The garden of love
where babies are grown
LEAF BY LEAF
The road to follow

The administrative documents to be sent:

1. TO YOUR HEALTH INSURANCE COMPANY
   a) request for reimbursement of the laboratory fees
   b) request for reimbursement of the medicines
   c) registration form for non-Belgian Europeans

2. TO THE PMU NURSES
   a) IVF consent duly signed by the couple
   b) the authorisations for reimbursement of laboratory fees
   > to come from the Insurance Company in the post

3. TO THE PHARMACY
   a) prescriptions
You are very welcome

It’s spring-time, the buds are opening [ANATOMY AND PHYSIOLOGY]
   In her…
   In him…
   The great meeting … naturally

A little problem in my garden [INFERTILITY]
   Examining the ground… in her
   Examining the ground… in him

If you have need our green fingers [IN VITRO FERTILISATION]
   Obtaining good seed… [1] to [4]
   The great…test-tube meeting [5]
   The return to nature [6]

The outlook? [PREGNANCY TEST]
   Is it journey’s end?
   A winding road?
   Some pitfalls: rare but they exist

What can one predict, what should one expect?
[RESULTS AND CAUSES OF FAILURE]
   Some figures…
   The sky is grey: why this failure?
   The long awaited sun! The young shoot will grow to be big

Sometimes there are other ways [DONATIONS AND ADOPTION]

For a peaceful journey [TEAM OF PSYCHOLOGISTS]

Down to earth but very necessary [LEGAL QUESTIONS, MONEY QUESTIONS]

The pro-active, preventative approach

A time to think… [ETHICAL QUESTIONS]

For a complete understanding, a lexicon of the garden! [GLOSSARY]
Welcome

[Image of watering cans with words: Sage, Passion, and Your Heart, pouring hearts down]

[Background of flowers and grass]
Dear Madam / Dear Sir,

We welcome you to our Assisted Reproductive Technology Center (ART).

If you are now reading through these pages, it is probably because your doctor has diagnosed a problem of infertility for you. In this booklet you will find a series of theoretical and practical pieces of information which will help you to understand and, we hope, to experience the various stages of in vitro fertilisation (IVF) in the best possible way.

If you decide to place your trust in us, we will meet regularly; the journey may be a long one and this is why we think it is important that you feel “at ease” within our team. We will do our best to ensure that you receive personalised and humane care, so that this stage of your life will not be a source of instability.

Like you, we know that a child is born of the love between two human beings. During in vitro fertilisation this love must be given a place of primary importance that both you and we will be careful to respect.

During the treatment, we will remain in close contact with your family doctor and your gynaecologist, who will continue to follow you for screening and who will take charge of you again as soon as pregnancy has taken place.

When you leave our department, whatever the outcome is, we would like to have news of you, because we really want this road we have travelled together to be constructive for everyone.

Good luck !!!

The ART team

CHC-Clinique Saint-Vincent
Rocourt-Belgium
It’s spring-time, THE BUDS ARE OPENING

In her...

The anatomy of the female reproductive system consists of the vagina, the uterus, 2 Fallopian tubes and 2 ovaries:

- The **OVARY (1)** each month produces an oocyte (or egg) which is released into the abdomen and then picked up by the Fallopian tube; this is called ovulation. If the egg is not fertilised after several hours, it is eliminated without any clinical sign.

- The **FALLOPIAN TUBE (2)** is a very fine duct linking each ovary with the uterus; it is here that the spermatozoa (sperm cells) can come into contact with and possibly fertilise the egg. By their movement the ciliae of the tubes move the egg, and then the embryo, towards the uterus.

- The **UTERUS (womb) (3)** is a muscular organ connected to the vagina by the cervix of the uterus; during each cycle the ENDOMETRIUM (4), which is the lining of the inside of the uterus, thickens to form a sort of nest able to receive the embryo; this nest is shed each month if no embryo is implanted in it: this is menstruation.

- The **CERVIX (5)** which connects the **VAGINA (6)** to the uterus contains glands which secrete the cervical mucus; this becomes more fluid during the ovulatory period allowing the passage of the spermatozoa which are deposited deep in the vagina during sexual intercourse. The spermatozoa may remain there for several days. Apart from this period the cervical mucus is impermeable.
The menstrual cycle is controlled by the sexual hormones, which are secreted by the glands.

The controller in chief is in the brain and is called:
- The HYPOTHALAMUS (7): it releases a hormone called the LHRH or GnRH; this then acts on another gland in the brain, the pituitary gland.

- The PITUITARY GLAND (8), in turn, during the first part of the cycle, releases an initial hormone, the FSH (Follicle Stimulating Hormone), which will stimulate the growth of several FOLLICLES (9) in the ovary; most of these will shrink and die except for the "dominant follicle" which will mature up to a diameter of about 2 cm; this is the point at which the pituitary gland releases the LH (Luteinizing Hormone) which gives the follicle the necessary impetus to release the egg it contains: this is ovulation.

Ovulation takes place 14 days before the start of menstruation, i.e., on the 14th day of a 28-day cycle. The FSH and LH are also called gonadotropins.

- The OVARY, the organ that produces the ovules, is also a gland. Under the influence of the FSH and LH, the cells surrounding the follicles, from the beginning of the cycle, secrete oestradiol, a type of oestrogen; this hormone acts on the breasts and uterus (endometrium and cervical mucus) to improve the chances of pregnancy; oestradiol also has an effect on other organs, such as the skin, bones and pituitary gland.

- Following ovulation, the follicle changes under the influence of the LH into a small gland, the CORPUS LUTEUM (10), which secretes progesterone; this hormone makes the endometrium receptive for the implantation of the embryo; if the implantation does not take place the corpus luteum shrinks and dies after 14 days and the endometrium is shed (menstruation).
The anatomy of the male reproductive system consists of the penis (1), testicles (2) and the system of excretory ducts linking them [epididymis (3), deferent ducts (4), ejaculatory ducts (5), urethra (6)], as well as the male accessory sex glands [prostate (7), seminal vesicles (8), Cowper’s and Littre’s glands (9)] which secrete the fluid surrounding the spermatozoa:

- The spermatozoa are produced in the TESTICLES (2). Production is continuous and there are about 3 months between the beginning of production of a spermatozoon and its ejaculation. The semen is made up of 95% fluid, called seminal fluid which is produced mainly in the prostate and the 2 seminal vesicles, and 5% spermatozoa.

- During sexual intercourse, the semen is brought to the exterior through the excretory ducts (epididymis → deferent ducts → ejaculatory ducts → urethra) to the extremity of the penial urethra; this is ejaculation. Tens of millions of spermatozoa are released in this way into the vagina; they move along the cervical canal, into the uterus and then the Fallopian tubes in search of an egg. Only 150,000 get this far; and only one can penetrate the egg; having survived for about 3 days the rest die in the female genital tract.

The functioning of the male sexual organs is dependent on the secretion of sexual hormones.

- As in the female the PITUITARY GLAND, which is controlled by the HYPOTALAMUS, release gonadotropins, which act on the testicles:
  - the FSH controls the production of spermatozoa.
  - the LH controls the secretion of male hormones (testosterone) ensuring the correct production of the spermatozoa, male physical characteristics (beard, voice etc.) and the correct functioning of the sexual organs (erection etc.)

The testicle, like the ovary, therefore has the double function of producing sexual cells (gametes) and also hormones.
The great meeting ... NATURALLY

- The successful spermatozoa therefore enters the Fallopian tube and combines with the egg by penetrating it; this is fertilisation.
- The external membranes of the egg change to prevent the entry of more than one spermatozoon.
- The two nuclei (male and female), each containing 23 chromosomes, unite to form a single nucleus with 46 chromosomes.
- The zygote (future embryo) then moves through the Fallopian tube, all the while multiplying its cells by successive divisions, before arriving in the uterus where it implants itself into the endometrium: during this journey, the fertilised egg divides into 2, 4, 8, … cells, forming a morula (small mulberry), then a blastocyst, a body of about 150 cells measuring about 0.15 mm. The zygote is now ready to implant (one week after its fertilisation).
- In 7 cases out of 10, the embryo does not implant and is eliminated without clinical signs in the days following fertilisation.

