

Kinderwunsch MITTELHESSEN zentrum

We want a *baby*
A matter of **body** and **soul**.

Welcome, dear Couple!

The desire to start a family is the basic need of each human being. The wish to have own children is the most natural in the world.

However, so obviously this yearning may be, a heavy strain lies on a couple if over a long time period the child blessing fails to appear. Questions, doubts and insecurity builds up and the partnership can be put on a very hard trial.

With our experience we stand by your side to show possible ways to fulfill your child wish. With pleasure, we would like to inform you in a personal meeting about possibilities of treatment, their prospects of success and risks.

We help nature to grow!

For the Team of the Fertility Center Mittelhessen

Dr. Amir Hajimohammad



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What happens within our body?

In understanding the causes of involuntary childlessness, it is important to understand the significance of the reproductive system and to visualise the processes involved which lead to egg fertilisation and pregnancy.

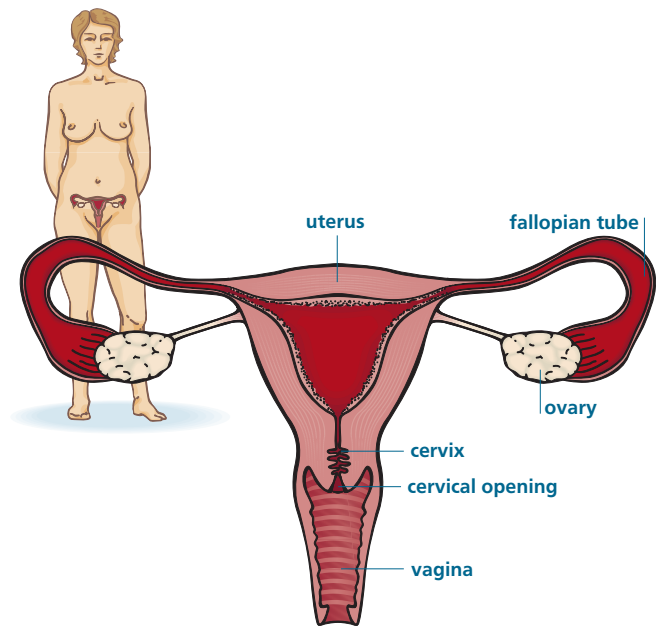
The female reproductive system

The reproductive system consists of both external and internal sexual organs. In women, these include the vulva (the outer and inner labia [lips], clitoris and the mound of Venus), the vagina, the womb (uterus), fallopian tubes and the ovaries.

The female menstrual cycle

The female menstrual cycle, a process which occurs on a regular basis, is one of the prerequisites for reproduction. During each cycle, egg cells (which are capable of being fertilised) mature and changes occur in the womb, as it prepares itself each month for the possibility of receiving a fertilised egg.

Both these processes, including the „right sequence“ in which they occur, are controlled by hormones, which are ultimately controlled and released by the brain.

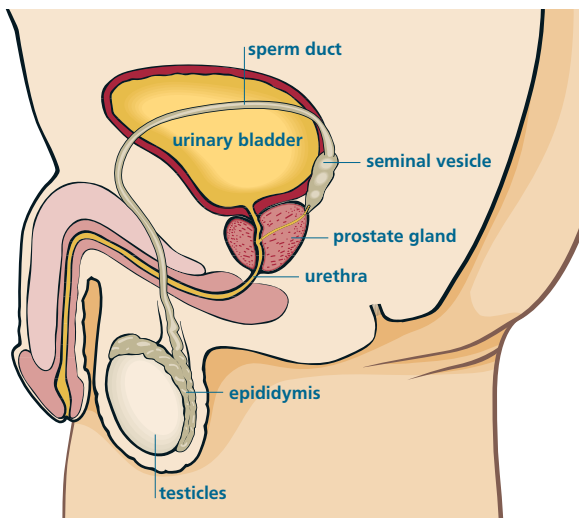


Hence, in terms of reproduction, as with other biological processes, the brain plays a vital role. Within our brain, all internal and external stimuli are received and processed. It also controls our emotions such as love, arousal and libido.

In this regard, the most important hormone is known as GnRH (gonadotrophin-releasing hormone). The secretion of GnRH in the brain triggers the release of two hormones: FSH (follicle-stimulating hormone) and LH (luteinising hormone). Both these hormones have an effect - via the blood - on the ovaries. To find out what roles hormones play in the process of conception, please read chapter „How does pregnancy occur?“.

The male reproductive system

External male reproductive organs include the testicles (gonads), epididymis (collection of tubes behind the testicle) and penis. Inside the body, reproductive organs include the prostate gland, seminal vesicle and the sperm duct.

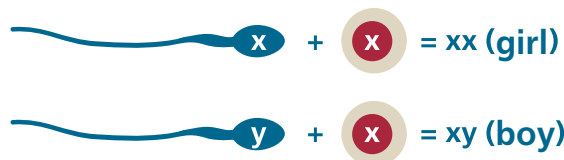


Sperm cell maturation in the male

As in women, male reproductive processes are regulated by hormones. As in the case of women, GnRH (gonadotrophin-releasing hormone) controls the secre-

tion of FSH (follicle-stimulating hormone) and LH (luteinising hormone) into the blood. Both these hormones regulate processes within the testicles. FSH is vitally important producing sperm, millions of which develop daily in the testicles within a system of tiny tubes known as the seminiferous tubules. From here, they enter the epididymis, where they eventually mature. During ejaculation certain muscles contract in order to force the sperm outwards via the sperm duct and urethra. Each ejaculation releases 3-4 hundred million sperm. However, of these, only a few hundred manage to reach the ovum (egg).

Each sperm cell consists of a head, body and tail. The sperm head contains the paternal genes, which, in the event of successful fertilisation, will determine whether the child will develop into a boy or girl. The sperm body is responsible for providing the sperm with energy, whilst the tail ensures a whiplash motion, which propels the sperm forwards.

