



IVF – ICSI – TESA



Information

Table of Contents

Table of Contents	2
Collection and storage of information	4
About this information	4
General information about IVF and ICSI	4
Treatment in Trianglen Fertility Clinic	4
All types of treatment	4
Legal regulations	4
Before IVF is started	5
Exams and tests of the woman	5
Exams and tests of the man	5
The steps in IVF/ICSI treatment	5
Hormone treatment	5
Hormone treatment with 'long down-regulation' (scheme 3)	6
Down-regulation	6
Hormone stimulation	7
Hormone stimulation with 'short antagonist' protocol (scheme 4)	7
Hormone stimulation	7
Antagonist	8
Other types of hormone stimulation	8
Clomiphene citrate plus FSH/hMG (scheme 1)	8
Un-stimulated treatment (scheme 0)	8
Final oocyte maturation injection	8
Final oocyte maturation with Suprefact® (or another 'GnRH agonist')	8
Oocyte pick-up without pain	8
The sperm sample	9
TESA (TEsticular Sperm Aspiration)	9
TESA	10
Possible complications to TESA	10
Fertilisation of the oocytes and the first cell divisions	10
Fertilisation	10
Fertilisation with ICSI	10
When is ICSI recommended?	10
Fertilisation with '½ICSI'	11
Risks associated with ICSI?	11
Fertilisation with donor semen	12
Legal and other aspects of using donor sperm	12
Donor testing	12
Selecting a sperm donor for treatment	12
'Anonymous' sperm donor	12
'Extended profile' sperm donor	13
'Open' sperm donor	13
'Own' sperm donor	13
Ordering donor sperm	13
Culturing the embryos	14
Culture for 2-3 days	14
Blastocyst-culture	14
MIRI-incubators for embryo culture	15
Cell culture at 'low oxygen concentration'	15
Assisted hatching ('AHA')	15
Embryo transfer	15
Hormone treatment after the embryo transfer	16
Pregnancy test	16
Positive pregnancy test	16
Negative pregnancy test	16
Pregnant by in vitro fertilisation	17
Pregnancy check-ups	17
Multiple pregnancy	17
Cancellation of a treatment cycle	17
Cancellation before oocyte pick-up	17
Cancellation around the oocyte pick-up	17
Cancellation after the oocyte pick-up	17

Other reasons for cycle cancellation	18
Dilated fallopian tubes	18
Acupuncture in connection with in vitro fertilisation	18
The chance of becoming pregnant by in vitro fertilisation	18
Detailed results for Trianglen	19
Complications and risks associated with the treatment.....	20
Undesirable effects of the hormone treatment.....	20
Hormone side effects	20
Ovarian hyperstimulation syndrome (OHSS).....	20
Allergic reactions	20
Does hormone treatment increase the risk of getting ovarian cancer?.....	20
Complications associated with oocyte pick-up	21
Pregnancy complications	21
Miscarriage	21
Ectopic pregnancy	21
Children born after in vitro fertilisation	21
Treatment in a new cycle.....	21
'Life style' and other factors	22
Folic acid	22
German measles (rubella).....	22
Medicine	22
Pain-relieving medicine	22
Tobacco.....	22
Alcohol.....	22
Coffee/caffeine	22
Physical exercise.....	22
Body weight.....	22
Environmental factors.....	23
Sex	23
Absence from work.....	23
§ 56 agreement (for women with Danish social security).....	23
Informing family and friends	23
Cryopreservation of embryos and transfer of thawed embryos	23
Thawing and transfer of cryo-preserved embryos	23
Transferring thawed embryos in your natural cycle	23
Transfer of thawed embryos in an estradiol-'stimulated' cycle	24
Treatment in public fertility clinics.....	24
Medicine used for in vitro fertilisation treatment.....	24
Medicine for down-regulation (GnRH agonists).....	24
GnRH Antagonists	25
Medicine for stimulation of the ovaries.....	25
Medicine for induction of final oocyte maturation.....	25
Estradiol and progesterone.....	26
Sedating and pain-relieving medicine	26
Other types of medicine	26
Subsidies for medicine.....	26
Trianglen's employees.....	26
Dictionary.....	27
Prices for treatment	28
Overview	28
'Flexible 3-treatment package'	28
Price list for other services.....	30
Opening hours, telephone hours and contact information.....	31
Mail-contact to the clinic for patients	31
Links.....	31
Videos.....	31
Notes.....	32

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 3 or more days the best embryo or embryos are transferred to the uterus so they can attach to the endometrial lining and continue their 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 embryos and oocytes

Cryo-preserved embryos may be stored until the woman turns 46 years. Cryopreserved oocytes (eggs) may be stored for up to five years.