TO CONCLUDE, so that a pregnancy can start there must be:

- An egg of good quality
- Cervical mucus permeable to spermatozoa
- A sufficient number of spermatozoa which are mobile and able to make the journey from the vagina and penetrate the egg.
- A permeable Fallopian tube (or better two) which can bring the gametes (sexual cells) together and the resulting embryo to the uterus
- A uterus which is lined with an endometrium of sufficient quality to ensure implantation of the embryo.
A little problem in my garden

- Natural FERTILITY in the human is not 100%; several stages must be completed to achieve a full-term pregnancy.
- For each cycle a fertile couple having regular and complete sexual intercourse has, on average, one chance out of five of starting a pregnancy.
- Age is a limiting factor as the fertility of the woman diminishes after 30 years of age and this reduction becomes greater after 35 years of age.
- Furthermore, the fertility of normal men and women varies from one time to another in their lives (fatigue, stress, smoking, weight and other circumstances).
- This explains the variation from one couple to another in the time that it takes to achieve a pregnancy; however, after one year 84% of couples will usually conceive a child, 92% after 2 years and 96% after 3.
- One couple out of six consults for INFERTILITY. Infertility is considered to be moderate after 2 years and severe after 5 years of unsuccessful attempts.
- TRUE STERILITY corresponds to a total inability to conceive (total absence of Fallopian tubes or uterus or of spermatozoa in the semen). It concerns only 2% to 3% of couples; such couples must get medical help in order to procreate.
- In practice the medical team will begin to examine and treat an infertile couple after at least one year of unsuccessful attempts. In certain circumstances the assessment and treatment may be earlier, for example in the case of “warning signs” (lack of periods, testicular problems known since childhood) or if the age of the woman means that waiting is not an option.

WHY DOESN’T IT GROW!

Overall in 30% of cases the problem is with the female, in 30% the problem is with the male and in 30% it is with both partners. In 5% to 10% of cases the infertility remains unexplained and is called idiopathic infertility.
Examining the ground ... in HER

After an anamnesis (medical history) and a complete general and gynaecological examination, we will carry out:

- A BLOOD TEST to screen for a hormonal problem, assess ovulation, determine the ovarian reserve, as well as to look for possible genetic (analysis of chromosomes) or infectious diseases to be treated or prevented before or during the pregnancy.

- An ULTRASOUND SCAN to determine the anatomy and correct functioning of the uterus and the 2 ovaries (the Fallopian tubes are rarely visible at this examination); the injection of a liquid enables a better approach to the cavity: SIS (saline infusion sonogram). ECHOSONO.

- A HYSSTEROSALPINGOGRAPHY, a radiological procedure to investigate the internal cavity of the uterus and the Fallopian tubes to find anomalies of the tubes or blockages on this path. The examination is done using a speculum, permitting the introduction through the cervix of the uterus of a liquid contrast medium which makes the examination somewhat unpleasant. This only lasts a few seconds, however; and is often carried out by your gynaecologist in a reassuring environment and under pain killers.

- A HYSSTEROOSCOPY makes it possible to see the interior of the uterus by introducing through the cervix, by the natural route, a very fine optical tube connected to a camera. This examination takes place under local, or even general, anaesthesia; it is not systematically carried out.

- A LAPAROSCOPY, carried out under general anaesthesia, consists of introducing an optical tube connected to a camera into the abdomen to see the internal organs, to determine their exact anatomical relations and to diagnose anomalies. It makes it possible to see any sequelae (consequences) of infections, uterine malformations, adherences or endometriosis. These anomalies can cause fertilisation problems (blockage, unfavourable environment) or implantation problems. Laparoscopy is a tool for diagnosing but also for treating (microsurgery, laser etc.) any pathology found. This examination, like the hysterectomy is only proposed in certain cases.

Problems? For every problem there is a solution!

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<th>THE CAUSES OF FEMALE INFERTILITY</th>
<th>TREATMENT</th>
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<td>Psychosexology treatment and possible artificial insemination</td>
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<td>Problems with cervical mucus</td>
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<td>Ovulation disorders</td>
<td>Hormonal treatment, rarely IVF</td>
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<td>Fallopian tube blockage or tubal ligation</td>
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<td>Endometriosis</td>
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<td>Uterine malformation</td>
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<td>Problems with cervical mucus</td>
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<td>Absence of oocytes and early menopause</td>
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<td>Woman unable to bear a child</td>
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<td>Failure of intrauterine insemination</td>
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</table>
INFERTILITY

Examining the ground... in HIM

- SEMEN ANALYSIS consists of a laboratory analysis of a sample of semen to assess the number, mobility and form of the spermatozoa, i.e. to assess the ability of the spermatozoa to reach the oocyte and complete the process of fertilisation.

This sample is obtained through masturbation, following an abstinence of 3 days, and will be brought to the laboratory within the hour of its production, in a sterile bottle at body temperature (bag...). If it is abnormal this examination must always be verified by a 2nd sample in the following 2 to 3 months.

- A BLOOD TEST is carried out to screen for a hormonal, infectious or genetic (analysis of chromosomes) problem.

- A clinical EXAMINATION of the GENITAL ORGANS, even a testicular ULTRASOUND SCAN, are sometimes necessary if the semen analysis is not normal. These examinations identify blockages or other problems of the genital organs. They will be carried out by a gynaecologist or a urologist with a training in andrology.

Although the causes of male infertility are rarely identified, it is important to look for them because some of them are treatable. The frequency of male infertility would seem to be increasing in recent years. Why? Various theories have been explored, in particular environmental and behavioural factors which might be toxic: pollution and related endocrine disruptors (pesticides, phthalates), heat, radioactivity, tobacco, obesity etc. It is therefore important to develop and encourage preventative procedures for male infertility; the andrology consultation also pursues this objective.

Problems? For every problem there is a solution!

<table>
<thead>
<tr>
<th>THE CAUSES OF MALE INFERTILITY</th>
<th>TREATMENT</th>
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<tbody>
<tr>
<td>Sexual intercourse disorders</td>
<td>Psychosexology treatment, physiotherapy</td>
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<td></td>
<td>or artificial insemination</td>
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<tr>
<td>Duct blockages</td>
<td>Surgery and/or IVF</td>
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<tr>
<td>Abnormalities in semen analysis data</td>
<td>Artificial insemination or IVF</td>
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<td></td>
<td>with or without ICSI according to the gravity</td>
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<tr>
<td>Absence of spermatozoa</td>
<td>Micro-injection of a surgically retrieved (from</td>
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<td></td>
<td>testicle or excretory tubes ) spermatozoon</td>
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<td></td>
<td>into the egg (ICSI) or artificial insemination</td>
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<td></td>
<td>with donor sperm</td>
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<tr>
<td>Hereditary illness in the man</td>
<td>Preimplantation genetic diagnosis (PGD),</td>
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<td>Unexplained infertility</td>
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</table>
**If you have need of our green fingers**

**BACKGROUND ...**

- The technique of in vitro fertilisation (IVF) was initially developed to promote the in vitro uniting of the spermatozoa and the egg when this was prevented by a blockage in the Fallopian tubes. Since the birth of Louise Brown, the first “test-tube baby” in 1978, the indications for this treatment have developed rapidly to include problems of ovulation, endometriosis and also male problems.

- The development of ICSI [Intra-Cytoplasmic Sperm Injection] in the early 90s made it possible to widen IVF indications to include severe male difficulties; this technique allows the injection of a single spermatozoon into each egg and therefore fertilisation with very few spermatozoa; it is now used in nearly 7 treatments out of 10 in Belgium and in our centre.

**OBTAINING GOOD SEED ... STIMULATION**

**THE STAGES OF IVF**

1. Suppression of ovarian activity
2. Stimulation
3. Ovulation induction
4. Retrieval of eggs
5. Fertilisation in laboratory ... the test-tube meeting
6. Embryo transfer ... return to nature
7. Pregnancy test ... or what’s on the horizon

**Why stimulation? To make the seeds grow!**

This is to ensure the development in both ovaries of several follicles (instead of a single one). Why several?

It is useful to collect several ovocytes to be sure to obtain after fertilisation a sufficient number of good quality embryos. From these the best is (are) chosen for fresh embryo transfer.

This will also allow to freeze good-quality supernumerary embryos for subsequent transfers.

In fact it will no longer be necessary to repeat in vitro fertilisation, which is a heavy treatment for couples (injections, ultrasound scans, possible anaesthesia) if frozen embryos are available.

Follicular growth, the number of eggs retrieved and fertilised, their maturity, as well as the number of embryos which develop are variable and finally only 15% of eggs will result in the transfer of an embryo and 17% in the freezing of an embryo; so 1 egg ≠ 1 embryo!