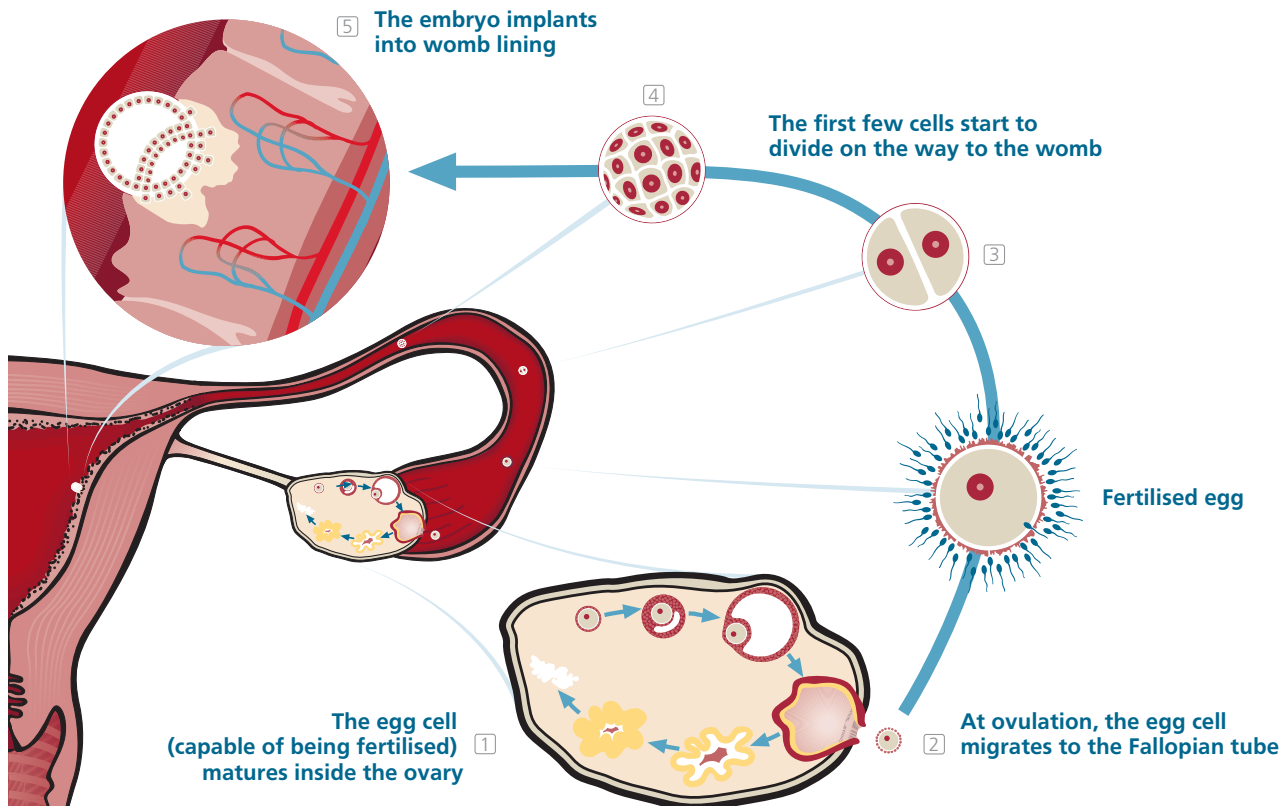


How does pregnancy occur?

- 1 During the first half of the menstrual cycle, the FSH hormone stimulates the growth and development of (usually) only one single egg follicle within one of the ovaries. Thereafter, a single egg cell matures inside this follicle. Estrogen, produced by follicles inside the ovary, stimulates the growth of the womb lining.
- 2 When an egg cell has matured and is ready, LH hormone levels suddenly rise, triggering off its release (ovulation). In a regular cycle of 28 days, ovulation takes place around Day 14-16. The egg follicle „explodes“, thus releasing the fertile egg, which then migrates to the Fallopian tube. Meanwhile, cell remnants of this spent follicle transform into corpus luteum („yellow body“), which goes on to produce a hormone known as progesterone. Progesterone prepares the womb for a possible pregnancy.
- 3 On its way from the Fallopian tube to the womb, the egg is fertilised. Out of the countless sperm that make it to this stage, only one manages to penetrate the egg's protective membrane thus fertilising the egg. During fertilisation the paternal and maternal genes combine to start the creation of the embryo and a new life begins.
- 4 As the first few cells divide, the embryo continues its course toward the womb. Here, just before implantation, it must „hatch“ out of the egg's protective membrane.
- 5 No sooner than six days after fertilisation, the embryo implants into the nutrient-rich lining of the womb.

A placenta forms at the site where the embryo is implanted, which serves to exchange nutrients and gases between mother and embryo, as well as producing hormones needed to maintain pregnancy.

If fertilisation does not occur, or if the embryo is unable to implant for any reason, the womb lining is expelled from the body, resulting in menstrual bleeding (period) and the cycle starts all over again.



When do we start speaking of infertility?

The specialist medical term for childlessness is infertility. In its literal sense, it means the inability to successfully carry out a pregnancy to full term. In common language, the term is synonymous with sterility, i.e. the inability to become pregnant or reproduce. We therefore define infertility as the inability to achieve or bring about pregnancy within one year, despite having regular, unprotected sexual intercourse.

In most cases, the cause of infertility is not hereditary but rather acquired, e.g. an occlusion (closure) of the fallopian tubes as a result of infection. Age is also a determining factor: in women, fertility starts to decline from the age of 30 and decreases quite considerably from the age of 35-40 onwards. In men, semen production and function go into slow decline from around the age of 40. Therefore, the decision to postpone family planning until later in life plays a significant role in infertility. These days, a quarter of all couples are over the age of 30 by the time their first child is born, whereas in 1970 for example, around 90% of men and women were under the age of 30 at the time of the birth of their first child. Incidences of the causes of infertility between men and women are roughly the same.

The causes of infertility in men

In men, the most common fertility problem is a deficiency in the production of normal, mobile sperm. There can be many causes of this; in many cases, it is difficult to give any clear-cut reasons.

- Mumps during childhood
- Varicose veins in the testicles
- Undescended testicles
- Hormone disorders
- Diabetes
- Tumour surgery
- Genetic disorders
- Stress
- Infections
- Environmental-related (toxins)
- Heavy nicotine and/or alcohol consumption

A less common cause is impaired sperm transport. In such cases, although enough sperm are produced, they are unable to reach the woman's body due to some form of blockage in the sperm duct. Often, the cause is due to a problem with the epididymal ducts (the collection of tubes behind the testicles), e.g. a blockage or malformation.



The causes of infertility in women

As with male infertility, there are also very many factors causing female infertility.

Ovulation disorders

A common cause of female infertility is an ovulation disorder that prevents the egg from maturing. Such disorders are mostly caused by a hormonal dysfunction in the ovaries. Any hormone imbalance can interfere with egg maturation, as well as affecting the ovulation process and the production of the corpus luteum („yellow body“).

Infertility as a result of a fallopian tube disorder

The fallopian tubes act as a „conveyor belt“, aiding sperm in their journey to the egg. They also transport the fertilised egg cells towards the uterine (womb) cavity. If the fallopian tubes are blocked or functionally compromised, egg transportation is made difficult, or even virtually impossible. Reasons for this may include an inflammation or a previous ectopic (tubal) pregnancy, surgery, or spontaneous growth of womb lining cells outside the uterus (endometriosis).

Endometriosis

Endometriosis occurs when functional cells of the womb lining grow in areas outside the womb, e.g. in the fallopian tubes, ovaries, or even the bladder or intestines. To a large extent, its cause is unknown. However, endometriosis makes it difficult for women to conceive.

Changes in the womb and cervix

For sperm, the cervix is the narrowest part of their journey to the egg. Fertilisation of the egg can therefore be prevented by cervical scarring (e.g. as a result of surgery), blockage or inflammation. Also, a myoma or fibroid (a benign tumour in the uterus) can sometimes be the reason for persistent infertility or miscarriage.

Malformations of the ovaries, fallopian tubes or womb

In very rare cases, reproductive system deformities, which are mostly congenital, can also be at the cause of infertility.

Polycystic Ovarian Syndrome (PCOS)

Often, female infertility can be associated with the appearance of multiple tiny cysts in the ovaries (polycystic ovarian syndrome). In most cases, this disorder is associated with a high level of male hormones.

Immune system disorders

Also, an impaired immune response can, on very rare occasions, be a cause of female infertility. With this dysfunction, the woman's immune system sees the egg or sperm as a foreign body, which is then attacked as an „intruder“ .