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 in order 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.

Exams 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) in order 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.

Exams 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 in order 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
- Embryo 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.

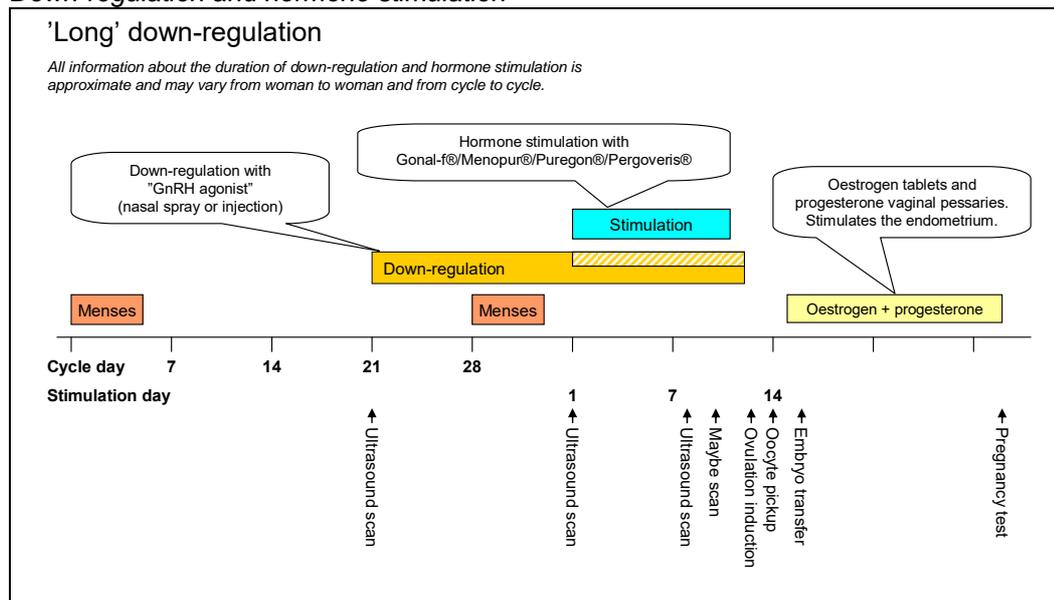
In our clinic, we use different hormone stimulation schemes. We mostly use treatment with 'long down-regulation' (we call it scheme 3) and the so-called 'short antagonist protocol' (we call it scheme 4). In some cases we use stimulation based on clomiphene citrate, 'agonist flare-up' or 'CRASH'. Very 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 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.

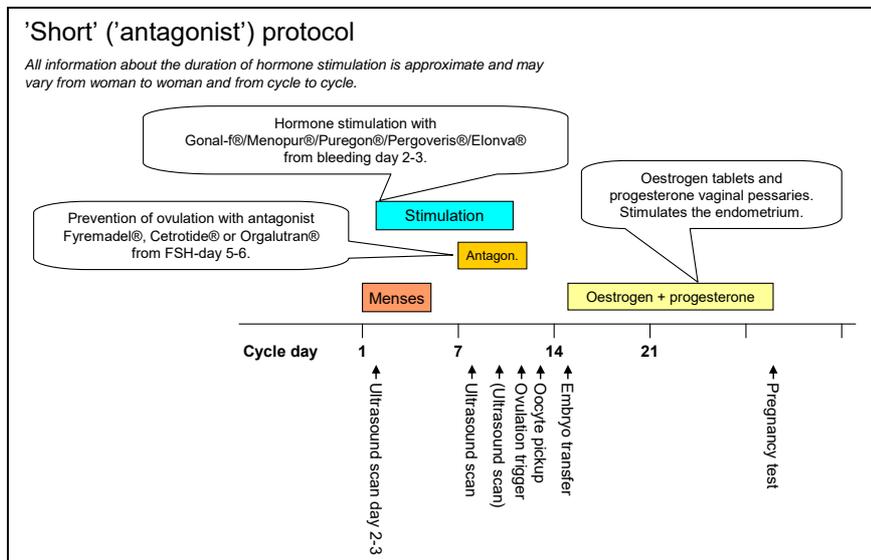
Before starting the hormone stimulation, we perform an ultrasound scan to make sure that the endometrium has been properly shedded and that no cysts are present in the ovaries.

