ASSISTED CONCEPTION

MSD

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INTRODUCTION

Infertility is a highly emotive and personal subject that affects tens of thousands of couples in our country. The common perception is that involuntary infertility has increased slightly. We have also gained better insight into the causes of infertility. Meanwhile treatment methods have developed, yielding better results.

This guide discusses reasons behind infertility, infertility evaluation and methods developed for treating infertility. Special emphasis is placed on assisted conception treatments. These are available in numerous forms depending on the situation.

It should be borne in mind that examination and treatment practices vary between clinics. Furthermore, everyone experiences treatments, both mentally and physically, in their own way. If a couple decides to have assisted conception, it is important to discuss personal experiences and feelings not only with the partner, but with the health care personnel as well. In terms of causes and treatment options, childlessness is unique for every couple. There is no universal treatment option that suits all. Assisted conception is planned individually and the duration of treatment may also vary. While some pairs are able to succeed relatively quickly, others may never bear a child despite years of treatment.

We hope this guide provides you with sufficient information on how to study and treat childlessness, and what results treatments can yield.

FERTILITY EVALUATION AND CARE PATHWAYS

- Evaluation and treatment are carried out by both public and private health care entities.
- In the public sector, evaluation is performed by all university, central and regional hospitals, but it always require a referral by a health centre physician or a private physician. The referral must contain background information of the couple, and often also basic examination data (FSH, TSH, PRL, and certain hospitals may require a sperm analysis).
- In the public sector, treatment is covered by the care guarantee. For more information on the care guarantee, please visit the Ministry of Social Affairs and Health website (www.stm.fi).
- In the private sector, evaluation is performed by any major health care facilities and private infertility clinics without a referral.

POSSIBLE CAUSES OF INFERTILITY

Infertility is a shared problem for a couple. Infertility can be of the primary type, which means that the woman has never been impregnated. Secondary infertility is defined as the absence of a live birth following a previous live birth or pregnancy. 25% of infertility is estimated to be attributable to females, 25% to males and 25% to both females and males. In the remaining 25% of cases, the cause of infertility cannot be clearly determined. This is referred to as unexplained infertility. Infertility can be due to any number of reasons. The most common reason for infertility in women is ovulation dysfunction or endometriosis. Fallopian tube damage and uterus-related problems are also common reasons behind infertility. Suboptimal semen quality may be caused by a dysfunctional testicle or hormonal imbalance of testicular function. However, testing often fail to pinpoint one isolated reason for infertility.

Ovulation dysfunction is often related to polycystic ovary syndrome (PCOS). The cause of the disorder is not known. Ultrasound examination reveal large ovaries with a large quantity of small ovarian follicles formed in line around the edges of the ovaries. Women with PCOS often experience abnormal menstruation, extended or irregular menstrual cycles, or may not have menses at all. The syndrome features excessive luteinizing hormone (LH) and male hormone (testosterone) excretion, which can cause acne and hirsutism. Predisposition to obesity is common and the condition is often associated with impaired glucose tolerance. Indeed, metformin, which is a medication typically prescribed for type II diabetes, is often used independently or together with other medication in assisted conception for patients with PCOS. The primary treatment for obese women is weight loss and increase in exercise. Often a weight loss of 5-10% can help to correct ovulation problems and contribute to successful pregnancy, even without additional treatments.

Endometriosis is a disease in which tissue similar to which lines the inside of the uterus grows outside the uterus. Endometriosis occurs most commonly in the lesser pelvis, ovaries, between uterus and rectum or elsewhere in the abdominal cavity. Endometriosis can cause significant menstrual pain and painful intercourse, and, in some women, reduce fertility. The treatment of endometriosis for women in fertile age should be carefully selected based on the patient's desire to get pregnant. Surgical procedures on the ovaries can significantly reduce the success rate of assisted conception. Repeated surgery is particularly problematic. On the other hand, pregnancy and breastfeeding can ease symptomatic pain. It is recommendable to treat hormonally even a mildly symptomatic endometriosis if the wish for pregnancy is not timely.

For men, reduced fertility is typically attributed to low sperm count or ejaculation problems. There are number of reasons for abnormal semen. Semen quality is affected by hormonal

disorders, immunological problems, anatomical abnormalities and environmental factors. Extremely low sperm count can be attributed to rare genetic factors. It is often difficult, sometimes impossible, to pinpoint the exact reasons behind reduced male fertility. It should be borne in mind that only a small amount of semen is produced in the testicle. Practically only sperm cells are produced in the testicle, while semen is produced in the seminal vesicle and the prostate gland.

Unexplained infertility can be caused by, for example, problems with oocytes, abnormal fertilisation or early cleavage abnormalities, Fallopian tube disorder or problems with embryo implantation. Unexplained infertility can be due to lifestyle-related factors, such as obesity, underweight, smoking, excessive use of alcohol, nutrition, environmental toxins, as well as mental factors, such as stress.

Infertility examinations are aimed at determining the cause of infertility. If conception has not occurred after one year of actively trying to conceive, it is advisable to seek help. It may be advisable to seek help even earlier if female is over 35 years of age or if the medical history or health of the couple includes factors that may be causing infertility. For example absent or irregular menstruation may indicate ovulation problems. In females, infections in reproductive system or abdominal surgery may damage the Fallopian tubes. Significant menstrual pain can also indicate endometriosis. In males, certain diseases or medication may affect sperm cell production. Malignant diseases, such as cancer, and related treatments experienced at a young age may contribute to infertility in both males and females.

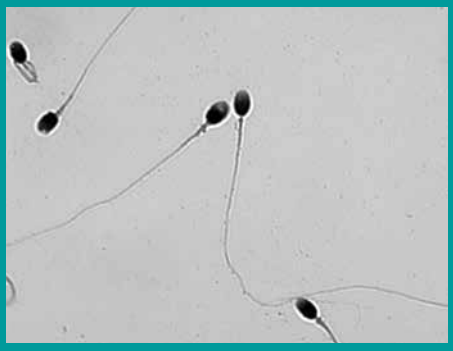
FERTILITY EVALUATION

Fertility evaluation is available at a reproductive endocrinology outpatient clinic at a central or university hospital by a referral from a local health care centre, where the physician can perform the initial tests. Alternatively, the couple may have the tests at a private reproductive care centre, in which case a referral is not necessary. Care for single female patients and female couples is currently only provided by the private sector (see graph Fertility examination and care pathways, p. 10).

Fertility examinations begin with a thorough interview in order to establish the physical status of the couple, including any previous disease, medical procedures and hospital care as well as current medication. In order to determine the duration of infertility, the physician will require information such as when contraception has been discontinued, how long the couple has been actively trying to conceive, as well as if there are any problems in their sex life. It is important to discuss nutrition, smoking, and the use of alcohol and other substances. The discussion will also cover puberty development, menstruation, and other symptoms related to endocrine diseases. Possible hereditary diseases should be also taken into consideration.

Possible reasons for infertility are examined with the actual fertility testing. Initially they aim to answer the following questions:

- Are there motile sperm cells in male´s sperm?
- Are uterus and ovaries healthy?
- Does oocyte mature and is it released during the menstrual cycle?
- Are the Fallopian tubes open?



Sperm cells (Pap stain)

Assessing male fertility is generally fairly straightforward, which is why it should be determined in the early stages of the fertility evaluation. A semen sample is examined, and, if necessary, supplementary tests can be performed. If the sperm analysis reveals abnormalities, it is essential to perform a clinical evaluation of the reproductive system. If necessary, it can be supplemented with an ultrasound scan. The most essential hormonal tests include testosterone, FSH and LH. Highly abnormal sperm results require further genetic tests (chromosomes, Y chromosome microdeletion test) in order to reach a more accurate diagnosis.