Life-style

Personal life-style can also affect fertility to the same extent in both men and women. Being overweight and having unhealthy eating habits can also play a major role, as can drinking too much alcohol/coffee and excessive smoking. Similarly, increasing detrimental environmental factors or too much stress can also have a negative impact on fertility in some cases.

In about 5-10% of couples, there is no apparent organ-related cause for the inability to conceive.



Which role does the mind play?

Saying „Yes“ to having a child together is a clear expression of deep affection and trust between two human beings. Saying „Yes“ also means that both partners are willing to accept responsibility for a new human being who is part of them both.

If the desire to have a baby remains unfulfilled, this can challenge the entire relationship, as the partners' common aim in life is seemingly under threat. Therefore, infertility all too often becomes a taboo subject. However, a lack of dialogue also means shouldering alone the burden that can sometimes develop from involuntary childlessness. In many cases, a vicious circle develops, whereby the body - laden with unexpressed reproaches or the feeling of failure - denies any chance of conception.

In such situations, talking to a therapist can be of great help. Professional psychological help can also contribute toward re-establishing dialogue between

both partners. A sex life dictated by the calendar, in which sexual desire all too often turns into frustration, can once again be steered towards mutual satisfaction. In order to be more aware of what childlessness means to you, you and your partner could ask yourselves the following questions during counselling:

- Why do we actually want a child at this moment in time?
- What does a child mean for our relationship?
- What has changed in our relationship since we „found out“?
- How are we experiencing our sexuality?
- Can we imagine our life without a child?
- Could adoption or being foster parents be an alternative?

You could also get in touch with interest groups that offer support to couples with fertility problems, such as the association Wunschkind e. V. (website and contact details are given in the appendix to this brochure). The website www.fertinet.de also provides further information on all matters concerning infertility. This site allows you to exchange your experiences with others who are also affected. In fact, talking to others with similar problems can often be a great support when facing your own challenges.

Give your emotional side all the attention it deserves

Why not seek professional help? In Germany, there are about 100 specialised infertility centres. Only by thorough investigation will you find out what is physically causing your infertility. This will then allow you to find the best solution for you.

Of course, there is no guarantee of successful treatment; indeed, human biology is not simply a mechanical process – complex interactions between body and mind have to be taken into account. As you will see:

Modern medicine has made enormous progress. These days, many childless couples can find help and success.



Medical history and diagnosis

At the beginning there is a dialogue with the doctor. Your medical history will offer valuable information as to the cause of the problem at hand.

You will be asked about your feelings and other very personal subjects by doctors equipped with a profound understanding of the aspects concerning infer-

tility-related issues and they will always treat this information respectfully and discreetly. Both partners will undergo examinations, as men and women can be affected equally by infertility. You may find it helpful to write down the questions you want to ask the doctor. Please don't hesitate to ask right away, if you don't



understand a detail fully. For your meeting with the doctors please bring all results of previous tests and possible surgery reports.

Infertility treatment can only be started after extensive diagnostic measures have been taken, to find out the possible causes. The diagnosis includes a physical examination and laboratory tests. The diagnosis of infertility disorders requires a special step-by-step process, which takes time and demands a good deal of patience.

In order to create a picture of the course of your infertility, your doctor might ask you some questions about your medical history, such as:

- How long have you been planning for a child?
- Have you ever received any previous medical treatment to help you/ your partner conceive?
- Do you think you might know why you or your partner is/ are unable to conceive?
- How much do you both suffer as a result of being childless?
- What changes have there been in your life since becoming aware of infertility (relationship, profession, self-esteem)?

In addition to talking to the doctor, diagnosis also includes a physical examination and laboratory tests. Overall, diagnosis of infertility disorders requires a special, step-by-step process, which takes some time and demands a good deal of your patience. However, if you take these steps together, you will come through in the end!

Medical examination methods concerning the male partner

Genital examination and ultrasound

As part of the infertility investigations, the man will see a urologist or andrologist (a doctor specialised in male genital disorders). First of all, in an examination known as palpation, the doctor will feel the testicles

and epididymis to check for any irregularities, as well as the prostate gland (via the rectum). A detailed investigation also includes ultrasound testing of the testicles and prostate gland.



In genetic testing, the structure and number of chromosomes is analysed.

Semen testing

Male fertility can be determined by a microscopic evaluation of the semen. Sperm, obtained via masturbation, are examined under a microscope and tested for shape and motility. As sperm cell quality can vary greatly, this test is repeated again at an interval of at least three months. A tissue sample from the testicles may be required if no or not enough intact sperm are found in the ejaculate, in order to determine whether there are problems in sperm production, furthermore these samples can be frozen for later use (TESE).

Hormone level tests

Excessively low sperm production can be caused by a hormonal imbalance. In order to rule out this possibility, hormone levels in the blood are tested. However, hormone disorders occur much more rarely in men than they do in women.

Genetic testing

Testing for genetic abnormalities is another possibility in men with an excessively low sperm count. This laboratory test is performed using a single blood sample.

Medical examination methods concerning the female partner

Palpation

First of all during the gynaecological investigation, the doctor will search for the presence of genital abnormalities or any other changes in the body that might be associated with infertility.

Ultrasound

The next stage involves examining the reproductive organs more closely by means of ultrasound. This safe and painless examination takes place via the vagina, as this ensures the best way of obtaining a view of the ovaries, fallopian tubes and womb.

Hormone level testing

In order to rule out any problems with egg maturation, levels of various hormones in the blood are tested on certain days during the monthly cycle. For example, at the start of the cycle, levels of estrogen, LH, FSH, androgens and prolactin are tested. The thyroid hormone TSH is also investigated, as both high and low levels of TSH can negatively affect fertility. During the second half of the cycle, progesterone and estrogen levels may also be measured.

Fallopian tube testing

If fallopian tube damage is suspected, imaging or surgical techniques may be used as a means of investigation. In imaging techniques, the function and condition of the uterine cavity and fallopian tubes are determined using either X-rays or ultrasound using a contrast solution. The tests can be performed on out-patients or in-patients under anaesthetic. For a more detailed investigation, it may be useful to have a laparoscopy performed (a surgical technique using a laparoscope), which might sometimes involve a short stay in hospital.

Laparoscopy

A laparoscopy is performed under anaesthetic. First of all, a laparoscope (a thin, tube-like instrument) is inserted through a tiny abdominal incision (just below the belly button) and into the abdominal cavity. This instrument is linked up to a monitor via a camera, thus allowing the doctor to obtain an extremely accurate image of the reproductive organs. If necessary, cysts, growths or endometriotic tissue can also be removed via laparoscopy.

Possible complications associated with this procedure are very rare (mainly injury to internal organs or infections). Anaesthetic-related problems are likewise very rare.



Fallopian tube filled with contrast media

Hysteroscopy

In order to determine the presence, in the uterine cavity, of malformations, myomas or fibroids (parasitic muscle tumours) or changes in the womb lining, a very thin probe is inserted into the womb via the vagina. By using this technique, the doctor can obtain an accurate image of the uterine cavity (womb) and openings of the fallopian tubes via a camera in the probe; if necessary, he/she can even perform minor surgery.