This helps us to understand that to optimise the chances of a pregnancy more than one egg is necessary initially.
STIMULATION scheme (long protocol)

The phases of IVF treatment are schematised along this timeline according to the technical procedures carried out. Long-protocol ovarian stimulation with GnRH involves 3 steps:

1. **SUPPRESSION OF OVARIAN ACTIVITY**
   - It may be necessary to suppress the activity of the ovaries before stimulating them in order to take control and avoid any natural ovulation (at the wrong time) which might cause failure of the treatment.
   - The activity of the pituitary gland is blocked by the administration, usually at the end of the cycle, of:
     - either a nasal spray 3 times daily
     - or a daily injection.
   - This treatment must be maintained for the entire duration of stimulation; it does not interfere with spontaneous menstruation which will take place almost normally.
   - The rest of the ovaries is controlled at the end of menstruation by ultrasound scan and a blood test.

2. **STIMULATION**
   - Starts 10 to 14 days after the commencement of ovarian suppression confirmed by an ultrasound scan and blood test (in certain cases this period of suppression must be extended).
   - Stimulation then begins by the daily administration of gonadotropins (1 to 4 ampoules per day or 50 to 300 Units).
   - This lasts for on average 12 days.
   - After several days of injections monitoring of follicle growth starts with endovaginal ultrasound scans (measurement of the number and size of the follicles) and/or blood tests (measurement of oestradiol, LH, progesterone levels) – to be carried out every 1 to 3 days.

3. **OVULATION INDUCTION**
   - This is the **MOST IMPORTANT** moment of the treatment.
   - Once the follicles are mature (17 to 24 mm) the medications are discontinued (spray and injections).
   - An injection of hCG (Pregnyl®) or (Ovitrelle®) will artificially induce the final reaction, necessary to ovulation.
   - This injection must be carried out at a definite time, always in the evening, in order to retrieve eggs just before they leave the follicles, i.e. the morning of the second day following the injection.
The good harvest: in Her [Day hospital]

Thirty-six hours after the injection of Pregny® (or Ovitrelle®) egg retrieval takes place. At this stage the egg is mature and is in the follicular fluid which can be easily aspirated.

The aspiration is carried out with a needle introduced through the vagina with ultrasound monitoring (lasting about 15 min.) under general or local anaesthetic in an operating theatre. The follicular fluid retrieved is immediately given on to the IVF biologists who isolate the egg it contains.

The number of eggs obtained is very variable but is, on average, about ten.

When an egg is retrieved it is not visible to the naked eye but is surrounded by a cluster of cells called the “cumulus oophorus” – a sort of mini cloud visible under a microscope and with a diameter of 1 mm.

The egg, once released from these cells in the laboratory only measures 0.1 mm, which is very small in comparison with the follicular cavity (2 cm) seen on the ultrasound.

The good harvest: in Him

Following the egg retrieval procedure (about 1 hour), the laboratory will need the sperm.

The sample is collected in a sterile bottle by masturbation.

Abstinence from the time of the Pregny® (or Ovitrelle®) injection is recommended.

In certain cases a testicular biopsy or aspiration of the sperm in the excretory tubes will be necessary. This takes place before (frozen sperm) or the same day (fresh sperm) as the retrieval of eggs under local or general anaesthesia.

The sample must get to the IVF laboratory within an hour of being produced, where it will be prepared (selection of normal and mobile spermatozoa) by the team of biologists.
[5] FERTILISATION IN THE LABORATORY... THE GREAT TEST-TUBE MEETING

THE LABORATORY WORK

D0  Retrieval of the gametes  IVF with or without ICSI

D1  Assessment of egg fertilisation and culturing of the zygotes

D2  Monitoring of the development of the embryos

D3  Transfer of the embryo(s) or continuation of culturing
     Freezing of remaining developing embryos or continuation of culturing

D5  Transfer of blastocysts where appropriate
     Freezing of blastocysts

INSEMINATION STAGE:

Some hours after retrieval, the eggs isolated in the IVF laboratory can be inseminated (put into contact
with the spermatozoa) = standard IVF. The quality of the sperm or other elements in the medical file
will determine whether standard fertilisation or micro-injection (ICSI) fertilisation should be used.

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**Standard insemination**

60 to 100,000 spermatozoa are left in culture with the eggs until the following morning.

**Intracytoplasmic Sperm Injection (ICSI)**

A micro-injection of sperm is carried out - If the quality of the sperm can not ensure a sufficient rate of fertilisation through the standard insemination technique, when there is a previous failure in standard IVF, if the sperm has been collected surgically from the testicles or the epididymis.

The technique called ICSI (intracytoplasmic sperm injection) was developed in 1992 by a Belgian team. It has been used in laboratories world-wide since 1994.

It consists of the introduction of a single sperm into the cytoplasm of the egg under the microscope, using a high-precision device (micromanipulator).

This micro-injection technique, now used in a very great number of cases (7 out of 10), achieves the fertilisation of 60% to 70% of the eggs injected.
EMBRYO DEVELOPMENT STAGE

**Monitoring fertilisation**
- The following morning, i.e. between 14 and 18 hours after insemination, the eggs are examined to see whether fertilisation has taken place. Normal fertilisation is shown by the expulsion of the 2nd polar body (excess genetic material contained in the egg) into the perivitelline space (outside the egg) and the presence of two pronuclei (that of the sperm and that of the egg). The pronuclei contain the genetic material of the mother and the father.
- The day after insemination you will be informed about the number of fertilised eggs or zygotes.
- The embryos are cultured generally for 2, even 6 days.

**Monitoring and care the embryos (2 to 6 days)**
- After verification, the normally fertilised eggs (2 pronuclei = zygote) are placed in a culture medium which promotes division of the cells and this is then quickly put in an incubator.
- The zygotes divide progressively; the first cell divisions are visible the day following detection of the pronuclei.
  
  Generally the embryo contains 2 to 4 blastomeres (cells) on day 2; 4 to 8 blastomeres on day 3 and reaches the blastocyst stage (about 100 cells) on day 5 or 6.
- Each day the embryos are monitored carefully but quickly.
- Very soon, the embryos show differences in their speed of division, the symmetry of their cells and their tendency to produce small cellular fragments.
  
  These three criteria are used to classify the embryos according to their developmental potential. Those which divide the most rapidly, with the most regular cells and the fewest fragments on the 3rd day of culturing have the best chance of producing a pregnancy.
- Only developing embryos can undergo transfer to the uterus or freezing with a view to subsequent transfer.
[6] EMBRYO TRANSFER... THE RETURN TO NATURE

- The embryo transfer technique is simple. A very fine and very flexible catheter containing the embryo or embryos (in a small drop of the medium preceded by a small bubble of air) is introduced through the vagina into the uterus; the patient is lying in the gynaecological position. This procedure is usually completely painless and does not require either anaesthesia or hospitalisation. Ultrasound scan is used by the gynaecologist to guide the catheter and ensure correct positioning of the small air bubble which accompanies the embryos into the uterus. Once the embryo(s) is (are) placed in the uterus, the catheter is delicately withdrawn and given to the biologist, who, using a binocular loupe, will check that no embryo remains in it.

- You are then generally advised to rest for ½ hour in a comfortable armchair. You can return to a normal life, avoiding sexual intercourse for 3 to 4 days.

- Since 2003, in Belgium, the number of embryos that may be transferred has been regulated by law. The number is fixed according to the age of the patient and the number of treatments already carried out, as detailed in the table on Page 28.

- In order to promote implantation a supplement of progesterone (Utrogestan®) is administered up to the pregnancy test. If the latter is positive the progesterone is continued up to between the 7th and 9th week of pregnancy. The long wait begins... the 12 longest days...

- Sexual intercourse is not forbidden during the treatment but abstinence is nonetheless recommended between the administration of Pregnyl® or Ovitrelle® and retrieval and during the 3 to 4 days following embryo transfer.
THE OUTLOOK?

Is it journey’s end?

- About 12 days after the transfer a blood test may be carried out to see if a pregnancy has started (a pregnancy test already carried out might be falsely positive because of the treatment).

- If the test is negative you are not pregnant.
  In this case we would ask you to get in touch quickly with the gynaecologist who is in charge of your treatment. He will assess this attempt and draw conclusions which will help to optimise any further attempt. This may only be considered after a resting period.
  If any cryopreserved ( frozen) embryos remain they can very often be transferred in the following cycle; this transfer may take place during a natural cycle (without treatment) or with oral treatment and not injections. The frozen embryos may be transferred cycle after cycle, without interruption, if the couple so wish.

- If beta-hCG levels are clearly higher than 50 U/ml, pregnancy has begun.
  This test will be carried out a week later to verify that this hormone level is increasing. If the pregnancy is developing properly, the levels should more or less double every 48 hours. It is important to continue to take your hormone treatment (Utrogestan®) for several weeks after the positive test.

