



# IVF – ICSI



# Information

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## Collection and storage of information

In connection with medical treatment and mandatory keeping of medical records we need to gather, organize and store information about the persons we treat. Medical treatment is possible only if you can accept this. The information is collected and stored according to the General Data Protection Regulation. More information is available on our website.

## About this information

The information given herein is a supplement to the information that you receive in connection with consultations and treatments in our clinic. If you have any questions, please do not hesitate to contact us. Please refer to the contact information.

We strive to ensure that all information is updated and correct. However, we cannot exclude the possibility of errors and typos.

## General information about IVF and ICSI

IVF is an abbreviation for In Vitro Fertilisation and is also called 'test tube' treatment.

During IVF treatment mature oocytes (eggs) are collected from the ovaries and fertilised with semen in a petri dish in an incubator in the laboratory. Here the fertilised eggs (embryos) develop during the first cell divisions. After 5 days the best embryo, now a blastocyst, is transferred to the uterus so it can attach to the endometrial lining and continue the development into a foetus, just like after normal conception.

ICSI is an abbreviation for Intra Cytoplasmic Sperm Injection. ICSI is used when the sperm quality is severely reduced or if there has been low fertilisation rate in a previous treatment cycle with normal IVF. With ICSI, one single selected sperm cell is injected directly into each of the oocytes. Except for this, ICSI and IVF treatments are the same.

## Treatment in Trianglen Fertility Clinic

### All types of treatment

- At Trianglen Fertility Clinic, we perform all types of fertility treatments that are legal in Denmark.
- We offer treatment of heterosexual couples, woman-woman couples and single women.
- The treatment may be with the husbands or male partner's semen or with donor semen.
- Donor semen may be from an 'anonymous donor', an 'extended profile donor', an 'open donor' or an 'own donor'.
- Donated eggs may be from an anonymous donor, an open donor or an 'own' donor.
- Double donation is allowed in Denmark.

*At Trianglen, treatment can start immediately.* The only exception is that we unfortunately have very limited possibility for treatment with oocyte donation since there are very few oocyte donors. It is legal to perform oocyte donation from a donor whom you know, and who has accepted to donate oocytes to you. It may be a friend or a family member (not mother or daughter). If you have your own oocyte donor, we can do oocyte donation without waiting.

We are open all year including holidays and weekends.

### Legal regulations

We can do treatments within the limits of the law in Denmark. Some of the central elements of the law are summarised below.

#### Age of the woman

Fertility treatment may not be performed after the woman has turned 46 years.

#### Sperm donation

May be from an 'Anonymous donor', an 'Extended profile donor', an 'Open donor' or an 'Own donor'.

#### Oocyte donation

Oocyte donation may be with eggs from an anonymous donor, an open donor or from a donor whom you know. The donor cannot be your mother or daughter.

#### Cryo-preserved blastocysts and oocytes

Cryo-preserved blastocysts and oocytes (unfertilised eggs) may be stored until the woman turns 46 years of age.

## Parent 'suitability'

There must not be doubt about the 'Parent suitability'.

## Before IVF is started

Before the treatment is commenced, we will go through your infertility history and the exams and tests that are necessary to select the best treatment for you. Many of the tests such as hormone assays, test for HIV and hepatitis, sperm analysis, contrast-ultrasound (HyCoSy) et cetera may have been performed already before you contact us. If not, we will make a plan for having the necessary work-up done.

You may have had fertility treatment before. If this is the case, we would like to have all available information about the treatment so we can consider it when advising you about treatment in our clinic.

### **Examinations and tests of the woman**

The woman is examined with an ultrasound scan of the uterus and ovaries. Blood tests are taken in order to evaluate the levels of hormones that are involved in the menstrual cycle, and which may be of importance for evaluating the chance of becoming pregnant. The function of the thyroid gland is also tested (TSH hormone) because normal thyroid function is very important in women trying to become pregnant. You must also be tested for HIV and hepatitis B and C.

If the fallopian tubes may be blocked, we recommend a contrast ultrasound exam (HSU) to find out if the fallopian tubes are fluid-filled and dilated. If they are, they should be surgically removed before IVF treatment because fluid filled fallopian tubes approximately halves the chance of becoming pregnant by IVF.

### **Examinations and tests of the man**

The man must have his sperm quality examined. He must also be tested for HIV and hepatitis B and C.

If the sperm quality is severely reduced with a total number of spermatozoa below 3 million so that the treatment of choice is ICSI, we recommend further work-up of the man to detect possible causes of the reduced sperm quality.

The testing may include hormone analyses, an ultrasound scan of the testicles and a test for 'micro-deletions' on the Y-chromosome.

If the cause of the reduced sperm quality is a micro-deletion on the Y-chromosome, you should consider possible implications for the choice of treatment. For example, use of donor sperm may be considered because a defect on the Y-chromosome will be inherited by male offspring who will then inherit their father's reduced sperm quality.

Men with azoospermia should also have a test for mutations in the gene that causes cystic fibrosis.

## The steps in IVF/ICSI treatment

IVF treatment follows the steps outlined below:

- Hormone stimulation of the woman monitored by ultrasound scans and in some case also blood tests for hormone levels.
- Final oocyte maturation injection
- Oocyte pick-up
- The sperm sample
- Fertilisation of the eggs and the first cell divisions in the laboratory
- Blastocyst transfer
- Hormone supplementation to strengthen the endometrium until the pregnancy test (and in some cases longer)
- The pregnancy test (blood test)
- Scanning of the pregnancy if the test is positive

### **Hormone treatment**

The purpose of the hormone treatment is to stimulate the ovaries to produce more than the one follicle that a woman produces in a normal cycle. The hormone stimulation aims at making 8-12 eggs for oocyte pick-up, but in some instances less will do. The number of cells can vary a lot depending on the woman's age and response to the stimulation.

We monitor the follicle growth by trans-vaginal ultrasound scans. In this way, the size and number of follicles can be determined. The size of the follicle indicates the maturity of the egg contained in the follicle. When the

follicles have reached a size of 17-20 mm the eggs are mature and ready for oocyte pick-up. The oocyte itself has a diameter of 0.12 mm and is not visible at the ultrasound scan.

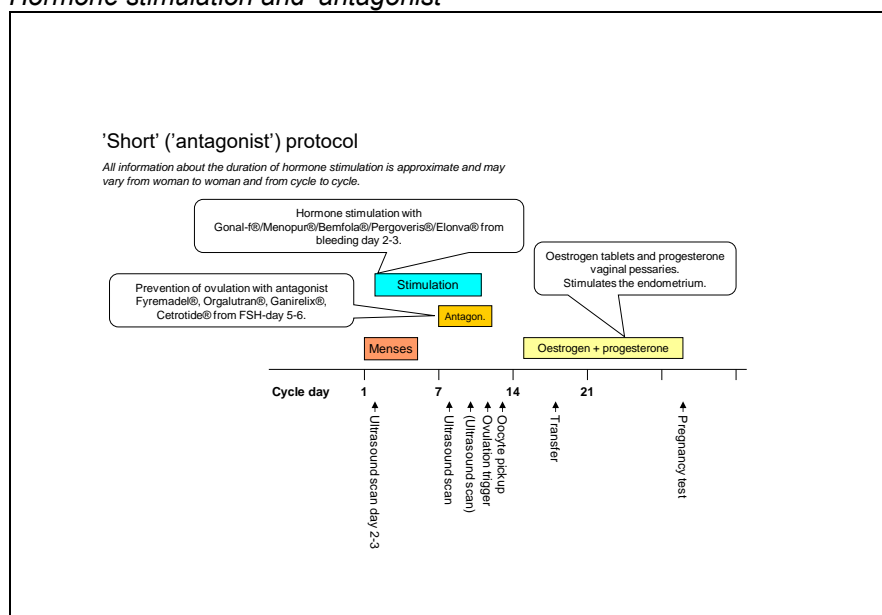
In our clinic, we use different hormone stimulation schemes. We mostly use treatment with 'long down-regulation' (we call it scheme 3) and the so-called 'short antagonist protocol' (we call it scheme 4). In some cases, we use stimulation based on clomiphene citrate, 'agonist flare-up' or 'CRASH'. Very rarely, we may do IVF without hormone stimulation.

The treatment is always tailored to the individual woman based on her cause of infertility and on experience from previous successful or less successful treatments.

When a treatment cycle starts, we will provide you with detailed information about the treatment plan, use of medicine, possible side effects and we plan the next consultation and ultrasound scan.

## Hormone stimulation with 'short antagonist' protocol (scheme 4)

### Hormone stimulation and 'antagonist'



### Hormone stimulation

The hormone stimulation is started on day 2-3 of the menstrual bleeding. The first day of 'real' bleeding is called day 1.

You must have an ultrasound scan before starting the stimulation. We make sure that there are no cysts (or a remaining 'corpus luteum' from the follicle that ovulated in the preceding cycle) in the ovaries and that the endometrial lining has been shedded.

If everything is ok you can start daily injections with stimulating hormone (Gonal-f®, Bemfola®, Puregon®, Pergoveris® or Menopur®). The injections should be taken once daily at approximately the same time (within +/- a few hours). The injections are given subcutaneously in the skin of the lower abdomen. In the clinic, we will instruct you how to do it, so you can take the injections yourself. Everybody can learn it. If it is not possible for you to take the injections yourself, our nurses can give them in the clinic during our opening hours. Or perhaps you can ask your doctor, nurse or another competent person to assist you.

In some cases, the long-acting stimulation hormone Elonva® is used. Elonva® is given as a single injection on day 2-3 and the effect lasts for 7-8 days, so it is not necessary to take additional injections of hormone stimulation for several days.

### Antagonist

Around 5-6 days after you started the hormone stimulation the treatment is supplemented with a so-called 'antagonist' (Fyremadel®, Orgalutran®, Ganirelix® or Cetrotide®).

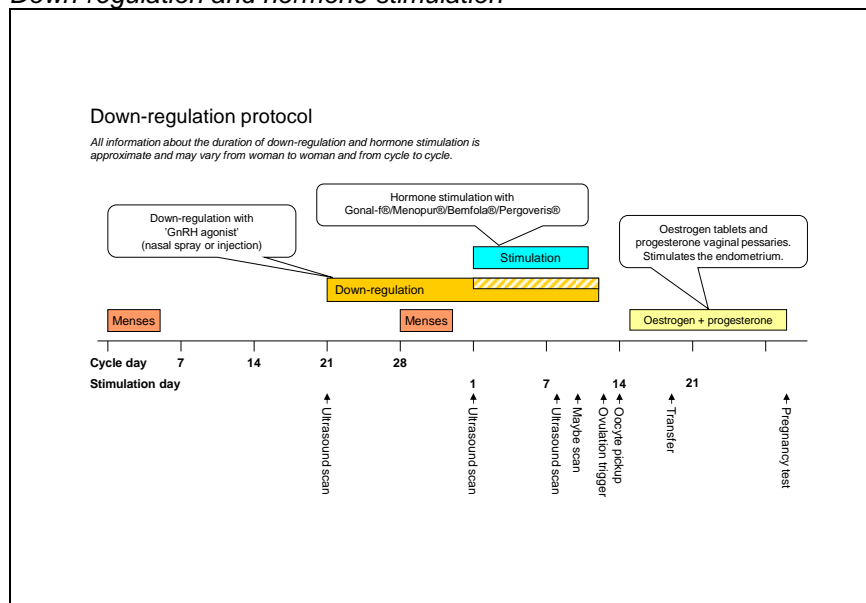
The antagonist prevents the pituitary gland from secreting FSH and LH, which are the hormones that stimulate the ovaries to produce eggs. The antagonist also prevents the pituitary gland from releasing the 'final

oocyte maturation' signal when there are mature eggs. In this way, the antagonist prevents the follicles from ovulating before the time of the oocyte pick-up.