There is a wide range of therapeutic procedures available which can help in cases of infertility; depending on the cause and the course of action needed, there are various steps which can be taken.

What treatment options are available?

Hormone therapy in men and women

In both men and women, a hormone disorder can be at the root of infertility. In men for example, if the testicles are not functioning properly as a result of a lack of FSH or LH, attempts can be made to supplement these hormones by external means.

If infertility in the woman is due, to an „underlying“ hormonal disorder (e.g. thyroid dysfunction or excess of male hormones), medicines with a specific mode of action can be used. If, despite normal hormone levels, ovarian function is impaired, the natural menstrual cycle can be simulated by clomiphene tablets, FSH injections (follicle-stimulating hormone) or, if necessary, LH injections (luteinising hormone). It is also possible to trigger ovulation by administering a pregnancy hormone known as hCG (human chorionic gonadotrophin). Therefore, in women, hormone therapy targets stimulation of egg maturation or ovulation.

Regular medical check ups can determine the optimum time for sexual intercourse (as close to ovulation as possible), i.e. when fertilisation is most likely to occur.

Hormone therapy is used to treat hormonal imbalances, disorders affecting egg maturation/ ovulation, or hormone-related testicular dysfunction.

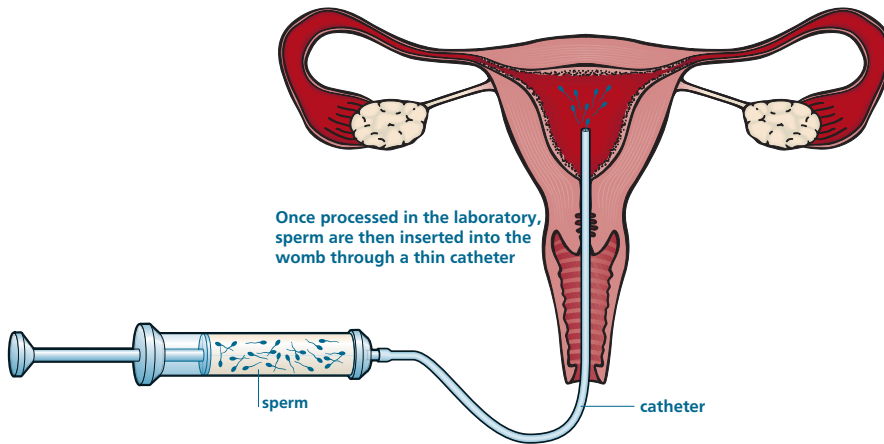
Assisted reproduction

These days, the term „artificial fertilisation“ has given way to „assisted reproduction“. This new term is intended to make it clear that fertilisation is merely assisted by the techniques available.

Conception, i.e. the fusion of egg and sperm, still remains an individual and natural process. There is a whole range of procedures that can be used, depending on medical history and the course of action needed.

- **Intrauterine Insemination (IUI)**

This technique is particularly suitable in cases of low sperm count, and in particular when sperm motility is poor. Before insemination is started, egg maturation can be stimulated by administering drugs (generally FSH), ovulation can be triggered by the administration of hCG. Semen is obtained by masturbation and then processed in the laboratory. Using a thin, flexible plastic tube (catheter), the semen is inserted into the womb cavity, as close as possible to the egg cell. The advantage of this technique is that large numbers of sperm come into close proximity with the egg cell. This method is chiefly used in cases of impaired sperm function or an immune reaction against sperm cells. It is al-



so used in cases of cervical stenosis (a narrowing of the cervix) and infertility with no recognisable cause.

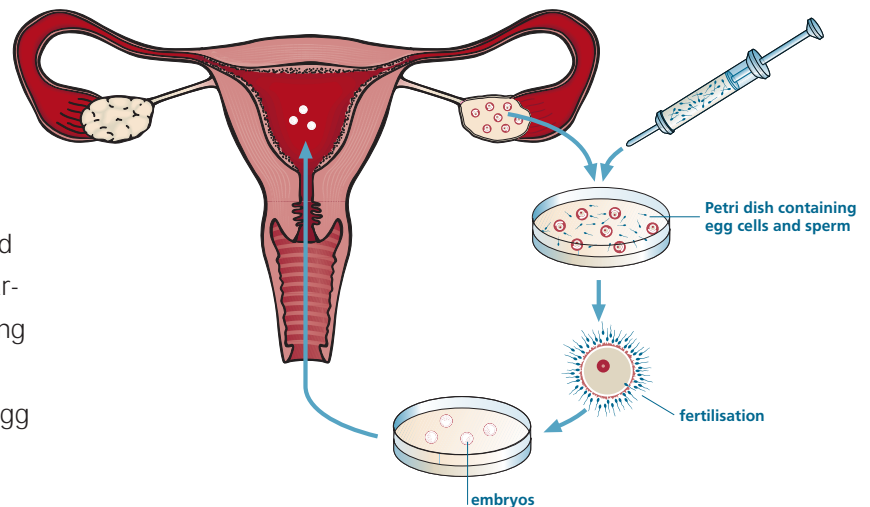
• In vitro Fertilisation (IVF)

In vitro is a Latin term meaning „in glass“, i.e. in a test tube subjected to processing techniques under laboratory conditions. Hence, IVF describes a fertilisation technique that takes place outside the body. Generally speaking, at the start of IVF treatment, egg maturation is also stimulated by means of FSH. However, in contrast to conventional stimulation, administration of a suitably adjusted hormone dose stimulates the maturation of not one, but several egg cells, which are then retrieved for fertilisation.

Whilst under general or local anaesthetic, the mature follicle (containing the egg cells) is punctured using a suction needle and the egg cells are then harvested. Next, they are placed in a Petri dish containing the sperm. After 24 hours in an incubator, a microscope is used to determine whether or not sperm/egg

fusion has taken place. If fusion has occurred, a maximum of three embryos are implanted into the woman after 2-3 days or 5-6 days (embryo transfer or blastocyst transfer, respectively; cf. also page 31).

Once all appropriate diagnostic stages have been performed to determine the cause of infertility, your doctor will talk at length with you and your partner, in order to explain the treatments that are suitable /available for you.



Which criteria must be fulfilled for IVF treatment?

The main eligibility criterion for IVF treatment is infertility that cannot be treated by any other means. In addition, egg and sperm cells must usually come from the couple involved (exceptions). Both partners are required by law to have a HIV test (a blood test to rule out the possibility of AIDS infection), as well as another test to exclude the possibility of hepatitis (a contagious liver infection).

Special requirements for the male partner

For men, the most important prerequisite is proof that they are able to produce sperm of sufficient quality in the first place. If sperm production is impaired, it is advisable to carry out blood DNA testing before considering any further treatment.

Special requirements for the female partner

Women should preferably be under the age of 40. As rubella (German measles) can damage the infant during pregnancy presence of antibodies is required. At least one ovary and the womb itself must be working properly.

In Germany, doctors must act in accordance with the Embryo Protection Act, which governs many aspects of assisted reproduction.

The preparation and stimulation phase

The first step in treatment is aimed at optimally preparing the body for hormonal stimulation.

