

Information brochure Intrauterine Insemination (IUI)

21.002E

Table of contents

1. The normal female cycle.....	3
1.1. Introduction.....	3
1.2. The different steps of the menstrual cycle	3
2. The normal production of sperm.....	4
3. Causes of reduced fertility	5
3.1. What is reduced fertility?	5
3.2. What are the causes of reduced fertility?	5
4. Ovulation induction.....	8
4.1. Medication in tablet form (clomiphene citrate)	8
4.2. Hormonal injections (gonadotrophins)	8
5. Intrauterine insemination with partner sperm	9
5.1. What is it?.....	9
5.2. For whom is intrauterine insemination utilised?.....	9
5.3. What preparations must be made when starting an intrauterine insemination procedure?	9
5.4. What is involved in the preparation for intrauterine insemination?	9
5.5. How is intrauterine insemination carried out?.....	9

1. The normal female cycle

1.1. Introduction

During the fertile period of a woman's life, one ovarian follicle matures every month. When this is sufficiently mature, the follicle bursts and the egg is released. This egg is picked up by the fallopian tube and can be fertilised by a sperm cell. In the meantime, the endometrium builds up and prepares itself in this way to catch any fertilised egg and let it implant there. If fertilisation does not occur, the egg disintegrates and the endometrium breaks down under the influence of hormonal changes. The breaking down of the endometrium is called 'menstruation'.

The female cycle lasts an average of 28 days and is the period from the first day of menstruation to the first day of the next period.

1.2. The different phases of the menstrual cycle

A normal menstrual cycle can be split up into four phases: the follicular phase, ovulation, the luteal phase, and menstruation.

The follicular phase

At birth, each woman has about 2 million egg cells in her ovaries. These egg cells are contained in small follicles. From puberty onwards, several follicles grow per cycle under the influence of hormones. In the end, there is only one dominant follicle that becomes sufficiently large (about 2 cm). When the dominant follicle bursts, the egg is released.

The dominant follicle produces the hormone oestrogen, which in itself causes the endometrium to thicken. In addition, oestrogen makes the mucus at the cervix more permeable to sperm cells.

Ovulation

In response to the peak in oestrogens, the pituitary gland begins producing the luteinising hormone. Under the influence of this luteinising hormone, changes occur in the wall of the follicle, causing it to crack so that the egg cell can be released: this is called ovulation. Ovulation generally occurs 14 days before the next menstruation. The egg is picked up by the fallopian tube. The egg is fertilisable for 24 hours after ovulation. If fertilisation occurs, it occurs in the fallopian tube and the fertilised egg is transported to the uterus to implant in the uterine lining.

The luteal phase

After ovulation, part of the dominant follicle remains in the ovary: this is called the corpus luteum (Latin for 'yellow body'). The corpus luteum produces progesterone, a hormone that stimulates the endometrium to mature further, so that a fertilised egg can implant itself.

Menstruation

If the egg is not fertilised after ovulation, the corpus luteum disintegrates. This reduces progesterone production, which stops the stimulation of the endometrium. The endometrium breaks down and is expelled: this is called menstruation.

Early pregnancy

If the egg is fertilised and the embryo has implanted, the woman is pregnant and menstruation will not occur. The corpus luteum continues to produce the progesterone that sustains pregnancy until this function is taken over by the placenta.

2. The normal production of sperm

The quality of the man's sperm is determined by the quantity, mobility, and shape of the sperm cells.

The **sperm count** is important for the chance of pregnancy. Normally, there are at least 15 million sperm cells per millilitre. The fewer sperm cells there are, the less chance there is of fertilisation. *Oligospermia* (too few sperm cells) occurs if there are less than 15 million sperm cells per millilitre. Sometimes, there is also azoospermia, which occurs when there are no sperm cells at all in the sperm sample.

The **mobility of the sperm cells** is also important. Sperm cells must be mobile enough to travel the entire route through the mucus of the cervix and then through the uterus and fallopian tube to reach the egg. If the sperm cells are insufficiently mobile, this is referred to as *asthenozoospermia*.

The **shape of the sperm cells** is the third parameter that is important for the quality of the sperm. Sperm cells with a normal shape are more likely to fertilise the egg. If there are too many sperm cells with different shapes, this is called *teratozoospermia*.

In case of reduced sperm quality, a combination of the three problems mentioned above is often seen: oligo-astheno-teratozoo-spermia.