Investigations of female fertility begin

Mature oocyte

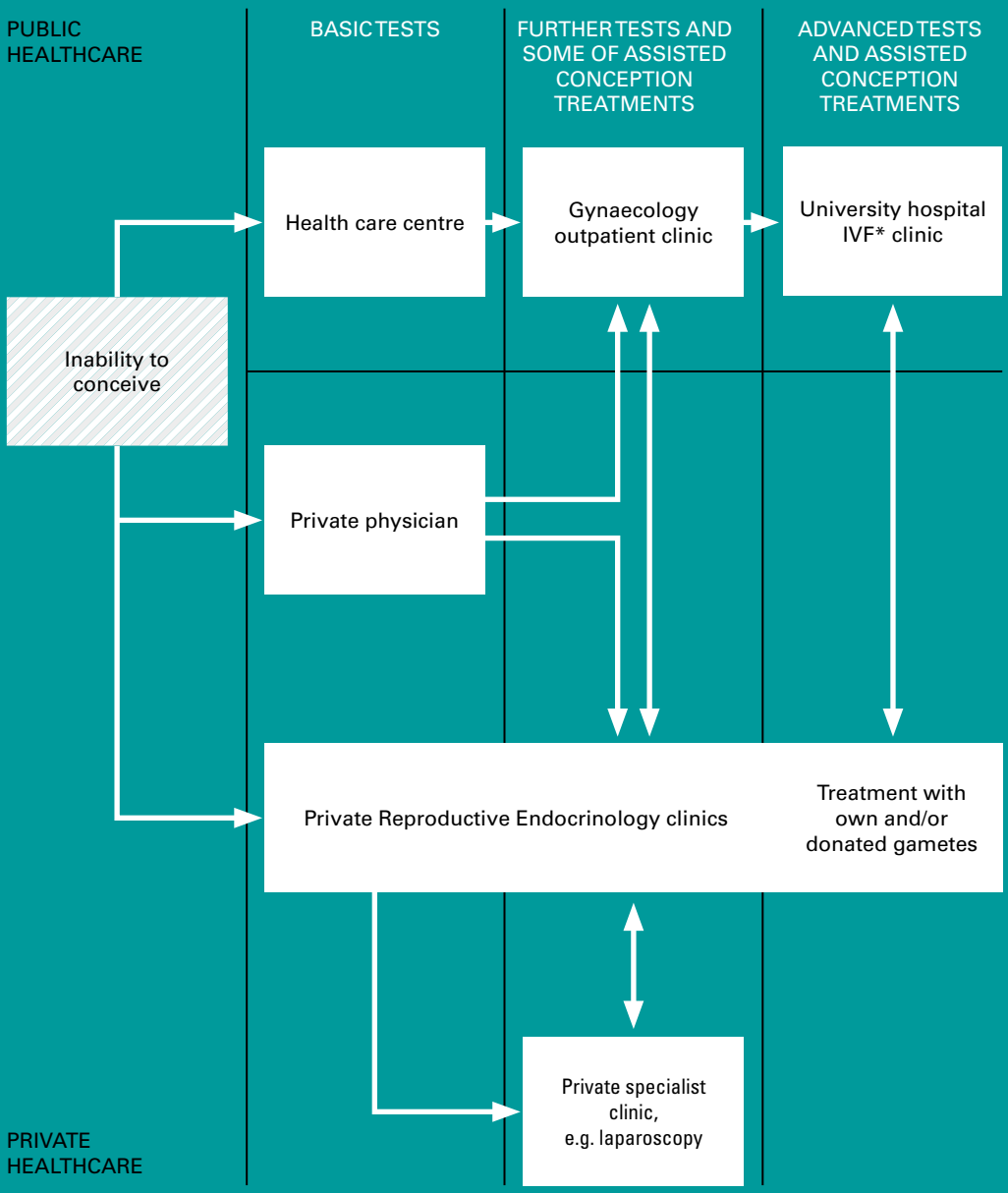
with a gynaecological examination. It can be supplemented with infection tests and a Pap smear, if necessary. A transvaginal ultrasound examination provides answers to several questions. It provides information on the structure of the ovaries and the ovarian reserve, which can be determined by the antral follicle count (AFC). If necessary, also Anti-Müllerian hormone (AMH) can be measured from a blood sample in order to estimate the remaining ovarian reserve. Follicle growth and oocyte release (ovulation) as well the thickness and structure of the endometrium can be examined at a suitable stage of menstrual cycle. The ultrasound is a pain-free and risk-free examination method, even during pregnancy. Typically female testing is supplemented with hormonal blood tests (thyrotropin (TSH), prolactin, as well as gonadotropins FSH and LH).

The Fallopian tubes can be examined for obstructions via ultrasound (SSG, sonosalpingoraphy) involving an injection of physiologic saline into the Fallopian tubes via the uterus. It is done with a thin catheter while monitoring the transfer of the saline solution to the fimbrial end. According to current practices, laparoscopy is rarely performed.

It is often the case that there are several reasons for infertility, which is why it is advisable to perform comprehensive investigations in the early stages. Following this, the physician will discuss with the couple regarding the necessity for assisted conception and whether the couple wishes to begin the treatments. Assisted conception may also be suggested in circumstances where studies are unable to pinpoint a reason for the infertility. The treatments may also yield information behind the reasons for infertility. If necessary, further testing can be performed to explore other possibilities.

FERTILITY EVALUATION AND CARE PATHWAYS

Basic tests are also performed at student health care centres.



*IVF = in-vitro fertilisation

Graph of Fertility examination and care pathways in Finland, 2012.

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ASSISTED CONCEPTION

ASSISTED CONCEPTION TREATMENTS INCLUDE

- Ovulation induction (OI)
- Insemination (IUI)
- In vitro fertilisation (IVF) and microinjection (ICSI)

OVULATION INDUCTION (OI), STIMULATION OF OOCYTE MATURATION AND RELEASE

Ovulation is one of the prerequisites of successful conception. If ovulation does not occur naturally, it can be induced with medication. This method is called ovulation induction (OI).

Ovulation induction is based on the principle of stimulation of the ovaries in order to produce one ovarian follicle and one mature oocyte per menstrual cycle in order to achieve fertilisation following intercourse. The initial medication is often provided in tablet form (clomiphene citrate or aromatase inhibitors). In rare cases the pituitary gland does not produce enough hormones (gonadotropins FSH and LH). In these cases, tablet medication is not possible. This may be caused by treatments (surgery, radiation) of pituitary gland tumours, severe underweight or excessive exercise (anorectics, endurance athletes, etc.), but the reason is often unknown. Underweight women can often reverse infertility and have normal menstrual cycles by increasing their weight. Elevated gonadotropin levels may indicate an abnormality in the ovaries, in which case medication will not be beneficial.

Tablet medication treatment is often fairly straightforward: medication is taken typically for five days in the beginning of the menstrual cycle. Treatment should be monitored with at least one ultrasound examination. Successful treatment requires that intercourse take place during ovulation. Ovulation test (LH test), available in pharmacies, helps with timing the intercourse correctly. If ovulation cannot be induced with tablets, or conception has not occurred within 4 to 6 menstrual cycles, other treatment options should be explored.

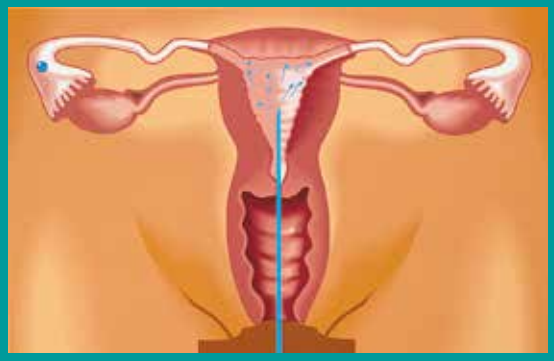
Gonadotropin treatments may be necessary if tablet treatments produce no results or pituitary gland hormone production remains low. Gonadotropin treatment begins between day two to five of the menstrual cycle with injections of 50-100 units (IU) of FSH. Treatment response is monitored with ultrasound examinations (number and size of ovarian follicles and thickness of the endometrium). Monitoring the treatment increases the likelihood of conception while eliminating possible risks (multifetal pregnancy).

INSEMINATION - IUI (INTRAUTERINE INSEMINATION)

Intrauterine insemination can be considered in case the infertility is caused by semen problems or unexplained infertility. Sometimes it may also be offered as a treatment for other types of infertility. Insemination can be performed during natural or hormone-induced menstrual cycle.

The male will provide a semen sample on the day of insemination. In some cases, insemination can be carried out with cryopreserved semen. The semen sample is prepared prior to insemination in order to separate the best, most motile sperm. Preparation helps in reducing any impurities and antibodies of the semen, which may help to improve sperm motility and ability to fertilise. The sperm is injected into the uterine cavity via the cervical canal with a small catheter. As conception with insemination occurs in natural environment, i.e. in the Fallopian tube, at least one of the tubes must be healthy. Successful insemination treatment requires sufficient sperm motility, otherwise the option is in vitro fertilisation treatment.

Insemination can be performed during natural menstrual cycle as close to ovulation as possible, or it can be combined with ovarian stimulation treatment. The timing of the insemination during natural menstrual cycle is determined with a home ovulation test that measures urine LH hormone content. Insemination is performed with pre-treated sperm 12-42 hours after a positive ovulation test, indicating the optimal time for conception.