As a rule, the menstrual cycle is adjusted with hormones in such a way that the time of ovulation and harvesting of egg cells can be well managed externally. This is achieved by medications that suppress the production of FSH and LH in the body. This process is known as „down regulation“. Medication given during this phase (e.g. GnRH agonists) target the part of the brain that releases these reproductive hormones.

GnRH antagonists can also be used to suppress the body's own production of hormones. GnRH antagonists have an advantage, in that they are not used until the stimulation phase. The total treatment time is thus shortened, and the possible onset of any hormone withdrawal symptoms is eliminated.

Stimulation of the ovaries is designed to bring several egg cells to maturity at the same time. This is necessary because not every egg cell is fertilised and not every embryo implants in the uterus.

Hormonal stimulation is very closely monitored by ultrasound examinations and by testing hormone levels in the blood. Such regular monitoring allows the doctor to observe the number and size of follicles and

the thickness of the womb lining. This enables determination of the most favourable time for triggering ovulation and for harvesting the egg cells. Furthermore, monitoring can reduce the risk of over-stimulation.

Which medications are used?

Certain medications, such as clomiphene tablets, stimulate the brain to secrete more of the reproductive hormones. For a targeted stimulation of egg cell maturation and to prepare for ovulation, other medications are used, which work in the same way as naturally secreted reproductive hormones:

- **FSH (follicle-stimulating hormone)**

In principle, the follicle-stimulating hormone (FSH) can be manufactured in various ways. FSH can either be extracted from the urine of women going through menopause (like hMG), or it can be manufactured in the laboratory using biotech techniques. These days, since purity and FSH content can vary greatly between urine-derived products, bioengineered FSH is preferred instead. This so-called recombinant FSH works in exactly the same way as naturally secreted FSH, and re-

flects the latest knowledge in medical research. It offers the maximum possible levels of purity, which means that it is much safer and better tolerated.

Furthermore – and this is the most important point for affected couples to know – one particular study has shown that substances produced in this way are more effective, i.e. the chances of conceiving are greater even though the actual dosage schedule is lower.¹

What's more, thanks to a brand-new manufacturing method (the so-called „filled-by-mass“ technique), a further step towards greater accuracy has been achieved. In FSH products manufactured via this technique, the active hormone component is measured to be exact in each batch. This means that with each injection, you will be using the exact amount of FSH which your doctor has individually calculated for you. Furthermore, the use of bioengineered products carries a lower risk of local reactions at the injection site, when compared with urine-derived products.²

FSH treatment generally starts 14 days after down regulation or within the first three days of the cycle (1st cycle day = 1st day of bleeding). Treatment lasts about 11–13 days. During this time, a specific amount

of the hormone is injected daily under the skin, preferably at around the same time of day.

If your doctor prescribes a GnRH antagonist to suppress natural hormone production, this is administered from the 5th – 7th day of stimulation onwards.

- **LH (Luteinisierendes Hormon)**

Nowadays, LH (luteinising hormone) as a pure substance is also produced using biotech techniques. LH is also used in women with LH deficiency. Since the advent of pure, biologically engineered LH, it is now possible to individually select a combination of FSH plus LH. However, since most women can produce enough LH by themselves, FSH is usually given on its own.

¹Ludwig et al., Journal Reproduktionsmed. und Endokrin. 4/2004: 284–88

²Ludwig & Rabe, Journal Reproduktionsmed. und Endokrin. 2/2004: 82–90

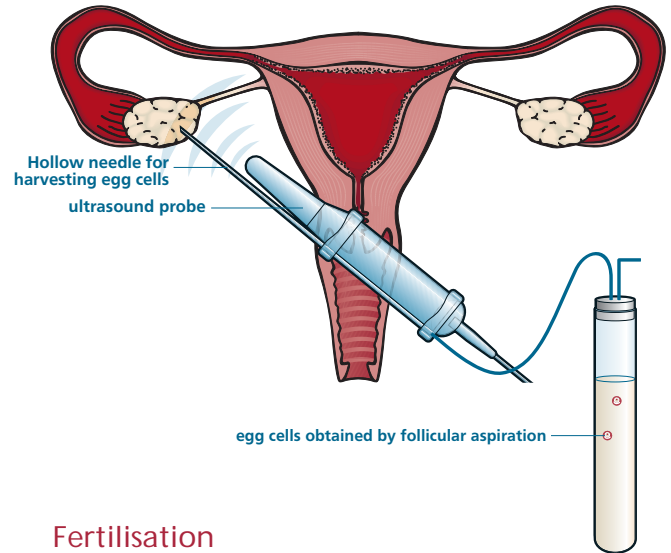
What happens once the egg cells are mature?

Once the egg cells inside the follicles are matured and ready, FSH treatment is suspended. By administering another hormone known as hCG (human chorionic gonadotrophin), the egg follicle is now prepared for ovulation.

As with FSH, modern bioengineering techniques are increasingly being used to extract hCG, in order to guarantee the highest possible levels of product purity.

HCG assumes the role that LH plays in the natural cycle. Within approximately 36 hours after administering hCG (i.e. just before ovulation), the eggs are harvested from the follicles by means of a long puncture needle (follicle aspiration or egg retrieval).

The eggs must be harvested before ovulation takes place. Otherwise, the egg cells would disappear into inaccessible areas of the Fallopian tubes and be lost. This ultrasound-controlled procedure is performed via the vagina. To make this procedure a little easier, you will be given a pain killer and/or sedative or even anaesthesia. After puncture, you may experience slight pain and minor bleeding.



Fertilisation

On that same day, fresh semen will be required from your partner in order to fertilise the egg cells. Masturbation „on demand“ is not always possible immediately. It is therefore important to address the problem of obtaining semen in good time, so that you, your partner and your fertility clinic can find a suitable solution together.

First of all, the semen is processed in the laboratory so as to optimise the fertilisation capability of the sperm. Thereafter, the egg and semen cells are placed together in a Petri dish containing culture medium and then cultivated in an incubator for 24 hours.

A maximum of three fertilised eggs are further cultured and allowed to mature for another 2-3 days (for embryo transfer) or 5-6 days (for blastocyst transfer) in the incubator.

Any remaining fertilised egg cells, in which fusion of genetic material has not yet occurred, can be frozen for subsequent cycles (cryopreservation). This is done one day after the egg retrieval. According to German law freezing of embryos (from day two onward) is only permitted in certain emergencies.

If the ejaculate (semen) contains no sperm

In some cases – e.g. where there is total blockage of the sperm ducts – there is no sperm at all in the ejaculate. However, it may still be possible to harvest sperm directly from the testicles (TESE) or from the epididymis (MESA).

- **Testicular Sperm Extraction (TESE) and Microsurgical Epididymal Sperm Aspiration (MESA)**

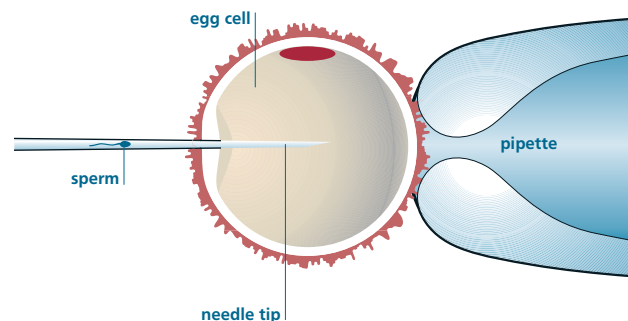
In this technique, a minor surgical procedure is used to remove tissue samples which may contain sperm. These sperm can later be used in the ICSI treatment.

