needle passed through the vaginal wall, and therefore has nothing to do with the place to where the embryos will be transferred.

Slight to moderate abdominal pain, to a certain extent, is a normal consequence of the puncture. You may definitely take pain relievers for this pain (preferably paracetamol: e.g. Perdolan®, Dafalgan®). The more egg cells that were collected, the greater the swelling of the ovaries and the more pain you can expect in the lower abdomen. These complaints might get stronger in the evening, especially the first day, since the effect of the pain relievers you were administered for the puncture will have stopped by then.

During the puncture, a needle must pass from the non-sterile zone (the vagina) to a sterile zone (the abdominal cavity). In doing so, it is unavoidable that bacteria end up in this sterile zone. Normally, the immune system of the woman is able to eliminate these few bacteria, but in some rare cases (risk of less than 1/1000) they may cause an infection. If the patient develops a fever ( $> 37.5^{\circ}\text{C}$ ) in the first days following the puncture, the doctor must be notified. In exceptional cases, this infection will require treatment with antibiotics or require surgery (keyhole surgery or laparoscopic surgery).

### 3. The processing of the sperm sample



#### The theory

On the day of the ovarian puncture, the partner's sperm is carefully prepared in the laboratory. The preparation ensures that the sperm is separated from harmful substances and dead or weak sperm cells.

It goes without saying that all of the laboratory technicians and embryologists from the Fertility Centre at AZ Sint-Lucas and the Department of Reproductive Medicine at the UZ Gent realise the grave importance of working as precisely and carefully as possible to avoid the mixing up of samples. A number of strict guidelines, which are consistently followed in the laboratory, have been established for this purpose.

In some cases, the sperm sample will not contain any sperm cells (azoospermia). A possible cause of this condition is the blockage of the semen discharge tracts after an infection or after a vasectomy (= sterilisation of the man), or the condition can be congenital. In other cases, the testes either produce no sperm cells or too few sperm cells. Before treatment, the precise cause must be determined via specific examinations and tests. For this, the male patient may be referred to dr. Jeroen De Smet.

When azoospermia exists due to a past vasectomy, dr. De Smet will discuss with the patient whether it is worthwhile to consider a vasovasostomy. This is a microsurgical procedure that reverses the effects of a vasectomy. This intervention is performed by one of our urologists. The results of this surgical procedure depend on various parameters, such as the number of years between the vasectomy and the planned repair and the length and the localisation of the piece of the seminal duct that was removed, among others. After the reparative surgery, living sperm cells are once again found in the ejaculate of 70-95% of the patients. Spontaneous pregnancies can be achieved in 30-75% of these couples.



The longer the interval is between the vasectomy and the planned repair, the lower the chance of successful results. That is why the chance of pregnancy falls to 30% if the obstructive interval is longer than 15 years. Female fertility declines gradually after the age of 35. Because it takes an average of 12 months to become pregnant after a successful vasovasostomy, the repair is usually not recommended if the female partner is older than 37 or if there are also female fertility problems present. In those cases, it is usually recommended that the sperm cells are collected using TESE (see page 15) so the cells can be frozen with the intention of using them later in an ICSI procedure. In consultation with the patient, this procedure can sometimes be performed at the same time as the vasovasostomy, just in case the repair is not successful. In cases where there is an obstruction at the level of the prostate, an endoscopic procedure (via the urethra) can open up the seminal colliculus. After this procedure, sperm cells appear in the ejaculate in 50-75% of the patients and pregnancy is achieved in 25% of the couples.

When surgical repair of the discharge disturbance is not possible, or when the testes produce so few sperm cells that no living cells can be found in the semen, living cells can often be found (in 50% of the cases) in the testicle. In order to be able to recover these sperm cells, one or more small pieces of tissue must be taken from the testicle (TESE or testicular sperm extraction). The procedure for obtaining sperm cells in this way is usually performed before the start of the IVF/ICSI procedure. The sperm cells collected in this way are then frozen and stored for later use once the egg cells are available. The frozen sperm cells do not always survive after thawing. When too few sperm cells are present and there is the risk of an insufficient number of them surviving the freezing and thawing procedures, the performance of the TESE procedure on the day of the ovarian puncture is an option. This way 'fresh' sperm cells can be used immediately. Fertilisation and pregnancy can be achieved after ICSI with sperm cells from TESE just as easily as with sperm cells collected after ejaculation.

The method of fertilisation of the egg cell that is ultimately chosen (IVF or ICSI; see page 16-17) depends on the quality of the sperm sample and, in principle, is determined ahead of time.

### In practical terms

On the day of the ovarian puncture, the sperm sample is usually produced at home just before leaving for the hospital. **When doing so, though, care must be taken to keep the sperm from cooling down during transport to the Centre (for example, keep it in the inside pocket of your jacket so that the sample remains at approximately body temperature). It goes without saying that the cup must be labelled, preferably with the name of the woman, using indelible marker or via the preprinted sticker that you will receive from us.** In case the transport of the sample would take more than one hour, it will be possible to produce the sample in the Fertility Centre, in a room specifically designed for this purpose.

If the quality of the sperm is very low (concentrations lower than 1 million per millilitre) or if a real risk exists that the production of a sample 'on command' on the day of the ovarian puncture will be a problem, then we advise that a sperm sample is generated ahead of time and frozen. This occurs in the IVF lab in the UZ Gent and the appointment for this must be made there. Regardless of the method chosen ahead of time, on the day of the puncture a fresh sample will be requested (since the quality of a fresh sample is generally speaking better than a thawed sample), although the realisation that 'there is a back-up supply just in case' is usually enough to make the production of a fresh sample just that much easier.

### TESE (testicular sperm extraction)

A TESE procedure is a minor procedure which will be performed under a short-term general anaesthetic. This procedure is performed in the day clinic of AZ Sint-Lucas. The tissue that is removed is sent in a special box kept at body temperature to the IVF lab in UZ Gent. This lab will send a fax the same day stating whether or not usable sperm cells were found in these tissues. When good sperm cells are found, the pieces of tissue will be frozen for use in a later ICSI procedure. The pain after the operation can usually be adequately relieved with an aspirin or a paracetamol tablet. The entire procedure requires temporary work incapacity of two days.

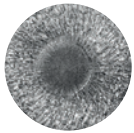


A vasovasostomy (reversal of male sterilisation) occurs under general anaesthetic during a short hospital admission of two to three days. In this case, the incapacity to work lasts for one week. The procedure is reimbursed by RIZIV (the Belgian National Institute of Sickness and Invalidity Insurance).

The freezing of sperm cells, the examination of the testicular biopsies for the presence of viable sperm cells and the freezing of these testicular biopsies carries extra costs which are not eligible for reimbursement.