The antagonist is taken as one injection every morning. Once the antagonist treatment starts, it must be continued until and including the day when you take 'final oocyte maturation' injection. The daily injections of stimulation hormone (FSH/hMG) are continued during this phase.

## Hormone treatment with 'long down-regulation' (scheme 3)

### Down-regulation and hormone stimulation



### Down-regulation

This treatment starts with 'down-regulation' close to day 21 of the menstrual cycle. Ideally the down-regulation is begun approximately one week before the next expected menstrual bleeding, so if your cycle is not between 26-30 days down-regulation may be initiated earlier or later than day 21. We perform an ultrasound scan to ensure that the down-regulation starts at the correct time in the cycle.

The down-regulation inhibits the secretion of FSH and LH from the pituitary gland. These hormones stimulate the ovaries to produce eggs. The down-regulation also prevents the pituitary from secreting the peak of LH that will induce ovulation when there are mature follicles. This prevents ovulation before the oocyte pick-up.

Down-regulation can be done with a nasal spray (Synarela® 3 puffs daily or Suprecur® 4 puffs daily) evenly distributed over the hours that you are awake. Alternatives are one daily injection with Suprefact® or Gonapeptyl® or one depot injection with Zoladex® or Decapeptyl®.

While you take the down-regulation medicine, you will have your menstrual bleeding. It may be slightly delayed. You should just proceed with the down-regulation. The bleeding may be slightly different than usual.

If the menstrual bleeding is more than one week delayed, you should take a pregnancy test. It may occasionally happen that the test shows that you are pregnant. If so, you should stop taking the down-regulation. It does not harm the pregnancy that you took the down-regulation medicine.

Because the down-regulation induces a hormonal stage that resembles the menopause, you may experience side effects resembling menopausal symptoms: Hot flushes, headache and mood disturbances. However, most women will have very few symptoms from the medicine. If you experience side effects, they normally disappear when the hormone stimulation starts.

### Hormone stimulation

The hormone stimulation normally starts approximately 14 days after the down-regulation began. At least three days should have elapsed since the onset of the menstruation. The down-regulation continues during the hormone stimulation.

Before starting the hormone stimulation, we perform an ultrasound scan to make sure that the endometrium has been properly shedded and that no cysts are present in the ovaries.

When everything is ok, the daily injections with stimulating hormone are begun (Gonal-f®, Bemfola®, Puregon®, Pergoveris® or Menopur®). The injections are taken once daily at approximately the same time (within +/- a few hours. The injections are taken subcutaneously. We will inform you about how to do it so you can take the injections yourself. Everybody can learn how to do it. If you – after having had detailed instruction from us – are unable to take the injections they can be given by our nurses in the clinic (during our opening hours), or you may know a doctor, a nurse or another competent person who can assist you.

After 8-10 days with the daily injections and the continued down-regulation, we will perform an ultrasound scan. We will determine the size and number of follicles and measure the thickness of the endometrium. Often, we will need to do one or two more scans before the follicles have reached a size (17-20 mm) where we can plan the time of the final oocyte maturation injection (hCG) and the oocyte pickup.

### ***Other types of hormone stimulation***

In some cases, we recommend other types of stimulation than 'long down-regulation' of 'short antagonist protocol'.

#### **Clomiphene citrate plus FSH/hMG (scheme 1)**

This stimulation is based on Clomiphene tablets and the stimulation is supplemented with hormone injections with Gonal-f®, Puregon®, Menopur® or Pergoveris®. This stimulation may be good for women who produce few eggs or low-quality eggs with the 'standard' treatments.

#### **Un-stimulated treatment (scheme 0)**

IVF without hormone stimulation may be considered when the woman does not produce more than 1-2 eggs with hormone stimulation.

Without hormone stimulation, only one follicle will develop. In such a 'natural' cycle without down-regulation and 'antagonist' there is always a risk that ovulation may occur before oocyte pick-up.

### ***Final oocyte maturation injection***

#### **Ovitrelle® (hCG)**

An injection with the 'final oocyte maturation' hormone hCG (Ovitrelle®) is given to induce the final maturation of the oocytes and make them ready for pick-up and fertilisation. hCG is a pregnancy hormone but it has the same effect as LH which is the natural 'ovulation' hormone.

Injection of Ovitrelle® is taken 36 hours prior to the scheduled oocyte pick-up. It is very important that the time of the injection be exactly as planned. We will inform you about exactly when to take the injection. The timing depends on the time of the planned oocyte pick-up.

#### **Final oocyte maturation with Gonapeptyl®, Suprefact® (or another 'GnRH agonist')**

An alternative to using hCG for final oocyte maturation is to give a single dose of Gonapeptyl®, Suprefact® (or another GnRH agonist). This method can only be used if you are not down-regulated, and therefore it is not used in 'scheme 3'.

Final oocyte maturation ('GnRH agonist triggering') with Gonapeptyl® or Suprefact® may be an option if there is risk of hyperstimulation or if the final maturation of the oocytes has not worked well with Ovitrelle®. GnRH agonist triggering is also useful in oocyte donors to avoid hyperstimulation.

### ***Oocyte pick-up without pain***

During the oocyte pick-up, the oocytes are picked up from the follicles. The oocytes are transferred directly to the lab where they will be fertilised and cultured.

The oocyte pick-up is virtually pain-free because we use a combination of local anaesthetic injection in the top of the vagina and small but frequent intravenous injections of a potent morphine-like medicine. It is important for you and for us that the oocyte pick-up is painless so you will not have to worry about this part of the treatment.

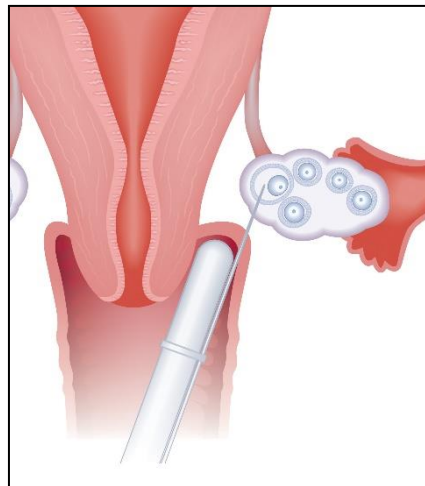


We use nurse anaesthetists to take care of the medication and pain relief during the oocyte pick-up. This has resulted in a very high level of satisfaction with the oocyte pick-up among our patients.

At the planned time, you and your partner (or possibly another accompanying person) come to Trianglen, normally between 9-11 a.m. You should bring the sperm sample with you (see below regarding the sperm sample).

When you arrive at Trianglen, we place a small plastic catheter in a vein. You will receive medicine through this catheter during the oocyte pick-up.

The oocyte pick-up is performed with ultrasound guidance. A thin needle is introduced through the vaginal wall and into the follicles in the ovaries. The individual follicles are emptied by aspirating the fluid. A laboratory technician immediately examines the fluid with a microscope to locate the oocyte. If the oocyte is not found in the initial follicular fluid, we will 'flush' the follicle to get the egg out of the follicle. We use a needle with two channels, one for aspirating the fluid and one for flushing. You can see both the ultrasound scan and the oocytes on monitors during the oocyte pick-up.



The pain-relieving medicine that you get during the oocyte pick-up will make you slightly drowsy, but you will be fully awake. We will talk with you during the procedure and explain to you what is going on. Your husband or another person can be with you during the oocyte pick-up, which normally takes 10-15 minutes.

After the oocyte pick-up you rest in the clinic for about one-half hour before you can go home.

*Because of the sedating and pain-relieving medicine, you get during the oocyte pick-up you must not drive a car yourself for the rest of the day.*

After the oocyte pick-up, you will be tired and need to rest.

If you experience discomfort or pain after the pick-up, you can use weak painkillers such as paracetamol (Panodil®). On the day of the pick-up and the following day you may use diclofenac or similar. After this time such drugs should be avoided because they may interfere with the process when a blastocyst attempts to implant in the endometrium.

#### **Fasting for the oocyte pickup**

You must come fasting for the oocyte pick-up. This means that:

- You must *not* eat or consume milk products for 6 hours before the oocyte pick-up.
- You *may* drink 'clear fluids' (not milk) until 2 hours before the oocyte pick-up. We recommend that you drink a large glass of juice approximately two hours before the oocyte pick-up.

### **The sperm sample**

The sperm sample is normally produced at home. It is produced by masturbation in a container that we provide when we plan the oocyte pick-up. We recommend that there has been ejaculation 1-2 days prior to providing the sample so that the sample we receive for fertilisation contains fresh sperm cells. A longer period of abstinence does not improve the sperm quality.

For some men with a very low sperm count, or when there may be a risk that the sample does not contain sperm cells at all we sometimes suggest that a sperm sample is provided both the day before oocyte pick-up and on the day of the pick-up.

Some men may have difficulty producing a sperm sample 'under pressure'. If you expect that this may be a possibility for you, some precautions may be taken. For example, you may provide a sperm sample in advance, which can be frozen and used as a back-up. The sperm quality will be reduced due to the freeze-thaw process but it will virtually always be usable for ICSI.

In the laboratory we prepare the sperm sample by washing and gradient centrifugation. The best motile sperm cells are concentrated and used for insemination of the oocytes. During or just after the oocyte pick-up we will inform you about the quality of the sample.

## TESA (TEsticular Sperm Aspiration)

Some men with azoospermia still have viable sperm cells in the testicles. TESA is also an option in men who have been sterilized by vasectomy because the testicles still produce sperm cells – they are just not present in the ejaculate.

In these situations, it is possible to obtain sperm cells directly from the testicles by a small procedure performed under local analgesia. A thin plastic catheter is inserted into the testicle and a small amount of the sperm producing tissue is aspirated. Sperm cells can be found in this tissue.

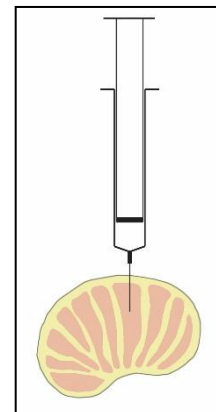
### TESA

TESA is performed on the day of the oocyte pick-up. The number of sperm cells obtained by TESA is always rather low. Therefore, ICSI is always necessary when fertilising the oocytes.

Before ICSI is planned, the man will be evaluated to try to determine whether it is likely that sperm cells can be aspirated from the testicles. Despite this, it may rarely happen that no sperm cells can be obtained by TESA.

Therefore, you should have thought about alternatives if this should happen. Should the oocytes be cryopreserved for later use? Should they be fertilised with donor semen? Or should they be discarded?

TESA is performed under local analgesia on the scrotum and the procedure takes less than 30 minutes. If you prefer, we can provide analgesia in the same way that we do for oocyte pick-up.



It is common to have some tenderness in the testicle for a few days after the procedure.