3. Causes of reduced fertility

3.1. What is reduced fertility?

Fertility is considered to be reduced when no pregnancy has occurred after 1 year of regular, unprotected sexual contact. In 33% of couples, the problem lies with the woman alone; in another 33% of couples, the problem lies with the man alone; and in the remaining 33%, the problem lies with both. No clear cause of reduced fertility is found in a small minority of couples.

3.2. What are the causes of reduced fertility?

A. Causes of reduced fertility in women

1. Absence of ovulation (anovulation)

Women with a regular menstrual cycle ovulate monthly. This is, of course, a basic requirement for becoming pregnant. Different hormones play a role in the menstrual cycle. If something goes wrong in the chain reaction of the different hormones, it is possible that ovulation will not occur. This is referred to as anovulation.

Anovulation can be caused by the woman's body weight being too high or too low, too much stress, and the most common cause: *polycystic ovary syndrome* (= PCOS).

What is PCOS?

PCOS occurs in 5 to 10% of all women. Their ovaries contain several small follicles without any of them being able to grow and burst open. Because of the absence of ovulation, they have an irregular cycle or even the absence of menstruation. The ovaries of these women produce more male hormones, which can lead to acne and excessive hair on the arms, legs, torso, and face.

How is PCOS diagnosed?

PCOS is diagnosed through a combination of blood tests and ultrasound.

How can we treat women with PCOS who want to become pregnant?

- **Weight control:** Weight loss in overweight women can already lead to a recovery of the cycle and the development of ovulation. Weight gain in underweight women can achieve the same result.
- **Ovarian stimulation:** Hormonal stimulation of the ovary is an attempt to ensure that one or more follicles mature, depending on the choice of fertility treatment.
- **Laparoscopic electrocoagulation of the ovary (ovarian drilling):** during a keyhole surgery, the capsule of the ovary is punctured in different places, which can lead to the easier occurrence of ovulation.

2. Disrupted egg transport

After ovulation, the ripe egg is picked up by the fallopian tube. This is how the egg is transported from the ovary to the uterus. Disrupted transport is caused by a poor throughput of the fallopian tube. This may be the result of an earlier infection or sterilisation.

3. Cervical issues

The passage of the sperm cells through the cervix is made more difficult when mucus production is reduced at the level of the cervix. This can be caused by insufficient hormonal stimulation in the first part of the cycle or by structural abnormalities in the cervix.

4. Implantation issues

Sometimes, implantation in the uterus is disrupted. This may be the result of insufficient progesterone production in the second half of the cycle (luteal insufficiency) or structural abnormalities in the uterus.

4a. Luteal insufficiency

If the corpus luteum produces too little progesterone after ovulation, the quality of the endometrium is insufficient to allow for adequate implantation.

4b. Structural uterine abnormalities

Structural uterine abnormalities include a bicornuate uterus, a septated uterus, or polyps/fibroids.

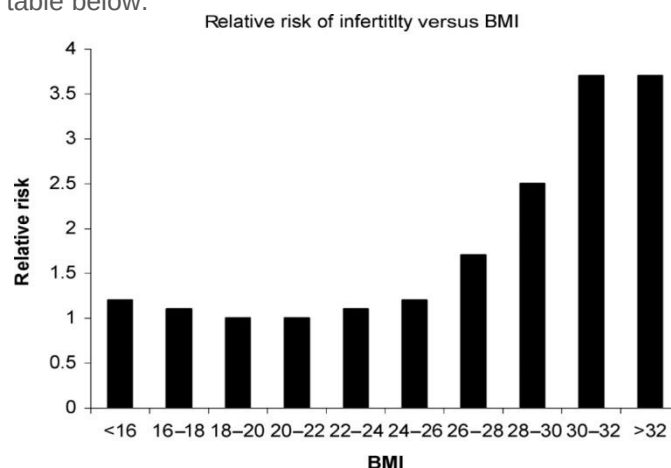
5. Endometriosis

Endometriosis means the presence of uterine mucosa outside the uterus. This can present itself as cysts on the ovaries or as affected areas on the peritoneum, intestines and bladder. Endometriosis is the result of the return of menstrual blood to the abdominal cavity. This causes abdominal pain, especially during menstruation or sexual contact, but it can also cause a kind of chronic abdominal pain. Some women with endometriosis have no symptoms. Endometriosis can cause reduced fertility, due to disruptions in ovulation or deformities, both of which make transport in the fallopian tubes more difficult. 3 out of 10 women with reduced fertility have endometriosis.