- If the beta-hCG levels are below 50 U/ml, but not negative, it is probable that pregnancy has started but is not developing.
  A test for this pregnancy hormone must therefore be carried out within 48 to 72 hours. Sometimes there may be an ectopic (extrauterine) pregnancy and this must be diagnosed quickly so that the least invasive treatment can be used.

- Two to three weeks after the first test, an ultrasound scan will be carried out.
  This is to check the progress of the pregnancy and determine the number of implanted embryos. After this, your pregnancy will be monitored by your own gynaecologist, with whom you will arrange an appointment in 2 to 3 weeks.
A winding road? (frozen embryos and other techniques)

The stimulation protocol that has just been explained is called the “the GnRH agonist long protocol”; this is still the one that is most used (48% of treatments in Belgium) (p. 12).

- Other stimulation protocols may be suggested according to the type of menstrual cycle of the patient, her age or sometimes because of an inadequate response to the long protocol: these are called “short” protocols because the blocking of ovulation does not start before menstruation.

- Either the same molecules are used as in the long protocol to block ovulation, GnRH agonist (Suprefact® or Decapeptyl®): “Agonist short protocol”.

- Or the start of stimulation is preceded by the taking of a contraceptive pill for at least 12 days. This causes down-regulation of the ovaries and allows the day of blocking ovulation with the GnRH agonists (Suprefact® or Decapeptyl®) to be scheduled often 3 days after discontinuation of the pill. Ovarian stimulation commences in the following days.

- Or blocking ovulation is started with the GnRH agonist (Suprefact® or Decapeptyl®) on the first day of menstruation. In this case a blood test and an ultrasound scan will be necessary before commencing ovarian stimulation (2 to 4 days later) in order to check that the ovaries and uterus do not show any abnormality (see page 21).

- Or other molecules than those of the long protocol are used to block ovulation; these are GnRH agonists (Orgalutran® or Cetrotide®) administered in the form of daily subcutaneous injections: during stimulation: “Antagonist short protocol”.

- Ovarian stimulation is begun between the second and fourth day of menstruation, after a blood test and ultrasound scan have been carried out to check that the ovaries and uterus do not show any abnormality. The antagonists which stop spontaneous ovulation are administered daily after a minimum of 5 days of stimulation, according to follicular development monitored by ultrasound scans and blood tests (see page 20).

Finally, an in vitro fertilisation cycle can be carried out without stimulation:

- The “natural cycle protocol” is performed for patients who have not responded to any other treatment or for whom stimulation is contraindicated (risk of thrombosis, history of hormone-dependent cancer etc.). The natural functioning of the ovaries is followed and a little before the onset of ovulation possible blockage of the pituitary gland may be carried out.
Retrieval therefore is of a single, maximum 2, egg(s) (often without anaesthesia). This treatment can be carried out cycle after cycle. Taking into account what has been said previously regarding the “efficiency” of the stimulated protocols, it will be understood that these natural cycles may be interrupted at different moments of the procedure: because of spontaneous ovulation before retrieval, or because the single egg is immature or not fertilised, or the single embryo does not develop. Overall 30% of natural cycles do not achieve embryo transfer. However, if there is transfer, the implantation rate of the embryos is identical to that in the stimulated cycles.

“AGONIST” SHORT PROTOCOL

“ANTAGONIST” SHORT PROTOCOL
NOT ALL OF THE SUPERNUMERARY EMBRYOS WILL BE FREEZABLE.

Only those which have shown an ability to develop during successive divisions are frozen. To freeze all the supernumerary embryos would lead to subsequent futile and costly treatment. When the embryos that are developing well are frozen, 2/3 of them survive the freezing process and restart their development after thawing. Their probability of implanting in the uterus is also less than that fresh embryos.

THE FREEZING OF SUPERNUMERARY EMBRYOS.

This can be done at different points in their development, from the pronuclei stage before the first cell division (day 1) up to the blastocyst stage (day 5 or 6). The freezing procedures must be adapted to the different developmental stages. To protect the embryos during freezing, they are plunged into a cryoprotectant solution. The embryos are then aspirated into straws which are placed in a device which allows to control very precisely the speed at which the embryos are cooled.

The embryos are then stored at a very low temperature in liquid nitrogen (−196°C).

THE TRANSFER OF FROZEN EMBRYOS.

If the couple has not achieved a pregnancy following the transfer of fresh embryos or if the couple desires further pregnancies after the birth, the cryopreserved embryos are thawed and those that have survived the freezing and thawing procedures are transferred, with the written agreement of both members of the couple.

IN BELGIUM, BY LAW, embryos can remain cryopreserved for 5 years. After this time their future depends on the choice that you have indicated in the informed consent form signed prior to treatment. After the period of 5 years, if you no longer wish for a child, you can request in this informed consent that the embryos be thawed and destroyed, or preserved for another 2 years for scientific research, or possibly donated to another infertile couple who desire a child. This donation is always strictly anonymous and strictly limited to couples for whom there is no other possibility of conception.
TRANSFER OF DEFROSTED EMBRYOS

One day before transfer, the embryos are thawed, washed to remove the cryoprotectants, then returned to a culture medium up to the moment of transfer. On average 66% of the embryos survive freezing; however, it can happen that none of them survive. In this case the transfer is cancelled.

The transfer of the thawed embryos only requires the patient to undergo light treatments and monitoring; it requires ultrasound and laboratory (blood test) monitoring to ensure proper implantation conditions (endometrium), either with the natural cycle, or semi-artificial cycle with the taking of hormones by the oral or vaginal route. There are no injections and few examinations.

PROLONGED CULTURE AND CRYOPRESERVATION OF BLASTOCYSTS

- In certain circumstances in order to have a better selection, culturing of the embryos may be continued up to 5 or 6 days after insemination. The aim of this particular technique is to increase the implantation rate of the embryos. At this stage the embryos must have reached the morula or blastocyst phase.

- A particular technique has been developed for the cryopreservation of embryos cultured for 5 to 6 days, because these embryos contain a greater quantity of liquid in a little cavity called the blastocoel. This technique, called "vitrification", would appear to produce very good results. It involves exposing the embryos to much stronger concentrations of cryoprotectant and, instead of slow freezing, carrying out very rapid freezing.
**PREIMPLANTATION GENETIC DIAGNOSIS**

- Certain in vitro fertilisation treatments can be associated with “embryo-choice” by genetic techniques, if one or both of the partners have genetic abnormalities which, if transmitted, could cause serious disease in the child. Examples of these conditions are mucoviscidosis, haemophilia, thalassaemia, Huntington’s disease, muscular dystrophy and various chromosome translocations.

- It is possible in a certain number of cases, on the 3rd day of embryonic development to take 2 cells of the embryo and to carry out a genetic diagnosis on these so that only “normal” embryos are transferred. The aim of the procedure is to diagnose anomalies before implantation and so avoid a somewhat delayed therapeutic abortion on the basis of an amniotic fluid test or a trophoblast biopsy.

**IN VITRO MATURATION**

- In a certain percentage of cases, it is possible to retrieve oocytes from the follicles at the beginning of growth and so avoid having to carry out long stimulation treatment. The oocytes retrieved from the follicles of less than 10 mm can be matured in the laboratory in an appropriate culture medium because they are still too “immature” to be fertilised. Oocytes matured in this way can be fertilised 24 to 48 hours after retrieval. This technique is reserved for patients with severe ovulation disorders who do not respond to standard ovarian stimulation treatment, such as patients suffering from micropolycystic ovaries.

**ASSISTED FERTILISATION**

- Certain fertilisation techniques compensate for the defective functioning of the sperm. This is the case of assisted **oocyte activation** which, by chemical activation of the oocyte, makes it possible to carry out a step in the fertilisation process that certain sperm lacking a normal enzymatic complement are unable to do.

- The **PICSI** technique allows the selecting of mature spermatozoa from a cohort of defective spermatozoa. It makes it possible to identify the sperm with the functional ability to recognise components of the oocyte cumulus complex.

- In **IMSI**, with very high magnification of the spermatozoa, the most “normal” ones are selected by the shape of their heads.
Some pitfalls: RARE BUT THEY EXIST

The incidence of complications is low and serious complications occur in less than 3% (2.5%) of cycles. However, these have to be given very particular attention because they involve iatrogenic side effects, i.e. treatments which can endanger young patients who theoretically will be in good health. Prevention therefore is of capital importance, as well as early diagnosis which will permit optimal treatment with a minimum of consequences.