### Possible complications to TESA

Local bleeding or infection may complicate TESA in 1% or less of the procedures. The symptoms will be pain, swelling or fever. The treatment is with antibiotics. Contact an emergency medical service or us if you have signs or symptoms of a complication.

## Fertilisation of the oocytes and the first cell divisions

Immediately after the pick-up the oocytes are transferred to small petri dishes with culture medium and placed in an incubator. An incubator is a specialised instrument that will maintain ideal conditions for the oocytes and early embryos. In the incubator the temperature, humidity, carbon dioxide tension and oxygen tension can be maintained within very narrow limits.

### Fertilisation

A few hours after the oocyte pick-up, the oocytes and the washed sperm cells are combined. With 'standard' IVF, the oocytes are placed in a small petri dish in culture medium and 100-500,000 sperm cells are added. After this, it is up to the sperm cells to compete about entering the oocyte.

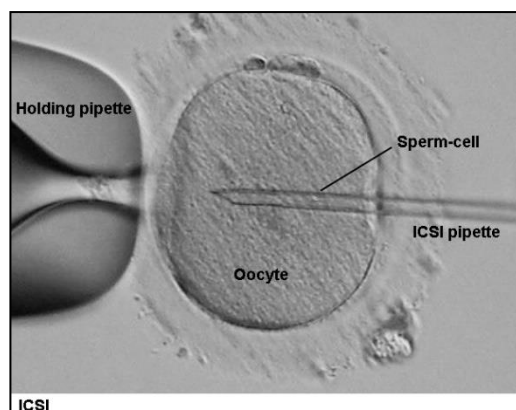
The following day the oocytes (now early embryos) are examined with a microscope for signs of fertilisation. Fertilised eggs contain two 'pro-nuclei' – one from the oocyte and one from the sperm cell. The early embryos are cultured until day 5-6 at which time they should have developed into the so-called blastocyst-stage.

### Fertilisation with ICSI

(*Intra Cytoplasmic Sperm Injection*, 'mikroinjection', 'mikroinsemination').

ICSI is an extension of the standard IVF method, which is used if the number of sperm cells is very low or if a previous 'standard' IVF treatment has resulted in a low fertilisation rate.

With ICSI, the hormone treatment and oocyte pick-up are done exactly as for IVF. The only difference is the way that the oocytes are fertilised.



The fertilisation with ICSI is performed with a special microscope with 'micromanipulators'. With this microscope, an oocyte can be held with a holding pipette and a normal-looking sperm cell can be selected and picked up with an extremely thin pipette. The sperm cell is then injected through the egg-'shell' and into the egg. After the ICSI fertilisation procedure, the cell divisions continue just like with standard IVF.

### **When is ICSI recommended?**

ICSI is used in situations where standard IVF fertilisation does not work. Some examples are

- Severely reduced sperm quality, i.e. less than 1-5 million sperm cells with good progressive motility.
- All cases where TESA has been done to obtain sperm cells.
- Situations where a previous IVF treatment has not resulted in satisfactory fertilisation of the eggs.
- If a previous IVF treatment has resulted in a low fertilisation rate, we often recommend ½ICSI in future cycles.
- In 'unexplained' infertility, we often recommend ½ICSI - (see below).

### **Fertilisation with '½ICSI'**

If the sperm quality is borderline and is likely that there will be a reduced fertilisation rate, we often recommend '½ICSI' ('half ICSI'). This means that we let the sperm cells themselves fertilise half of the oocytes while we perform ICSI on the other half of the oocytes. We also recommend ½ICSI in cases of unexplained infertility because the problem in some situations may have to do with the fertilisation process.

### **Risks associated with ICSI?**

Several studies have looked at children born after ICSI fertilisation.

The studies have shown that the risk of miscarriages and malformations are slightly higher in pregnancies resulting from IVF or ICSI compared with natural conceptions. However, this does not seem to be caused by the IVF/ICSI procedure per se. But the infertile couples who are in need for IVF/ICSI treatment already have a slightly increased risk of pregnancy complications and malformations in the children.

Chromosome abnormalities can be demonstrated in approximately 1.75% of the children, which is slightly higher than in the background population. It is not believed that the ICSI procedure as such is the cause.

With ICSI it is slightly more common to find chromosomal abnormalities inherited from the father. Approximately 5% of men with severely reduced sperm quality may have chromosomal abnormalities. These may be passed on to the child. In addition, it has been demonstrated that up to 10% of men with severely reduced sperm quality have small deletions on the Y-chromosome ('Y-microdeletions'). Because genes on the Y-chromosome are involved in sperm production it is very likely that boys born after ICSI fertilisation with a sperm cell with a Y-microdeletion will grow up to have reduced sperm quality. Just like their father.

## Fertilisation with donor semen

In some cases, the oocytes will be fertilised with donor sperm. This may be done if the man does not produce usable sperm cells. Or it may be when a woman is treated without a male partner.

It is possible to use different types of donor semen as described in more detail below.

### Important legal aspects when using donor sperm

When a woman with a male or female partner is treated with donor semen, there are important legal issues to consider. The father or 'co-mother' to be must sign a form about the fatherhood or 'co-motherhood' before the fertility treatment. Please see *The State Administration's* website, [www.familieretshuset.dk](http://www.familieretshuset.dk).

## Legal and other aspects of using donor sperm

The legal implications of sperm donation depend on the type of sperm used. Please see below for a brief description of some of the legal aspects associated with different types of donor semen.

The Danish Health Authorities demand that the following information be given to all women/couples treated with semen from a sperm donor.

*'When donors are selected, it is sought to limit the risk of inheritable diseases, malformations et cetera by only using donors who have declared that they are not aware of such inheritable risks in their kindred and who have been asked about such conditions by an experienced health professional. Despite these precautions, the risk of inheritable diseases is not excluded. If the child unexpectedly has a condition at birth or during the first years of life which you are informed could be inheritable it is therefore important that you inform the clinic or the health professional who has treated, you so it can be decided whether the donor can still be used. The same applies if you find out that a contagious disease may have been transferred by donor semen or donor eggs. Even though the donor is tested and found not to have transmittable diseases such as HIV or hepatitis the risk is never zero'.*

## Donor testing

Please see the sperm banks' websites for details about donor testing.

The extent of testing performed by the various sperm banks differ. Therefore, we recommend that you consult the individual sperm bank's website for detailed information about the donor testing in that sperm bank.

The sperm bank's doctor examines donors. They must be physically and mentally healthy, and there must not be inheritable diseases in their family. The donors must have a normal chromosome test. They are tested for serious infectious diseases (venereal diseases, hepatitis B and C and HIV). The sperm is only released for use after having been stored frozen for 6 months and after a repeated negative HIV test.

## Selecting a sperm donor for treatment

As described below it is possible to choose between different types of sperm donors ('Anonymous', 'Extended profile', 'Open' and 'Own'). Depending on the type of donor, you may base your selection on basic characteristics such as eye colour, hair colour, height, weight and skin colour or more detailed information, such as childhood photos, voice samples et cetera.

The sperm banks offer different donor types and thus various levels of information about the donor. We recommend that you select a donor from a sperm bank (for example [www.cryos.dk](http://www.cryos.dk) or [www.skejbycryobank.com](http://www.skejbycryobank.com)). When you have found a suitable donor, you can have sperm 'straws' sent to our clinic. We can then store the straws at minus 196 °C until they are used for treatment.

Different sperm preparations and sperm qualities are available. For us the important issue is that we for one treatment cycle (insemination or IVF) have at least 5 million sperm cells of good quality. You can confirm with the sperm bank that the sperm straws fulfil this.

*Please note that The Danish Health and Medicines Authority and the sperm banks use different definitions of 'anonymous'.*

## 'Anonymous' sperm donor

For an anonymous donor the sperm bank may provide information about the donor's eye colour, hair colour, height, weight, and skin colour. You may select sperm donors from the sperm banks' websites.

The donor will forever remain anonymous, and his identity will never be revealed to you or the child. Neither will the donor ever have any information about the children resulting from the treatment with his sperm.

*It is conceivable that DNA analyzes on the donor or his children and family and on children created with sperm from donor can be used to find out who the donor is. This may happen if some of the aforementioned*

*publish their DNA profiles so that they are available on the internet. In this way, it can theoretically happen that the anonymity is broken.*

When donor insemination is used to treat a heterosexual couple, the man must declare that he will be the father of the child/children and assume all the responsibilities associated with fatherhood.

The 'Anonymous' donor has no legal obligations or rights in relation to the child.

#### **'Extended profile' sperm donor**

A sperm donor with an 'Extended profile' is a donor where there is more information available than the basic information that may be provided for an 'Anonymous' donor. 'Extended profile' donors are per definition non-anonymous. The 'Extended profile' may contain information about blood type or more detailed information such as family relations, interests, education, voice sample, baby photos et cetera.

When donor insemination is used to treat a heterosexual couple, the man must declare that he will be the father of the child/children and assume all the responsibilities associated with fatherhood.

The 'Extended profile' donor has no legal obligations or rights in relation to the child.

#### **'Open' sperm donor**

An 'Open' donor is a donor who delivers sperm to a sperm bank and the sperm bank provides the sperm to fertility clinics. The 'Open' donor has made an agreement with the sperm bank that children resulting from treatment with his sperm may contact their donor when they turn 18 years old, if they wish.

*The specific terms are agreed between the donor and the sperm bank. Therefore, users of 'Open' profile donor semen must themselves obtain detailed information from the sperm bank about the agreement that has been made with the donor concerning later contact between children resulting from treatment with his sperm and him.*

The 'Open profile' donor has no legal obligations or rights in relation to the child except for the 'contact' possibility.

#### **'Known/own' sperm donor**

An 'Known' sperm donor is a donor whom the woman or couple knows and who has accepted to donate sperm for treatment of the woman, even though the woman and the donor are not married or living together as a couple.

An 'Own' donor must be tested for contagious diseases and deposit sperm like other sperm donors. This testing is done in a sperm bank, that can freeze the sperm for later use in a fertility clinic. Please note that it is not possible to use 'fresh' not frozen sperm from a known sperm donor. It must be frozen in a sperm bank prior to treatment.

The donor must be examined medically to determine if he is suitable as sperm donor. This testing can be done at Trianglen. For prices, please consult our pricelist or the secretaries. When the known donor has been evaluated and accepted, the frozen sperm can be transferred to the fertility clinic for use.

*According to Danish Law, a 'known' donor is legally the father of the child/children resulting from the treatment i.e., the 'known' donor has duty to financially support the child, and the child will inherit from the 'known' donor. An exception from this rule applies when the woman being treated lives in a 'marriage-like' relationship with a male partner or if she has a female partner who assumes for 'co-motherhood' for the child.*

*The legal aspects regarding the donor's fathership or the female partner's co-motherhood must be settled before the fertility treatment. The form called 'Blanket 9' from Familieretshuset ('The Family Law House') is used for this purpose.*

There are some important issues to consider when using a 'known' donor

- The known donor must give his written consent prior to each use of his sperm or blastocysts fertilised with his sperm. The treatment will be cancelled if the sperm donor's consent is not in place before the stage in the treatment where his sperm or the blastocyst must be thawed.
- The known donor can - at any time - request that the fertility clinic discards any unused sperm and any frozen blastocysts created with his sperm.
- If the donor should pass away, any stored sperm samples and blastocysts fertilised with his sperm cannot be used for treatment and must be discarded.