Egg cell before fertilization



Egg cell after fertilization with two pronuclei



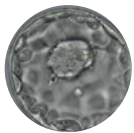
Embryo of good quality (4-cell stage)



Embryo of lesser quality (more fragments)



Early blastocyst (moderate quality)



Expanded blastocyst (good quality)



Hatching blastocyst (excellent quality)

## 4. What happens in the IVF lab?

### The theory

After the ovarian puncture, the vials in which the egg cells are kept are immediately sent to the lab and the highly mobile sperm cells are added to them. The egg cells, together with the sperm cells, are placed in an incubator at body temperature and at a set relative humidity and CO<sub>2</sub> concentration.

One day later, the cells can be examined microscopically to determine whether or not they have been fertilised. Fertilisation is the fusion of a sperm cell with an egg cell. At that point, a fertilised egg cell has not yet divided but contains two pronuclei, which are visible under the microscope. Each pronucleus contains the genetic material of the woman or the man.

From day 2, the cells start to divide and if all goes well, the embryo develops from 2 to 4 to 8 cells, up to the blastocyst stage on day 5 (a group of approximately 50 cells surrounding a cavity). Each embryo will be scored for quality, which will enable the laboratory to select the embryo with the very best chances for success.

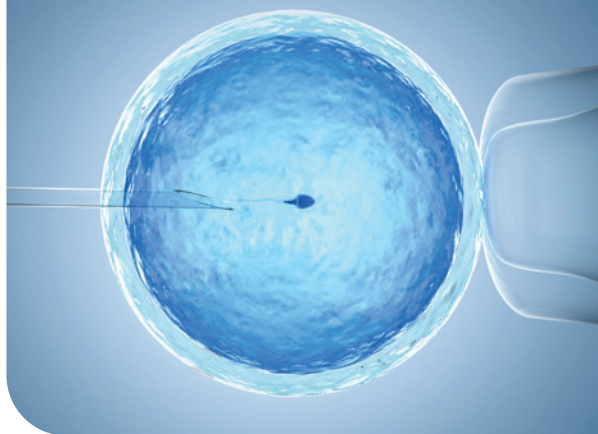
It is important to realise that embryo development from fertilisation till the blastocyst stage is not always optimal. The embryos go through some kind of a "last-man-standing" contest: some of them will develop well, others will fragment, others will arrest at a certain stage. This is not due to the fertility problem, but in fact is proper to the human species in general. Outside of an IVF context, we do not realise ourselves this is happening: a natural cycle, not leading to a pregnancy might have been a cycle where an embryo was formed, but where the embryo did not develop further. On average, one third of the embryos on day 5 will be usable (to transfer or to freeze). We should therefore take the possibility into account that no embryo is available to be transferred on day 5. This probability is higher when there is a low number of oocytes to start with. The good news

is that if we have embryos to be frozen, they represent a realistic chance of success: on average 40% per embryo (between 15 and 50%, depending on the embryo quality, age of the woman, etc ...). Embryo transfer will be performed on the fifth day after the puncture.

When pregnancy is achieved after the implantation of less than ideal embryos, the result of the pregnancy and the health of the child are as just as good as after the implantation of a 'perfect' embryo. The quality of the embryo is therefore not related to whether or not the child will be normal. Embryos of lesser quality will have a lower chance of leading to a pregnancy, and a somewhat higher risk of miscarriage.

### In practical terms

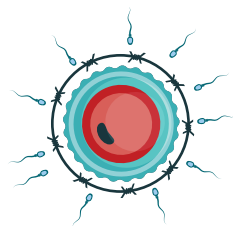
The day after the ovarian puncture, the IVF laboratory will contact you to tell you the result of the fertilization procedure (the number of embryos) and to make an appointment for the actual embryo transfer. In case there would be no embryo available for transfer, the laboratory will contact you on the day of the transfer, in order to avoid that you present yourself in vain for the transfer. In this case, you will be given an appointment for discussion of the results. This does not mean that your case is hopeless.



## 5. What is ICSI and when is it needed?

### The theory

Normal sperm cells are equipped with natural mechanisms that allow them to penetrate the egg cells, while the egg cell makes sure that only one sperm cell is allowed to enter. In a number of cases, fertilisation fails to occur because the sperm cells are not present in great enough numbers or because they are too weak to penetrate through the egg cell membrane. In rare cases, the failure of the fertilisation can be caused by an egg cell membrane that is impenetrable to sperm cells.



Several years ago, a method was developed which allowed one sperm cell to be picked up with a microscopically fine needle and to inject it directly into the egg cell (intra-cytoplasmic sperm injection, shortened to ICSI). ICSI results in the fertilisation of an average of 75% of the injected egg cells, regardless of the quality of the sperm sample and even when fertilisation was not achieved with traditional IVF. The reasons that 25% of the egg cells cannot be fertilised with this method include the following: immature egg cells, abnormal egg cells, damage to the egg cell during injection or defects in the sperm cell.

Once fertilisation has occurred, the chance of pregnancy is the same as after a regular IVF treatment. The ICSI technique will only increase the chance of fertilisation if the results of the traditional IVF were less than ideal, and therefore it is by no means a guarantee of pregnancy. When traditional IVF results in good fertilisation, there is no reason that ICSI will provide better results.

The ICSI method can even be considered in the case of sperm samples which do not contain even one normally

formed sperm cell. When sperm cells do not appear normal on a microscopic level this usually has no relationship to the genetic contents of the sperm cells.

Initially, it was feared that the elimination of a natural selection process among the sperm cells used in ICSI would bring with it many risks (after all, it is the lab technician who decides which sperm cell should fertilise which egg cell).

From the numerous pregnancies which up until now have been achieved using this technique, it appears that this fear is largely unfounded. There is a slightly increased incidence of genetic abnormalities in children born after ICSI, with, in particular, sex chromosome defects occurring somewhat more frequently after ICSI. By somewhat more frequently, we mean that the risk increases from 1 in 500 to 1 in 200, which also means that in 98 to 99% of cases everything is normal. It is also worth asking whether this risk is caused by the ICSI procedure itself or by the predisposition of the group of people for whom ICSI is necessary to achieve pregnancy.

In addition, there is a chance that the fertility problem is passed along to future sons via the ICSI treatment. These children, just like their father before them, are otherwise perfectly healthy. The couple can decide for themselves whether this is an impediment to the continuation of the treatment. Genetic testing should be able to predict the chance of passing along the fertility problem to a son. Yet, a positive genetic test is still not a guarantee that there is no hereditary factor present, since there are genetic defects that cannot yet technically be detected.