When everything is ok, the daily injections with stimulating hormone are begun (Gonal-f®, 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.

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®, 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® 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.

Other types of hormone stimulation

In some cases, we recommend other types of stimulation than 'long down-regulation' or '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® eller 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 in order to induce the final maturation of the oocytes and make them ready for pick-up and fertilisation. hCG is actually a pregnancy hormone but it has the same effect as LH which is the natural 'ovulation' hormone.

Injection of Ovitrelle® is taken 34-36 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 Suprefact® (or another 'GnRH agonist')

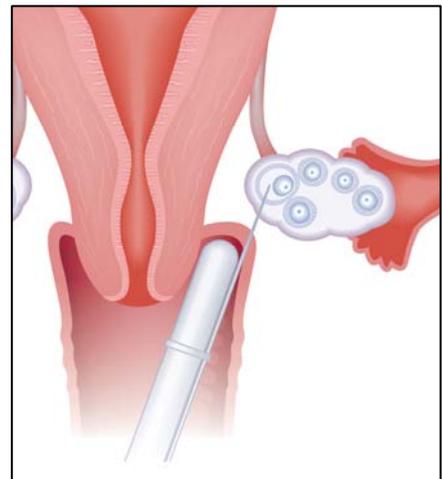
An alternative to using hCG for final oocyte maturation is to give a single dose of Suprefact® (or another GnRH agonist). This method can only be used if you are not down-regulated, and therefore it is not used in 'scheme 3'.

Final oocyte maturation ('GnRH agonist triggering') with 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.

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 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 an early embryo attempts to implant in the endometrium.

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.

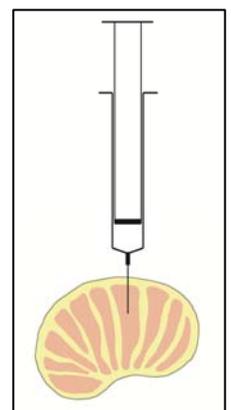
Some men may have difficulty producing a sperm sample 'under pressure'. If you expect that this may be a possibility for you, some precautions may be taken. For example, you may provide a sperm sample in advance, which can be frozen and used as a back-up. The sperm quality will be reduced due to the 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 generally performed the day before the oocyte pick-up. It improves the sperm cells' ability to fertilise if they have a day to mature after the testicular aspiration. 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 tested 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 fertilised with donor semen? Should they be cryopreserved for later use? Should they be donated to another couple? 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 now transferred to a new growth medium that is free of sperm cells. Here the embryos are cultured for one or more additional days. The cell divisions are visualised with a microscope.

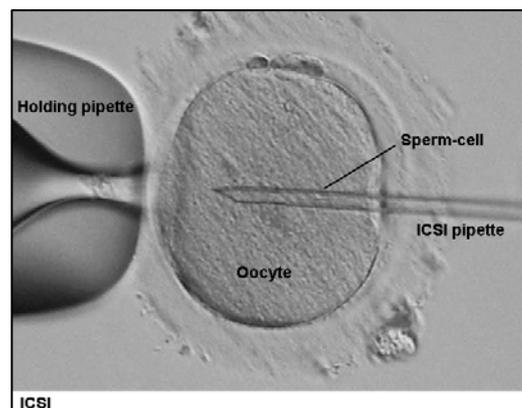
Fertilisation with ICSI

(*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 is 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.

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 sperm bank's doctor examines donors. They have to 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 or www.nordiccryobank.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.