Insemination involves injecting sperm into the uterine cavity with a catheter.

Best insemination results can be achieved by combining insemination with hormone medication. Treatment must, however, be monitored in order to avoid the development of too many ovarian follicles which may increase the risk of multifetal pregnancy. The ideal number is one to two follicles and mature oocytes. In ovulation induction, the insemination is timed with an ultrasound examination. Insemination is performed 24-42 hours following the hCG injection that induces ovulation.

While female age is the most significant determinant of successful treatment, the semen quality and timing of insemination are also important factors. Success rate for insemination combined with hormone injections is 10-20 % per treatment. Treatment is typically repeated two to four times. If insemination treatment fails to yield positive results, the next option is IVF treatment.

IUI STEP-BY-STEP

1. Can be performed in natural menstrual cycle. Ovulation is confirmed with a home ovulation test. Further steps pursuant to 3 and 4.
2. Alternative hormone treatment for producing one to two oocytes: tablets or injections for stimulating ovarian follicle development. This is followed by inducing ovulation with an hCG hormone injection.
   - Treatment monitoring is essential: vaginal ultrasound monitoring (one to three times per treatment).
3. Semen sample is delivered on the morning of the day of insemination. Semen is processed and injected into the uterus later that day.
4. Pregnancy test two weeks from insemination.
5. Pregnancy ultrasound three weeks from a positive pregnancy test.

Another treatment option is insemination with donated sperm. The introduction of intracytoplasmic sperm injection (See page 19) has significantly decreased the need for donated sperm for treatments in cases of male-related infertility. Donated sperm is only used when the male cannot produce sperm cells or he suffers from a difficult hereditary disease. Donated sperm is also necessary for providing assisted conception treatment for female couples and single women.

IN VITRO FERTILISATION (IVF)

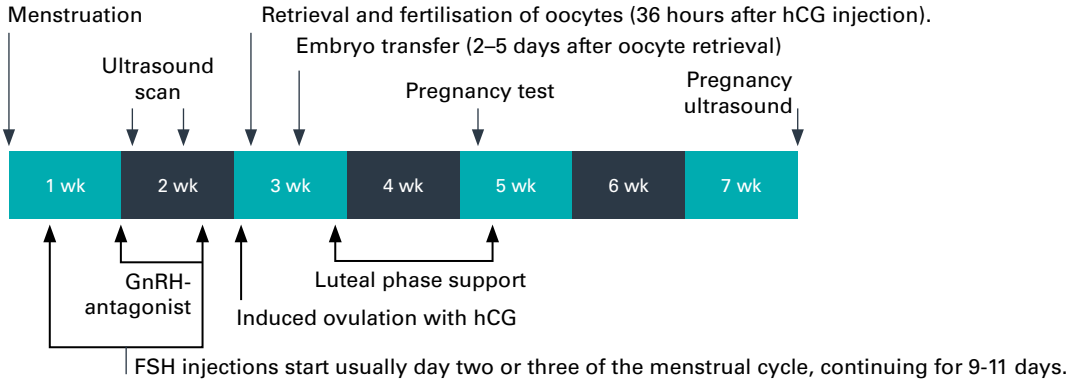
Today, in vitro fertilisation is the most commonly used assisted conception method in the world. The first IVF baby was born in 1978. Since then, the treatment has offered a solution to an increasing number of infertile couples. There are over 5 million children that were conceived with IVF and ICSI treatments.

IVF treatment involves collecting and fertilising gametes in a laboratory and transferring the embryo into the uterus.

The treatment involves gonadotropin stimulation of the ovaries in order to produce several oocytes during the treatment cycle. The GnRH hormone antagonists prevent premature maturation and release of oocytes prior to oocyte retrieval. Assisted conception treatment is always planned and implemented on an individual basis. There are several treatment options. The most commonly used treatments are the short GnRH antagonist or the long GnRH agonist treatment. There is no significant difference in results between short and long protocol. The treatment is aimed at producing several good quality embryos, of which one or two will be transferred into the uterus, while the rest are frozen for possible later use.

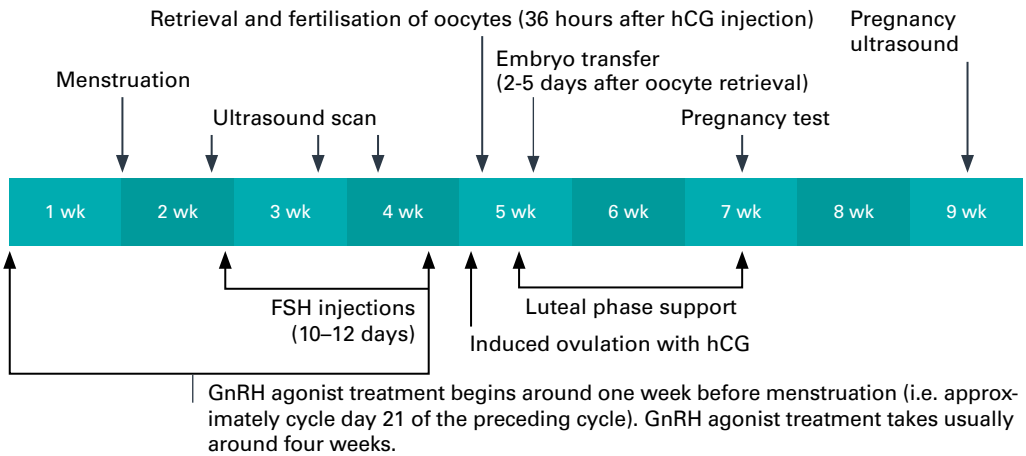
Short protocol, i.e. GnRH antagonist therapy

In short protocol, the female starts gonadotropin injections typically on the second or third day of the menstrual cycle. Daily gonadotropin injections can also be replaced with a long-acting FSH product where the first injection replaces the first seven gonadotropin injections. Typically onwards the fifth day of stimulation the treatment is supplemented with a daily GnRH antagonist injections. The antagonist treatment continues alongside the stimulation treatment for four to six days. The benefits associated with this treatment are shorter duration and less adverse effects. The duration of the short protocol is less than two weeks, typically around twelve days, from the start of the medication to the oocyte retrieval. Short protocol is not as easy to program compared to long protocol.



Long protocol, i.e. GnRH agonist therapy

Long protocol involves GnRH agonist treatment (by injections or nasal spray) for two weeks before gonadotropin injections are started. The GnRH agonist treatment will begin suppress hormonal function in the luteal phase of the preceding menstrual cycle, lasting for around two weeks, and continuing further 10-14 days together with the gonadotropin treatment. Agonist treatment may induce a menopause-like condition with symptoms such as irritability, sweating and hot flushes. The duration of the long protocol is typically around four weeks, from the start of the medication to the oocyte retrieval. Oocyte retrieval can be timed more precisely during the long protocol, in case it is important to establish the retrieval time beforehand.



GONADOTROPIN TREATMENT

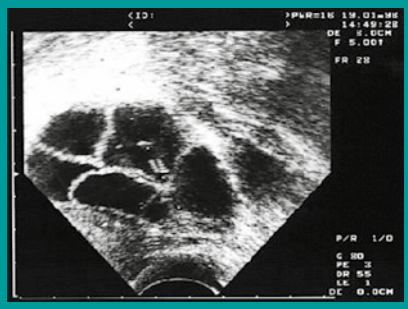
Gonadotropin treatment involves FSH or hMG hormone injections. Currently there are several products on the market, containing either only FSH hormone or FSH with LH/hCG. The latest innovation is a long-acting FSH that produces a stimulation effect for one week with a single injection.

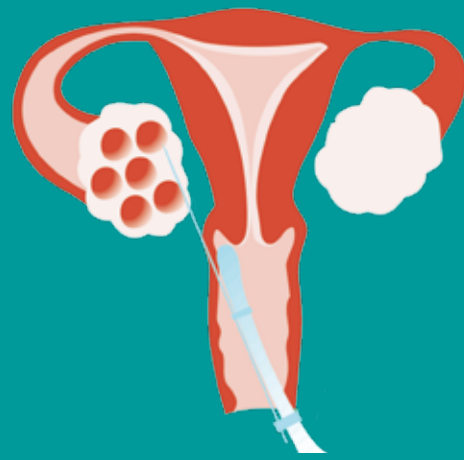
Hormone treatments are highly individualised in terms of dosage and the duration of treatment. Typically gonadotropin treatment is given approximately 9-12 days with a daily dosage of 100-300 units (IU). The total gonadotropin dose depends on age, weight and antral follicle count (AFC) of the female. When the largest follicles reach over 17 mm in diameter, ovulation is induced with an hCG injection (human chorionic gonadotropin), and the follicles are collected 34-38 hours later.