When there are no sperm cells present in the semen because the man has no vas deferens (tube through which the sperm leave the testis), more extensive genetic testing is indicated. Indeed, the absence of the vas deferens can be congenital and can also be the only indication that the man is a 'carrier' of the disease called mucoviscidosis or cystic fibrosis. When the man is a carrier and the woman is also a carrier, then the couple has 1 chance in 4 of having a child with mucoviscidosis

after ICSI. Given that mucoviscidosis is a disorder that has a significant influence on the life expectancy of the child, it is important to determine whether or not the parents are carriers before the start of an ICSI treatment. For the sake of clarity, we repeat once again that this is not the case in every ICSI treatment but only in cases where the man has no vas deferens. There is less experience with children born after ICSI with sperm cells obtained by MESA or TESE. Up until now, research has shown that, just as in ICSI with ejaculated sperm cells, the chance of new genetic defects is only increased slightly and is primarily related to the characteristics of the persons using the technique rather than to the ICSI technique itself.

### In practical terms

There is no significant difference for the couple between the practical steps of a traditional IVF treatment and those of an ICSI attempt. The only difference lies in what occurs in the lab.

Sometimes it can be that the quality of the sperm on the day of the ovarian puncture is so poor that only an ICSI offers a real chance of fertilisation, even though a traditional IVF was originally planned. Often, as a first course of action, a second sperm sample will be requested in the hope that it will be better. If that does not turn out to be the case, then, in the hours following the ovarian puncture, the IVF laboratory will consult with the treating fertility doctor about whether or not, due to the extremity of the case, the ICSI procedure should be followed instead. The number of oocytes available could also influence the choice.

When it is known ahead of time that the sperm are a 'borderline' case for traditional IVF, a decision can be made beforehand to split the egg cells into two groups, one group to undergo traditional IVF and the other ICSI. This allows the simplest technique to be attempted, while eliminating the risk that none of the egg cells will be fertilized with this sperm sample.

## 6. Embryo transfer

### The theory

In the vast majority of IVF cases (85%), we replace one single embryo. Since embryo culture has been extended to day 5, embryo selection has been improved significantly. As a result, the success rates per embryo transfer have increased up to 40%. Moreover, spare embryos can be frozen efficiently, which offers extra chances.

In cases of repeated failures, in women with advanced age and when the embryo quality is less good, the transfer of two embryos might be considered. If you know that a twin pregnancy entails many more risks for both the mother and the children, it becomes clear why we try to avoid multiple pregnancies.

Since the reimbursement of the IVF laboratory expenses by the Belgian Health Insurance Fund began, the maximum number of embryos to be transferred has been established by law. The numbers established for fresh transfers are listed in the table below. Take notice of the fact that the maximum number of embryos allowed to be transferred is not always similar to the optimal number or medically justified number to be transferred (rather one single embryo in 85% of the cases). The final number of embryos to transfer will be decided at the moment of transfer, since the embryo quality will only be known by then. This will be a common decision made the gynaecologist together with the couple and the laboratory. Of course, a couple can always decide to replace less than the number proposed by the gynaecologist and the laboratory.

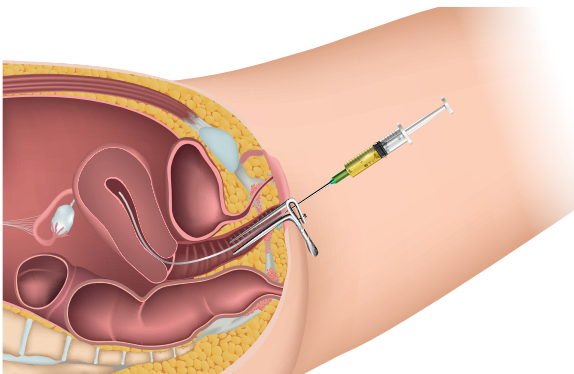
Woman < 36 years of age	
1 <sup>st</sup> attempt	One embryo
2 <sup>nd</sup> attempt	One embryo (unless insufficient embryo quality: then two)
3 <sup>rd</sup> to 6 <sup>th</sup> attempt	Maximum two embryos
Woman between 36 and 40 years of age	
1 <sup>st</sup> & 2 <sup>nd</sup> attempt	Maximum two embryos
3 <sup>rd</sup> to 6 <sup>th</sup> attempt	Maximum three embryos
Woman of 40 years of age onwards	
1 <sup>st</sup> to 6 <sup>th</sup> attempt	No maximum established

### In practical terms

**The embryo transfer occurs in the IVF laboratory of UZ Gent so that we can place the embryos directly from the incubator into the uterus without having to transport them. The transfer in UZ Gent is performed by the fertility doctor from AZ Sint-Lucas so that you will see a familiar person while you are there.**

The transfer itself is a simple procedure which does not require hospital admission or anaesthetic. The embryos are gathered up from the laboratory dish in a fine catheter or tube and are transferred to the uterine cavity via the cervix. For the woman, this procedure is comparable to having a cervical smear or to an insemination. The transfer is performed under abdominal ultrasound monitoring. Therefore it is best not to go to the toilet just before the transfer. A full or half-full bladder is ideal for smooth insertion of the catheter into the uterine cavity.

You may get up immediately after the transfer.



## 7. After the transfer

After the transfer, we can do very little to influence the chance of pregnancy. We do prescribe medicine to support the lining of the uterus, but other than that, it is primarily a question of being patient for 14 days until the final result can be known.

It is important that you also realise that there is nothing else you can do at this point to change the outcome. In particular, it is not worthwhile to get extra rest, to avoid physical exertion, to abstain from sex or to adhere to specific dietary rules. Doing these things would only make the fertility treatment more complicated and more stressful than it already is, without having any proven effect on the final result. At first glance, these measures could seem inoffensive, but from a psychological point of view, this is not always the case. Indeed, if the treatment was not successful, certain patients try to find an answer to the question why this was the case. They sometimes tend to link the negative end result with these self-imposed extra rules, supposing these were still not strict enough. Doing this, the couple ends up in a vicious circle of guilt feelings which, in turn, can become so difficult to bear that further IVF ultimately becomes intolerable. It is however recommended to 'take it easy' after a transfer when the ovaries are still quite swollen (high number of egg cells). The goal of this is not so much to influence the chance of pregnancy but to ensure that you do not experience too much pain in the abdomen.

The period after the transfer is perceived by the majority of the couples as the most nerve-racking episode of the IVF treatment. The best way to somewhat reduce the psychological load of this period is to live as 'normally as possible' and to keep the IVF from disrupting your daily activities.

Whether or not pregnancy occurs depends mainly on the quality of the embryos, which in fact cannot be influenced. The implantation must be regarded as an active process, the most important steps of which originate from the embryo itself. So when an IVF attempt is not successful, this can be attributed in most cases to natural selection and is purely a question of chance (being lucky or unlucky).

## 8. The result: pregnant or not?

The date on which the result can be determined is arranged at the time of the transfer. A blood test will usually be performed on the day you come for the result. 'Being late' in and of itself is not reliable proof of pregnancy and vaginal blood loss can also not be considered proof of a failed attempt, although this is a sign that the chance of a normal pregnancy is somewhat reduced. Taking a urinary pregnancy test is usually not advised since the medication you received during the IVF treatment can cause false results. Therefore, in every case, a blood test must be performed after an IVF cycle in order to be certain about the final result. The blood test results will usually be given to you via telephone the same day.