'Own' sperm donor

An 'Own' sperm donor is a donor who 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 live as a couple.

An 'Own' donor must be tested for contagious diseases and deposit sperm in a sperm bank for later use in a fertility clinic. Presently, only European Sperm bank offers this service in Denmark.

The donor must be examined medically to determine if he is suitable as sperm donor. This testing can be done at Trianglen. You may enquire with the secretaries about prices.

An 'Own' donor is legally the father of the child/children resulting from the treatment. The 'Own' donor has duty to support the child and the child will inherit the 'Own' donor. In Denmark, there is an exception from this when the woman being treated has a male or female partner who assumes fatherhood or co-motherhood for the child.

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.

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

In Denmark, there are two major sperm banks:

- **European Sperm Bank** (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.

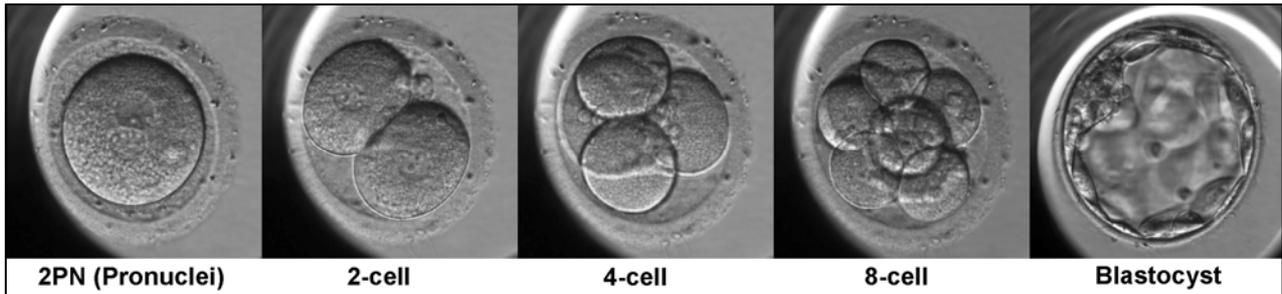
- **Cryos** (www.cryos.dk). We collaborate with Cryos. You can find more information about the collaboration on our website. Please note that we recommend that you order MOT20 or better when ordering from Cryos. MOT10 and MOT5 straws are not recommended.

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

Culturing the embryos

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 3.

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 'egg-shell', 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 will always select the best embryo for transfer into the womb. We only transfer embryos 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 at least two transferable embryos. On average one third of the oocytes will develop into embryos suitable for transfer. If more good quality embryos than the one we can transfer are available we can cryo-preserve ('freeze') the surplus embryos 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 (<http://en.wikipedia.org/wiki/Blastocyst>). 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. Embryos in the blastocyst stage hatch out of the surrounding 'egg-shell' ('zona pellucida') and begin to implant in the endometrium around 6-7 days after fertilisation.

For blastocyst culture, we change the gas composition in the mini-incubators in order to make it more like the conditions found in the fallopian tubes. This means reduced oxygen concentration and the usual high carbon dioxide concentration.

For blastocyst culture, it is desirable that there are five or more good quality embryos on day 3 after the oocyte pick-up. This gives a good probability that one or more embryos will reach the blastocyst stage. When blastocyst culture is intended, there is always a risk that none of the embryos reaches the blastocyst stage and that embryo transfer therefore must be cancelled. In some cases when blastocyst culture is intended, we may suggest embryo transfer on day 3 if it already at this stage is obvious that one or two of the embryos are of better quality than the rest. During the culture period, the laboratory will keep you informed about the development of your embryos on their way towards the blastocyst stage.

MIRI-incubators for embryo culture

Our Miri incubators allow us to keep the temperature, air composition more constant than is possible in classical incubators where embryos from several patients are cultured in the same incubator.

The Miri-incubators also 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. In traditional incubators, the concentration of oxygen cannot be adjusted but will be that of atmospheric air.

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 Miri incubators enable adjustment of the concentration of carbon dioxide and oxygen surrounding the embryos.

Assisted hatching ('AHA')

The oocyte is surrounded by a 'shell' called the *zona pellucida*. The first cell divisions take place inside this shell. When the embryo reaches the blastocyst stage, it must 'hatch' out through the shell in order to be able to implant in the endometrium in the uterus.