To do this, all IVF centres have a hotline service which ensures continuity of care and a gynaecologist on-duty who can see you at any time. Complications can occur following ovarian stimulation, following egg retrieval and following pregnancy after in vitro fertilisation.

LINKED TO OVARIAN STIMULATION

- **Ovarian hyperstimulation** is the most frequent complication in IVF. It consists of an over-response of the ovaries to the gonadotropins. It occurs generally some days after the transfer of the embryos and presents different degrees of gravity.

  The first symptoms are abdominal discomfort, accompanied by nausea, even vomiting and diarrhoea. The ovaries are increased in size due to the presence of cysts of the corpus luteum. The severe forms (0.5% of IVF cycles) are characterised by the appearance of fluid in the abdomen, around the intestines (ascites), and an increase in the concentration of the blood (haemocencentration) which can lead to thromboses and abnormalities in kidney and liver function. Patients become bloated and can be out of breath. This condition requires special treatment, preferably in an ART center. In most cases the symptoms disappear spontaneously but sometimes a short hospitalisation is necessary.

- **Ovarian torsion: one retrieval in 1000**

  This is a torsion of the blood vessels that supply the ovary, caused by a rotation on itself of the heavier ovary. The ovary is no longer vascularised and, if this situation continues, it can become necrosed. The patient will suffer abdominal pain and nausea following the retrieval of the eggs. Torsions can occur up to 11 weeks after OPU (ovum pick-up) in case of pregnancy and ovarian hyperstimulation, which are risk factors.

  The treatment is uncoiling of the torsed ovary by laparoscopy and this must be carried out as quickly as possible once the diagnosis has been confirmed.
Although the complications of in vitro fertilisation are rare, they do exist. You should contact a member of the ART team as quickly as possible if you experience any symptom that worries you (pain or significant blood loss).

[COMPLICATIONS]

LINKED TO THE OOCYTES RETRIEVAL

- The risk of infection

Even though strict precautions are taken during egg retrieval there is a minimal risk, of about 3 cycles out of 1000, of gynaecological infection. These complications are related to the vaginal approach which allows the infection of the abdomen by germs imported from the vagina by the needle. In case of infections, fever and abdominal pain in the week following retrieval occur but these symptoms can still appear up to 8 weeks later. If the infection is diagnosed before the transfer of the embryos, some doctors recommend freezing the embryos and postponing the transfer because of the lower pregnancy rate in the presence of such an infection.

The accidental entry of the needle into the bladder during retrieval is often without consequence; it can, however, be complicated by a urinary infection and the presence of blood in the urine (haematuria), which must be treated but is not serious.

- The risk of haemorrhages:

Blood loss from the vagina is the most frequent form of haemorrhage (8.6%), but it is not serious. Less than 1% of these haemorrhages require treatment following egg retrieval, either by simple pressure on the bleeding point or, more rarely, by the insertion of a stitch in the vaginal wall.

Slight abdominal bleeding is usual during the ovarian puncture and is the cause of the discomfort felt by the patients for 48 hours after retrieval. During retrieval the needle passes through the blood vessels of the ovarian capsule but in most cases blood losses are moderate and without clinical consequences.

Where there is more significant bleeding the doctor will suggest longer monitoring in hospital and sometimes subsequent blood tests to make sure that the bleeding has stopped and is not endangering the patient.

Significant blood loss around the intestines is rare (0.08 % to 0.20%). It usually occurs within the 48 hours following retrieval, as abdominal pain and signs of hypotension, rarely fainting. Such bleeding is slow and diffuse and the symptoms therefore appear some time after the surgical procedure. Treatment is limited to monitoring the patient in hospital and it is only very rarely that a laparoscopic procedure will be required.
MULTIPLE PREGNANCY:

- Multiple pregnancy:

  The chances of pregnancy, but also the risk of a multiple pregnancy, increase with the number of embryos transferred.

  The new law governing in vitro fertilisation procedures limits the number of embryos that may be transferred and therefore has also reduced the rate of multiple pregnancies.

  Before this legal limitation on the number of embryos that could be transferred, the rate of twin and triplet pregnancies was respectively 28% and 0.8%; at present this has fallen to 10.2% and 0.5%.

  It must not be forgotten that multiple pregnancies are subject to obstetrical complications: late miscarriages, hypertensive disorders in the mother during pregnancy, 3 times more hospitalisations during pregnancy, fifty percent premature births with long stays in neonatal units and by caesarean section occurring three times more often. This often compromises the quality of life of the entire family.

  Furthermore, prematurity can have long-term consequences, particularly neurological and respiratory. Multiple pregnancies are also not without subsequent significant social, psychological and financial consequences for the family.

  The aim of the entire team is that you should have a pregnancy without complication, achieving the full-term birth of a child in good health. For this reason the number of embryos transferred must be limited.

- Ectopic pregnancies:

  The incidence of ectopic pregnancies varies from 0.43% to 1.6% for natural conception and from 2% to 11% with IVF. Despite the transfer of the embryos directly into the uterine cavity, so avoiding the Fallopian tubes, the embryos can migrate passively into the tubes, particularly when the tubes are dilated by an obstruction. The possibility of an ectopic pregnancy must be considered where there is an abnormal increase in the pregnancy hormone levels in blood tests or blood loss and abdominal pain. The treatment may be medical if the diagnosis is early, if not, it will be surgical.

  Finally, in IVF “heterotopic pregnancies” are found (a pregnancy which is inside and outside the uterus at the same time) in 0.75% to 1% of pregnancies. The diagnosis of a heterotopic pregnancy is difficult and must be considered in the case of abdominal pain and/or bleeding following an IVF.

In the presence of any of the symptoms described above, you should contact the ART Center which will inform you about the treatment that is the most suitable for your symptoms and your situation. There is an on-call service round the clock which can always contact your ART gynaecologist or the physician who is on-call for the ART when your gynaecologist is absent.
What can one predict, what should one expect?

Some figures ...

- The chances of pregnancy vary according to age and type of cycle
  (Rocourt results in 2009):
- With a stimulated cycle:
  • if you are under 35 years, you have a 40% chance of becoming pregnant following
    transfer of your embryo,
  • from 36 to 39 years, 35%
  • after 40 years: 19%
- With a natural cycle:
- The chances are very different depending on whether one is talking of pregnancy by transfer or
  by cycle, because 30% of cycles are discontinued before transfer:
  • if you are less than 40 years of age and if you go as far as a transfer your chances
    of becoming pregnant are 29%; after 40, 12%.

The sky is grey: why this failure?

For various reasons, each stage of treatment has a failure rate

[1] STIMULATION FAILURE
[2] RETRIEVAL FAILURE
[3] FERTILISATION FAILURE
[4] IMPLANTATION FAILURE
[5] MISCARRIAGE

Miscarriages 11%
Retrieval failure 1%
Full-term pregnancies 30%
Stimulation failure 7%
Implantation failure 45%
Fertilisation failure 6%
[1] **STIMULATION FAILURE**

- Sometimes the doctor is obliged to stop the treatment due to an insufficient or an excessive response of the ovaries. An insufficient response is most often related to the age of the patient (over 35 years) and/or an insufficient egg reserve due to another cause (ovarian surgery, smoking etc.). An excessive response is due to ovulation disorders of the micropolycystic-ovary type. The discontinuation of a treatment does not mean the end of the treatment of your problem but only readjustment of the doses or stimulation protocols.

[2] **RETRIEVAL FAILURE**

- It sometimes happens that no mature egg is obtained at retrieval. Here also the type of cycle determines the failure rate. For a natural cycle, where only one egg reaches maturity, the rate of retrieval failure is 6% and for a stimulated cycle it varies from 0% to 1%.

  In the stimulated cycle the principal cause of failure is an error in the administration of Pregnyl®: forgetting the powder, wrong time or wrong day etc. It is therefore very important to comply with the instructions that you will be given for this stage of the treatment.

  In general, in a cohort of oocytes, 86% of those retrieved are mature.

[3] **FERTILISATION FAILURE**

- It can happen that none of the inseminated eggs is fertilised. This can be due to abnormalities in the sperm (insufficient mobility, atypical morphology, presence of antisperm antibodies etc.) which prevent penetration of the egg envelopes. The immaturity of the eggs can also be a cause of the failure of fertilisation.

  Although more unusual, absence of fertilisation is also found after ICSI. This is generally due to an abnormality of the sperm or the egg (no activation). The rate of fertilisation failure for all eggs varies from 6% in stimulated cycles to 26% in natural cycles. There are certain specific treatments to get around this problem.