Some people wonder whether a menstrual period will occur when one of the embryos becomes implanted and the other one does not. This will not happen because the menstrual period is not a direct result of an embryo that does not implant but of the breakdown of the uterine lining that is no longer supported hormonally when no implantation (of one or more embryos) has occurred.



### What is the chance of pregnancy?

Based on the figures gathered from the cases in our centre, we can say that globally speaking your chance of achieving pregnancy is 30% per puncture and 40% per transfer. In each individual case, this chance is determined by the age of the woman, the number and quality of the egg cells and the quality and the number of the embryos transferred. Yet, it is extremely difficult to determine beforehand exactly what the personal chances are in each individual case. Initially the chance of success might not seem very high. Yet you must realise that even in cases where there are no fertility problems, the chance of spontaneous pregnancy is 'only' 20% per cycle. Furthermore, 30% per cycle is a significant improvement over the maximum 5% chance of pregnancy per cycle without further treatment. Incidentally, a 30% chance of pregnancy per cycle means that the chance of pregnancy is 66% over three attempts.

If pregnancy has still not been achieved after six cycles, which luckily is only the case in 15% of the couples, then the case can be individually evaluated as to whether the chances remain high enough to continue treatment. Naturally, in these cases, the attitude of the couple will be of decisive importance because, medically speaking, the chances can never be said to be reduced to zero. As long as embryos are transferred, there is a possibility that one of them will succeed in becoming implanted. Whether the chance of pregnancy is great enough to justify the efforts and investment (on the physical, psychological and financial levels) is a personal matter over which the couple themselves must decide. Medical and non-medical aspects must then be considered in conjunction with one another, for we do not want to become entangled in a situation driven by irrational persistence.





## 9. Freezing of embryos (cryopreservation)

### The theory

When one or more good-quality embryos are left over after an embryo transfer, the possibility exists to freeze it/them. Freezing occurs on day 5 in the IVF lab of UZ Gent; each embryo is frozen individually. This will only occur with the written consent of the couple (see declaration of consent for the freezing of embryos). If the embryos are of insufficient quality and therefore do not have a chance of resulting in pregnancy, we then, of course, let nature take its course. That way they will not develop further and die naturally. On average, one embryo on four is of sufficient quality to be frozen. Therefore, bear in mind that there is a realistic chance that no embryos will be available to be frozen. In these cases, we can of course consider a new treatment with stimulation and puncture.

After thawing, an average of 90% of the embryos survives. The other 10% are so fragmented after thawing that they have no chance of resulting in pregnancy. There is a wide distribution around this average, which means that in some cases all of the embryos survive after thawing, and in some cases not one single embryo survives thawing. As a rule, only one embryo is thawed at a time. When immediately after thawing it appears that the embryo has not survived, a second embryo is thawed.

The chance of becoming pregnant after the transfer of thawed embryos which are still viable is approximately 35%. Therefore the results are comparable to a 'fresh' transfer. This must be seen as an extra chance on top of the chance offered by the IVF cycle and one which requires relatively little effort. Since, in fact, no additional

stimulation or ovarian puncture is needed. In addition to this, the transfer of frozen embryos does not count as a cycle in the official count of the number of reimbursed attempts. A new attempt is only counted as such when all of the embryos resulting from a fresh cycle are completely 'used up'.

### In practical terms

The number of unused embryos that can be frozen can be determined on day 5 after the ovarian puncture. Embryos will only be frozen if the consent form is present in the patient file. If a pregnancy is achieved after the transfer of fresh embryos, then the remaining embryos remain frozen for a period of 5 years, as agreed upon in the contract. Do not forget to request an extension of this agreement, if necessary, before this period elapses. Without this extension, the embryos will be subject to the outcome agreed upon in the contract. If no pregnancy results after the fresh transfer, then the frozen embryos must be transferred first.

If a regular spontaneous cycle occurs, then no medication must be taken for this. Usually, though, medication is necessary if no spontaneous ovulation occurs. The first cycle after a fresh attempt is always a rest cycle, given that it may be disrupted by the after effects of the medication administered during the previous attempt. The second cycle after a fresh cycle can be used for the transfer of frozen embryos, just as the following cycles can. The monitoring of such a cycle is usually limited to a couple of ultrasounds after which the thawing and possibly the transfer are scheduled. The possibility that none of the thawed embryos is good enough to be transferred must always be taken into account. This means that the IVF lab will always call the patient on the day of the transfer to confirm the fact that the transfer can take place.

Before freezing the embryos, a **consent form for freezing of embryos** must be signed by both partners at the latest on the day of the puncture. This contract also regulates the outcome of the embryos in the long-term and in exceptional circumstances (divorce, death of one of the partners). For each transfer of frozen embryos, a new written consent should be signed by both partners before thawing.



### What is the cost of an IVF treatment?

Not all fertility treatments are covered by the compulsory health insurance in Belgium. For the most part, the following items are reimbursed: consultations during the treatment, ultrasonography for the monitoring of a stimulation, blood tests, the ovarian puncture, the majority of the medication needed for the stimulation of the ovaries and the laboratory costs for a standard IVF or ICSI treatment (age of the women less than 43 and a maximum of 6 attempts).

The total amount of the non-refundable portion for check-ups, blood tests, medication, the hospital stay for the puncture and the transfer lies between 150 and 200 euros (for patients covered by the Belgian National Health Service).

You can recuperate the non-refundable portion of the costs of the hospital stay for the ovarian puncture via some hospitalisation insurance policies. However, these policies often stipulate that fertility treatments are exempt from reimbursement. If you have supplemental hospitalisation insurance coverage, we advise you to take a look at the detailed policy information to see whether or not you can recuperate these expenses in this manner.

If you can, then please bring the hospitalisation insurance claim form with you on the day of the ovarian puncture so that the gynaecologist can fill it out.

There are extra costs for services that are not considered part of a standard IVF procedure, such as the freezing of a sperm sample, the analysis and freezing of testicular biopsies, pre-implantation genetic diagnoses (see further on) etc.

The costs for the cycles which are not reimbursed (> 6th cycle and/or older than 43 years of age) amount to approximately 2600 euros (laboratory costs + cost of medications).

Foreign patients must pay for the treatment in advance. You will be informed of the specific conditions for these cases in advance. You will also be provided with a receipt for each payment made so that you have the possibility of submitting them to the health insurance in your own country.

## 10. The course of an IVF pregnancy

The course of a pregnancy achieved after IVF or ICSI is almost just like that of any other pregnancy. Yet, we would like to draw your attention to a few important points.