It has been theorised that some embryos fail to hatch and therefore do not develop into pregnancies. For this reason, it may in some situations increase the pregnancy chance if the hatching process is assisted by weakening the shell. This may be done by making very tiny holes in the shell by a laser beam, so-called 'assisted hatching'.

The Cochrane Library is an independent international organisation that evaluates the scientific evidence for many types of treatment. In the most recent review of assisted hatching the conclusion is:

Assisted hatching is a technique sometimes used for IVF (in vitro fertilisation) and similar procedures. It involves thinning the coat surrounding the fertilised egg, or making a hole in it. It is suggested that this may improve the chance of the embryo attaching to the womb so that pregnancy can begin. In this review of randomised controlled trials there was no evidence of a benefit in the live birth rate with assisted hatching although there was an increase in multiple pregnancy rates. There was some evidence that assisted hatching improves the chances of pregnancy in women for whom IVF has been repeatedly unsuccessful, but more research is needed

We can perform assisted hatching with the most advanced laser equipment available. As described above AHA may increase the pregnancy chance in some women.

Embryo transfer

The embryo transfer is normally performed 3-5 days after the oocyte pick-up. If blastocyst culture is performed and if blastocysts have 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.

On the day of embryo transfer, the lab will call you in the morning to tell you about the embryos that will be transferred. You will be informed about the number of cells in the embryos and about their 'quality'.

The embryo transfer is usually simple and painless and only takes a few minutes. You will see the embryos 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 embryo(s) are 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 or occasionally two embryos in order to minimise the possibility of multiple gestations.

After the embryo transfer, you may rest in the clinic for 30 minutes or so before you leave. There are no special precautions after the embryo transfer but we recommend that you avoid hard physical activity including high intensity exercise for some days.

You should not swim or take a bath tub 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 embryo transfer.

Filled urinary bladder for the embryo-transfer

It may facilitate the embryo 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 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 embryo transfer.

Urine in the urinary bladder at embryo transfer

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

Hormone treatment after the embryo 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 embryo 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 embryo 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 in order to determine if any adjustments should be made in a future treatment cycle.

After a hormone-stimulated cycle, there should be at least one pause-cycle before a new treatment cycle is initiated.

Pregnant by in vitro fertilisation

Pregnancy check-ups

All women who have become pregnant in our clinic are offered an ultrasound scan in the 7th or 8th 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 embryos, whether the heart is beating and whether the size of the embryo 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, two embryos are sometimes transferred to the womb in order to increase the chance of pregnancy. However, this also increases the possibility of a twin pregnancy. With transfer of two embryos, approximately 20-25% of younger women who become pregnant will have 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 embryos.

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 a sufficient number of 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 despite the fact that 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 are not of a quality sufficient for transfer.

Please also read the paragraph about blastocyst culture for more information about possible cancellation of embryo 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 embryo 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.

Acupuncture in connection with in vitro fertilisation

Acupuncture is a traditional Chinese treatment, which may have a beneficial effect on the chance of becoming pregnant with fertility treatment. We offer acupuncture in connection with embryo transfer.

A number of studies have been conducted in order to evaluate the effect of acupuncture in connection with in vitro fertilisation. One study was performed at Trianglen to determine the effect of acupuncture around the time of embryo transfer. The results showed an increased pregnancy chance in the women who got acupuncture. The results were published in *Fertility and Sterility* (Westergaard LG et al., *Fertility and Sterility* 85:1341-46, 2006).

There is an ongoing scientific debate about whether or how much acupuncture may improve the success rate with fertility treatment.

The Cochrane Library is an independent international organisation that evaluates scientific evidence for a number of treatments. In Cochrane's analysis of the effect of acupuncture in connection with IVF the conclusion is:

The data from this meta-analysis suggests that acupuncture does increase the live birth rate with in vitro fertilisation (IVF) treatment when performed around the time of embryo transfer. However, this could be attributed to placebo effect and the small number of trials included in the review. Larger studies are necessary to confirm the results.

We offer acupuncture in connection with the embryo transfer for those who would like it.