- Another possibility is “bad fertilisation” where more than two nuclei (pronuclei) are visible in the embryo the day after fertilisation. In standard in vitro fertilisation this phenomenon is very probably due to the entry of more than one sperm into the egg. When it happens after ICSI, it would appear to be due to the non-expulsion of a part of the genetic material of the egg (2nd polar body) which should have happened naturally. Sometimes a single nucleus (pronucleus) is visible the day after fertilisation. It may be caused by an early fusion of the sperm and egg nuclei, or activation of the development of the egg taking place without the participation of the sperm. The culturing of such embryos is generally not continued.
[4] IMPLANTATION FAILURE

- The implanting of the embryo in the endometrium is an important factor and is still not very well understood. Anatomical factors (regularity of the cavity) are involved but also immunological factors, which are much more difficult to assess and correct.

Before any recourse to IVF, your gynaecologist will have assessed the normality of the cavity in which the embryo must implant, but it must be remembered that in the human species the rate of implantation of the embryo is constitutionally low and is rarely more than 25% to 30%.

In certain situations the “reception site” for the embryo is not good enough and it must be prepared in the best way possible (e.g.: history of pelvic inflammatory disease, Fallopian tubes infection, endometriosis, polyps etc.); where there is repeated failure to implant certain of the supplementary examinations may have to be repeated between two stimulation attempts to ensure better local conditions.

[5] MISCARRIAGE

- This risk is similar to that seen with a natural pregnancy, i.e. in the order of 11% and increasing with the age of the patient, particularly over 35 years (20%).

The long awaited sun! The young shoot will grow to be BIG...

The health of the child to come:

The health of children conceived by ART has been assessed in extensive epidemiological studies, in particular after the use of ICSI. Initial studies assessing the karyotype (the chromosomes) of the child conceived by ICSI showed a slight increase in abnormalities; this concerned 3% of children. These disorders were in part acquired or newly occurring (de novo) (1.6%) and in part inherited from the parents (1.4%), mainly the father (1.1%). More than half the acquired abnormalities concern the X and Y chromosomes; among the other chromosomes concerned, the majority were Trisomy 21 related to the age of the mother. Acquired abnormalities being three times more frequent than in the general population, it cannot be excluded that the cause of some of these anomalies is linked to the ART technique or to the infertility itself. Fortunately the majority of these disorders are considered benign, because they have limited or no clinical repercussions for the children.
The assessment of children born following ICSI has shown a slight increase in malformations at birth (1.3 to 3 times more), explaining the more frequent need for medical attention and minor surgery found in comparisons of these children at 5 years with those of the same age conceived naturally. The development of these children has been studied for a longer period and at 8 years the assessment of their puberty stage, growth, neurological and intellectual development did not show any difference to that of children conceived naturally.

However, these studies are difficult to interpret, because the control groups of children born after natural conception were probably less carefully examined than those born after ICSI, which could lead to an overestimation of the abnormalities following ICSI. Furthermore, an increase in malformations, not only with ICSI, but also with IVF and with IUI has been found, which would suggest here also that it is more the infertility than its treatment that is at the origin of the these abnormalities.

It is still not known whether the ART which help infertile couples to have children result in the transmission of this infertility to these children. This is not excluded, in particular following ICSI; however, studies of several generations are not realisable at present as ICSI only dates from 1992.
Sometimes **THERE ARE OTHER WAYS**

**EGG DONATION**

This involves the donation of female reproductive cells (eggs or oocytes) from one woman to another. In Belgium there is a law governing the donation of eggs: the request must be made before the woman’s 45th birthday and the embryo transfer may not take place after 46 years of age. The soundness of the indication is left to medical assessment.

In our centre the donation of eggs is carried out only in the context of medical indications. It is intended for couples who want a child and in which the woman is suffering from an early depletion of her ovarian reserve. It can also be carried out if there are significant oocyte abnormalities which have caused the failure of multiple in vitro fertilisation attempts, or in certain cases where there is a genetic anomaly which is incompatible with the normal development of a pregnancy and a child. Here it is the voluntary donor in good health who will receive the stimulation treatment up to the time of retrieval.

To donate eggs in our centre you have to be older than 18 years but less than 36 years old, be already a mother and have a health status corresponding to the criteria defined by the gynaecologist. The donation can be anonymous or not. A specific brochure concerning the donation of eggs is available to you.

**SPERM DONATION**

- In certain cases extensive examinations carried out in the man, including surgical examinations, fail to find any spermatozoa. There is therefore no possibility of conception with gametes from the male partner. One of the alternative solutions for the couple is to use a donor sperm who is usually anonymous. Non-anonymous donation is authorised in Belgium.
RE COURSE TO EMBRYO DONATION (OR ANTENATAL ADOPTION)

Every year a certain number of couples having frozen supernumerary embryos in our laboratory and having fulfilled their desire for children, donate these embryos, through our centre and anonymously, to other infertile couples.
These embryos (while being rare) are at the disposal of any couples who have infertility problems involving both partners.
In order to benefit from this a complete file must be drawn up in our centre by one of the coordinating gynaecologists.

N.B. : In Belgium the donation of embryos is always COMPLETELY anonymous. Neither the couple nor the child will be given the identity of donors.

ADOPTION

Like procreation, adoption finds it raison d’être in the quest for a child to love. If medical techniques do not prove successful, it still offers hope.
It provides parents for a child who has not been favoured by fate and creates a true parent-child relationship.

For more information about adoption you should contact the Reproductive Health Department of the Communauté Française. http://www.adoption.be
AT YOUR SIDE... for a peaceful journey

“Meeting place – An opportunity to take a break for the couple”

THE MONTHLY INFORMATION SESSION:

Every first Monday of the month, in a room in the general hospital, the ART team will welcome you to an audiovisual presentation to explain all the treatment to you. Your presence together as a couple is strongly recommended because the explanations and question-answer exchanges which are scheduled for 2 hours allow couples to embark on treatment with greater equanimity. You can listen to and question the doctor, biologist, nurse and our well-being specialists (psychologist and sophrologists).

The session starts at 7.30 p.m. and it is not necessary to register.

CONSULTATIONS WITH NURSES:

Our nurses will give you support throughout your treatment. They will be present at the information session, during blood-sample taking, on the telephone the afternoon of your consultation, at your side in the operating theatre during the retrieval and transfer and when the results of your pregnancy test are made known.

They will be there for your questions or particular requests, your remarks or complaints. They may also receive you for a “nursing consultation”, as a couple or individually before or during the treatment. This is the time when they can examine with you the conditions in which your treatment is about to start and adjust your lifestyle: food, smoking, sport etc.; they can even refer you to specialists, such as a dietician or tobacco-addiction specialist. They can go over all the stages of your treatment with you in a relaxed and face to face session where you can ask them all your questions calmly. They can help you to manage the administrative steps and to fill your informed consent.

For these consultations the appointment is made directly with the nurses (see details on Page 37).
TALKING TO THE PSYCHOLOGIST

ART does not only concern the body; it also concerns your person as a whole and your life and your partner’s life together. The medical team therefore, apart from the “technical” aspects of ART, will accompany and support you in the plans you have for your life. It is important for this medical team to protect the human dimension as far as possible during the diagnostic and therapeutic stages. While those involved in the medical procedures will do their best in this regard too, there are also the well-being professionals attached to the ART Center who will be there to listen to you.

At the beginning of the programme, an interview with one of our 2 psychologists is therefore systematically recommended by the gynaecologists.

WHY DOES THE MEDICAL TEAM ADVISE THIS VISIT?

- The discussion is an opportunity for the couple to talk, to meet with a professional who can, without judging and in complete confidentiality, accept your tears, understand your anger, listen to you laugh, allow your contradictions, recognise your fears, witness your stress and relaxation, restrain your incertitudes and contain your certitudes.

- The discussion can also be a time and a space for information. It offers you the possibility to anticipate problems which might occur during or after the ART process, so that you can control the steps that you are about to take and their consequences in the best way possible.

- The discussion is therefore not a consultation with an expert intent on screening for incompetencies or difficulties in order to select good parents.

Subsequently, on request, you may of course contact the psychologists again for another or several other meetings.
**WHY CONTINUE THESE MEETINGS?**

During and after the ART programme some couples experience great emotional and interpersonal strain due to the continual pressure and stress of the situation.

As the rate of success for the programmes is estimated at between 25% and 30%, some couples will have to face failure, sometimes repeated failure. These failures often lead to phases of depression. In such a situation the role of the psychologist is to offer support to the couple, or to one member of the couple. This support may also be desirable for some couples who may have to give up the ART attempts.