During the short protocol, the hCG injection can be replaced with a GnRH agonist injection in order to prevent the onset of ovarian hyperstimulation syndrome (OHSS). Hyperstimulation refers to the overreaction of the ovaries to the hormonal stimulation given during assisted conception. For further information, see page 26.

OOCYTE RETRIEVAL

Oocyte retrieval is done by ultrasound guided transvaginal aspiration, where a small needle is passed to ovarian follicle through the vaginal wall. The follicular fluid is collected into a test tube and delivered to a fertilisation laboratory. The oocytes are collected from the follicular fluid, placed on petri dishes and transferred into an incubator. The patient is given sedatives and analgesic and/or paracervical block (PCB) anaesthetic. If necessary, the procedure can be performed under general anaesthesia. The procedure takes approximately 10-20 minutes in total. The oocytes are fertilised either by placing them on a petri dish with sperm cells and storing them in an IVF cabinet overnight (IVF), or by intracytoplasmic sperm injection (ICSI).





Oocyte retrieval by ultrasound guided transvaginal aspiration

EMBRYO TRANSFER AND LUTEAL PHASE SUPPORT

One or maximum two embryos are transferred into the uterus with a small flexible catheter following two to five days of culture. Embryo transfer is a painless procedure that is done under ultrasound guidance.

Luteal phase support begins typically on the following day after the oocyte retrieval. Any spare good quality embryos can be frozen for later use.

The embryos transferred into the uterus are subject to natural selection. Similar to natural conception, only some of the embryos implant and begin developing into a child.

According to studies, the chance of pregnancy is around 20-40% per treatment cycle. These figures are similar to the pregnancy rates of fertile couples. Pregnancy rates start to decline in women fairly rapidly with age, which is why it is recommended that women over the age of 35 should seek treatment as soon as possible.

If pregnancy test is negative following the treatment, a new treatment or a frozen embryo transfer can be performed in the subsequent menstrual cycle (for GnRH antagonist treatment) or after a break of one cycle (for GnRH agonist treatment).

FROZEN EMBRYO TRANSFER

Frozen embryo transfer can be performed during natural or hormone-induced menstrual cycle. When the embryo is thawed and transferred during natural menstrual cycle, thawing is timed according to ultrasound examination and ovulation. Medication is given in case the menstrual cycle is irregular or ovulation does not occur. In this case, the embryo transfer is timed with an ultrasound examination.

Most of the frozen embryos survive the freezing and thawing process. In order to obtain a viable embryo for transfer, it may be necessary to thaw several embryos at once. The embryos can also be cultured further after thawing them in order to ensure proper development. This ensures that the most viable embryo is chosen for the transfer. The frozen embryo is transferred as indicated above. See also Embryo freezing (p. 21).

IVF/ICSI, STEP-BY-STEP

1. Hormone treatment to stimulate maturation of several oocytes
   - Gonadotropin (FSH, hMG, long-acting FSH) to stimulate growth of ovarian follicles
   - GnRH antagonist injections for around 5 days together with gonadotropin injections in order to prevent premature oocyte maturation and ovulation
   - Alternative GnRH agonist treatment (by injections or nasal spray) in order to suppress own hormonal activity for two weeks before and 10-14 days during the gonadotropin injections
   - hCG for inducing ovulation and timing of oocyte retrieval.
2. Monitoring the treatment in order to measure follicle growth, to determine hormone dosage and to minimise adverse effects.
   - Transvaginal ultrasound monitoring (two to three times during treatment cycle)
   - Hormone level tests (E2, estradiol) from blood samples, if necessary
3. Oocyte retrieval (34-38 hours after hCG injection)
   - Intravenous sedative and analgesic and/or local anaesthetic.
4. Semen sample is delivered on the day of oocyte retrieval.
5. Fertilisation
   - Oocytes are fertilised either by placing them with sperm cells on a petri dish and storing them in a thermal cabinet overnight (IVF), or by intracytoplasmic sperm injection (ICSI)
   - Microscopic examination of oocytes on the following day in order to check fertilisation
6. Embryo transfer two to five days after oocyte retrieval
   - Typically one, sometimes two, embryos are transferred into the uterus with a small catheter
   - Spare good quality embryos are frozen for possible later use
7. Luteal phase support with progesterone
8. Pregnancy test two weeks after embryo transfer
9. Monitoring of pregnancy. Ultrasound examination is done typically three weeks after a positive pregnancy test.

LABORATORY METHODS RELATED TO ASSISTED CONCEPTION

SPERM ANALYSIS

Sperm analysis is the most important basic examination in terms of male fertility. Semen sample is provided with a container provided by the clinic and delivered to the laboratory for tests. In order to obtain more reliable test results, the male should avoid ejaculation two to five days before providing a sperm sample. The sample should be stored in a warm place and the tests should be performed within one hour of sample collection. Following the provided guidelines is essential for successful sperm analysis and reliable results. The treating clinic will provide detailed instructions on how to provide a sample.

The sperm analysis determines the quality of the semen with the following criteria: total amount of sperm cells, sperm density, motility, sperm antibodies, and, if necessary, the shape and structure of the sperm cells. Reduced sperm fertilisation capacity can often be detected with microscopic examinations. If necessary, the physician may recommend further examinations, such as sperm DNA fragmentation test. According to studies, the DNA fragmentation has importance in semen quality. If high level of DNA fragmentation is detected in sperm cells it may have an impact on male fertility, and, subsequently, on the success of assisted conception.

Temporary factors, such as medication, stress or illness, may impact semen quality, which is why abnormal sperm analysis results are always verified with a second sample. If no sperm cells are found in the semen, this may indicate an obstruction in vas deferens. In this case, a testicular biopsy may be attempted in order to retrieve sperm cells for fertilisation. This is also typical if the male has had a vasectomy.

IN VITRO FERTILISATION (IVF)

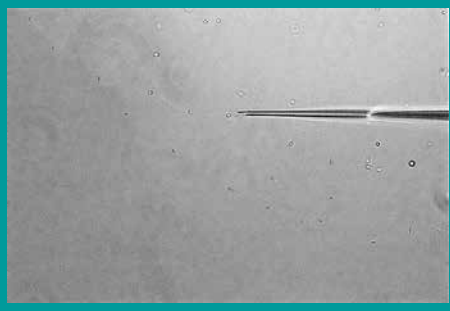
Semen sample is collected on the day of the oocyte retrieval. The motile sperm cells are separated from the sample by preparing the sperm in laboratory. The form of assisted conception (IVF or ICSI) is determined according to the quality of the sperm. Treatment history and the number of oocytes are also taken into consideration. Fertilisation is performed in a laboratory four to six hours after oocyte retrieval. IVF treatment involves placing the motile sperm cells on a petri dish with an oocyte and storing them in an IVF cabinet overnight. Normally one sperm cell fertilises the oocyte, preventing other sperm cells from entering the oocyte.

In IVF treatment the motile sperm cells are placed ona petri dish with an oocyte and stored in an IVF cabinet overnight.

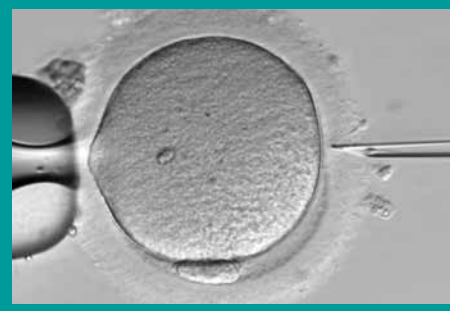
MICROINJECTION – ICSI (INTRACYTOPLASMIC SPERM INJECTION)

ICSI is the most commonly used method for treating male infertility. In case the sperm cell count or sperm motility is significantly reduced, conception via petri dish fertilisation may not be possible. In this case, intracytoplasmic sperm injection may provide an answer. The method involves injecting a single sperm cell into an oocyte with micromanipulation equipment. ICSI can also be used in case a fertilisation in an IVF treatment has not been successful. ICSI fertilisation is also used in case the sperm cells have been collected directly from the testicle or vas deferens, or if frozen oocytes are used.

The oocytes are matured and retrieved with the same way in ICSI and IVF. Once the embryos developed with the ICSI method have been transferred into the uterus, the pregnancy rates are similar to IVF treatment.