6. Age, excess weight, smoking, alcohol, drugs

A woman's age has a major influence on fertility. The most fertile period for women is between the ages of 20 and 35. After that, fertility gradually decreases, mainly due to the reduced quality of the eggs and the decreasing egg cell reserve. As a woman ages, the risk of spontaneous miscarriage also increases.

With a BMI (body mass index) of under 18 or over 25, the chance of spontaneous pregnancy decreases, as can be deduced from the table below.



Smoking, alcohol, and drugs are harmful to the quality of the egg and are also a cause of reduced fertility. They also increase the risk of miscarriage.

B. Causes of reduced fertility in men

1. Disrupted sperm transport

1a. Erectile dysfunction

In cases of erectile dysfunction, the sperm cells cannot be introduced up to the cervix via the vagina in a normal way. This reduces the chance that sperm cells will reach the eggs quickly.

1b. Premature ejaculation

The sperm cells do not go deep enough into the vagina in cases of premature ejaculation. Therefore, the chances of normal fertilisation are also smaller.

1c. Retrograde ejaculation

In cases of retrograde ejaculation, the sperm cells end up in the man's bladder. Retrograde ejaculation can be the result of a deviation of the seminal ducts or the side effect of taking certain high blood pressure medication. Retrograde ejaculation is also seen in men with diabetes or after prostate surgery.

1d. Obstruction of the seminal ducts

In the event of obstruction of the seminal ducts, the sperm cells cannot, of course, end up in the sperm sample. Causes of obstruction of the seminal ducts may be congenital (cystic fibrosis) or acquired (after sterilisation).

1e. (Partial) absence of the seminal ducts

If the seminal ducts are absent, normal transport of the sperm cells is, of course, impossible. Therefore, there are no sperm cells present in the sperm sample.

2. Disrupted sperm production

2a. Improperly descended testicles

If the testicles have not descended, the temperature in the testicles will be too high, which negatively affects the quality of the sperm cells. Testicular descent must be closely monitored in children. Surgery is occasionally necessary to solve this problem. The testicle is then attached to the scrotum.

2b. Previous infection of the testicle

When going through mumps in puberty, the young man can develop an inflammation of the testicle (orchitis). Sexually transmitted diseases such as gonorrhoea can also cause an infection in the testicle. This then hinders production or transport of sperm cells.

2c. Varicocele

A varicocele is a mass of varicose veins in the testicle. A varicocele occurs in about 15% of men. A large varicocele can be operated on. However, it is still unclear whether surgery increases the chances of pregnancy.

2d. Testicular torsion

Testicular torsion is when the spermatic cord rotates and becomes twisted, which cuts off the supply of blood to the testicle, leading to death of the testicle. The latter can only be prevented if action is taken very quickly. Fortunately, testicular torsion is rare. This can occur due to intense physical activity or not have any clear cause at all.

3. Smoking, drugs, alcohol, heat, chemicals

Smoking, drugs, and alcohol all have a negative effect on sperm quality.

If the temperature of the testicles is too high, this can be detrimental to the sperm quality. This can be caused by frequent visits to the sauna or hot baths.

Certain substances with which men come into contact can also cause fertility problems. Examples are certain pesticides, welding fumes, solvents for certain paints, etc.

4. Ovulation induction

A slight hormonal stimulation can be given to women with an irregular cycle so that one or a maximum of 2 follicles will grow. This hormonal stimulation can take the form of medication ingested during 5 days of the cycle or daily hormonal injections until ovulation is achieved.

4.1. Medication in tablet form

On the third day of the cycle, the woman starts to take one tablet/day for five days. An initial ultrasound is performed around day 10-12 of the cycle to assess the ovaries' reactions. If one or two follicles are growing, the ultrasound is repeated until the largest diameter of the follicles is about 20 mm, with or without blood sampling. At that moment, we expect the egg to be mature and ovulation is started with an HCG injection. From this moment on, the woman is fertile and can initiate spontaneous sexual relations if the sperm quality is normal.

If there is little to no reaction from the ovaries, the medication dose can be increased to a maximum of three tablets a day.