### Blood loss during the first months of the pregnancy

Blood loss during the first weeks of these pregnancies occurs slightly more often than it does in spontaneous pregnancies. An ultrasound examination can clarify the meaning of this blood loss. In most cases, this blood loss is not a threat to the pregnancy and is a result of the so-called implantation bleeding. The chance of a miscarriage after IVF however is somewhat higher than after a spontaneous pregnancy.

This is probably not so much a result of the IVF procedure itself but more likely due to the fact that people with fertility problems are more at risk of miscarriages than others, regardless of the method used to become pregnant. Furthermore, with fertility treatments we are monitoring the pregnancy right from its inception so that very early miscarriages are also detected. This is not the case in spontaneous pregnancies. In those cases, this type of bleeding is not interpreted as a miscarriage but as a late menstrual period. Therefore the number of miscarriages recorded in non-fertility treatment cases is likely underestimated.

### Ectopic pregnancy

If a woman becomes pregnant after IVF treatment, the chance of an extrauterine pregnancy is approximately 5%. The risk is higher than in spontaneous pregnancies, in particular because people who undergo IVF already have damaged Fallopian tubes, which increases the risk of ectopic pregnancy.

It sounds incredible that even after the transfer of embryos to the uterus, extrauterine pregnancies can occur. The reason for this is that contractions of the uterine muscle can cause the embryo to be moved outside of the uterus. The common term used for embryo transfer is often 'implantation', which sounds as if the embryos attach themselves to the inside of the uterus. However this is by no means the case. During trans-



fer, the embryos are introduced unattached to the uterine cavity. This cavity continues through to the Fallopian tubes, which means that the embryos are able to change location to a certain extent.

Through careful hormonal and ultrasound monitoring, the diagnosis of extra-uterine pregnancy is usually made very quickly, enabling it to be treated in time. This treatment usually occurs via laparoscopy ('key-hole surgery through the navel').

### Multiple pregnancy

As mentioned above, there is still currently approximately a 5 to 10% chance of a multiple pregnancy after IVF. Of course, the ideal situation is to prevent a multiple pregnancy by limiting the number of embryos per transfer.

When, in spite of this, a multiple pregnancy occurs, the pregnancy must be very carefully monitored. A multiple pregnancy, in fact, has a number of extra risks associated with it: the risk of miscarriage, of premature dilation and premature birth, of slowed development and low birth weight, of high blood pressure ... If it becomes necessary, your gynaecologist will discuss each of these risks in detail with you.

What does occasionally occur in multiple pregnancies is that one of the implanted embryos dies or stops developing during the first trimester; this is then considered to be a partial miscarriage. This may or may not be accompanied by vaginal blood loss, which does not mean that the other foetus is also lost.

## Complications associated with fertility treatment

### Ovarian hyperstimulation syndrome

The number of egg cells that can be brought to maturity per cycle varies greatly from individual to individual. The optimal number of egg cells is between 10 and 20. In some cases, the ovaries react insufficiently which can influence the result of an IVF treatment. In other cases however the reaction of the ovaries is unexpectedly strong and 30 to 40 egg cells are developed. As a result, after ovulation and egg cell pick-up, the ovaries can swell and produce fluid that accumulates in the abdomen. In most women this will cause only temporary swelling and some abdominal pain. In rare cases (1 on 500) this condition causes an enormous shift in the fluid balance of the body which may require treatment in a hospital. The most significant symptoms at that point are swelling and pain in the abdomen, shortness of breath (especially when lying down), dizziness, stomach pain, nausea and heart palpitations. The treatment for this consists of bed rest, intravenous administration of protein-rich fluid and, if necessary, the removal of excess fluid from the abdominal cavity. Even though a hospital admission of one to two weeks may be necessary, the hyperstimulation syndrome will have no adverse effects on the health of the woman or the foetus, as long as its treatment occurs under medical supervision. A comparable, yet less severe phenomenon can result in a weight gain of several kilos due to the accumulation of fluid during IVF stimulation. This is normal and since the weight gain is due to fluid as opposed to fat tissue it disappears again after treatment.

### Multiple pregnancy

Although some couples hope for a twin pregnancy and most couples would also thankfully accept one, we would like to take this opportunity to explicitly caution against excessive optimism and enthusiasm in relation to multiple pregnancy. Without a doubt, multiple pregnancy is still the most significant complication of IVF treatment. Apart from the burden for the woman during the pregnancy itself and the socio-familial burden after the birth, there is the medical risk for the children themselves. For example, we know that the chance of losing one or both children from a multiple pregnancy is five times higher than in a single pregnancy, primarily as a result of pre-mature birth. This risk becomes even more pronounced in the case of triplet pregnancies. Pre-mature birth and low birth weight can have lifelong consequences on both the physical and the mental health of the children. The risk is so high that an embryo reduction is proposed in cases of triplet pregnancy.

# Insemination with donor sperm

Previously, insemination with donor sperm was proposed as a possible treatment for infertility when the man either had no sperm cells or when the quality of the sperm cells was so poor that pregnancy with partner sperm was effectively ruled out. Thanks to the development of ICSI and TESE, it occurs only very rarely that this treatment must be considered. In other more rare cases, insemination with donor sperm can be indicated to prevent hereditary disorders in the child. It goes without saying that a treatment like this is only elected after thorough deliberation and counselling and only upon the explicit request of the couple.

Donor inseminations can also be performed for lesbian couples as well as for single women who wish to have children. In the latter case, this is only possible with prior approval after thorough evaluation of the request.

The inseminations usually occur during a spontaneous cycle. The fertile moment is determined by way of urinary ovulation tests, ultrasound and/or hormonal (blood) tests. When pregnancy fails to occur after three to six cycles, further fertility testing is performed. If no abnormalities are found, the inseminations are resumed. Sometimes, in order to increase the chances of pregnancy, the egg cell maturation process is slightly stimulated with Clomid®, and ovulation is induced with an injection of Pregnyl®. The same procedure is used when ovulation is not forthcoming or when the moment of ovulation is extremely variable. To keep the number of twins and triplets to a minimum, no insemination is performed if there are more than three mature follicles.

## The donor

If this method also fails, the treatment method can be shifted to IVF with donor sperm upon the request of the couple and after twelve insemination attempts.

The sperm that is used for donor insemination originates from healthy donors with normal sperm quality. It is preferable to use donors with proven fertility (read: the donor himself already has healthy children). This sperm is frozen and only used after it is unequivocally established that the donor is not a carrier of HIV, syphilis or the hepatitis B or C virus. In addition, there can be no question of any hereditary disorders in the donor's family and the donor himself may not have had any serious health problems in the past (for example, cancer or psychiatric disorders). The donor is subject to urological and psychological tests, so that we are convinced of his good health, both physical and mental.