Sperm collection



Oocyte in a pipette

Microinjection

Oocyte following microinjection

FERTILISATION AND EMBRYO CULTURE

Fertilisation is examined the following morning from oocyte retrieval. 60-70% of oocytes are expected to fertilise, and two pronuclei can be seen in the oocytes. In case of abnormal fertilisation, the oocytes may contain one, three or more pronuclei. If fertilisation has not occurred, there are no pronuclei. Fertilisation is dependent on the maturation of the oocytes and the quality of both oocytes and sperm.

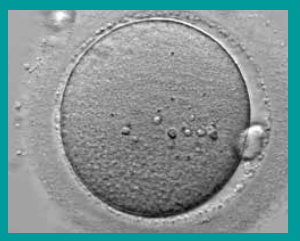
First cell division can be observed in approximately one day from the fertilisation. Two days after fertilisation, typically the oocytes have divided twice, forming four-cell embryos.

The length of embryo culture and transfer day is planned on a case-specific basis. Typically the embryo is transferred into the uterus when there are two to eight cells, i.e. during the second or third day following the oocyte retrieval. If necessary, culture can be extended until the fifth day (to form blastocysts).

Embryo classification and selection for transfer or freezing is based on daily microscopic examination of the embryos. Embryo quality is determined according to timing of the division and morphology.

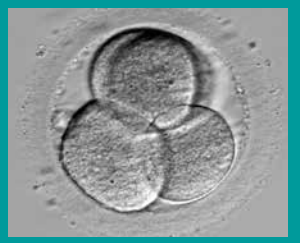
On day two following fertilisation, the embryo has optimally four cells, and eight cells on day three. The morphological classification of embryos is mainly based on fragmentation, size differences between cells and the symmetry of division. Cytoplasm or zona abnormalities and multinuclearity may impact the prognosis of the embryo.

The latest method for facilitating the embryo selection is the so-called time-lapse method. The method involves monitoring the development of embryos by repeated imaging during culture. The image set provides information that can be used in determining the most viable embryos.

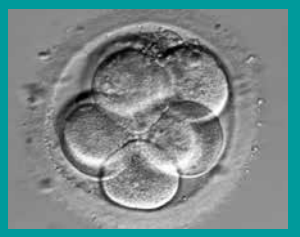


Mature oocyte

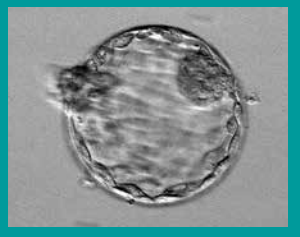
Fertilised oocyte



4-cell embryo



8-cell embryo



Blastocyst

EMBRYO FREEZING

Usually IVF treatment produces several embryos, of which one, or two at most, is transferred into the uterus during a stimulated menstrual cycle. Any remaining, viable embryos can be frozen for later use, which means that a single IVF treatment may enable several embryo transfers. Furthermore, if the physician considers there to be a high risk of OHSS, all viable embryos can be frozen. This helps to prevent the onset or persistence of OHSS initiated by pregnancy. (OHSS, see p. 26)

Embryo freezing is done on estimate in over half of all in vitro fertilisations. The freezing plan is typically discussed no later than during the transfer of the embryo. Embryos are stored in liquid nitrogen at -196 degrees Celsius. Freezing does not damage the embryos.

Freezing can be done in two ways. Slow freezing involves lowering the temperature of the embryo in carefully calculated steps in an embryo freezer. Vitrification is an ultra-rapid freezing method where the temperature of the embryo is lowered rapidly down to the cryopreservation temperature. Several clinics use both methods, determining the most suitable option on individual basis.

The embryos are frozen individually or in batches, depending on the number and quality of the embryos as well as further treatment steps. Freezing is performed with cryopreservation straws or ampoules. The freezing solution contains cryoprotectant that prevents the formation of harmful ice crystals. The frozen embryos must be good enough in quality in order to survive the freezing and thawing process.

Frozen embryos are common property of the couple that produced them, and can be stored for several years, if necessary.

OTHER METHODS

Blastocyst culture

The embryo is typically transferred into the uterus at four-cell stage (two days after oocyte retrieval) or at eight-cell stage (three days after oocyte retrieval). Alternatively the embryos can be cultured for five days on a petri dish. At this point, the embryos typically reach the blastocyst stage of development (over 100 cells). The method helps determine the most viable embryos for transfer. The drawback of the technique is that in some cases, the fertilised oocytes do not divide as expected and the blastocyst stage is not reached.

Assisted Hatching (AHA)

Assisted hatching is a technique that may improve embryo implantation on the endometrium. The embryo develops into a blastocyst surrounded by an embryonic shell (zona pellucida). The shell becomes thinner during embryo development, and finally around the sixth day from fertilisation, breaks, allowing the embryo to hatch. The embryo must hatch in order to be able to implant onto the endometrium. If the embryo shell is thicker than normal, or has an abnormal structure, hatching may not be possible.

Assisted hatching involves using a laser beam, acid, or a mechanical aid in order to make the zona thinner or to make a small hole to it, facilitating embryo hatching and implantation. Assisted hatching is a somewhat controversial method, as there is no reliable evidence of its impact on embryo implantation. The procedure can be considered in case assisted

conception treatments have failed repeatedly for no apparent reason, or if the embryonic shell is abnormally thick.

Preimplantation Genetic Diagnosis (PGD), Preimplantation Screening (PGS)

Preimplantation genetic diagnostics has seen rapid development in the recent years, thanks to new investigation methods. Current methods enable more accurate examination of any chromosome abnormalities of embryos. The advanced methods enable the examination of both chromosome and gene mutations that cause specific hereditary diseases.

The examination requires a biopsy from the embryo on the third day, or on the fifth or sixth day at the blastocyst stage. It is advisable to perform the biopsy during the blastocyst stage, as this allows for a larger sample size for more reliable results. If results are ready on time, it enables the fresh embryo transfer into the uterus. Embryos examined at blastocyst stage are frozen following the biopsy and transferred into the uterus later. This procedure produces the best pregnancy results.

PREIMPLANTATION GENETIC DIAGNOSTICS IS PARTICULARLY BENEFICIAL FOR PATIENTS WHO HAVE

- Hereditary disease or chromosome abnormality that may cause severe developmental issues (gene mutation, chromosome translocation) (PGD)
- Several unsuccessful IVF treatment cycles (PGS)
- Repeated miscarriages (PGS)
- Women over 38-40 years of age who require assisted conception treatment (PGS)

Preimplantation genetic screening is clearly beneficial for all females who are receiving IVF treatment. Studies have indicated that in young women, around half of the embryos with normal morphology are abnormal, while women over 42 years of age may have abnormalities in over 80% of embryos. In some cases the treatments are unable to produce any chromosomally normal embryos for transfer. Transferring a chromosomally normal embryo into the uterus produces better results in all age groups, while reducing miscarriages and unnecessary treatments.

FERTILITY PRESERVATION

Assisted conception methods can also be used in fertility preservation. In public healthcare fertility preservation procedures, such as cryopreservation of gametes or ovarian tissue, can be offered before cancer treatments that affect on fertility, for patients with endometriosis requiring recurring operations, or for patients who are genetically predisposed to early menopause. Freezing gametes enables the preservation of fertility for post-pubertal males and females. For young children, however, the only options are ovarian and testicular tissue cryopreservation techniques that are still in experimental stage.

Sperm cryopreservation has been used for decades. Preserving female fertility is significantly more challenging due to the limited amount of oocytes and shorter period of fertility. The circumstances are further complicated by the susceptibility of oocytes to damages occurring during freezing and thawing due to their size and high liquid content. Previously the only viable female fertility preservation technique was embryo cryopreservation, but recent advancement in techniques such as vitrification has introduced new options.

These new techniques have seen increasing interest in gamete cryopreservation for non-medical purposes as well, for example, in the event that the timing is not optimal for having a child. For men, cryopreservation of sperm before sterilisation enables conception at a later point in life, if necessary. Female fertility begins diminishing after the age of 30, and the risk for childlessness between the ages of 40-44 is over 60%. Furthermore, pregnancy rates for IVF treatment are lower for women over the age of 35, and significantly lower for women over the age of 40. Thus, oocyte cryopreservation may provide an alternative for women who are unable attempt conception at an optimal age.

Oocyte cryopreservation provides women with more time to, for example, find a suitable partner and to retain the possibility of having genetic offspring. The technique also reduces the need for donated oocytes. It should be emphasised, however, that oocyte cryopreservation is not meant for treating women who are past the fertile age, but for women between 30 to 35 years of age who wish to preserve their fertility a bit longer. Proactive oocyte cryopreservation should be done before the age of 35, while observing differences in individual circumstances, particularly the remaining ovarian reserve. Finnish Fertility Society (SFY) published good practice guidelines in 2013 on the proactive oocyte cryopreservation and related psychotherapeutic counselling. In Finland, gamete cryopreservation for non-medical reasons is only possible in private fertility clinics.