If there are not enough functional sperm

If the sperm count is extremely poor (i.e. the number of fully functioning sperm is low), the chance of success, using only the IVF method, is very low. In such cases, ICSI techniques can be used instead.

- **Intracytoplasmic Sperm Injection (ICSI)**

As with IVF, before ICSI can be performed, egg cells must first be obtained by hormonal stimulation and follicular puncture. Under a special microscope, a single sperm is sucked into a fine hollow glass tube and injected directly into the egg cell (i.e. into the cell plasma, hence the term „intracytoplasmic“). This microinjection thus imitates the natural process of penetration of one semen cell into the egg cell. As in the IVF procedure, if fertilisation and cell division has taken place, a maximum of three embryos will be inserted into the uterus after 2-3 days.



Transferring embryos

The transfer of a maximum of three embryos into the womb cavity is performed by means of a thin, flexible plastic tube, which is inserted into the womb cavity through the vagina. This procedure is painless.

The more embryos that are introduced into the uterus, the higher the risk of a multiple pregnancy. It is therefore advisable to limit the number of embryos to two or three (maximum).

- **Assisted Hatching of the Embryo**

Under certain conditions (for example, after a number of unsuccessful embryo transfers), an attempt is made to increase the chances of pregnancy, by making it easier for the embryo to „cast off“ the egg membrane. This involves using a laser, which makes a tiny opening in the outer shell of the embryo just before its implantation into the womb.

- **Freezing egg cells (cryopreservation)**

It is possible to keep egg cells at the pronuclear stage for several years by freezing them. „Pronuclear stage“ means that whilst fertilisation has been successful, fusion of the genetic material has yet to occur. Cryopreservation should only be considered if there are at least three excess, high-quality eggs available. Then, even if only two embryos are to be transferred in a „frozen embryo cycle“, there is a „back-up“ embryo, if one of the cells should not survive the thawing process.

The advantage of cryopreservation: If pregnancy has not occurred in the „fresh“ treatment cycle and treatment has to be repeated, it will not be necessary to repeat the process of hormonal stimulation and egg cell retrieval.

The procedure is proven and safe. However, it does result in a lower pregnancy rate. Before you undergo IVF treatment, it is therefore important that you discuss with your doctor whether any surplus pronuclear-stage egg cells should be frozen.

Egg cells at the pronuclear stage can be kept for several years in containers filled with liquid nitrogen (cryopreservation).

Once you have become pregnant

Approximately two weeks after the embryo transfer, an initial pregnancy test is performed. At this point in time, however, it is too early to tell which course the pregnancy will take.

NB: You and your body should try to take things easy. Although it is understandable that you will feel nervous and tense, you should try to relax mind and body. At the same time, however, you should not make any radical changes in terms of your private and professional life.

For safety's sake, your gynaecologist or fertility specialist will perform a number of follow-up examinations. Furthermore, during the second half of the cycle or if you are actually pregnant, the administration of progesterone may be useful in promoting embryo implantation/ maintaining pregnancy. This is known in the medical profession as luteal phase support.



Chances and risks

There are many factors that decide whether treatment procedures will be a success. In addition to the type of fertility disorder and how long it has existed, the woman's age also plays an important role. It is therefore impossible to give any exact success ratios.

The treatment methods used today have approximately the same success rate per cycle as a natural pregnancy. By exhausting all available options - and if conditions are favourable - 60% of all affected couples can be successfully treated. However, there are a few (albeit rare) risks involved, which are given below:

- **Over-stimulation**

Your hormone treatment will be carefully monitored by your treating doctor, on account of the possible risk of over-stimulation. This means that the ovaries produce very large numbers of egg follicles, which in turn secrete an increased amount of hormones.

This over-activity can result in nausea and fluid retention, with pains in the abdomen. If you experience increasing body discomfort, you must notify your doctor at once. Severe over-stimulation may necessitate hospital treatment.

Fortunately, regular monitoring can bring the risk of severe over-stimulation down to 1–2%. Here, your active co-operation is requested. You should keep your regular appointments, even if it sometimes might be difficult.

- **Multiple pregnancies**

As a rule, the likelihood of multiple pregnancy in IVF is greater (20–30%), because, in order to assure success, several embryos (three as a maximum) are usually transferred into the uterus.

- **Miscarriage**

In older patients and as a result of subfertility (impaired ability to procreate or conceive), the risk of miscarriage is slightly increased.

- **Surgical complications**

Complications are very rare within the context of surgical procedures used in IVF. For example, during egg retrieval, infection can occur, as well as injury to organs in the pelvic area.

- **Psychological stress**

Infertility treatment is very time-consuming and involves many different appointments and sometimes complex examinations. It therefore requires a good deal of patience on the part of both partners.

Couples go through a time of intense emotions, during which their feelings can sometimes swing greatly between hope and fear, joy and disappointment. All of this can easily result in psychological stress. It is therefore important to keep communicating: Tell others how you are feeling, both physically and mentally. Talk to your partner. Communicate with your friends and exchange experiences; possibly in a self-help group and in particular with the doctor treating you.



The costs of infertility treatment

In Germany, the costs of diagnosing fertility problems, as well as examining individual case histories and providing subsequent counselling, are generally covered by the statutory health insurance fund. If IUI, IVF or ICSI treatment is needed, patients so insured are required to pay 50% of all treatment and medication costs. The remaining 50%, met by the statutory health insurance fund, is limited to three insemination procedures in the stimulated cycle, and/or three IVF/ICSI cycles. In non-stimulated cycles, eight insemination procedures are 50% reimbursable by the statutory health insurance fund.

Thereafter, any subsequent treatment is deemed „without prospect of success“, which in effect means that the patient ceases to be entitled to reimbursement from the statutory health insurance fund. However, if the treatment cycle results in a pregnancy, insured patients can make a new claim for reimbursement from the statutory health insurance fund, i.e. for up to the maximum number of unsuccessful cycles, depending on the method used. In Germany, the age range for reimbursement entitlement is between 25-40 years for women and between 25-50 years for men.

In Germany, private health insurance generally covers the cost of all IVF and ICSI attempts. However, patients are advised to check their own personal policy very closely in this regard. Couples wishing to make a fourth attempt must pay for the costs of this themselves, irrespective of the policy they hold. Should a second child also be born with the help of reproductive medicine, the statutory health insurance fund will grant the same financial help as with the first child. Similarly, private health insurance companies are also obliged to cover the costs of a second child, provided that the likelihood of pregnancy is around 15%. This generally no longer applies to women over 40; however, individual factors might be favourable, so an application to your private health insurance might be successful.

Prior to therapy, your fertility clinic will draw up a treatment plan (one for each partner), listing all the costs involved. In Germany, patients have to submit this plan to the statutory health insurance fund, whose approval must be gained before treatment can begin.

The cost of medication

In Germany, patients have to pay 50% of medication costs involved in fertility treatment, plus an additional prescription charge of ?10 maximum. Prescriptions are issued by the prescribing doctor, with a comment that the medication is for IUI or IVF treatment. The 50% of medication costs borne by the patient is paid directly to the pharmacist.