Obviously, donor insemination is not only a medical matter but affects both partners on all levels of their personal life and their relationship. Not only must the fertility problem itself be worked through in this case but also, more importantly, the realization that in order to come to a solution another party (the donor) must be involved. Therefore it is also necessary to spend adequate attention on this process and to provide specific psychological guidance for it.

There is a specific information brochure available which contains detailed information about donor insemination.

# Egg cell donation

The indications for requesting egg cells from another woman in order to achieve pregnancy are:

- a congenital absence of egg cells,
- premature menopause (premature loss of the reserves of egg cells),
- deformities of the egg cells which result in infertility,
- hereditary considerations,
- repeated poor embryo quality with IVF or ICSI with own egg cells.

The age limit for receiving donor egg cells in our centre is 45 years of age.

In contrast to the donation of sperm, egg cell donation is an invasive procedure. After all, the donor must undergo hormonal stimulation and an ovarian puncture. It is for this reason that the supply of egg cell donors is extremely limited. Although it is rare that a patient must resort to egg cell donation, the demand for donor egg cells is substantially larger than the supply. There is a waiting list for egg cell donation. At this time, the waiting time is one to one and a half years. And, unfortunately, you cannot be placed on the waiting list once you have reached the age of 40.

You can be helped by this method much sooner if you find a donor yourself. This is also the only possibility for patients over 40 years of age. The donor must preferably not be older than 35, already have a complete family, be free of hereditary and infectious diseases and be willing to go through an IVF procedure. When two or more couples who are eligible for egg cell donation have found a donor, the egg cells from that donor can be exchanged for the egg cells of another donor who is anonymous to the recipients. This is called exchange donation and ensures that anonymity is maintained. If a woman is eligible for egg cell donation, she will first,

together with her partner, have to have a comprehensive interview with a psychologist.

If you become pregnant after treatment with us or somewhere else or if you are older than 40, your name is removed from the list, and you must submit a new request if you would like to try again.

In addition, every couple that starts an IVF treatment in our centre and from whom we expect a moderate amount of egg cells is presented with the option of voluntarily donating extra egg cells for anonymous donation.

Although legislation regarding donation explicitly forbids the donor from asking for monetary compensation for the donation, this does not mean that the egg cells are free. The treatment of the donor, after all, must be paid for. On the one hand, this includes the cost of the treatment itself and on the other hand the expenses that the donor incurs in the process (consultations, travel expenses ...). For these expenses, the egg cell donor receives reimbursement.

It has recently become possible to freeze unfertilised egg cells using the so-called vitrification technique. This technique makes it possible to store the cells for a longer time in a cell bank. This also means that it is also no longer necessary to use fresh egg cells for an egg cell donation treatment. This makes the logistics of an egg cell donation treatment considerably easier than before, since the treatment of the donor no longer must be synchronized with the treatment of the recipient.

For more information about egg cell donation, we refer you to the specific information brochure on this topic.

# Medical precautions

## General health

- It goes without saying that a healthy lifestyle which includes sufficient physical activity, a balanced diet and good sleep habits is important for the general health. These conditions also form the optimal conditions for becoming pregnant. **The use of alcohol must be limited.**
- **Smoking** has a negative effect on fertility (in both men and women). Research has shown that the chance of achieving pregnancy after IVF in smokers is approximately 50% less than in non-smokers. Smoking is harmful to the unborn foetus, and the combination of smoking with elevated hormone levels increases the risk of thrombosis. We therefore emphatically advise smokers to quit smoking before initiating treatment. For help with this, you can turn to the stop-smoking programme of Sint-Lucas (simply request the brochure).
- **Obesity** is also a factor with a clearly negative effect on the chances of success of a fertility treatment, and it also brings with it high risks for the health of the child. The supervision of a dietician can definitely be helpful.
- It is the responsibility of the woman to also continue to go to her **gynaecologist for her annual check-up** throughout the course of the fertility treatment. This check-up will not be performed by the gynaecologist who supervises the fertility treatment. And if a general gynaecological problem arises during the fertility treatment (lump in the breast, vaginal infection, ovarian cysts), you will have to go to your general gynaecologist for treatment.

## Screening for infections in both partners

Both for the couple as well as for the personnel who will come in contact with your blood, sperm cells and egg cells, it is necessary to know whether this biological material is free from infection with HIV, syphilis and/or the hepatitis B and C virus(es). For this reason, a blood sample will be taken from both partners before the start of the treatment for the purpose of detecting the presence of the aforementioned, infectious diseases. If necessary, this examination will be repeated annually. In the event that the man is a carrier of the hepatitis B and/or C virus(es), no ICSI treatment can be performed. The reason for this is that the theoretical possibility exists that virus particles, which can be attached to a sperm cell, can be injected into the egg cell via the ICSI procedure. This may have negative consequences for the health of the child.

## Whooping cough vaccination

Whooping cough (or pertussis) is a serious, infectious disease of the airways that can potentially be dangerous for babies and young children. It is caused by a bacterium that is transmitted via small droplets generated when coughing or sneezing or via the hands. The whooping cough vaccine protects you against the disease and prevents you infecting others (including babies). The protection provided by the whooping cough vaccine is not permanent. If you were vaccinated a long time ago, you can become infected and transmit the disease to others. In order to prevent that you, as an adult, infect babies with whooping cough, a so-called booster vaccine is recommended for all future parents. To get this vaccine, it is best that you contact your general practitioner.

## Genetic testing

When there is a suspicion that one of the two partners has a genetic abnormality, genetic testing is advised. Especially in serious cases of male infertility, it is advisable to determine whether this infertility has a hereditary cause. This option is also considered when in spite of repeated IVF attempts and for no clear-cut reason pregnancy is not achieved.

## Pre-operative examination

As you probably already know, the ovarian puncture is performed under light anaesthetic. If you have general health problems for which you take medication (for example, high blood pressure, diabetes, asthma ...), you must report this fact to the doctor because this may mean that a pre-operative examination is necessary.

## Prevention of nervous system defects in the child

The chance that a disturbance in the closing of the spinal column will arise during pregnancy is approximately 1 in 1000. The presence of an open spinal column (spina bifida) produces a permanent handicap in the child. Research has shown that the majority of the cases of spina bifida arise due to a shortage of folic acid during the first weeks of the pregnancy. Although some folic acid is present on our food (in grain products, leafy vegetables, legumes and liver), all women who are trying to become pregnant are advised to take a daily folic acid supplement of 0.4 mg. This precaution has greatly reduced the number of children with spina bifida. This supplementation is best started several weeks before fertilization and must be continued until the 16<sup>th</sup> week of the pregnancy. Folic acid can be purchased without a prescription in your pharmacy.