Other forms of support may be proposed to you in order to help you approach and manage the treatment better. We work with a **sophrologist** who can help you through this process in other ways than with words.

**DISCUSSION GROUPS:**
Apart from private discussions with a psychologist, some couples appreciate and are enriched by the sharing of experiences.

This is why the psychologists, in association with the sophrologist, make “discussion groups” available to you, in which you can exchange your experiences with other couples. Many couples become aware in this way that they are not alone and that the contradictory feelings they have are also felt by others and, continuing from this awareness of a shared problem, they support each other mutually, give and receive messages of hope and can look forward to a future.
DOWN TO EARTH BUT VERY NECESSARY!

Since July 2003 the health mutual insurance companies may reimburse IVF laboratory work (i.e. up to about €1400) for 6 attempts (egg retrieval and fertilisation) if the patient is less than 43 years of age. Since the introduction of this reimbursement, the number of embryos that may be transferred is governed by certain conditions; this in order to limit the risk of multiple births.

<table>
<thead>
<tr>
<th>Age of the patient</th>
<th>First attempt</th>
<th>Second attempt</th>
<th>Subsequent attempts</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; than 35 years</td>
<td>One</td>
<td>1 or 2 according to quality</td>
<td>Never more than 2</td>
</tr>
<tr>
<td>From 36 to 39 years</td>
<td>Never more than 2</td>
<td>Never more than 2</td>
<td>Never more than 3</td>
</tr>
<tr>
<td>Over 40 years</td>
<td>No limit imposed</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Compliance with the directives has brought the rate of twin pregnancies following IVF down to 11%.

N.B. The maximum number of transfers of thawed embryos is 2 irrespective of age.
Your particular case will be discussed in consultation with your gynaecologist and the laboratory biologists following the particular conditions given above.
Six complete treatment cycles will be reimbursed whether or not the patient has been pregnant in previous attempts and this is the maximum allowed for any one individual.

We will try to assess roughly what a test-tube pregnancy would cost for a couple with health insurance and entitled to the reimbursement of the laboratory costs, by listing for you the costs which are not covered by the health insurance organisation (patient’s contribution/supplements):

- +/- 4 consultations with ultrasound Scan: 40€ no reimbursement
- +/- 5 blood samples: 60€ no reimbursement
- Oocytes retrieval:

<table>
<thead>
<tr>
<th>Added</th>
<th>multiple bed room</th>
<th>2 bed room</th>
<th>Private Room</th>
</tr>
</thead>
<tbody>
<tr>
<td>Room</td>
<td>0,00 €</td>
<td>0,00 €</td>
<td>0,00 €</td>
</tr>
<tr>
<td>Surgery</td>
<td>55,97 €</td>
<td>90,00 €</td>
<td>120,00 €</td>
</tr>
<tr>
<td>Ultrasound scan</td>
<td>3,29 €</td>
<td>15,00 €</td>
<td>0,00 €</td>
</tr>
<tr>
<td>Anesthésia</td>
<td>0,00 €</td>
<td>47,00 €</td>
<td>94,00 €</td>
</tr>
<tr>
<td>WE surcharge (surgery)</td>
<td>22,05 €</td>
<td>0,00 €</td>
<td>0,00 €</td>
</tr>
<tr>
<td>WE surcharge (anesthesiologist)</td>
<td>22,05 €</td>
<td>0,00 €</td>
<td>0,00 €</td>
</tr>
</tbody>
</table>

- The cost for drugs: around 10 €
- Cost for embryo transfer: no reimbursement
  - 25 € for the medical procedure
  - Reception in the rest area: 70 €
  - Medical surcharge: 50 €
- Consultation with the anesthesiologist: 20 € (once a year) no reimbursement

N.B.:

For all special situations (EEC, foreigners without social insurance cover etc.) you can ask prior to any treatment for a personalised quote from one of our administrative secretaries (details on Page 37)
The pro-active, preventative approach

Very often when they become involved in this kind of very technical treatment, couples like to know how they can improve the prognosis by doing something themselves: by adopting a new lifestyle, behaviour and habits which would make them active participants in the construction and achievement of their project.

While the chances of success depend on the experience and competence of the ART team, they are also greatly influenced, not only by the pathology involved, but also by the LIFESTYLE of the couple.

Some very important elements:

Smoking:
The effects of tobacco on the unborn child are well known, as well as its impact on pregnancy.
Smoking furthermore reduces the chances of spontaneous pregnancy and prolongs the time to conceive. These observations concern both male and female and include both active and passive smoking. Smoking also increases the risk of a miscarriage and reduces the ovarian reserve, advancing the age of the menopause by 2 to 3 years.

In IVF the chances of success are also reduced by smoking and it is considered that, if a woman smokes, the number of IVF attempts must be doubled before she becomes pregnant; however, in Belgium only 6 attempts for any one person are reimbursed. The retrieval of oocytes is reduced because of the effect of smoking on the ovarian reserve levels and it is considered that a smoker who undergoes IVF will have the same results as a woman 10 years older than her, particularly in the years between 20 and 30. This reduction in ovarian reserve will be added to the reduction already taking place in women of over 35 years. The length of time the person has been a smoker is an important element, as well as the number of cigarettes smoked; it would appear that even less than 10 cigarettes a day can have an effect.

Smoking in the male partner has an added effect, but even if the woman does not smoke, the results for IVF will be reduced by 40 %, and this includes the case of recourse to ICSI. The rate of miscarriage is multiplied by 2 due to a direct effect on the integrity of the chromosomes transmitted by the sperm.

This is why it is absolutely necessary to stop smoking BEFORE undergoing an IVF attempt. To help you with this process, which is often very difficult in a period of stress due to infertility and the heavy forms of treatment involved, we would suggest that you seek the assistance of a tobacco-addiction specialist.
Weight:
It is the ratio between weight and height that is important and this is called the “body mass index” or BMI (weight divided by squared height). The BMI is used in the assessment of the impact of excess weight on fertility, on IVF results and on the progress of the future pregnancy.
A BMI over 25 is considered overweight, over 30 obesity, over 35 severe obesity and a BMI of 40 is considered pathological and life threatening disease.
Being overweight reduces the chances of becoming pregnant naturally, and this is true for both partners. Where there is overweight and obesity the chances of successful IVF are reduced by 30% and the rate of miscarriage is also increased by 30%.
But the most important effect is without any doubt on the future pregnancy, with a significant increase complications during the pregnancy: high blood pressure, diabetes, thrombosis, premature birth, caesarean section and also malformations and death of the foetus. The frequency of these complications is proportional to the excess weight, multiplied by 2 to 3 on average, but with up to 8 times more complications for a BMI of over 40.
This is why we work together with a team of dieticians who will see you BEFORE the beginning of treatment and will propose a lasting weight-control management and will monitor you during the treatment. If there is a major risk for the future pregnancy, prior treatment for this problem will always be required.

And more:
Excessive consumption of alcohol by either member of the couple, and particularly during an IVF attempt, would seem to affect the retrieval of eggs and lead to fewer pregnancies and more miscarriages.
A high consumption of drinks containing caffeine (coffee, coca-cola) should also be avoided.
Regular physical exercise and a balanced diet are associated with greater fertility.
Finally, you will be recommended to take folic acid, alone or in a multivitamin supplement. This vitamin has proved to be effective in the reduction of certain foetal malformations (neural tube) but also in increasing fertility. You should start it before the treatment and take it continuously until pregnancy is achieved, including during periods when treatment has been stopped.
Assisted reproductive technology raises a number of ethical questions. We propose to examine three of them and hope to give you some elements to think about.

**IS HAVING A CHILD A RIGHT (LIKE THE RIGHT TO HEALTH AND LIFE) AND IS IT THE DOCTOR’S DUTY TO HELP EVERYBODY TO ENJOY THIS RIGHT?**

For many of us having children is a desire rather than anything else. Some would go further and talk of a need. One has a need to have children as one has a need to eat, to have shelter, to rest etc. If having children is a need, then obviously it is normal, if this need is not satisfied, to look for help.

Medicine is an important element in Western society and it is more and more to medicine that people turn when a need is not satisfied. However, talking in this way of the need for a child is a little too easy and obscures some of the complexity of the problem. We do not know why at a certain time in our lives we feel the desire to have a child. Many factors are involved; some are essentially cultural, others much more personal. But we can live very well without satisfying all our desires.

Having said this, not being able to have a child when one badly wants one can spoil one’s life and have repercussions on both physical and mental health.

If this is the case, it is probably the duty of the doctor to respond to this distress.