For each treatment cycle, patients have to pay total medication costs of around ?400 (stimulation in the insemination cycle) or around ?800 (IVF cycle). NB: These figures are merely average costs, as actual costs will depend on the type and dosage of medication prescribed by the treating clinic.



Legal principles

Since the birth of the first IVF baby in 1978 in England, discussions regarding the legal framework are still raging in Germany. On January 1st 1991, the Embryo Protection Act was adopted, which regulates the use of reproductive technologies and the handling of embryos.

The Embryo Protection Act legislates on several issues in detail, e.g.: artificial insemination may only be used for the purpose of procreation and not for research purposes. Within the context of assisted reproduction, the creation of surplus embryos (i.e. those which subsequently cannot be reinserted into the womb) must be avoided. Within any one treatment cycle, women may only have a maximum of three embryos transferred.

Experiments with and on the embryo are forbidden. Also, tampering with genetic material (e.g. selection of sperm according to sex chromosomes) is illegal. Similarly, egg cell donation and surrogate motherhood are also forbidden.

Assisted reproduction may only be performed by specially trained doctors. Furthermore, in most German states, assisted reproduction may only be performed on married couples. However, even in German states where unmarried couples are allowed treatment, statutory health insurance funds will not cover any of the costs. Unmarried German patients with private insurance are advised to check with their insurance companies.

Addresses and further information

The name Serono is not only associated with the latest in medicines. It also has extensive experience in matters of infertility. By working closely together with preeminent scientists, Serono is always at the cutting edge.

In order for you, after reading this brochure, to benefit further from our knowledge, we have set up a free-call telephone hotline, where you can talk to one of our trained team members. Your questions will be answered immediately, or if further research is needed, you will be called back.

At our web portal www.fertinet.de, you will find a wide range of up-to-date information and services, as well as a moderated forum, where you can swap your experiences with other affected couples and talk online to our experts.

Communication Center

Free-call telephone hotline (German / English speaking):

08 00/0 46 62 53

Your major information portal:

www.fertinet.de

In addition to medical and psychological counselling, contact with a self-help group is often helpful. Here, you can swap your experiences and concerns with other people in a similar situation. Wunschkind e.V., an association that deals with infertility issues, will be happy to provide you with the address of a self-help group near you. You can also obtain further information on the issue of infertility at their website.

German Organisations

Wunschkind e. V.

Verein der Selbsthilfegruppen für
Fragen ungewollter Kinderlosigkeit
Fehrbelliner Straße 92
10119 Berlin
Telefon: 01 80/5 00 21 66
Telefax: 0 30/69 04 08 38
Hotline: Dienstags von 19 bis 21 Uhr
E-Mail: wunschkind@directbox.com
www.wunschkind.de

Bundesverband

reproduktionsmedizinischer Zentren Deutschlands e. V.

Dudweilerstraße 58
66111 Saarbrücken
Telefon: 06 81/37 35 51
Telefax: 06 81/37 35 39
E-Mail: brz@repromed.de
www.repromed.de

pro familia-Bundesverband

Stresemannallee 3
60596 Frankfurt
Telefon: 0 69/63 90 02
Telefax: 0 69/63 98 52
E-Mail: info@profamilia.de
www.profamilia.de

Do you feel that psychotherapeutic counselling might be required? Kinderwunsch Deutschland (BKID) is a counselling network, which maintains a comprehensive list of addresses online:
www.bkid.de

In exceptional cases, fertilisation with donor sperm (heterologous or donor insemination) is another therapeutic option available. A comprehensive list of addresses can be found at the following website:
www.donogene-insemination.de

Literature tips

There is a range of books available, which deal with the question of infertility. Following – a small selection of entertaining and informative literature.

Fiction

Barbara Brassel:

„**Alles wird gut**“ ... sagt ein kinderloses Paar

Bakiba, 2002, EUR 17,95

Nancy Thayer:

Das Glück am Rande des Wassers/

Ein Morgen am Meer

Zwei Romane in einem Band

Ullstein, 2000, EUR 7,95

Ben Elton:

Die Unempfänglichen/Seitensprünge

Roman

Goldmann, 2001, EUR 21,00

Uwe A. O. Heinlein:

Eisprung

Thriller

Middelhaue, 1999, EUR 17,95

Judith Uyerlinde:

Eisprung

Geschichte über die Liebe

und den Wunsch nach einem Kind

Goldmann, 2002, EUR 17,90

Rachel Morris:

Ella und ihre Mütter

Roman

Droemer/Knaur, 1999, EUR 8,90

Nina Lekander:

**Ich will keine Schokolade,
ich will unbedingt ein Kind**

Roman

Klein, 1997, EUR 16,36

Maria Hechensteiner:

**Orchideenblüte –
Mein Weg zum Wunschkind**

Mutmacher-Tagebuch für

ungewollt kinderlose Frauen

Diametric, 2003, EUR 12,80

Non-fiction

Martin Spiewak:

Wie weit gehen wir für ein Kind?

Eichborn Verlag, 2002, EUR 19,90

Tewes Wischmann, Heike Stammer:

Der Traum vom eigenen Kind

Kohlhammer, 2001, EUR 18,00

Heike Hunneshagen:

Die Qual der Wahl

Centaurus, 2000, EUR 15,24

Sybille Ried, Gertrud Beck-Mannagetta:

Epilepsie und Kinderwunsch

Blackwell Wissenschafts-Verlag, 2001, EUR 14,95

Krista Federspiel:

Kinderlos, was tun?

Hirzel, 2000, EUR 9,90

Günter Freundl, Christian Gnoth,

Petra Frank-Hermann:

Kinderwunsch

Gräfe & Unzer, 2001, EUR 15,90

Gabriele Grünebaum:

Ich will ein Baby

VGS Verlag-GmbH, 2000, EUR 20,50

Roger Neuberg:

Ich will ein Kind!

Ehrenwirt, 1999, EUR 9,95

Niravi B. Payne, Brenda L. Richardson:

Wenn das Wunschkind auf sich warten lässt

Scherz, 1999, EUR 20,40

Thomas Strowitzki:

Wenn das Wunschkind ausbleibt

Haug Sachbuch, 1998, EUR 11,45

Hans H. Pusch:

Wie kommt der Mann zum Kind

ARISTON, 1996, EUR 18,51

Martin Sillem:

Wirksame Hilfe bei Endometriose

Trias, 1998, EUR 11,45

Technical terms – a quick guide

So that you know „what's what“ at all times, we have put together a list of specialist medical terms, together with their definitions.

Androgene

Male hormones.

Assisted hatching

Cutting a tiny gap into the embryo's outer shell (e.g. by means of a laser), in order to make it easier for the embryo to implant into the womb lining.

Chromosomes

Cell nucleus components and carriers of hereditary material. Chromosomes mainly consist of deoxyribonucleic acid (DNA). DNA is the actual genetic material and is passed on during cell division to the daughter cells. Humans have $2 \times 23 = 46$ chromosomes. Out of these, 22 chromosome pairs play no role in determining gender. The 23rd pair, the sex chromosomes, are formed differently in men and women. In women, each cell nucleus has two X chromosomes, whereas men have an unequal pair, i.e. an X and a Y chromosome. Gender of the foetus (boy or girl) is dependent on which chromosome the successful sperm (i.e. which fertilizes the egg cell) is carrying.