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.

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 embryos.

The highest success rates are obtained when the woman is young (less than 38-40 years). When there are two fertilised embryos of good quality for transfer the pregnancy chance is optimal. In this situation, the chance of a positive pregnancy test is between 40-50% per transfer. After subtracting the miscarriages (approximately 20% of the pregnancies) the chance for giving birth to one or two children 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

Year 2017 Day 2-3 transfer	Transfer of 1 embryo (eSET)		Transfer of 2 embryos	
	<i>under 40</i>	<i>40-45</i>	<i>under 40</i>	<i>40-45</i>
Age				
Number of transfers	321	84	165	257
Mean age (years)	34,3	41,6	36,0	42,3
Number of positive hCG	133	24	86	103
% Positive hCG	41,4	28,6	52,1	40,1
Number with heartbeat	108	13	65	58
% With heartbeat	33,6	15,5	39,4	22,6
Number of twin pregn.	0	1	17	13
% Twin pregnancies	0,0	7,7	26,2	22,4

Year 2017 Blastocyst transfer	Transfer of 1 blastocyst (eSET)		Transfer of 2 blastocysts	
	<i>under 40</i>	<i>40-45</i>	<i>under 40</i>	<i>40-45</i>
Age				
Number of transfers	75	30	2	8
Mean age (years)	35,2	42,0	39,0	42,6
Number of positive hCG	48	14	0	3
% Positive hCG	64,0	46,7	0,0	37,5
Number with heartbeat	41	9	0	3
% With heartbeat	54,7	30,0	0,0	37,5
Number of twin pregn.	0	0	0	0
% Twin pregnancies	0,0	0,0	0,0	0,0

Year 2016 Day 2-3 transfer	Transfer of 1 embryo (eSET)		Transfer of 2 embryos	
	<i>under 40</i>	<i>40-45</i>	<i>under 40</i>	<i>40-45</i>
Age				
Number of transfers	211	49	185	288
Mean age (years)	34,7	41,9	35,5	42,3
Number of positive hCG	94	13	106	83
% Positive hCG	44,5	26,5	57,3	28,8
Number with heartbeat	73	9	78	44
% With heartbeat	34,6	18,4	42,2	15,3
Number of twin pregn.	1	1	19	2
% Twin pregnancies	1,4	11,1	24,4	4,5

Year 2016 Blastocyst transfer	Transfer of 1 blastocyst (eSET)		Transfer of 2 blastocysts	
	<i>under 40</i>	<i>40-45</i>	<i>under 40</i>	<i>40-45</i>
Age				
Number of transfers	80	35	5	13
Mean age (years)	35,4	41,5	35,6	42,0
Number of positive hCG	52	14	3	9
% Positive hCG	65,0	40,0	60,0	69,2
Number with heartbeat	39	12	3	8
% With heartbeat	48,8	34,3	60,0	61,5
Number of twin pregn.	0	1	1	0
% Twin pregnancies	0,0	8,3	33,3	0,0

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 embryo 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 to freeze 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?

A number of 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 (<1/2%) 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 embryo transfer the embryos are placed centrally in the endometrial cavity. However, for unknown reasons the embryos 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 surplus embryos that were cryo-preserved these will often be used first. There has to be a 'pause' cycle before the treatment with thawed embryos.

If there are no frozen embryos 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 similar to the previous treatment or if

something should be changed. There should be a break between the treatments so that there are 2 months/cycle between oocyte pick-ups.

‘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.

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®, Iprex®, 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.

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* exercise – but at moderate or low intensity.

Body weight

Both a too low and a too high body weight will reduce the chance of becoming pregnant. Over weight 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:

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

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

A normal sex life does not seem to negatively 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 embryo 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 make an arrangement 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.

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 embryos and transfer of thawed embryos

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

In general, we culture embryos to the blastocyst stage before cryopreserving them.

Even though we only freeze embryos of very good quality, not all embryos will survive the freezing and subsequent thawing.

The current legislation in Denmark states that embryos may be stored for up to 5 years. 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 embryos

In women with a regular menstrual cycle shorter than approximately 35 days, the thawed embryos 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 'stimulated' cryo-cycle.