## Ordering donor sperm

If you are going to use donor sperm for treatment, the sperm should be ordered from one of the certified sperm banks, and the donor sperm should be transferred to us. We can store the frozen sperm samples in liquid nitrogen until they are used for treatment.

You can find the desired information about the donors on the sperm bank's websites. You can find additional information about ordering donor sperm on [trianglen.dk](http://trianglen.dk).

We prefer 'washed' semen, also called 'IUI-ready'.

In Denmark, there are three major sperm banks:

- **Skejby Cryobank** ([www.skejbycryobank.dk](http://www.skejbycryobank.dk)). We have a collaboration agreement with Danish Skejby Cryobank, which, like Trianglen, is part of Virtus Health. This means that you get free delivery and save our handling fee when you order sperm from Skejby CryoBank. We recommend MOT20 for straw for insemination treatment.
- **European Sperm Bank** ([www.europeanspermbank.com](http://www.europeanspermbank.com)). We collaborate with European Sperm Bank so you can access their donor register without having to pay. If you go to ESB's website using this link <http://clinics.europeanspermbank.com/trianglen> they can see that you were referred from us. All sperm straws from European Sperm Bank are MOT20 or better and thus meet Trianglen's recommendations for quality.
- **Cryos** ([www.cryos.dk](http://www.cryos.dk)) We collaborate with Cryos. You can find more information about the collaboration on our website. Please note that we recommend that you order MOT20 or better when ordering from Cryos. MOT10 and MOT5 straws are not recommended.

*Please note that The Danish Health Authorities and the sperm banks use different definitions of 'anonymous'.*

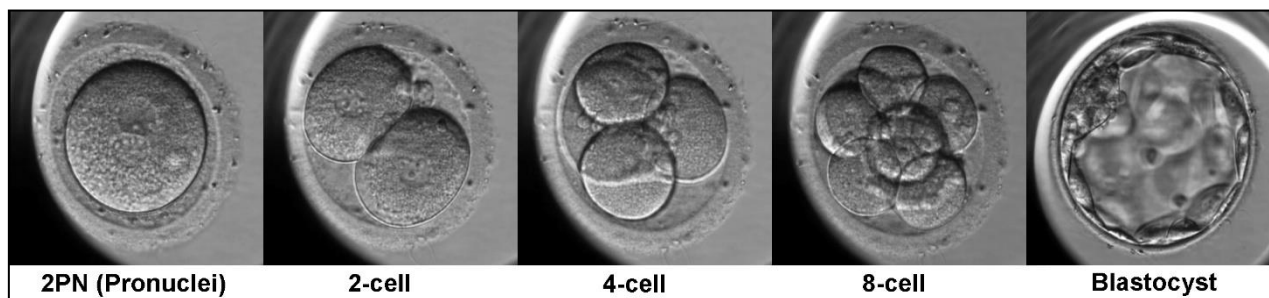
## Reservation of sperm from the same donor for future treatment

You can reserve/buy sperm from the same donor for future treatment. When you have become pregnant with a donor, you may contact the sperm bank and buy 'straws' from the same donor for future use. The straws should remain in the sperm bank until the time when you want to use them.

## Culturing the embryo into blastocysts

### Culture for 2-3 days

A fertilised oocyte which has begun dividing is called an embryo. Two days after the oocyte pick-up and fertilisation, many embryos have divided into 2-4 cells.



The cells in the embryo appear as round 'balls' surrounded by a translucent shell (zona pellucida). Ideally, an embryo should contain four cells on day 2 after the oocyte pick-up and around eight cells on day three.

Several criteria determine the quality of the embryos. The number of cells at specific time points is important. In addition, the individual cells in the embryo should be of approximately the same size. When the cells divide within the limits of the 'eggshell', little fragments sometimes occur between the cells. A few fragments do not affect the quality of the embryo, but severe fragmentation indicates that the embryo has a reduced chance of developing into a foetus.

We follow the development of the early embryos as they divide and preferably reach the blastocyst stage by day five or six after the pick-up. We can then select the best blastocyst for transfer into the womb. We only transfer blastocysts that are of such high quality that they have the potential to develop into a child.

Sometimes many embryos are of good quality sometimes it is just a few. In most cases, there will be embryos developing into blastocysts, the stage at which the transfer is done. If more than one blastocyst of good quality is obtained we can cryo-preserve ('freeze') the surplus blastocysts for later use.

### **Blastocyst-culture**

A blastocyst is the developmental stage that an embryo normally reaches 5-6 days after fertilisation. A blastocyst consists of approximately 100 cells. Blastocysts consist of a fluid-filled centre surrounded by a wall of cells. A small group of cells on the inner side of the wall ('the inner cell mass') are those cells that will develop into the embryo. At the blastocyst stage cells begin to "hatch" out of the surrounding 'eggshell' ('zona pellucida') and begin to implant in the endometrium around 6-7 days after fertilisation.

For embryo and blastocyst culture, we adjust the gas composition in the incubators to make it similar to the conditions found in the fallopian tubes. This means reduced oxygen concentration and an increased carbon dioxide concentration.

When blastocyst culture is intended, there is a risk that none of the embryos will develop into a good quality blastocyst that is suitable for transfer.

In some cases, we may suggest embryo transfer on day 3, especially if previous cycles have not resulted in one or more blastocysts suitable for transfer.

### **Incubators for blastocyst (embryo) culture**

Our Miri and EmbryoScope incubators allow us to keep the temperature and air composition constant and optimised for the development of the early embryo into a blastocyst.

The incubators make it possible to control the concentration of oxygen, carbon dioxide and nitrogen in the air inside the incubators, so the concentrations of these gasses can be kept as close as possible to the conditions in the fallopian tubes.

In natural conception, the first cell divisions occur in the fallopian tube where the concentration of oxygen is lower than in 'normal' air and the concentration of carbon dioxide is higher.

These conditions are mimicked in our incubators.

### **Cell culture at 'low oxygen concentration'**

The normal conception and the first cell divisions until the blastocyst stage is reached take place in the fallopian tube. In the fallopian tube, the carbon dioxide concentration is higher, and the oxygen concentration is lower than in atmospheric air. We seek to imitate these special conditions. Our incubators enable adjustment of the concentration of carbon dioxide and oxygen surrounding the embryos.

### **Add-ons (adjuvant treatments)**

*In connection with fertility treatment, it may for some cases be considered to supplement the 'standard treatment' with various additional measures. These so-called 'add-ons' or adjuvant treatments should not be used for everyone but may in certain situations improve the chance of achieving pregnancy and birth.*

*Below we briefly review some of the most common add-ons.*

*The use of add-ons must be paid separately. The prices can be found on our website.*

### **Zymot sperm purification**

Zymot is a method that can be used for the purification of the sperm sample, which is always carried out before the sperm is used for IVF/ICSI or insemination. The method is based on the sperm cells having to swim through thin fluid channels, in principle to imitate what sperm cells go through in connection with natural fertilization in the fallopian tubes. There are some studies that suggest that the method selects good sperm with less DNA damage. It may increase the chance of pregnancy and decrease the risk of miscarriage.

You can consider using this sperm purification if you have repeatedly had disappointing results from the treatment, for example low fertilization rate, poor embryo development, no pregnancies, or several pregnancy losses, and where a sperm factor may be suspected.

### **EmbryoGlue**

EmbryoGlue contains hyaluronan (also called hyaluronic acid), which is naturally present in many of the body's tissues. There are several studies that indicate an increased chance of pregnancy by adding hyaluronan to the culture medium in which the blastocyst is placed when it is transferred to the uterus. There may

be a slightly increased likelihood of twin pregnancy. If there have been several attempts without pregnancy, you can consider using EmbryoGlue.

### **Ca-ionophore (calcium ionophore)**

Ca-ionophore is an agent that activates many processes in the egg around fertilization. It can be added to the medium the eggs are in if there has been previous IVF/ICSI treatment(s) without fertilization or with very poor division of the eggs. Ca-ionophore can also be used if there are sperm cells with round heads ('globozoospermia'). There are several studies that suggest that in these cases Ca-ionophore can improve the fertilization rate and the subsequent division of the eggs in the laboratory.

### **Assisted hatching (AHA)**

The first cell divisions in an early embryo take place within the 'eggshell' (zona pellucida) that surrounds the egg. When the embryo has developed into a blastocyst, the surrounding shell must 'hatch'. There are theories that failure to hatch can prevent the blastocyst from penetrating through the shell when it needs to grow into the uterine lining. AHA is a weakening of the shell with a very precise laser beam that does not damage the cells of the blastocyst. It is still debated whether AHA increases the chance of pregnancy or not. AHA appears to increase the likelihood of twin pregnancy. AHA can be considered if the eggshell in the lab looks too thick when the embryologists look at it, or if many good quality blastocyst transfers have been done without pregnancy.

### **Endometrial priming (scratching)**

Priming of the endometrium is a superficial scraping or scratching of the endometrium, which is usually carried out in the cycle before the cycle in which the blastocyst is to be transferred. The procedure is carried out with a thin 'suction catheter' and takes a few seconds. There are theories that this superficial 'damage' to the endometrial lining can initiate repair processes that make the endometrium more receptive to an embryo in the following cycle and perhaps more cycles. Studies have not shown a positive effect of using priming for everyone in IVF/ICSI treatment. We believe that there may be a possibility for a beneficial effect of priming in situations where multiple transfers of high-quality blastocysts have been performed without pregnancy being achieved, because in this situation it is possible that the endometrial lining may be a limiting factor. There is short-term discomfort in connection with the priming.

### **Prednisone**

Prednisone is a corticosteroid that is produced naturally in the body. Prednisone has many effects, including a reduction in the activity of the immune system. You can consider using prednisone in cases where there have been repeated miscarriages or lack of pregnancy and where it is suspected that the body has a 'too active' immune system, for example if the woman has an 'autoimmune' disease, where the body's immune system attacks the body itself. In some cases, we also use prednisone in women with endometriosis based on a consideration that increased activity of the immune system around endometriosis cysts in the ovaries might negatively affect the nearby eggs. Prednisone in the low doses and for the few weeks of treatment does not appear to cause significant side effects in the woman or the foetus.

### **Clindamycin (Dalacin)**

In some cases, there may be an 'unfavourable' bacterial composition in the vagina or a chronic inflammatory condition in the uterine cavity (chronic endometritis). If there is an excess of 'bad' bacteria, it can probably make it more difficult to get pregnant and increase the risk of spontaneous miscarriage. It can be difficult to carry out good studies of the exact bacterial composition, because everyone has many different bacteria in that region. If you have undergone several treatments without pregnancy or have had several miscarriages, we may consider giving antibiotics for 5 days in the days leading up to blastocyst transfer.

### **Blastocyst transfer**

The blastocyst transfer is normally performed 5 days after the oocyte pick-up. If a blastocyst has not developed before day 6 we will freeze the blastocysts and do transfer in a subsequent 'freeze' cycle. This is because the endometrium becomes less receptive if six days has passed since the oocyte retrieval. In some situations, transfer of an embryo may be done on day three after the pick-up.

On the day of blastocyst transfer, the lab will call you in the morning to tell you about the quality of the blastocyst that will be transferred.



The transfer is usually simple and painless and only takes a few minutes. You will see the blastocyst on a monitor before the transfer. A gynaecological examination is performed, and a very thin catheter (tube) is introduced through the cervical canal into the endometrial cavity where the blastocyst is transferred in a small drop of fluid. We may also do an ultrasound through the abdominal wall during the transfer.