Corpus luteum

The remnant of the follicle after ovulation, which, after undergoing transformation, takes on a yellowish colour; hence, yellow body. The corpus luteum secretes estrogen and progesterone.

Cryopreservation

Greek word: kryo = cool, frosty. Egg cells at the pronuclear stage or sperm can be deep-frozen and stored by means of cryopreservation.

Down regulation

A reduction in the body's own hormone production, by use of certain drugs.

Embryo

Once the genetic material has merged, the term „embryo“ is used. From the 13th week of pregnancy, the developing child is referred to as a foetus.

Embryo transfer

Transfer of an embryo into the womb after the egg has been fertilized outside the body.

Endometriosis

A word compounded from the Greek: endo = inside + metra = uterus. A frequent cause of infertility. In endometriosis, tissue from the womb lining migrates outside of the uterus, resulting in possible scarring.

Endometrium (womb lining)

A richly vascular mucous membrane that is formed periodically by the uterus. The embryo implants into the endometrium.

Estrogen

Latin: oestrus = readiness to copulate + gen = produce. Estrogen is a female sex hormone that is produced in the ovaries and promotes growth of the womb lining.

Fallopian tube

A funnel-shaped „conveyor belt“, along which sperm cells are guided towards the egg, and fertilised eggs are conveyed to the womb cavity.

Follicle

A fluid-filled egg capsule, in which the egg cells are found. The follicles mature in the ovaries.

Follicular puncture

Puncture of the follicle with a very fine suction needle, in order to harvest an egg cell.

FSH

Follicle-stimulating hormone, which promotes egg cell growth and development.

Gametes

A collective term for male and female sex cells, which have only one single chromosome pair before fertilisation.

Gamete intrafallopian transfer (GIFT)

A reproductive technique, in which the development of several egg follicles is achieved by means of drugs (such as gonadotrophins), and mature egg cells thus obtained are harvested from the ovary. Thereafter, semen and egg cells are immediately and separately introduced into the fallopian tubes, where fertilisation takes place.

GnRH

Gonadotrophin-releasing hormone. A Greek-English compound word: gonos = procreation + trop = action on. Hormone that causes the release of LH and FSH.

GnRH agonist

A drug which inhibits the release of LH and FSH (after an initial increase of their secretion).

GnRH antagonist

From the Greek (anti = against). Drugs that prevent secretion of the reproductive hormones LH and FSH (without initial increase).

Gonadotrophic

Stimulating the gonads

Gonadotrophins

Collective term for gonadotrophic hormones of the anterior pituitary, placenta or womb lining, which promote and control growth of the gonads (sexual glands, in which the gametes develop).

Hormones

Carriers of information produced by the body that transmit information from one organ to another.

Human chorionic gonadotrophin (hCG)

Latin compound term: human, chorion = egg skin, gonad = sex glands, trop = stimulate on. A hormone that is used in medicine for triggering ovulation. HCG is extracted from the urine of pregnant women or is manufactured using bioengineering techniques.

Human menopausal gonadotrophin (hMG):

Latin compound word: human, menopause = end of menstruation. HMG is extracted from the urine of women going through menopause. HMG is used for stimulating the ovaries.

Intracytoplasmic sperm injection (ICSI)

Latin compound word: intra = in, into, cytoplasma = cell contents, spermium = male gamete. A method of artificial insemination, in which a single sperm is injected into an egg cell using a thin, glass capillary.

Intrauterine insemination (IUI)

Insemination is the transfer of semen into the vagina or uterus using technical means. In IUI, the semen is placed into the uterus as close as possible to the egg.

In vitro fertilisation (IVF)

Latin: in vitro = in glass. IVF means fertilisation outside of the body.

Laparoscopy

Endoscopic investigation of the abdominal cavity and its organs. Is performed to determine the position, size and status (condition) of the abdominal organs.

Luteinising hormone (LH)

A hormone that triggers ovulation.

Myoma

A benign tumour in the uterus consisting of muscle tissue. Myomas can often be the cause of persistent infertility or miscarriages.

Out-patient

Not involving admission into hospital (the opposite of in-patient).

Ovaries

Two, plum-sized female organs, in which egg cells capable of being fertilized are produced. The ovaries produce the hormones estrogen and gestagen (gestatio = pregnancy, gen = producing).

Ovulation

When the egg cell leaves the ovary and passes into the Fallopian tube.

Placenta

The placenta provides the developing child with nutrients. After delivery of the infant, the placenta detaches from the uterine wall and is expelled as the „after-birth“.

Polycystic ovary (PCO)

Derived from the Greek kystis = capsule and poly = numerous. An ovary with numerous small cysts

Progesterone

Latin: pro = for + gestatio = pregnancy. Progesterone is produced by the corpus luteum. Progesterone prepares the womb lining for implantation of the embryo.

Prolactin

Latin: lactis = milk. A hormone produced in the brain. Prolactin stimulates lactation (flow of breast milk).

Sterility

If no pregnancy occurs with regular sexual intercourse over the course of one year, doctors suspect sterility. However, this is not necessarily final or absolute.

TESE/MESA

If there are no sperm at all in the ejaculate, they can be directly extracted from the testicles (TESE = testicular sperm extraction) or from the epididymis (MESA = microsurgical epididymal sperm aspiration).

Tubal or ectopic pregnancy (extrauterine pregnancy)

Implantation of the embryo in one of the Fallopian tubes, instead of in the womb cavity.

Uterus (womb)

Pear-shaped organ, in which the baby develops. The uterus consists of: the ectocervix (cervical opening), the cervix and the womb (uterine) cavity. The two Fallopian tubes open into the uterus.

Route explanation:

A 45 – exit Wetzlar south – direction Wetzlar on L3451 – after approx. 1km turn right to the industrial area "Spilburg" – in the traffic circle first exit – Sportparkstraße 9

B 49 – direction Wetzlar – exit A 45 direction Frankfurt – exit Wetzlar south – direction Wetzlar – after approx. 1km turn right to the industrial area "Spilburg" – in the traffic circle first exit – Sportparkstraße 9

Bus – line 11, 12 or 13 – Bus stop "Spilburg"

Kinderwunschzentrum Mittelhessen – Sportparkstrasse 9 – 35578 Wetzlar





Kinderwunschzentrum Mittelhessen


MD Amir Hajimohammad

Specialist for women's welfare and maternity


Specialist in gynaecological endocrinology and reproductive medicine

 Sportparkstraße 9
35578 Wetzlar

 (06441) 2 00 20 20

 (06441) 20 02 02 99

 info@ivf-mh.de

 www.kinderwunschzentrum-mh.de

Consulting Hours

Monday – Friday 7.30 a.m. to 12.00 p.m.

in addition

Monday 1.00 p.m. to 6.00 p.m.

Tuesday 1.00 p.m. to 6.00 p.m. (*By appointment until 7:00 p.m.*)

Wednesday 1.00 p.m. to 4.00 p.m.

Thursday 1.00 p.m. to 6.00 p.m.

Friday 1.00 p.m. to 4.00 p.m.