## Social support

If you would like, you can request advice and guidance for the psychosocial aspects of fertility treatment. Not only can you turn to the gynaecologist or the midwife for this support, but you can go specifically to a psychologist for counselling. At important decision-making points during the treatment, we will provide you with a specific list of questions that will make it easier for you to evaluate, given your specific situation, the extent to which it could be helpful to see a psychologist. It is completely normal that you are highly passionate about your desire for children. As long as you are still unsure of whether or not you will ultimately have children, you may have the tendency and be prepared to take this desire too far. The anxiety and concerns that accompany this journey can sometimes be unexpectedly intense. At those times, courage and optimism can fade away. Indeed, every fertility treatment is a chain of moments of vigorous hope, expectation and joy, with moments of deep discouragement and grief.

The first requirement for coping with the stress of a fertility treatment is a healthy portion of realism. For that, keep the numbers in mind as much as possible (30% chance of pregnancy also means a 70% chance of no pregnancy), try not to consider pregnancy alone to be your only life's goal (definitely do not give up your job at the start of IVF) and, finally, find a confidante to whom you can pour out your heart. To a certain extent, the following people can help you with this: your partner, the doctor who is supervising the treatment, your general practitioner, the psychologist, a family member, a good friend, a self-help group ...

In any case, keep talking and do not hold it all in. Talking always reduces stress and offers relief, these conversations can keep the discouragement and the grief from leading to real depression. Counselling support for working through the failures, loss or grief is an important factor in ensuring that you can continue on together afterwards. Working through the fertility problem can be a heavy load, but on top of that an imbalance in the coping process can also arise in the relationship. One partner processes the disappointments more quickly

than the other, one partner struggles more with feelings of guilt than the other, one partner is more inclined to go further into treatment than the other ...

The physical and psychological burdens of medically assisted fertility will also often bring about disruption in the normal sex life of the couple, which can also lead to additional stress in the relationship. It is obvious that within this whole problematic situation, having a partner with whom you can speak freely, like a psychologist, can be very helpful.

The following are a few examples of questions that are often asked during a conversation with one of our psychologists:

- We really want a child, what do we do now?
- How do we arrange all of this with our work schedules? What do I say to my boss?
- My best friend is pregnant. Do I really have to feel happy about it? Why does everyone I know get pregnant without any effort at all? Am I just becoming too preoccupied with the whole project?
- How do we explain to family and friends that we would rather not attend that party for the newborn?
- How far can we go in the fertility treatment? What if my partner has other views about this?
- Are our plans for the future now completely ruined?

In practice, the psychologists can offer you the following support:

- individual/couples counselling during the various steps of the medical process;
- attention to strengthening your coping mechanisms;
- teach you to better handle your problems so you can put the various aspects of the situation into perspective;
- lower the stress level;
- support during the coping process.

Consultations with the psychologists require an appointment and can be booked via our secretary. At this moment, these appointments are only reimbursed partly by the National Health Service.

# Notes

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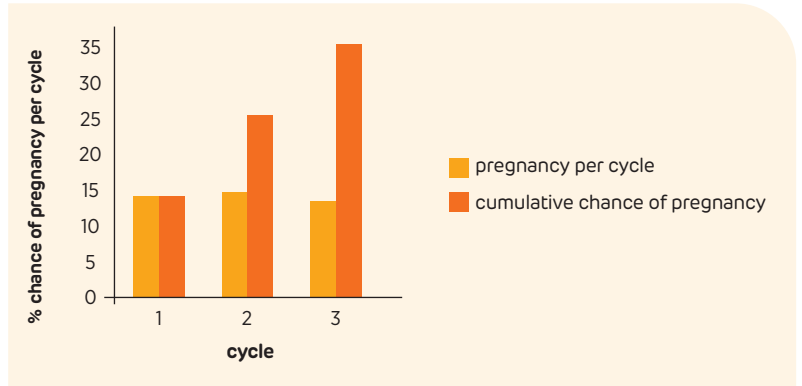


# Appendix

## Activities and results of our center

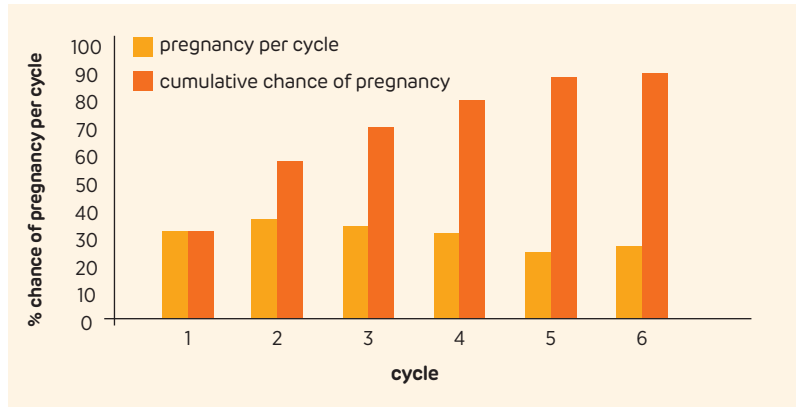
### • Global chance of pregnancy per insemination cycle

The chance of pregnancy remains quite constant over the first 3 treatment cycles. This is to be expected since coincidence plays such a large role. Cumulatively, the rate of pregnancy is 35% within the first 3 cycles.



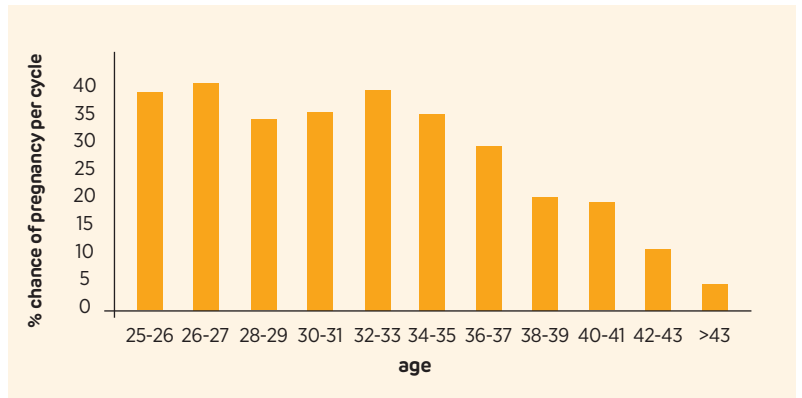
### • Global chance of pregnancy per IVF/ICSI cycle

The chance of pregnancy is quite constant over the first 4 treatment cycles, which is to be expected since coincidence plays such a large role. Cumulatively, 80% of the pregnancies are achieved within the first four cycles.