It is common to transfer one blastocyst. In rare situations two may be transferred, but this will increase the risk of a twin pregnancy. Twin pregnancies are associated with a higher risk of premature birth and other complications than singleton pregnancies.

There are no special precautions after the transfer, but we recommend that you avoid hard physical activity including high intensity exercise for some days.

You should not swim or take a bathtub bath the first week after the transfer.

In general, you can lead a normal life. Things are largely up to nature now. You may also lead a normal sex-life after the blastocyst transfer.

### **Filled urinary bladder for the transfer**

It may facilitate the transfer if your bladder is somewhat full. You should just have a mild sensation of a filled bladder. It need not be very full. There are two reasons why it may be advantage that the bladder is filled. The full bladder straightens the

#### ***Urine in the urinary bladder at transfer***

On the blastocyst transfer day, please come with a slightly filled urinary bladder. This may make it easier for us to do transfer.

uterus, which makes easier to pass through the cervical canal and into the endometrial cavity with the very soft catheter. The other reason is that the bladder is located in front of the uterus. Urine in the bladder provides a good ultrasonic window to look through into the uterus when we scan during transfer.

### ***Hormone treatment after the blastocyst transfer***

In order to stimulate the endometrium and thereby increase the chance that the embryos will implant you must be treated with the natural hormones progesterone (vaginal pessaries) and estradiol (tablets) for the next 14 days until the pregnancy test.

Both these hormones are normally produced by the corpus luteum in the ovary after ovulation. But in IVF treatment the hormone production from the ovaries is reduced due to down regulation, hormone stimulation and oocyte pick-up. Therefore, the pregnancy chance is improved by taking progesterone and estradiol. Progesterone is given as vaginal pessaries (usually Cyclogest®) three times daily with approximately 8-hour intervals. Estradiol is given as tablets three times daily.

The treatment continues until the pregnancy test. Some women may have to continue taking progesterone and estradiol also after the pregnancy test. We will inform you if this applies to you.

### ***Pregnancy test***

Approximately 15 days after the oocyte pick-up a blood test for pregnancy hormone (hCG) is performed. The blood test can be taken in the clinic in the morning, and you will then have the result later the same day. The blood test must be performed even if you have begun bleeding (menstruation). It is best if you do not bleed but the pregnancy test may be positive even if you have had some bleeding. It may also be negative even though you have not had any bleeding at all.

## Positive pregnancy test

If the pregnancy test is positive, we will make an appointment for an ultrasound scan three weeks later corresponding to a pregnancy length of 7-8 weeks and about five weeks after the blastocyst transfer.

The chance of a positive pregnancy test is approximately 40% for women under 40 years of age and around 25% for women above 40 years. See more results below. The younger the woman is the higher the pregnancy chance because the egg quality starts to decline already at age 25. The chance of life birth is severely reduced in women above 43 years of age.



Sometimes the level of pregnancy hormone is lower than expected. If this is the case, a repeat blood test should be taken a few days later to find out if the concentration of pregnancy hormone (hCG) increases as it should. If the rise is too slow it may indicate that the pregnancy is not developing normally and could end up as a miscarriage. It may also raise the suspicion of an ectopic pregnancy.

## Negative pregnancy test

We have sometimes been asked the question: 'What went wrong since I did not become pregnant'.

It is understandable to seek an explanation. However, only rarely is it possible to pinpoint one specific reason. Several factors have to work together optimally for a pregnancy to occur. Often, small details determine whether a treatment cycle is successful or not.

If the pregnancy test is negative, we will analyse all elements of the treatment to determine if any adjustments should be made in a future treatment cycle.

After a negative result, it is often possible to start a new hormone stimulated cycle immediately after, when the menstrual bleeding starts. Sometimes the ovaries may not be ready to start a new stimulation so soon, and we will then recommend a pause cycle. We can decide this when we see you for a 'start-up' scan..

## Pregnant by in vitro fertilisation

### Pregnancy check-ups

All women who have become pregnant in our clinic are offered an ultrasound scan in the 7<sup>th</sup> or 8<sup>th</sup> week of pregnancy, which is approximately 3 weeks after the positive pregnancy test. You may also have an additional scan a few weeks later.

The scan will show if the pregnancy is developing normally, the number of fetuses, whether the heart is beating and whether the size of the fetus is as expected for the gestational age.

The gestational age and the due date are calculated from the day of the oocyte pick-up. The 'first day of the last menstrual period (LMP)' is 14 days before the day of the oocyte pick-up. The 'due date' is 280 days after the LMP. You should contact your doctor (GP) after the first pregnancy scan in our clinic. Your GP will do check-ups during the pregnancy and assist you with selecting the hospital where you will give birth.

If necessary, we can do additional ultrasound scans within the first 12 weeks of your pregnancy.

A 'nuchal translucency' scan and a blood test is now offered to all pregnant women in Denmark. The scan and a blood test will give a good estimate of the risk of a chromosomal abnormality in the foetus (see below).

### Multiple pregnancy

In in vitro fertilisation treatment, it is the golden standard to transfer one blastocyst per treatment cycle. In rare cases it may be considered to transfer two. However, transfer of two blastocysts increases the possibility of a twin pregnancy. Multiple gestations are associated with an increased risk, in particular miscarriage and preterm delivery.

These risks are even more pronounced in triplet pregnancies. Therefore, we never transfer more than two blastocysts.

## Cancellation of a treatment cycle

### Cancellation before oocyte pick-up

Approximately 5% of treatment cycles are cancelled before the oocyte pick-up.

The most common cause is insufficient response to the hormone treatment, meaning that the ovaries do not respond by producing enough mature follicles. If this should happen, an increase in the hormone dose in a future cycle will often result in more follicles.

In 'older' women, the expected number of follicles is generally low. Therefore, a low number of follicles may not lead to cancellation of the cycle.

### **Cancellation around the oocyte pick-up**

Very rarely the follicles have ovulated before the oocyte pick-up even though we try to avoid this by careful timing and use of ovulation-preventing medicine. If all follicles have ovulated, we cannot do oocyte pick-up and the cycle must be cancelled.

Very rarely all follicles are 'empty' so that we cannot obtain eggs from them. During the oocyte pick-up, we will do everything that is possible to obtain the eggs including repeated flushing of the follicles if the eggs are not easily retrieved.

### **Cancellation after the oocyte pick-up**

Approximately 10% of cycles are cancelled after the oocyte pick-up. One reason may be fertilisation failure caused by poor sperm quality or poor egg quality. If we suspect that the sperm quality is too poor to fertilise the eggs, we will suggest fertilisation by ICSI. Another reason for cancellation may be that the embryos develop poorly and do not develop into a blastocyst that is suitable for transfer.

Please also read the paragraph about blastocyst culture for more information about possible cancellation of transfer when blastocyst culture is planned.

If a cycle is cancelled, we will discuss with you the possible reasons for the poor result and relevant treatment changes that may improve the outcome of a future treatment.

### **Other reasons for cycle cancellation**

Fever and illness during treatment could be a reason to consider cycle cancellation. Fever above 38.5°C may adversely influence the follicle development. The pregnancy chance will also be reduced by fever after the blastocyst transfer.

Fever may harm the sperm production in the man. If the man has had fever within a month or so before the oocyte pick-up it may be worth checking the sperm quality. If the man has had fever the sperm quality may be reduced for 2-3 months after the fever episode.

### **Dilated fallopian tubes**

If during hormone stimulation the fallopian tubes are seen dilated on ultrasound, we will discuss with you whether the cycle should be cancelled. Dilated 'hydrosalpinges' are only seen when the fallopian tubes are blocked at their distal ('ovarian') end. The reason that we suggest cycle cancellation in this situation is that dilated fluid filled fallopian tubes reduce the chance of pregnancy by IVF by approximately half. Fortunately, the chance may be improved by removing the dilated fallopian tubes by a usually simple, laparoscopic operation.

If it is known before treatment that one or both fallopian tubes are dilated (for example visualised by contrast ultrasound (HSU)) we recommend removal of the affected tub(es) before IVF treatment.

## **The chance of becoming pregnant by in vitro fertilisation**

In order for IVF treatment to result in a pregnancy all steps in the treatment must be successful. It is never possible to predict if the treatment will be successful in a particular woman and cycle. Our statistics are based on average probabilities from our own clinic and on data from the international scientific literature. National Danish results may be found on The Danish Fertility Society's website [www.fertilitetsselskab.dk](http://www.fertilitetsselskab.dk).

Since the start of our clinic in 1993, we have performed more than 15.000 IVF/ICSI cycles and several thousand treatments with cryo-preserved blastocysts and embryos.

The highest success rates are obtained when the woman is young (less than 38-40 years). When there is a good quality blastocyst for transfer the pregnancy chance is optimal. In this situation, the chance of a positive pregnancy test is around 50% per transfer. After subtracting the miscarriages (approximately 20% of the pregnancies) the chance for giving birth to one child is around 30-35%. After three successfully completed treatment cycles on average 70-75% of the women will have given birth. The pregnancy chance declines gradually as the woman's age increases regardless of the cause of infertility. Therefore, the pregnancy chance is higher the younger the woman is. In women above 40 years the average chance for pregnancy/birth is approximately half of the figures mentioned above.

## Detailed results for Trianglen

Day 5 transfers IVF and ICSI in 2022	<35 years	35-<38 years	38-<40 years	40-<43 years	43-45 ye- ars
Embryo transfers on IVF/ICSI day 5	152	98	82	123	48
Positive pregnancy test per embryo transfer	93	52	35	53	9
<b>Positive pregnancy test per embryo transfer (%)</b>	<b>61,2%</b>	<b>53,1%</b>	<b>42,7%</b>	<b>43,1%</b>	<b>18,8%</b>
Ongoing clinical pregnancy in week 8	69	35	17	25	0
<b>Ongoing clinical pregnancy in week 8 (%)</b>	<b>45,4%</b>	<b>35,7%</b>	<b>20,7%</b>	<b>20,3%</b>	<b>0%</b>
Multiple pregnancy	3	1	0	1	0
<b>Multiple pregnancy (%)</b>	<b>2%</b>	<b>1%</b>	<b>0%</b>	<b>0,8%</b>	<b>0%</b>

Day 3 transfers IVF and ICSI in 2022	<35 years	35-<38 years	38-<40 years	40-<43 years	43-45 ye- ars
Embryo transfers on IVF/ICSI day 5	27	23	14	55	28
Positive pregnancy test per embryo transfer	6	8	3	12	2
<b>Positive pregnancy test per embryo transfer (%)</b>	<b>22,2%</b>	<b>34,8%</b>	<b>21,4%</b>	<b>21,8%</b>	<b>7,1%</b>
Ongoing clinical pregnancy in week 8	2	5	2	6	1
<b>Ongoing clinical pregnancy in week 8 (%)</b>	<b>7,4%</b>	<b>21,7%</b>	<b>14,3%</b>	<b>10,9%</b>	<b>3,6%</b>
Multiple pregnancy	0	0	0	0	0
<b>Multiple pregnancy (%)</b>	<b>0%</b>	<b>0%</b>	<b>0%</b>	<b>0%</b>	<b>0%</b>

Embryo transfers in freezing cycles with own eggs in 2022	<35 years	35-<38 years	38-<40 years	40-<43 years	43-45 years
Embryo transfers in freezing cycles	269	142	87	122	58
Positive pregnancy test per embryo transfer	151	72	44	54	21
<b>Positive pregnancy test per embryo transfer (%)</b>	<b>56,1%</b>	<b>50,7%</b>	<b>50,6%</b>	<b>44,3%</b>	<b>36,2%</b>
Ongoing clinical pregnancy in week 8	113	45	25	31	6
<b>Ongoing clinical pregnancy in week 8 (%)</b>	<b>42%</b>	<b>31,7%</b>	<b>28,7%</b>	<b>25,4%</b>	<b>10,3%</b>
Multiple pregnancy	2	1	1	0	0
<b>Multiple pregnancy (%)</b>	<b>0,7%</b>	<b>0,7%</b>	<b>1,1%</b>	<b>0%</b>	<b>0%</b>

## Complications and risks associated with the treatment

It may be stressful to undergo fertility treatment not least mentally because the hope for success is very pronounced. The possible physical side effects are described below. There is no indication that there should be any long-term side effects of the treatment.