TREATMENT INVOLVING DONATED GAMETES OR EMBRYOS

Despite the advancements in assisted conception methods, not everyone is able to conceive with their own gametes. Donated gametes can be used for treating male and female infertility.

DONATED GAMETES MAY BE REQUIRED IF

- The couple is unable to produce gametes
- Gamete production has ended due to a serious illness
- The female has experienced recurring miscarriages
- There is a risk of a difficult genetic disorder
- The couple has had several futile IFV/ICSI treatment cycles
- Infertility is due to social reasons (female couples and single women)

Gametes are provided by voluntary donors. Current legislation requires donors to agree to record their personal information in the national donor registry. By law the child has the right to know the identity of the donor once the child reaches the age of eighteen.

Healthy women who are no older than 35 years of age can be accepted as oocyte donors. Oocyte donation requires that the donor receive hormone treatment and monitoring similar to IVF treatments. Retrieved oocytes are fertilised with the sperm of the recipient's partner. Embryo transfer is performed two to three days after the fertilisation. Any remaining, viable embryos are cryopreserved. The recipient's endometrium is prepared for transfer and implantation with two to three weeks of oestrogen treatment. Embryo implantation is also aided with progesterone. Hormone treatment is given for at least two weeks following the transfer. In case of successful conception, the treatment is continued until 10th to 12th week of pregnancy.

Donated sperm can be used for insemination and IVF/ICSI treatment. The sperm is frozen and stored in a sperm bank, then thawed for insemination during ovulation, or on the day of oocyte retrieval in IVF treatment. Embryo donations are available in the form of spare embryos from IVF treatments, when the donor couple no longer needs the embryos and decides to donate them. The embryos are transferred to the recipient´s uterus in natural cycle during ovulation or in hormone replacement therapy cycle.

When providing assisted conception involving donated gametes, it is essential to provide sufficient counselling and support to the couples from a medical, psychological and juridical standpoint.

RISKS ASSOCIATED WITH ASSISTED CONCEPTION

RISKS ASSOCIATED WITH ASSISTED CONCEPTION INCLUDE:

- Risks related to procedure (bleeding, infection)
- Ovarian hyperstimulation syndrome (OHSS)
- Ovarian torsion
- Risks in early pregnancy (miscarriage, ectopic pregnancy)
- Risks related to multifetal pregnancy

OVARIAN HYPERSTIMULATION SYNDROME (OHSS)

The only risk directly related to hormone treatment is the ovarian hyperstimulation syndrome (OHSS). Ovarian follicles fill up with liquid, resulting in painful enlargement of the ovaries following ovulation or oocyte retrieval. The onset of OHSS can result from any medication used for inducing ovulation. Symptoms of OHSS include abdominal pain, swelling, nausea, vomiting, diarrhoea and sometimes breathing difficulties.

Among the most severe conditions related to hyperstimulation is fluid build-up particularly in the abdominal cavity. Mild forms of OHSS are fairly common, while severe cases are quite rare (occurs in less than 1% of treatment cycles).

Anticipating OHSS is difficult because the condition may not be related to the medication dosage or duration of the treatment. Risk group includes young, slender females and PCOS patients. Effective ultrasound monitoring seems to have reduced the risk of OHSS related to gonadotropin medication. Mild cases can be treated with rest, but severe cases may require hospitalisation. Pregnancy following treatment may result in the onset or prolongation of OHSS. If the risk of OHSS onset is considered significant, all embryos will be cryopreserved and the embryo transfer will be postponed until a later menstrual cycle.

ECTOPIC PREGNANCY

With assisted conception there is also a slightly increased risk of ectopic pregnancy. It is possible that the transferred embryo travels from the uterine cavity into a Fallopian tube, if the Fallopian tubes have not been removed. This can be checked with ultrasound examinations during the first weeks of pregnancy. Lower abdominal pain and bleeding are the most severe symptoms of ectopic pregnancy.

MULTIFETAL PREGNANCY

One of the most significant risks attributed to assisted conception is the high number of multifetal pregnancies. Risks related to multifetal pregnancy include higher risk of miscarriage, premature birth and low birth weight. The probability of multifetal pregnancy can be avoided in IVF treatments by transferring only one embryo at a time into the uterus.

HEALTH OF CHILDREN BORN FOLLOWING FERTILITY TREATMENT

So far IVF treatments have produced more than five million babies. According to estimates, every 25th birth is the result of assisted conception. 25-40% of babies were conceived with frozen embryos. Most babies conceived with assisted conception are healthy.

There can, however, be risks involved with pregnancies resulting from assisted conception. These risks can be attributable to the pregnancy and the health of the newborn baby. Previously, health problems have been related to multifetal pregnancies. The current practice is to transfer one embryo at a time into the uterus, which has resulted in fewer multifetal pregnancies. However, even monofetal pregnancies following IVF/ICSI treatments have 1.5-3 times higher risk of hypertension, pre-eclampsia and bleeding during pregnancy, as well as premature birth and low birth weight. While the reasons for these risks are not known, they might be at least partially related to infertility.

Babies conceived with assisted conception run a slightly higher risk of defects. While approximately three out of 100 live births are affected by a birth defect, four out of 100 babies born after assisted conception treatments are affected by a birth defect. Most of the defects are urinary and reproductive organ abnormalities that can be corrected with operations. If the cause of infertility is a significant problem of spermatogenesis, babies conceived with ICSI have a slightly higher risk of having a male chromosome defect. According to studies, the increased risk of a chromosome defect is related to infertility factors, not the assisted conception treatment.