Medicine, however, is not all powerful in matters of reproduction, any more than in other dysfunctions, and can only act within the limits of its possibilities. Therefore, rather than talking about a right to have a child, one should talk of the right to be assisted, including medically, when one is unable to have the child that one desires.

**DO THE TECHNIQUES FOR MEDICALLY ASSISTED REPRODUCTIVE TECHNOLOGY THREATEN THE NORMAL FILIAL RELATIONSHIPS? DO CHILDREN CONCEIVED BY ART HAVE THE SAME RELATIONSHIPS WITH THEIR PARENTS AS OTHER CHILDREN?**
ART techniques are often accused of dissociating the biological aspect of paternity (or maternity) from its social aspect, so upsetting family stability. It is true that when recourse has to be made to a gamete donor (eggs or sperm) outside the couple, the biological father or mother of the child will be different to the social father or mother. Some people think therefore that it is not possible to say who the parents of a child conceived in this way really are.

However, in Western culture, as in numerous other cultures, the filial relationship is above all a social one. For many of us the parents of a child are those who are recognised both by themselves and society to be so, irrespective of the biological relationship.

**Being a parent is therefore, and above all, becoming a parent.**

WHAT THEN IS THE MORAL STATUS OF THE EMBRYOS THAT THE ASSISTED REPRODUCTIVE TECHNOLOGY PRODUCE AND MANIPULATE? ARE THE EMBRYOS OBTAINED THROUGH FERTILISATION OF THE EGG ALREADY PEOPLE?

The problem of the status of the human embryo has always haunted humanity but ART has made this problem more concrete by bringing out into the open what previously was hidden in the womb. The majority of doctors and biologists who manipulate human embryos consider that it is something other than just biological material that can be treated like any object. But while it is not an object, the embryo is not necessarily a person. In fact scientists lack the information necessary to determine with certainty the moral status of an embryo. Being uncertain, many doctors and scientists adopt as normal good practice the respect of the embryo for its own sake but also, and above all, because it is often very precious to its parents.

Laurent RAVEZ
Ethics Expert
For a complete understanding, a lexicon of the garden!

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adhesions</td>
<td>binding of 2 tissues by scar tissue within the abdomen after an injection or operation.</td>
</tr>
<tr>
<td>AID</td>
<td>artificial insemination using donor sperm.</td>
</tr>
<tr>
<td>AIH</td>
<td>artificial insemination by the husband's sperm.</td>
</tr>
<tr>
<td>Amenorrhoea</td>
<td>absence of menstrual periods.</td>
</tr>
<tr>
<td>Andrology</td>
<td>study of diseases of the male reproductive system.</td>
</tr>
<tr>
<td>Anejaculation</td>
<td>absence of ejaculation.</td>
</tr>
<tr>
<td>Anovulation</td>
<td>absence of ovulation.</td>
</tr>
<tr>
<td>ART</td>
<td>Assisted Reproductive technology.</td>
</tr>
<tr>
<td>Asthenospermia</td>
<td>poor sperm mobility.</td>
</tr>
<tr>
<td>Azoospermia</td>
<td>total absence of spermatozoa in the semen.</td>
</tr>
<tr>
<td>Biochemical pregnancy</td>
<td>a pregnancy which is only identifiable by hormone testing and the development of which stops before it can be identified by ultrasound scan.</td>
</tr>
<tr>
<td>Blastocyst</td>
<td>embryo aged 5 days already consisting of around a hundred cells and a central cavity.</td>
</tr>
<tr>
<td>Blastomere</td>
<td>embryonic cell.</td>
</tr>
<tr>
<td>Cervical mucus</td>
<td>viscous liquid secreted by the cervix of the uterus and facilitating the passage of the spermatozoa during the ovulatory period.</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>bacterium which in the woman can cause a relatively unnoticed infection; it is dangerous for fertility because it spreads in the Fallopian tubes and without being notice may cause irremediable damage to them.</td>
</tr>
<tr>
<td>Cryopreservation</td>
<td>Storage of cell at a very low temperature. (products used: cryoprotectants)</td>
</tr>
<tr>
<td>Culture medium</td>
<td>a nutrient liquid in which the gametes, and then the embryos, are cultured.</td>
</tr>
<tr>
<td>Cumulus oophorus</td>
<td>a cluster of cell that surround the oocyte.</td>
</tr>
<tr>
<td>Deferent duct (vas deferens)</td>
<td>duct in male reproductive organs for the transfer of spermatozoa.</td>
</tr>
</tbody>
</table>
Ectopic pregnancy: a pregnancy developing outside the uterus and often requiring termination by medical or surgical means.

Ejaculate: semen released at ejaculation.

Electronic microscopy: a particular technique for in-depth analysis of the structure of a cell, e.g. of a spermatozoon to assess its ability to fertilise; this examination may be carried out in addition to a standard semen analysis.

Embryo: the group of cells resulting from the fertilisation of an egg by a spermatozoon. It continues to be called an embryo for 3 months after conception.

Endometriosis: presence of endometrial mucosa outside the uterine cavity: in the abdomen, in the ovaries. This can cause infertility. Treatment can be medical, surgical or… pregnancy!

Endometrium: the uterine mucosa covering the interior of the cavity; it changes during the cycle becoming an environment for the implantation of the embryo.

Epididymal micropuncture: surgical procedure for epididymal sperm aspiration.

Epididymus: elongated organ situated at the back of the testicle and serving to convey the sperm from the testicles to the deferent ducts.

Fallopian tube: tube connecting the uterus with the ovary; this is where natural fertilisation takes place.

Fertility: ability to reproduce

Fibroid or Fibromyoma: benign tumour of the uterine muscle present in 1/3 of women of over 35 years and which has no risk of becoming cancerous.

Fœtus: at the end of the 3rd month of development the embryo is called a fœtus and continues to be so called up until childbirth.

Follicle: fluid cavity developing every month in the ovary and containing the oocyte. The follicle is visible in ultrasound and measures 2 cm at ovulation while the oocyte measures 120 microns and is invisible to the naked eye.

Gamete: reproductive cell whether male or female (sperm or egg).

Hormone: a substance made by glands which acts on a target organ.
ICSI: intra cytoplasmic sperm injection.

IVF: in vitro fertilisation.

IVF-ET: in vitro fertilisation and embryo transfer.

Infertility: the inability of a couple to conceive.

Insemination: in IVF putting the egg and sperms in contact

IUI: Intrauterine insemination.

Karyotype: analysis of the number and structure of the chromosomes carried out on blood cells; in either member of the couple it can provide evidence of certain causes of infertility or miscarriage.

Micropolycystic ovary: syndrome associating ovulation disorders excess of male hormones and typical aspect of ovaries at the echography scan.

Oestrogen: female hormone secreted by the ovary, in the first part of the cycle, as oestradiol.

Oligozoospermia: reduction in the number of spermatozoa ejaculated.

Oocyte = egg: female reproductive cell (gamete).

Ovary: female sex gland producing eggs or oocytes.

Pituitary gland: A gland situated at the base of the brain and controlled by the hypothalamus, which is situated higher up in the brain. The pituitary gland secretes the hormones which, among other things, act on the ovaries and testicles.

Polar body: small cell containing 23 chromosomes which is discarded during the development of a fertilisable oocyte and at ovulation.

Progesterone: hormone secreted by the corpus luteum in the 2nd half of the cycle; the corpus luteum is the gland which takes the place of the follicle ruptured at ovulation.

Pronuclei: nuclei of the sperm and oocyte before their fusion in the fertilised egg.

Prostate: gland of the male reproductive system situated at the base of the urethra and the secretions of which contribute to producing semen.
Spermogenesis: process of producing sperm.

Spermatozoa: male reproductive cell.

Spermoculture: screening for infection of the semen, often carried out at the same time as a sperm count.

Straw: fine tube containing the sperm or embryos frozen in the laboratory. A straw may contain one or several embryos or thousands of spermatozoa.

Teratospermia assessment: sperm morphology screening. The fertilising power of the sperm is related to the rate of “normal” forms and structures.

Testicle: male reproductive gland producing the sperm and hormones responsible for male physical characteristics.

Testicular biopsy: surgical removal of small sample of testicular tissue in which the spermatozoa necessary for fertilisation can be found.

Uterine polyp: small benign tumour developing in the uterine cavity from the endometrium.

Uterus: organ with a potential cavity where the embryo implants and develops up to childbirth (normally called the womb).

Varicocele: varicose veins around the testicles which can reduce fertility.

Zona pellucida: membrane surrounding the egg which must be penetrated by the spermatozoa at fertilisation.

Zygote: fertilised egg.
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