### *Undesirable effects of the hormone treatment*

#### Hormone side effects

Some women will experience side effects, but most women will only have very mild symptoms.

During down-regulation, you may experience headache, hot flushes and mood disturbances because of the reduced production of estrogen. These side effects will disappear once the hormone stimulation is started.

Stimulation of follicle growth is done with the pituitary hormones (FSH or hMG), which are natural hormones. In preparation for oocyte pick-up we aim for a follicle number of 8-14.

Some women will feel discomfort or tension in the lower abdomen because of the high number of growing follicles. In rare cases many more follicles than intended will grow. In this situation, there is a risk of developing ovarian HyperStimulation Syndrome (OHSS). See more information below.

### **Ovarian hyperstimulation syndrome (OHSS)**

If too many follicles are growing a condition known as the ovarian hyperstimulation syndrome may occur after the hCG injection for final oocyte maturation is given. In OHSS, the ovaries are markedly enlarged. Because fluid may also accumulate in the abdominal cavity, the abdomen may become distended.

Signs of OHSS may occur in the days after the final oocyte maturation injection (hCG) is given (early onset OHSS). Symptoms may also arise approximately one week after the transfer (late onset OHSS). The late OHSS will almost only occur if you are pregnant. This reason is that the early pregnancy produces hCG which is the hormone that together with many follicles may cause OHSS.

OHSS may be mild, moderate, or severe. The mild to moderate OHSS does not require hospitalisation and will often improve if the woman drinks a lot of fluid after the oocyte pick-up. The severe form of OHSS requires hospitalisation. Often it is of short duration, but it is a potentially serious condition. Symptoms include a very distended abdomen, trouble breathing, reduced urine production and circulatory problems.

Less than 1% of our patients will need hospitalisation because of OHSS. If hospitalised most women will be discharged within a few days, but unfortunately, we have seen very few (<1%) patients with severe hyperstimulation who will need prolonged hospitalisation.

If you think that you may be hyperstimulated you should always contact us.

We always try to avoid hyperstimulation by adjusting the dose of stimulation hormone to fit the individual woman. We intend to stimulate so that a suitable number of follicles will grow, but in some women, it is not so easy to achieve. Hyperstimulation is always temporary and does not cause long-term effects.

If hyperstimulation is imminent we may recommend freezing the embryos as blastocysts and not do transfer in the fresh cycle. Transfer can then be done in a later cycle.

### **Allergic reactions**

Allergic reactions may occur during the hormone treatment.

Most often it will be mild reactions like erythema or itching around the site of injection. It will often solve the problem if you switch to another of medicine.

Very rarely, there could be severe allergic reactions with rash, trouble breathing or fever. If you experience such serious reactions, you must *not* take more of the medicine. You should contact us or another doctor immediately.

### **Does hormone treatment increase the risk of getting ovarian cancer?**

Several studies from Denmark, Sweden and other countries have demonstrated hormone treatment used for IVF does not appear to increase the risk of getting ovarian cancer or endometrial cancer.

### ***Complications associated with oocyte pick-up***

The oocytes are aspirated through a needle that is inserted into the follicles in the ovaries through the vaginal wall. Therefore, there may be slight bleeding from the vagina after the oocyte pick-up. Very rarely (<1%) does the bleeding require further treatment. The bleeding may be stopped by placing a suture or two at the origin of the bleeding. The suture will disappear by itself. Bleeding after the oocyte pick-up does not alter the chance of becoming pregnant. After the oocyte pick-up, you may have some discomfort in the lower abdomen. If you experience pain after the oocyte pick-up, you may use pain relieving medicine such as Panodil® (paracetamol).

Infection after oocyte pick-up is very uncommon (<½%) and should be treated with antibiotics. At the oocyte pick-up women with an increased risk of infection (e.g. endometriosis or previous infection) will receive a prophylactic injection of an antibiotic to minimise the risk.

## **Pregnancy complications**

### **Miscarriage**

After a positive pregnancy test, the risk of a miscarriage is approximately 20% when the woman is younger than 40 years. If she is older than 40 years, the risk is higher.

### **Ectopic pregnancy**

Implantation outside of the endometrial cavity ('ectopic pregnancy') occurs in about 1-3% of IVF/ICSI pregnancies.

At the transfer the blastocyst is placed centrally in the endometrial cavity. However, for unknown reasons the blastocyst may occasionally migrate out into the fallopian tube and implant there.

Signs of an ectopic pregnancy include pain and bleeding early in the pregnancy. Another sign may be that the pregnancy hormone (hCG) starts at a too low level and that the concentration increases at a slower than normal rate.

If there is suspicion that you may have an ectopic pregnancy, we will take repeated blood tests for hCG to follow the development. If the hCG level does not increase the way it should or if you develop symptoms indicating an ectopic pregnancy (pain or vaginal bleeding) we will refer you to a hospital for further treatment. The treatment may be with medicine or an operation (most often a laparoscopy).

If we suspect that you may have an ectopic pregnancy, we will inform you that you should go to a hospital immediately if you experience abdominal pain or if you do not feel well. If you should experience abdominal pain and you do not feel well, you must seek immediate medical assistance. The symptoms may be caused by bleeding from the ectopic pregnancy into the abdominal cavity and may be fatal if not treated immediately.

## **Children born after in vitro fertilisation**

Several large studies have shown that the risk of miscarriage and malformations after ICSI and IVF treatment is slightly increased. This does not appear to be because IVF/ICSI treatment as such increases the risk. But the infertile couples who are in need for IVF/ICSI treatment already have a slightly increased risk of pregnancy complications and malformations.

There is no special indication for CVS (chorion villus sample) or amniocentesis because the pregnancy is achieved by IVF or ICSI.

All pregnant women in Denmark are offered a nuchal translucency scan in week 11-14 and a blood test (double test) in week 9-12 of the pregnancy. Based on the woman's age and the results of the tests the risk of a chromosomal abnormality in the fetus can be evaluated.

## **Treatment in a new cycle**

If you did not become pregnant in a completed in vitro fertilisation cycle, it is often reasonable to do another treatment cycle.

If there are cryo-preserved blastocysts these will normally be used first. It is often possible to initiate a cryo cycle immediately after a 'fresh' cycle where you did not become pregnant.

If there are no frozen blastocysts the next treatment will be a 'fresh' treatment with hormone stimulation, oocyte pick-up et cetera. Together we will decide if the treatment should be like the previous treatment or if something should be changed. If you wish to start a new 'fresh' treatment in the cycle immediately after the completed treatment, we will by ultrasound on cycle day 2-3 determine if the body is ready or needs a pause cycle in between the stimulations.

## **'Life style' and other factors**

### **Folic acid**

It is recommended that all women take folic acid daily when they try to become pregnant and during the first 12 weeks of pregnancy. Folic acid reduces the risk of foetal malformations in the central nervous system.

In Denmark the health authorities recommend a daily dose of 400 micrograms folic acid.

If you have previously had a child (or a miscarriage) with malformations in the central nervous system (neural tube defects), it is recommended that you take 5 mg folic acid daily. This also applies if you use medicine against epilepsy.

## Physical exercise

Physical exercise is good – in moderation. Very hard physical exercise or training may reduce the chance of becoming pregnant. Most likely, high heart rate for extended periods reduces fertility. We recommend that exercise is kept at moderate intensity. This means that you should not go beyond 2/3 of your capacity equal to a level where you can easily keep up a conversation during exercise.

## German measles (rubella)

It is recommended that the woman has a blood test to determine if she has antibodies against German measles. If she is not immune, she should be vaccinated because it may cause serious foetal malformations if she is infected with German measles during pregnancy.

## Medicine

If you take medicine, you should consider whether the medicine may affect your chance of becoming pregnant or if it could harm the foetus/baby when you are pregnant. You may discuss this subject with your doctor. It may be possible to switch to another medicine, which will not affect your fertility or the foetus. *We recommend* that you do not take medicine that is not strictly necessary for you and that you do not use herbal medicinal products, since too little is known about their possible effects on your fertility.

## Pain-relieving medicine

We recommend that you do not use pain-relievers of the 'NSAID' type (e.g. Brufen®, Iprel®, Diclon®) during fertility treatment. You may use paracetamol (e.g. Panodil®) if necessary.

## Tobacco

Smoking reduces the fertility in women and the sperm quality in men. Therefore, it is advisable for both the woman and the man not to smoke at all. *We recommend* – no smoking at all.

## Alcohol

The woman should consume as little alcohol as possible, when she tries to become pregnant. It is likely that even a small alcohol intake (1-5 units per week) may reduce fertility. When a woman is pregnant, she is advised not to drink alcohol at all. Alcohol seems to affect the man's fertility to a lesser degree. A daily consumption of up to 3 units does not seem to affect the sperm quality. A higher intake of alcohol may reduce the sperm quality. *We recommend* that the woman does not drink alcohol at all or keeps the alcohol consumption at a minimum.

## Coffee/caffeine

Coffee, tea and cola contain caffeine. There is no indication that a moderate consumption of caffeine-containing beverages affects fertility. It is possible that a large consumption (more than 3-5 cups/glasses per day), may reduce the chance of becoming pregnant.

## Body weight

Both a too low and a too high body weight will reduce the chance of becoming pregnant. Overweight also increases the risk of complications during pregnancy and delivery. Normal body weight and too low or too high weight may be determined by the so-called 'Body Mass Index' (BMI) which is calculated as follows:

$$\text{BMI} = \frac{\text{Weight}}{\text{Height}^2} \quad \text{the weight is in kilos and the height in metres.}$$

BMI between 20 and 25 is optimal. Your fertility may be reduced if your BMI is below 19 or above 29. *We recommend* that the BMI should be between 19-29.

## Environmental factors

Most kinds of work will not affect the fertility. If you work with chemical substances such as organic solvents or pesticides or if you are exposed to radiation, your fertility may be affected. You may discuss this with your workplace or with your doctor.

## Sex

Sex does not seem to influence the chance of becoming pregnant by IVF/ICSI.

## Absence from work

You should expect not to go to work on the day of the oocyte pick-up and probably not the following day either.

On the day of the blastocyst transfer, it may be advisable to rest at home after the transfer. In the following days you may do normal daily activities and 'office type' work. You should refrain from hard physical exercise of any kind until the pregnancy test has been taken.