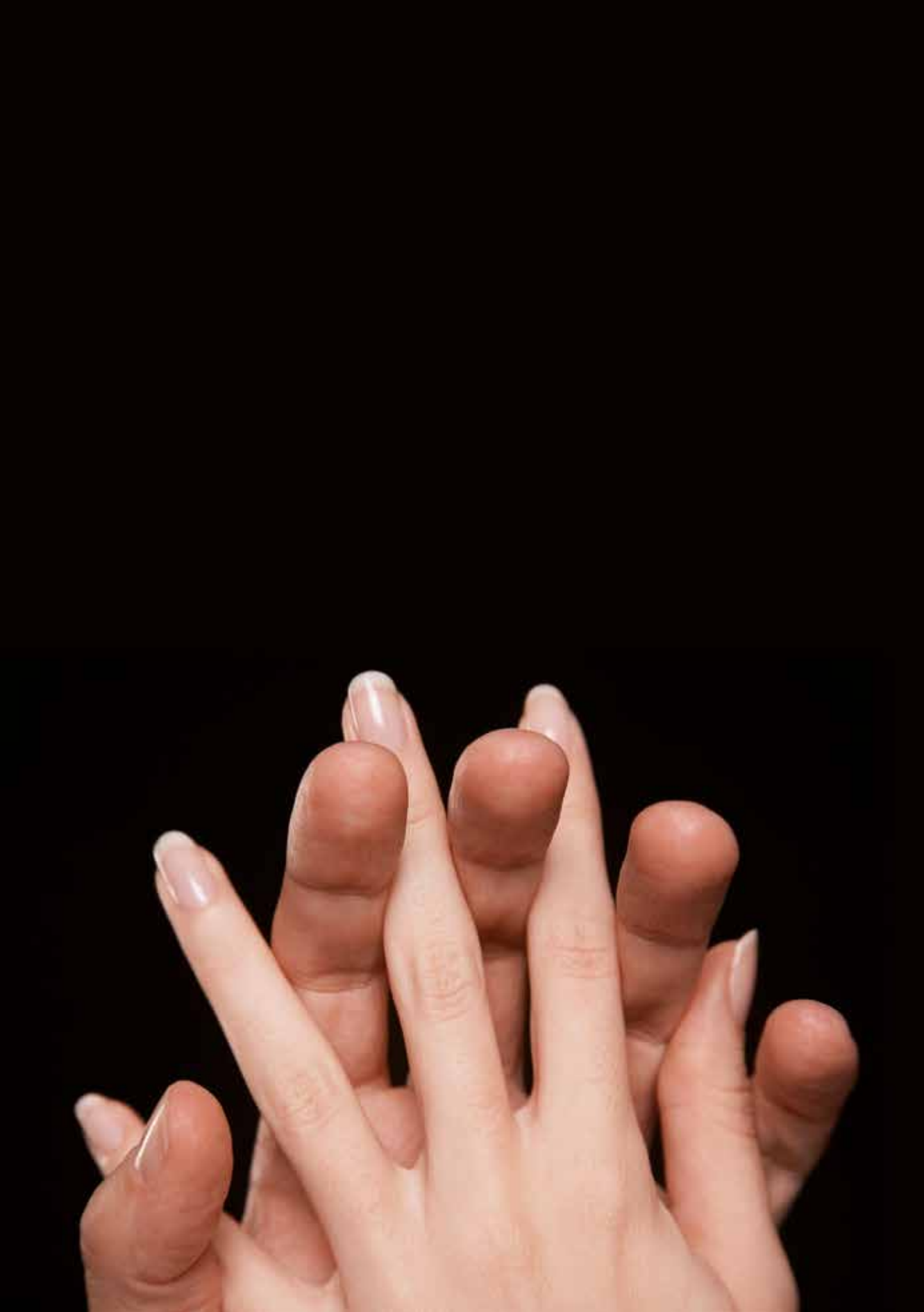
ACT ON ASSISTED FERTILITY TREATMENTS AND TREATMENT STATISTICS

The Act on Assisted Fertility Treatments (1237/2006) applies to the provision of assisted fertility treatment in which a human gamete or an embryo is placed into a uterus of a woman for the purpose of creating a pregnancy. The act also applies to the donation and storage of gametes and embryos for use in assisted fertility treatment. According to the act, in Finland an assisted fertility treatment can be provided to married or unmarried couples, female couples and single women. The service providers must also have a license granted by the National Supervisory Authority for Welfare and Health (Valvira). Fertility treatment is also subject to the Human Tissue Act (2004) under the license and supervision of the Finnish Medicines Agency (Fimea).

The Act on Assisted Fertility Treatments allows the use of preimplantation genetic diagnosis for preventing a serious, hereditary disease. Selection of sex for non-medical purposes is not allowed. Surrogate treatment is illegal in Finland. The law does not contain specific statute on assisted conception. The care provider is obligated to report and clarify any medical and juridical matters related to treatments with the relevant parties. A written consent is signed before the treatment. The consent indicates the applied methods and conditions under which care is given, as well as the period of validity.

If the treatment involves use of donated gametes or embryos, the donor must be registered in the donor registry (Luoteri) maintained by Valvira. The care provider is obligated to disclose to all relevant parties all medical and juridical matters related to donated gametes. The treating clinic is also obligated to provide counselling regarding the possible impacts of the biological origin of the child may have on the relations between family members, and on ways to prevent or alleviate any problems that may arise. The service provider must provide an opportunity for the person receiving treatment to discuss these matters with an expert. Typically gamete donation counselling is provided by a psychologist specialising in this field. The donor must not be informed of whom their gametes have been provided to, nor do the parents of the conceived child have the right to know the donor's identity. An exception to this is a situation where the donor is a person familiar to the family (known donor). A person who has been born from a donated gamete or embryo has the right to obtain information regarding their biological origin after reaching the age of 18. This requires that the parents disclose their child the information regarding their origin. Parents are encouraged to be open about the matter.

Clinics providing assisted conception treatments are obligated to provide annual reports on treatments to the National Institute for Health and Welfare (THL, www.thl.fi). The information is provided anonymously so that they cannot be used for identifying patients. Furthermore, archived information cannot be used to identify a hospital or a clinic. Information is collected on the number of treatments performed, treatment results, number of multifetal pregnancies and the health of conceived babies. Any complications will also be recorded.



INFERTILITY AND RELATIONSHIP

Infertility is an increasingly common problem. About one couple in six will experience involuntary infertility. For many, the experience of infertility can be the first major challenge of their lives. This is the harsh, uncontrollable part of nature. For 50% of women and 20% of men, infertility is the worst crisis they have faced so far in their lives. Infertility is a highly emotive and personal subject, that may be difficult to discuss with outsiders, sometimes even with the partner.

Infertility touches on the most private subjects: procreation and sexuality. The fear of being alone and without a family is the most significant fear related to infertility. Every couple approaches the issue of infertility differently. While some are eager to solve the problem and decide to contact a fertility clinic, others may go through a lonely mourning process before they can even consider seeking assisted conception treatment.

Modern assisted conception treatments are efficient, but they also bring along a large number of outsiders into the intimate life of the couple. This incursion of outsiders in intimate matters can result in various emotions, including helplessness and confusion.

EMOTIONAL ROLLERCOASTER AND COPING WITH REPEATED TREATMENTS

Fertilisation treatments alone take a physical and emotional toll. During the treatment, the couple receive information on their fertility, which may be difficult to process, or even accept. The couple will learn to accept that the results of assisted conception treatment cannot be known beforehand. Although most of the examinations and treatments are performed on females, the emotional rollercoaster of infertility examinations and treatments is experienced by men as well.

Experiencing infertility often brings up emotions that are difficult to bear and process. The couple are forced to look at themselves as exposed and inadequate, having to evaluate their manhood and womanhood. It is common for women to experience more negative emotions and blame themselves for the infertility. Being left outside the traditional world of women, seeing pregnant women and the happiness of others who have experienced the joy of birth are painful experiences, often resulting in feelings of inferiority.

Men tend to react differently to infertility. The ability to impregnate their partner, to continue their bloodline and to become a father are important milestones for many men. Men experience increased stress and anxiety following a failed assisted conception. These feelings may intensify after repeated failures of treatments. Men are worried about the impacts of infertility on their partner, the relationship and friendships.

Life may begin revolving around the hope of having a child; friendships become neglected, and it is difficult to find satisfaction in other areas of life. Being in a cycle of repeated treatments is a period that the couple is simply trying to survive.

LEARNING HOW TO COMMUNICATE

Each relationship will go through crises. Childless couples are no exception. Infertility will undoubtedly change the relationship as well as the way the couple view their own sexuality. Good interaction, communication and ability to listen to the other party may help bring the couple closer together through the shared experience of infertility. These challenges are generally positive, as in most cases going through the crisis together will make the relationship stronger. It is important to learn to talk about difficult matters with the partner. In some cases, however, old problems may resurface and new ones may be created due to infertility. The closest person, who is the one to provide the most support and comfort, can also be the reminder of the sadness of infertility. Children born out of a previous relationship may also serve as a painful reminder of the partner's fertility. It is easily forgotten that in the current relationship, both of them are childless. Even if conception has occurred easily in the previous or current relationship, it does not mean the next conception would be as easy.

SEXUALITY

Fulfilling sexual life is based on an encouraging and loving relationship. Avoiding communication breakdowns requires learning. The better the communication skills, the better equipped the couple is to process issues related to sexuality.

Although issues related to sex life are rarely the cause of infertility, infertility may have a significant impact on sex life. Attempting conception makes sex life scheduled and performance-oriented, which may suffocate spontaneous sexuality. The psychological impacts of infertility are related to the sexual self-image of an individual. Particularly in case of extended treatments or failure to conceive, both women and men tend to feel that their bodies are dysfunctional and inadequate. Caring, loving and considerate contact will help heal mental bumps and bruises.

WHAT IF ASSISTED CONCEPTION TREATMENT DOES NOT WORK?

Although most couples receiving assisted conception treatment are able to have the child they have been longing for, there are some to whom the treatments do not produce the desired results. Letting go of the dream of having a child is one of the most significant decisions in life, and may often result in a difficult personal crisis. This crisis can be overcome by taking it step by step, by dealing with personal emotions, allowing enough time and space for the process to take place and by discussing the matter and personal feelings with family members and others with similar experiences. In this situation, psychotherapeutic counselling can be beneficial for many couples. Both partners should be allowed to find new directions and joy in life, both individually and together. In case the infertility treatments become a prolonged struggle, the couple needs realistic information and support in terms of making a decision to stop the treatments. In order to help the couple find closure, it is important to emphasise that all assisted conception measures have been taken.

At the end of assisted conception treatments, the couple should consider whether to continue their life together without a child or to seek parenthood via adoption or foster parenthood.

IMPORTANCE OF MENTAL SUPPORT

Couples seeking help for infertility require comprehensive counselling and mental support throughout the care process, ideally as a part of the care process. Mental support is particularly important when the couple is seeking assisted conception treatments, or when ending the treatments or using donated gametes should be considered.

Mental support is also necessary following successful assisted conception. Fears related to pregnancy, miscarriage and parenthood may be intensified after years of wishing for a child. Natural childbirth may also bring about conflicting emotions that are difficult to process.

The need for mental support varies greatly. Some couples are able to go through the process with typical medical care and family support, while taking care of themselves. It is important for both partners to actively participate in decision-making. The treating physician and the rest of the care staff should also address the psychological aspects of assisted conception throughout the treatment process. Two out of three infertile couples feel that they receive sufficient support from family and friends.