4.2. Hormonal injections (gonadotrophins)

If the woman does not respond to three tablets a day during stimulation or if the uterine mucosa does not build up sufficiently under the stimulation in tablet form, it is possible to switch to daily injections. Here, too, the reaction of the ovaries is monitored via ultrasound and blood sampling until the largest diameter of the follicles is about 20 mm. At that moment, we expect the egg to be mature and ovulation is started with an HCG injection. From this moment on, the woman is fertile and can initiate spontaneous sexual relations if the sperm quality is normal.

If there is little to no reaction from the ovaries, the injection dose can be increased until a mature follicle has grown.

If, in both cases, stimulation leads to three or more follicles, the cycle is stopped to avoid the risk of multiple pregnancy.

5. Intrauterine insemination with partner sperm

5.1. What is it?

Intrauterine insemination is the insertion of the sperm using a fine catheter high in the uterus at the time of ovulation. The inserted sperm has been pre-processed in the laboratory.

5.2. For whom is intrauterine insemination utilised?

Intrauterine insemination is utilised in the following situations:

- for couples where the quality of the man's sperm is slightly abnormal (abnormalities in number, shape, and/or mobility of the sperm cells)
- for couples with normal sperm quality who have not become pregnant after a few ovulation induction attempts
- for couples where the quality of the woman's cervical mucus is poorer
- for couples for whom no clear cause of reduced fertility has been found

5.3. What preparations must be made when starting an intrauterine insemination procedure?

- For the man, a virus serology (hepatitis B and C, HIV, and syphilis) must be determined in the laboratory of the Jan Yperman Hospital. This blood sample is valid for a period of 6 months.
- The couple must sign a contract with the Jan Yperman Hospital.

5.4. What is involved in the preparation for intrauterine insemination?

For the woman

Intrauterine insemination can occur in a spontaneous cycle or after hormonal stimulation.

For the man

The man is asked to provide a sperm sample at the agreed time. A sexual abstinence of two to three days before the production of the sample is recommended. Specific guidelines concerning the collection of sperm can be found on the lab's application form.

Sperm consists largely of liquid in which the sperm cells are located. The sperm cells are separated from the liquid. The reprocessing of the sperm takes about two hours. Afterwards, the intrauterine insemination using the reprocessed sperm sample may take place.

5.5. How is intrauterine insemination carried out?

Intrauterine insemination takes place during the visit to the clinic. The gynaecologist inserts a speculum into the vagina. Then, a very thin catheter is passed through the cervix, through which the reprocessed sperm is fed into the uterus. This is painless. Once the sperm has been injected, you can return home immediately.

Authorisation for artificial insemination with partner sperm

Between

1/ the Jan Yperman Hospital, with its registered office at Briekestraat 12, 8900 Ypres, represented by Doctor H. Feys (Medical Director), who shall appoint the Gynaecology Department for the further implementation of this contract, represented by Doctor J. Quintelier, department head and intermediate structure administrator and the treating physician (the undersigned).

Hereinafter referred to as the Jan Yperman Hospital,

and

2/ Ms
born in on
residing at
.....

Mr
born in on
residing at
.....

hereinafter referred to as the prospective parents,

The following is agreed:

Mr
grants permission to Jan Yperman Hospital
to inseminate Ms
with his sperm.

Ms
grants Jan Yperman Hospital permission to inseminate her with the
sperm from Mr

The prospective parents are aware that, for Jan Yperman Hospital, the treatment forms the subject of a best-efforts obligation and that the success of the treatment cannot be assured.

The prospective parents explicitly declare to have been sufficiently informed about the medically assisted procreation treatment (hereinafter referred to as the treatment) and the possibility of obtaining the necessary psychological support before and during the treatment in accordance with the law of 6 July 2007.

The prospective parents declare that they have received this information in the form of a printed information brochure (**21.002E**), in which all aspects of the treatment are discussed, including the associated examination procedures and the risks and inconveniences that the treatment may entail.

They declare that they have received, read, and understood that information and that it was sufficient to support their informed decision.

The prospective parents agree that their medical data will be available to the gynaecologists at Jan Yperman Hospital involved in the treatment and also give their consent to pass on the data obtained to an external body for national and international registration. This is done in encrypted form so that the recipient of this information cannot trace anyone's identity.

Drawn up in duplicate in Ypres on/...../20.....,
of which each party declares to have received one copy.

The prospective parents,

..... (I) (I)

Name: Name:

Signature: Signature:

Name of the treating physician:

Stamp and signature:

(I) Handwritten in full: 'read and approved'.