### **§ 56 agreement (for women with Danish social security)**

If your amount of sick leave is increased because of a long-lasting or chronic illness, you arrange with your employer and the county that will reduce your employer's expenses during your sick leave. Your condition should result in at least 10 days of absence from work per year. You can find additional information at [www.sundhed.dk](http://www.sundhed.dk).

### **Informing family and friends**

Studies have shown that it may be easier for couples to cope with the stresses of treatment if they tell their close ones about what they are going through. There may be individual variation on this matter, but it appears to be a good idea to tell family and close friends about the treatment.

## **Cryopreservation of blastocysts and transfer of thawed blastocysts**

If the treatment results in more high-quality blastocysts than the one transferred, 'surplus' blastocysts can be cryopreserved and stored in liquid nitrogen at -196°C. The blastocysts can later be thawed and transferred usually without the need for any hormone stimulation.

We culture embryos to the blastocyst stage before cryopreserving them.

We only freeze blastocysts of very good quality. When we later thaw a frozen blastocyst for transfer around 95-98% of the cryopreserved blastocysts will survive and be suitable for transfer.

The current legislation in Denmark states that blastocysts may be stored until the woman turns 46 years of age. They must be discarded if the couple breaks up or if one of the partners should die. However, the couple may agree in writing that the embryos can be transferred to the woman even if the man should pass away.

If the embryos are the result of treatment of a couple the following applies:

- Both partners must accept in writing that the embryos are cryo-preserved and stored.
- The embryos can only be thawed and transferred if both partners give written consent before each 'cryo-cycle'

### **Thawing and transfer of cryo-preserved blastocysts**

In women with a regular menstrual cycle shorter than approximately 35 days, the thawed blastocyst will be transferred in your own natural cycle.

If your cycle is long (longer than approximately 35 days) we will prepare the endometrium to receive the embryos by having you take estradiol tablets or patches. This is called a 'substituted' cryo-cycle.

### **Transferring a thawed blastocyst in your natural cycle**

Transfer of thawed blastocyst is most often done without any hormone treatment. Sometimes we will recommend stimulating the follicle growth with a mild hormone stimulation. You should call us when your menstrual bleeding starts and make an appointment for an ultrasound scan on cycle day 10-12. The scan will evaluate the size of the growing follicle and the thickness of the endometrial lining. When the follicle reaches a diameter of 17-20 mm you should take an injection of Ovitrelle® to induce ovulation. Six days later, we thaw a frozen blastocyst and transfer it to the uterus on the same day.

On the day when we thaw the blastocyst, you should call the laboratory. The lab will inform you about the quality of the thawed blastocyst.

The transfer takes place on the day of thawing for cryopreserved blastocysts. The transfer procedure is the same as for 'fresh' blastocysts.

On the day of the transfer, you shall take a small dose of Ovitrelle® (10 'clicks') and also start taking vaginal progesterone (Cyclogest® or Lutinus®) three times daily.

The injection of Ovitrelle® will make the ovary produce more progesterone, which in turn will stimulate the endometrium.



### **Transfer of a thawed blastocyst in an estradiol-'substituted' cycle**

On day 2-3 of your menstrual bleeding, you start taking estradiol tablets.

After 10-12 days, we will perform an ultrasound scan. When the endometrium has reached an appropriate thickness (preferably over 7 mm) you start taking progesterone (Cyclogest® or Crinone®) vaginal pessaries or gel in addition to the estradiol.

Six days later, we thaw a frozen blastocyst and transfer it to the womb on the same day. You must continue taking estradiol tablets and progesterone vaginal pessaries until the day of the pregnancy test. *If your pregnancy test is positive, you must continue the treatment with estradiol and progesterone until you are approximately 10 weeks pregnant.*

The chance of becoming pregnant after transfer of thawed blastocyst is approximately 50%.

### **Referral for treatment in a public fertility clinic**

It is possible to be referred to fertility treatment in the fertility clinics in the public hospitals.

In general, you must meet the conditions below to be referred to a public fertility clinic. We are happy to assist you with the referral.

- There must be reason for fertility treatment.
- You must not already have a child (for couples: a common child).
- The woman must not have turned 40 at the time of referral.

### **Medicine used for in vitro fertilisation treatment**

At Trianglen Fertility Clinic we have made an agreement with Holte Apotek (Pharmacy) which means that we have a stock of medicine in the clinic. You may buy medicine from this stock so that you do not have to pick up the medicine at a pharmacy. When we provide medicine from Holte Apotek, the pharmacy will send an invoice directly to you. We mention this service here to avoid misunderstandings.

### **Medicine for down-regulation (GnRH agonists)**

#### **Synarela®, Zoladex®, Gonapeptyl®, Decapeptyl®**

These medicines are so-called GnRH agonists. They influence the secretion of the hormones FSH and LH from the pituitary gland. FSH and LH regulate the maturation of follicles and eggs in the ovaries. These medicines temporarily block the secretion of FSH and LH. In this way, it is possible to control the maturation of oocytes in the ovaries. The GnRH agonists block the ovulation signal (LH) that would otherwise be released from the pituitary gland when the ovaries contain mature oocytes. In this way it is prevented that ovulation occurs before the scheduled oocyte pick-up.

GnRH agonists (for example Gonapeptyl®) may also under certain conditions be used to trigger ovulation. It may be done in women who are not down-regulated. It will not work in the 'long down-regulation' protocol.

Synarela® is a nasal spray that must be taken several times every day.

Gonapeptyl® is taken as one daily injection.

Zoladex and Decapeptyl are depot preparations that only need to be taken once per cycle.

Side effects: Headache, hot flushes, and mood changes.

### **GnRH Antagonists**

#### **Fyremadel®, Ganirelix®, Orgalutran®, Cetrotide®**

GnRH antagonists prevent the pituitary gland from secreting LH, which is the normal ovulation-inducing signal. It is used to avoid ovulation before the oocyte pick-up. We recommend that you take this injection in the morning.

Side effects: Itching and redness at the injection site.

### **Medicine for stimulation of the ovaries**

#### **Gonal-f®, Bemfola®, Puregon®**

Contain FSH which stimulates the ovaries to produce follicles containing eggs. This is the natural follicle-stimulating hormone.

With the doses used for stimulation for IVF/ICSI, the ovaries will produce more than the one egg that is matured in a normal cycle. These hormones are taken as one daily injection.

Side effects: Local irritation at the site of injection. Tenderness in the lower abdomen. May cause ovarian hyperstimulation.

### **Menopur®, Pergoveris®**

Contain FSH and LH. FSH is the most important hormone stimulating the ovaries to produce eggs. It is the natural follicle stimulating hormone. LH is necessary in small amounts to assure an optimal follicle development. Normally there is enough LH present in the body, so it is much debated whether it is necessary to add the LH component for ovarian stimulation.

With the doses used for stimulation for IVF/ICSI, the ovaries will produce more than the one egg that is matured in a normal cycle. These hormones are taken as one daily injection.

Side effects: Local irritation at the site of injection. Tenderness in the lower abdomen. May cause ovarian hyperstimulation.

### **Elonva®**

Contains a long-acting FSH hormone that stimulates the ovaries to produce follicles containing eggs. It works in the same way as normal follicle stimulating hormone, but the stimulating effect lasts for several days after one injection.

With the doses used for stimulation for IVF/ICSI, the ovaries will produce more than one egg. Elonva® is mostly used for stimulation in the 'short antagonist' protocol (scheme 4) where it is given as a single injection on cycle day 2-3.

Side effects: Local irritation at the site of injection. Tenderness in the lower abdomen. May cause ovarian hyperstimulation.

### **Clomid®**

The active ingredient in Clomid® is clomiphene, which indirectly stimulates the ovaries and thus makes more than one follicle grow. Usually, Clomid® will result in growth of less than 5 follicles. We may use it if traditional stimulation with FSH/LH medicines has not worked well. Clomid® is taken in the form of tablets.

Side effects: Hot flushes, nausea, blurred vision and headache. However, most women taking Clomid® will not experience side effects.

## ***Medicine for induction of final oocyte maturation***

### **Ovitrelle®**

These medicines contain hCG and induce final oocyte maturation and initiate the ovulation process. The ovulation will occur approximately 40 hours after the hCG injection. The oocyte pick-up is performed 35-36 hours after the injection. At this time, the oocytes are mature, but ovulation has not yet taken place. These medicines are taken as a single injection at a time that is carefully scheduled based on the planned time of the oocyte pick-up.

Side effects: None – except that it may together with stimulation hormones result in ovarian hyperstimulation if (too) many follicles have developed.

### **Gonapeptyl® and Suprefact® (GnRH agonists)**

An alternative to hCG to induce final oocyte maturation is to give a single dose of Gonapeptyl®, Suprefact® or another GnRH agonist. This 'agonist triggering' may be employed if down-regulation has not been given and therefore it cannot be used in scheme 3.

## ***Estradiol and progesterone***

### **Estradiol, Progynon®, estradiol-patches**

Estradiol and Progynon® contain the female sex hormone estradiol. This hormone makes the endometrial lining grow so it reaches a thickness that makes it ready to receive a blastocyst. Estradiol is a hormone normally produced in the ovaries.

In connection with in vitro fertilisation, estradiol is used to strengthen the endometrium after the oocyte pick-up. For treatment with thawed cryo-preserved blastocysts in women with a long menstrual cycle and for women receiving donated eggs estradiol is used to stimulate the endometrium to increase in thickness.

Estradiol can be taken as tablets several times daily or as transdermal patches.

### **Lutinus®, Crinone®, Cyclogest® (progesterone)**

Progesterone is a natural hormone that makes the endometrial lining ready to receive a blastocyst after the endometrium has been stimulated with estradiol. Progesterone is taken as vaginal pessaries (Lutinus®, Cyclogest®) or as vaginal cream (Crinone®). Progesterone strengthens the endometrium.

Possible side effects: Bloating, diarrhoea.

## ***Sedating and pain-relieving medicine***

### **Propofol®**

A sedative. Is given intravenously at the oocyte pick-up.  
Side effects: Tiredness, vertigo.

### **Rapifen®**

Strong pain-relieving medicine. Related to morphine. Is given intravenously at the oocyte pick-up.  
Side effects: Nausea, tiredness, vertigo.

### **Panodil® (paracetamol)**

Mild pain-relieving medicine. Taken as tablets.  
Side effects: None – when the daily dose does not exceed eight tablets (of 500 mg).

## ***Other types of medicine***

### **Prednisone**

Prednisone is a corticosteroid. It has several effects. One effect is to dampen immune responses to some extent.

We occasionally recommend prednisone in connection with IVF treatment. We may do it in women with repeated miscarriages or in women who have not become pregnant despite several treatments. There is no scientific proof for the effect of prednisone.

Side effects: With the low doses and the short duration, we use prednisone there are very few side effects.

### **Metformin**

Metformin is a type of medicine that is sometimes used for treating type-2 diabetes. It increases the insulin sensitivity of cells.

We sometimes suggest treatment with metformin in women with PCOS because such women may have a degree of 'insulin resistance'.

### **Antibiotic**

In women with an increased risk of infection at oocyte pickup (e.g. endometriosis or previous infection) a single dose of antibiotic is given at the pickup in order to minimise the risk of infection.