IMPORTANCE OF PEERS

All couples can benefit from having even a single person, with whom they can discuss about infertility and assisted conception treatment once they are ready to address the issue. Mutual support provided by infertile couples is extremely important. In Finland, this type of support is provided by the Finnish Infertility Association Simpukka. The members of Simpukka cover the entire spectrum of infertility: couples in various stages of the treatment process, couples that have had successful assisted conception treatment, couples that have decided to engage in adoption, as well as couples that have decided to stay childless. The most vital role of the association is to help childless people connect and share their experiences.

During a hard period in life, it is important to take care of oneself and fully enjoy other areas of life. Fun, shared activities help reduce stress and provide more content to life. Taking care of the relationship should be a priority for all infertile couples.

GLOSSARY

AFC: Antral follicle count. Antral follicles are small, growing ovarian follicles under 10 mm in diameter.

AMH: Anti-Müllerian Hormone, a hormone produced by ovarian follicles in the early stages of development. Can be used for predicting gonadotropin response in IVF treatment.

Anabolic steroids: Hormone products that have an impact similar to testosterone.

Assisted hatching (AHA): Facilitating embryo hatching by using a laser beam, acid, or a mechanical aid in order to make the zona thinner or to make a small hole to it.

Biopsy: Removal of cells for testing.

Blastocyst: Embryo that has been cultured for five to six days.

Chromosome examination: Basic genetic examination that aims to establish possible connections between chromosome mutations and genetic disorders. Typically, chromosome examination is done from a blood sample. Chromosome examination can also be performed by taking a sample from placenta or amniotic fluid, in case there is a reason to suspect difficult illness affecting the foetus.

Embryo: A fertilised oocyte that has divided into several cells, and may implant onto the endometrium.

Endocrine system: Collection of glands that secrete hormones.

Endometriosis: Presence of tissue similar to the lining of the uterus (endometrium) in abnormal anatomical location.

Estradiol (E2): Hormone produced by ovarian follicles. Estradiol can be used for measuring follicle growth during ovarian stimulation treatment.

Fimbria: Fringe tissue at the end of the Fallopian tubes.

Follicle: Ovarian follicle containing an oocyte.

FSH: Follicle stimulating hormone secreted by the pituitary gland, regulating female ovarian follicle growth and male sperm production. FSH is used during IVF treatment cycle for developing several oocytes.

Gene: The basic physical and functional unit of heredity.

GnRH: Gonadotropin releasing hormone, produced by the hypothalamus for the release of gonadotropins.

GnRH-agonist: Medication given before FSH injections in order to suppress natural hormonal function.

GnRH-antagonist: Medication used simultaneously with FSH (instead of GnRH agonist) to prevent premature ovulation.

Granulosa cell: A somatic cell of the sex cord (in the ovary).

hCG (human Chorionic Gonadotropin): Placenta hormone which is produced following the implantation of the embryo into the uterus. Pregnancy tests are based on measuring hCG levels. The hormone is also used for producing a hormone product for enabling timed oocyte retrieval during IVF treatment.

hMG (human Menopausal Gonadotropin): Extracted from urine of menopausal women, used in IVF treatments in a similar way as FSH.

Hypotalamus: Part of the brain located below the thalamus and above the pituitary gland.

Hypothyreosis: Insufficiency of thyroid gland to produce thyroid hormones.

ICSI (Intracytoplasmic Sperm Injection): Microinjection fertilisation procedure in which a single sperm is injected directly into an oocyte.

Immunology: Branch of biomedical science covering the immune system.

Implantation: Attachment of the embryo onto the endometrium.

Induction: Production, causing.

Injection: Insertion of liquid with a syringe.

IUI: Intra Uterine Insemination.

IVF: In Vitro Fertilisation.

IVM: In Vitro Maturation.

Laparoscopy: Keyhole surgery, allows access to abdomen from small incisions in the skin.

LH: Luteinising hormone produced by the pituitary gland. Causes female ovulation and the development of corpus luteum, regulates male testosterone production.

Menarche: The first menstrual cycle indicated by menstruation.

Microdeletion study: Y chromosome screening study done from a blood sample.

Morula: Embryo resulting from cell divisions, usually around four days after fertilisation.

Myoma: Bening tumour that grows within the muscle tissue of the uterus.

OHSS: Ovarian Hyperstimulation Syndrome.

Ovarian reserve: The capacity of the ovaries to provide oocytes.

Ovulation: Release of oocyte.

Ovulation induction: Stimulation of oocyte maturation and release.

PAP smear: Screening test for cervical cancer.

PCOS: Polycystic ovary syndrome.

PGD: Preimplantation genetic diagnosis.

PGS (Preimplantation genetic screening): embryo chromosome screening.

Pituitary gland: An endocrine gland located on the bottom of the hypothalamus, producing seven hormones from the anterior and two from the posterior side.

Polyp: Benign bulge of a mucous membrane.

Progesterone: Endogenous steroid hormone.

Prolactin (PRL): Hormone regulating milk production.

Puncture: Insertion of a hollow needle, e.g. into the ovary in oocyte retrieval.

Sperm washing: Preparation of sperm prior to infertility treatment.

Spermatogenesis: Process in which spermatozoa are produced.

SSG: Salpingosonography (ultrasound examination), used for examining possible Fallopian tube obstructions.

Testosterone: Male hormone produced by testicles.

Time-lapse embryo imaging: Non-invasive embryo selection technique involving taking a series of photographs for determining the most viable embryos.

Translocation: Rearrangement of parts between nonhomologous chromosomes.

Trophoblast: The outer layer of a blastocyst, forms the placenta.

TSH: Thyroid-stimulating hormone, which regulates thyroid gland functions.

Varicocele: Abnormal enlargement of pampiniform venous plexus.

Zona pellucida: Glycoprotein layer surrounding the oocyte.

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IVF CLINICS IN HELSINKI

■ PUBLIC HEALTH CARE
■ PRIVATE HEALTH CARE

Dextra Fertility Clinic ■
www.dextralapsettomuusklinikka.fi

Fertinova Infertility Clinic ■
www.fertinova.fi

HUS/Women's Hospital ■
PL 140, Haartmaninkatu 2, 00290 Helsinki
Tel. +358 9 4711

Mehiläinen Felicitas ■
www.felicitas.fi

Family Federation Infertility Clinics,
Helsinki clinic ■
www.vaestoliitto.fi

IVF CLINICS IN JOENSUU

North Karelia Central Hospital,
Infertility Outpatient Clinic ■
www.pkssk.fi

IVF CLINICS IN JYVÄSKYLÄ

Fertinova Jyväskylä ■
www.fertinova.fi

IVF CLINICS IN KOTKA

Appelmedi Oy ■
www.appelmedi.fi

IVF CLINICS IN KUOPIO

InOva klinikka Oy ■
www.inova.fi

Kuopio University Hospital,
Gynaecological Outpatient Clinic ■
www.psshp.fi

IVF CLINICS IN LAPPEENRANTA

Mehiläinen Felicitas ■
www.felicitas.fi

IVF CLINICS IN OULU

Oulu University Hospital, Department of Obstetrics and Gynaecology ■
www.gyn.oulu.fi and www.ppshp.fi

Family Federation Infertility Clinics, Oulu clinic ■
www.vaestoliitto.fi

IVF CLINICS IN TAMPERE

Ovumia Oy ■
www.ovumia.fi

Tampere University Hospital, Gynaecology Outpatient Clinic and Reproductive Endocrinology Outpatient Clinic ■
www.tays.fi

IVF CLINICS IN TURKU

Fertinova Turku ■
www.fertinova.fi

Turku University Hospital, Gynaecological Outpatient Clinic ■
www.tyks.fi

Family Federation Infertility Clinics, Turku clinic ■
www.vaestoliitto.fi

CONCLUSION

Involuntary infertility affects thousands of couples in Finland. The emotional burden of infertility affects both parties. Most couples suffering from infertility can find a solution from current treatment methods. The decision on treatment options ultimately lies with the couple.

The first step in treating involuntary infertility is to seek information and expert help. When starting examinations and possible subsequent assisted conception treatments, it is important that the couple shows mutual compassion and understanding. Assisted conception treatments can be a very hard period in the couple's life, which is why it is important to try to find joy in other aspects of life, such as physical activity, cultural experiences, or simply enjoying peaceful time together.

For more information on infertility and assisted conception, please visit:
www.parempaaelamaa.fi/lapsettomuus

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