Transferring thawed embryos in your natural cycle

Transfer of thawed embryos is most often done without any hormone treatment. 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 embryo.

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

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

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

Transfer of thawed embryos in an estradiol-'stimulated' 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 (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 you become pregnant, 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 embryos is approximately 30-40%.

Treatment in public fertility clinics

In vitro fertilisation may be done in public fertility clinics (for couples covered by Danish social security) if the following conditions are met:

Medical: Indication for performing IVF or ICSI

Age: The woman must not be older than 40 years.

Family/social: The couple must not have a child together.

We can make a referral to a public fertility clinic if you ask us to.

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 in order to avoid misunderstandings.

Medicine for down-regulation (GnRH agonists)

Synarela®, Suprecur®, Suprefact®, 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 Suprefact®) 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® og Suprecur® is a nasal spray that must be taken several times every day.

Suprefact og Gonapeptyl® is taken as one daily injection.

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

Side effects: Headache, hot flushes and mood changes.

GnRH Antagonists

Fyremadel®, 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®, 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.

Pergotime®

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

Side effects: Hot flushes, nausea, blurred vision and headache. However, most women taking Pergotime® 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.

Suprefact® (GnRH agonists)

An alternative to hCG to induce final oocyte maturation is to give a single dose of 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 an embryo. 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 embryos 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 an embryo 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, diarrhea.

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)

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 embryo. Embryos in the blastocyst stage hatch out of the surrounding 'egg-shell' ('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 embryos 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 prevents the pituitary gland from secreting FSH and LH. The key function is to prevent premature ovulation before the oocyte pick-up. Examples: Synarela®, 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**..... IntraCytoplasmic Sperm Injection. Mikroinjection of a sperm cell into the oocyte.
- Implantation rate** The proportion of embryos 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 embryo transfer.
- Progesterone** A hormone that is produced in the ovary after ovulation. Progesterone is important for preparing the endometrium to receive an early embryo.
- 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 embryo '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 01.09.2021	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
Price (all prices in DKK)	26.000	49.000	57.200	29.000	55.000	64.400
Completed cycle <i>The cycle is considered completed if oocyte retrieval has been done and one or more eggs has been obtained.</i>	26.000	16.333	19.067	29.000	18.333	21.467
Additional services (can be drawn from 3-package)						
Blastocyst freezing and storage up to 1 year.	6.500	6.500	6.500	6.500	6.500	6.500
Thaw cycle with embryo transfer.	6.000	6.000	6.000	6.000	6.000	6.000
ICSI (Intracytoplasmic Sperm Injection).		3.000	3.000	Included	Included	Included
Cycle cancelled after stimulation but before oocyte pickup.	<i>pr.cns.</i> 1.150	<i>pr.cns.</i> 1.150	<i>pr.cns.</i> 1.150	<i>pr.cns.</i> 1.150	<i>pr.cns.</i> 1.150	<i>pr.cns.</i> 1.150

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 one or more eggs has been obtained.
- 3) If the contract is suspended, payment is as specified under "Single" treatments. Cannot be suspended during pregnancy.
- 4) Donor sperm (if used) must be paid separately (to the sperm bank).
- 5) TESA (if used) and Assisted Hatching (if used) must be paid separately. Cannot be drawn from the 3-pack.
- 6) Acupuncture (if used) must be paid separately. Cannot be drawn from the 3-pack.
- 7) Medicine is NOT included in the prices in the price list
- 8) Services in the 3-cycle package must be used within two years.

'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 cryo-preserved embryos after a 'fresh' treatment. Often the next treatment will then be with transfer of thawed embryos before you go through a new 'fresh' treatment, if still not pregnant. The payment for the use of thawed embryos 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 embryo 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 55.000

Treatment	Comment	Spent	Left
1st IVF treatment	First 'fresh' treatment. Three blastocysts cryopreserved. Pregnancy test positive.	18.333	36.667
Cryopreservation	Surplus blastocysts frozen.	6.500	30.167
Birth	Birth of live baby means that the card is completed.	The rest	0