## ***Subsidies for medicine***

For patients with Danish social security coverage the medicine is subsidised. If you are a member of the health insurance 'Danmark' you may have some of the medicine expenses reimbursed from there.

The public subsidy means that within one 'subsidy-year' your own payment for medicine is limited to approximately DKK 4000,-.

You may find additional information on the website of The Danish Medicines Agency ([www.laegemiddelstyrelsen.dk](http://www.laegemiddelstyrelsen.dk))

## **Trianglen's employees**

Please go to our website to see all the people that make up Trianglen

## **Dictionary**

Blastocyst ..... An embryo with approximately 100 cells. Blastocysts consist of a fluid-filled centre surrounded by a wall of cells. A small group of cells on the inner side of the wall ('the inner cell mass') are those cells that will develop into the fetus. Embryos in the blastocyst stage hatch out of the surrounding 'eggshell' ('zona pellucida') and begin to implant in the endometrium.

Chromosome ..... A part of the cell's DNA. Contains a collection of genes.

Cleavage rate ..... The fraction of oocytes that develop into embryos.

Cumulus ..... The 'cloud' of supportive cells that surround the oocyte inside the follicle. The cumulus still surrounds the oocyte after the oocyte pick-up.

Embryo ..... A fertilised oocyte that has begun dividing.

Estradiol ..... Female sex hormone produced in the ovary. Stimulates growth of the endometrium.

ET ..... Embryo Transfer, transfer of a blastocyst to the endometrial cavity.

Fertilisation rate ..... The fraction of oocytes that become fertilised.

Fertility ..... The ability to become pregnant.

Follicle ..... A fluid-filled 'pocket' in the ovary that contains an oocyte.

Fragments.....	Small waste particles that may occur when the cells in an early embryo divide.
FSH.....	Follicle Stimulating Hormone. Stimulates the ovaries so they produce follicles/oocytes.
GnRH-agonist.....	Gonadotropin Releasing Hormone agonist or analogue. Hormones that prevent the pituitary gland from secreting FSH and LH. The key function is to prevent premature ovulation before the oocyte pick-up. Examples: Synarela®, Gonapeptyl®, Suprefact®, Suprecur®, Zoladex® and Decapeptyl®.
GnRH-antagonist....	Gonadotropin Releasing Hormone antagonist. Hormones that prevent the pituitary gland from secreting its LH ovulation induction signal. The key function is to prevent premature ovulation before the oocyte pick-up. Examples: Fyremadel®, Cetrotide®, Orgalutran®.
Granulosa cells .....	The cells that constitutes the wall of a follicle in the ovary.
hCG.....	human Chorion Gonadotropin. A pregnancy hormone. Is very similar to LH and may be used to induce final oocyte maturation.
ICSI .....	IntraCyttoplasmic Sperm Injection. Mikroinjection of a sperm cell into the oocyte.
Implantation rate .....	The proportion of transferred blastocysts that implant in the endometrium and produce a gestational sac.
Incubator .....	A 'box' where temperature, air composition and humidity can be kept constant and tightly controlled. It is used for culturing embryos in the laboratory.
IUI .....	IntraUterine Insemination, insemination in the womb.
IVF .....	In Vitro Fertilisation.
LH .....	Luteinising Hormone. Is important for follicle maturation and is the hormone that induces final oocyte maturation and ovulation.
Morula .....	An embryo with so many cells that it resembles a mulberry.
Nucleus .....	The central part of the cell that contains the cell's genetic information.
OHSS.....	Ovarian HyperStimulation Syndrome.
Oocyte.....	Egg-cell, approximately 0.12 mm in diameter.
Pregnancy rate .....	Proportion af pregnancies per oocyte pick-up or blastocyst transfer.
Progesterone .....	A hormone that is produced in the ovary after ovulation. Progesterone is important for preparing the endometrium to receive a blastocyst.
Pronuclei.....	Early nuclei. Nuclear material in an egg cell. After fertilisation 2 pronuclei can be seen, one from the egg and one from the sperm cell.
Scanning.....	Ultrasound scanning. In connection with fertility treatment, ultrasound scans are almost always performed transvaginally.
Spermatozoa .....	Sperm cell, approximately 5 µm in diameter.
TESA.....	Testiculær Sperm Aspiration. Aspiration of sperm cells directly from the testicles.
Zona pellucida .....	The 'shell' (zona pellucida) surrounding the oocyte. It is within the boundary of this shell that the first cell divisions take place. When the embryo reaches the blastocyst stage the cells in the blastocyst 'hatch' and break out of through the shell.

## Prices for treatment

### Overview

**Please note:** Because of 'money laundering' laws, we cannot receive cash payment of DKK 50.000 or more. Such amounts must be paid by card or bank transfer.

Price List 01.01.2024	IVF			ICSI		
	Single cycle any age	3-pack until 35 years	3-pack from 35 years	Single cycle any age	3-pack until 35 years	3-pack from 35 years
<b>Price (all prices in DKK)</b>	<b>27.900</b>	<b>52.000</b>	<b>61.000</b>	<b>31.400</b>	<b>60.600</b>	<b>70.950</b>
<b>Completed cycle</b> <i>The cycle is considered completed if oocyte retrieval has been done and one or more eggs have been retrieved.</i>	27.900	17.333	20.333	31.400	20.200	23.650
<b>Additional services (can be drawn from 3-cycle package)</b>						
Blastocyst freezing and storage up to 1 year.	6.300	6.300	6.300	6.300	6.300	6.300
Cryo cycle with blastocyst transfer.	9.000	9.000	9.000	9.000	9.000	9.000
ICSI (Intracytoplasmic Sperm Injection).		3.500	3.500	Incl.	Incl.	Incl.
Cycle cancelled before oocyte pickup or oocyte pickup without eggs (pickup counts as consultation).	<i>pr.cons.</i> 1.300	<i>pr.cons.</i> 1.300	<i>pr.cons.</i> 1.300	<i>pr.cons.</i> 1.300	<i>pr.cons.</i> 1.300	<i>pr.cons.</i> 1.300

### Notes and remarks

- 1) In the 3-cycle packages birth of a living child fulfils/ends the contract.
- 2) The cycle is considered completed if oocyte retrieval has been done and at least one egg has been obtained.
- 3) A freeze all cycles due to medical reasons is paid as a completed cycle.
  - The first subsequent cryo cycle is included if done within 6 months of freezing.
  - If more than one blastocyst is frozen, freezing of the surplus blastocysts must be paid
- 4) Freeze all due to patient wish is paid as a completed cycle. Freezing is included regardless of number.
  - Subsequent transfer of frozen blastocysts must be paid.
- 5) If the 3-cycle contract is suspended, payment is as specified under "Single" treatments.
  - Cannot be suspended during pregnancy.
- 6) Donor sperm (if used) must be paid separately (to the sperm bank).
- 7) Any additional services such as TESA, assisted hatching, priming etc. cannot be drawn from the 3-cycle package.
- 8) Medicine is not included in the prices in the price list
- 9) Services in the 3-cycle package must be used within two years. Any remaining amount will be lost hereafter.
- 10) If 'DuoStim' is performed, the 2nd DuoStim cycle costs 50% of the price for a full cycle.

Payment must be settled at the latest on the day of oocyte pick-up.

If payment is not done before the oocyte pick up a fee of DKK 1000 may be added.

### 'Flexible 3-treatment package'

We have what we think is a fair and flexible 3-treatment package. If you buy such a package you are entitled to three treatments in the package (or until you give birth to a live baby). However, during a treatment it may be relevant to perform more than the three standard IVF/ICSI treatments. For example, there may be cryopreserved blastocysts after a 'fresh' treatment. Often the next treatment will then be with transfer of a thawed blastocyst before you go through a new 'fresh' treatment, if still not pregnant. The payment for the use of thawed blastocysts may be deducted from the 'Flexible 3-treatment package'. We do not want you to have paid for a 3-treatment package and then charge you for a thawed blastocyst transfer while you still have money left on the 3-package.

A 'Flexible 3-package' is completed when the total amount on the 'card' is spent or when you have given birth.

If the 3-package is cancelled for other reasons our services will be charged according to the price list for single treatments.

#### Examples

##### Example 1

#### ICSI under 35 Price 60.600

Treatment	Comment	Spent	Left
1st treatment	First 'fresh' treatment. Three blastocysts cryopreserved. Pregnancy test positive.	20.200	40.400
Cryopreservation	Surplus blastocysts frozen.	6.300	34.100
Birth	Birth of live baby means that the card is completed.	The rest	0

##### Example 2

#### ICSI under 35 Price 60.600

Treatment	Comment	Spent	Left
1st treatment	First 'fresh' treatment. Two blastocysts cryopreserved. Unfortunately the pregnancy test is negative.	20.200	40.400
Cryopreservation	Two blastocystss frozen.	6.300	34.100
Cryo-cycle	All cryopreserved blastocysts are thawed. One is transferred. Unfortunately the pregnancy test is negative.	9.000	25.100
2nd treatment	Second 'fresh' treatment. No blastocysts for cryopreservation. Unfortunately the pregnancy test is negative.	20.200	4.900
3rd treatment	There is now 'only' 4.900 left on the card. We ask you to pay 15.300 to reach the amount of 20.200 that one cycle costs.	20.200	-15.300
Comment	<i>This means that not until now do we ask for payment for cryo-preservation and transfer of thawed blastocysts. You will not have to pay for the 'frozen' cycle unless the entire amount on the card is used.</i>		

### Price list for other services

Prices for other services can be found on the clinic's website.

## Opening hours, telephone hours and contact information

### Opening hours

The Clinic is open all days year-round, including weekends and holidays.  
On weekdays, the opening hours are from 8-16 (8 a.m. – 4 p.m.).  
Weekends and holidays we are open from 8-12 (a.m.).

In case of an emergency outside of our opening you should contact an emergency room or a doctor on call.

### Telephone numbers and telephone opening hours

Phone: +45 3940 7000

Please find our telephone opening hours on weekdays and on holydays and weekends on our website.

### Address

Our address is:  
Strandvejen 104A  
DK-2900 Hellerup  
Denmark.

### Mail-addresses

Due to security and because of the General Data Protection Regulation all email correspondence must be 'secure'. Please refer to 'Contact' information on our website [www.trianglen.com](http://www.trianglen.com).

### Mail-contact to the clinic for patients

Please only use *secure email*, see 'Contact' information on our website [www.trianglen.com](http://www.trianglen.com).

If you send an email to us about an ongoing treatment, please provide your *full* name and your *date of birth*.

There is more information on our website: [www.trianglen.com](http://www.trianglen.com) and [www.trianglen.dk](http://www.trianglen.dk)

### Bank

Nykredit Bank  
Reg. nr. :5490 Account no. 0007032755  
Swift Code: NYKBDKDK  
IBAN: DK1354900007032755

### Links

Trianglen Fertility Clinic ..... [www.trianglen.dk](http://www.trianglen.dk)  
Danish Fertility Society ..... [www.fertilitetsselskab.dk](http://www.fertilitetsselskab.dk)  
Danish Health and Medicine Authority ..... [www.sst.dk](http://www.sst.dk)  
Sundhed.dk..... [www.sundhed.dk](http://www.sundhed.dk)  
Medicin.dk..... [www.medicin.dk](http://www.medicin.dk) - detailed information about medicine

### Videos

Videos of procedures are posted on our website, e.g. ICSI, blastocyst culture and assisted hatching.

# Notes