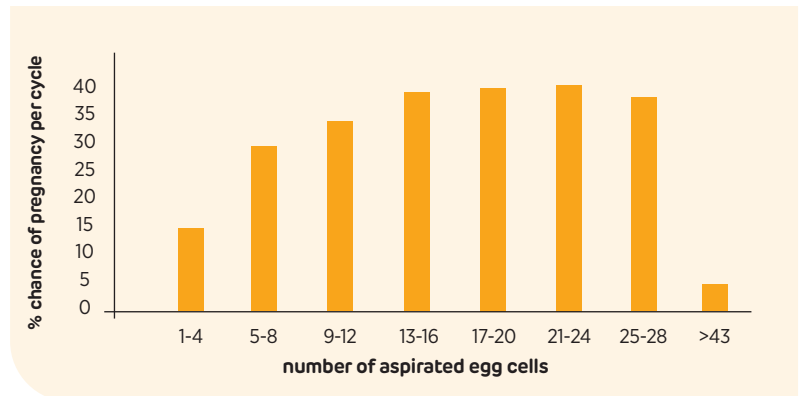
### • Chance of pregnancy per age after IVF

Up until the age of 36, the chance of pregnancy per cycle remains quite constant. After that, the chances decrease gradually. This decrease is related to a reduction in the quality of the egg cells after the age of 37.



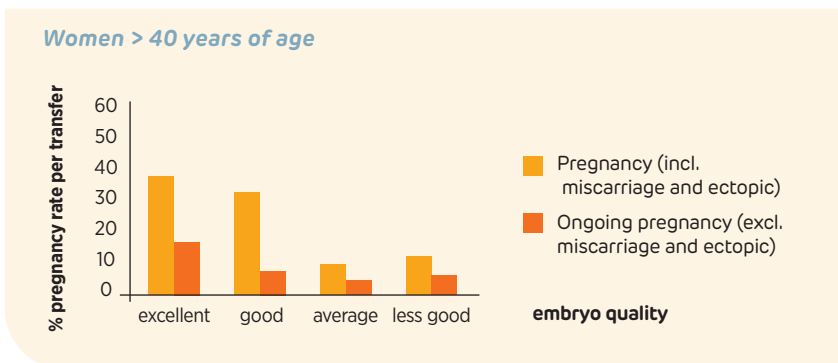
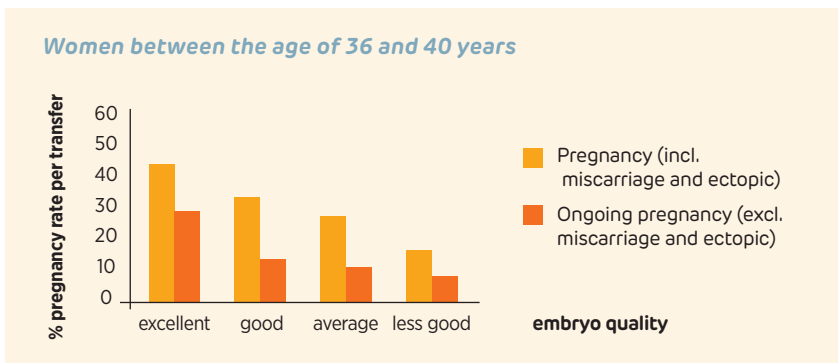
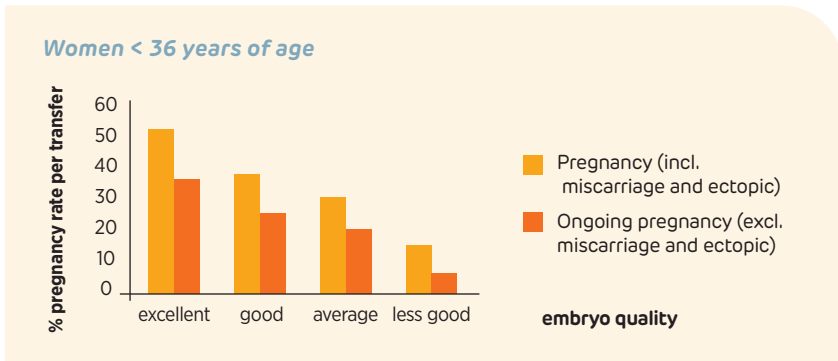
### • Chance of pregnancy and number of eggs

The chance of pregnancy is closely related to the number of egg cells that are produced. However, after 15 to 20 egg cells, the chance of pregnancy does not continue to increase. Ten to fifteen egg cells is the ideal target.



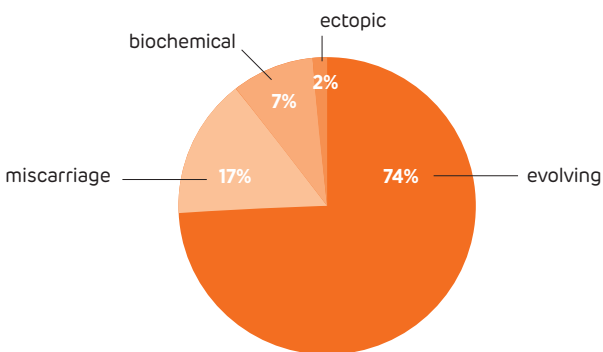
**• Probability of success according to age and the quality of the embryos**

The embryo quality will be discussed at the moment of the transfer. The success rate per transfer is between 15% and 50% for women younger than 36, and between 10% and 40% between 40 and 43 years of age. You can estimate your own chances in the corresponding graph, depending on your personal characteristics.



**• Pregnancy outcome after IVF/ICSI**

Just as in the natural situation, 74% of all pregnancies that are initiated persist (continue on), 7% end in a very early miscarriage (biochemical; i.e., not yet clinically discernible), 17% end in clinical miscarriage and 2% are ectopic.



# How to contact us

For short, practical and/or urgent questions relating to an on-going treatment, you can always (24/7) call our **Fertifoon at 09 224 64 39**. There, a midwife or gynaecologist who is qualified in these matters and who is part of the Fertility Centre team will answer the phone to assist you.

Please note: You cannot use this telephone number to make appointments. For appointments, you must contact the secretary of the office in AZ Sint-Lucas.

## **Fertility centre AZ Sint-Lucas**

### *Street 7*

**T** 09 224 60 92

**E** [fertiliteit@azstlucas.be](mailto:fertiliteit@azstlucas.be)

## **Gynaecologists**

Dr. Tom Coetsier ([tom.coetsier@azstlucas.be](mailto:tom.coetsier@azstlucas.be))

Dr. Jeroen De Smet ([jeroen.desmet@azstlucas.be](mailto:jeroen.desmet@azstlucas.be))

Dr. Isabelle Meire ([isabelle.meire@azstlucas.be](mailto:isabelle.meire@azstlucas.be))

Dr. Nele Van Renterghem ([nele.vanrenterghem@azstlucas.be](mailto:nele.vanrenterghem@azstlucas.be))

## *Psychologists Pspypunt*

Heidi De Vylder & team

**T** 09 224 60 92

## **IVF laboratory + embryo transfer UZ Gent**

P4, 2<sup>nd</sup> floor (embryo transfers)

**T** 09 332 31 39

**T** 09 332 21 94 (weekend)

**E** [arg@uzgent.be](mailto:arg@uzgent.be)

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