Example 2

ICSI under 35 Price 55.000

Treatment	Comment	Spent	Left
1st IVF treatment	First 'fresh' treatment. Two blastocysts cryopreserved. Unfortunately the pregnancy test is negative.	18.333	36.667
Cryopreservation	Two blastocysts frozen.	6.500	30.167
Cryo-cycle	All cryopreserved blastocysts are thawed. One is transferred. Unfortunately the pregnancy test is negative.	6.000	24.167
2nd IVF treatment	Second 'fresh' treatment. No embryos for cryopreservation. Unfortunately the pregnancy test is negative.	18.333	5.833
3rd IVF treatment	There is now 'only' 5.833 left on the card. We ask you to pay 12.500 to reach the amount of 18.333 that one cycle costs.	18.333	-12.500
Comment	<i>This means that not until now do we ask for payment for cryopreservation and transfer of thawed embryos. You will not have to pay for the 'frozen' cycle unless the entire amount on the card is used.</i>		

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

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

Price list for other services

Price List 01.09.2021	
Consultations	DKK
First consultation. Is covered if you have a referral from your Danish doctor. Is included if you pay for IVF/ICSI treatment.	1.250
Subsequent consultations. Are included if you pay for IVF/ICSI treatment.	1.150
Ultrasound scanning	
Ultrasound scan (when not part of paid IVF/ICSI/IUI treatment).	1.150
Sperm analysis	
Sperm analysis (if not covered by 'Sygesikringen').	1.150
Handling fee when receiving sperm straws from a sperm bank	
Handling fee for sperm straws received from sperm bank regardless of number of straws.	750
TESA - aspiration of sperm cells from testicles for use with ICSI	4.600
AHA	
Assisted Hatching - with laser	2.600
Ca-Ionophore	
Addition of Ca-Ionophore when fertilizing eggs	1.500
IVF/ICSI without stimulation - in natural cycle	
IVF without stimulation (must also be paid if the cycle is cancelled after oocyte pick-up). If the cycle is cancelled before the oocyte pick-up payment is per consultation.	11.300
ICSI without stimulation (if no oocytes are retrieved at the oocyte pick-up the price is 11.000). If the cycle is cancelled before the oocyte pick-up payment is per consultation.	14.500
Cryo-storage of frozen embryos and oocytes	
Continued storage of frozen embryos or oocytes, per year. (Storage for the first 1 year is included in the price for cryo-preservation).	2.600
Cryopreservation of oocytes - Note: May be stored for up to 5 years	
Hormone stimulation, oocyte pickup and cryopreservation (including 1 year storage).	26.000
Cryopreservation and storage of semen	
Cryopreservation of sperm sample (including storage for 1 year).	2.100
Continued storage of frozen sperm samples (beyond 1 year), per year.	2.600
Administration when transferring sperm/oocytes/embryos to or from another clinic	
Administrative work for transfer - does <i>not</i> include transport	3.100
Transfer of sperm from Rigshospitalet department GR	
Transport and administrative work for transfer.	2.100
Blood tests (covered if you have Danish social security coverage)	
Test for hepatitis B and C and HIV in EU tissue-centre laboratory.	850
AMH blood test.	650
Other blood tests - per test.	250
Acupuncture	
Acupuncture. Per treatment.	600
Hysteroscopy	
Hysteroscopy (is covered if you have a referral from your Danish doctor).	2.575
Priming	
Priming - superficial 'scratching' in the endometrium.	2.100
Handling fee for blood tests for 'foreign' clinics	
For example for a clinic in another country (does not include price for analysis).	800
Prescription fee for 'foreign' clinics	
For example for a clinic in another country.	550
Filling out forms/certificates etc.	
For example for foreign clinics, insurance companies etc.	750

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 holidays and weekends on our website.

Address

Our address is:
Lundevangsvej 12
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.

Mail-contact to the clinic for patients

Please only use *secure email*, see 'Contact' information on our website 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 and www.trianglen.dk

Bank

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

Links

Trianglen Fertility Clinic www.trianglen.dk
Danish Fertility Society www.fertilitetsselskab.dk
Danish Health and Medicine Authority www.sst.dk
Sundhed.dk www.sundhed.dk
Medicin.dk 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

