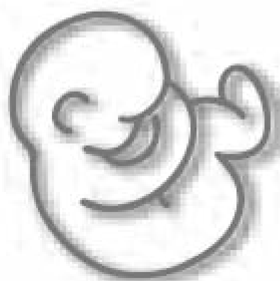
Treatment Guide

In-Vitro Fertilisation (IVF)

Intra-Cytoplasmic Sperm Injection (ICSI)

Testicular Sperm Extraction (TESE)

Frozen Embryo Transfer (FER)



DANISH FERTILITY CLINIC

www.danfert.dk

Tel. +45 38 34 90 30

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The treatment: IVF, ICSI, TESE, frozen embryos

General

This Guide is handed out to everyone seeking in-vitro fertilisation treatment at The Danish Fertility Clinic due to involuntary childlessness. It is not intended as a guide that must be read from beginning to end (although you are of course welcome to). Instead, you may use it as a reference guide in the course of your treatment. In this way, you can read the most important information in the quiet of your home and be prepared to ask specific questions when you visit the fertility clinic. In addition, the Guide contains the most relevant information which you may be unsure about at home. We are naturally happy to answer all questions you may have when you visit us at the fertility clinic.

In our waiting room, you will find various leaflets describing different subjects in more detail.

What are IVF and ICSI?

IVF is an abbreviation for **I**n-**V**itro **F**ertilisation which means that fertilisation takes place outside the body (in vitro - in glass). This procedure is also known as "test tube fertilisation" or "artificial fertilisation".
ICSI stands for **I**ntra-**C**ytoplasmic **S**perm **I**njection which literally means injection of the sperm cell into the egg.

Who can be treated with IVF and ICSI?

- This treatment must be medically indicated and have a reasonable success rate.
- The woman may not be over 45 years of age.
- Both single women, heterosexual and homosexual couples can be treated.

Medicine prices

Unfortunately, the medicine used is quite costly. Without any repayment, the sum amounts 1000 to 4000 Euro (usually 2000-3000 Euro) per treatment, depending on, how many hormones you need.

Medication and side effects

<u>Synarel, Suprefact, Profact and Suprecur (down regulation):</u>
Effect: Reduces the amount of FSH and LH released from the pituitary gland.
Side effects: Nasal spray: In particular, women suffering from allergies may experience nasal irritation. Headache towards the end of the treatment, hot flushes, sleep disturbances and mood swings. Many women experience hardly any side effects. When the next medication is administered, any side effects usually disappear quickly.

<u>Puregon, Gonal-F and Menopur/Menogon:</u>
Effect: Stimulates egg production (FSH).
Side effects: Local irritation at the injection site (small), with high doses non-specific tiredness, bloating and oppression/pain in the abdomen as the ovaries grow and take up space in the abdomen.

<u>Luveris:</u>
Effect: Luteinising hormone (LH). Normally used in combination with FSH.
Side effects: Local irritation at the injection site, headache, tiredness, nausea, abdominal pain, ovarian cysts, tender breasts.

<u>Cetrotide/Orgalutran:</u>
Effect: Regulates the release of women's own FSH and LH from the pituitary gland.
Side effects: Local irritation at the injection site, (infrequently) nausea, headache and skin rash.

<u>Ovitrelle/Pregnyl:</u>
Effect: Ovulation-triggering hormone causing women to ovulate about 40 hours following injection.
Side effects: Local irritation at the injection site. If there are many follicles, pain may be experienced after 30 hours and in connection with ovulation, as many eggs are released. If there is a risk of hyperstimulation, the symptoms will be aggravated, for which reason we sometimes choose not to administer the ovulation-triggering injection of hCG.

<u>Progestan or Utrogestan suppositories/Crinone gel:</u>
Effect: Acts on the uterine mucosa and prepares it for implantation of the embryo.
Side effects: Tender breasts, nausea, fluid retention, will sometimes delay the menstrual period, psychological side effects in rare cases.

General side effects: All medication may cause an allergic reaction. However, experience shows that allergic reactions are very rare in patients taking the preparations mentioned above. Do not hesitate to ask if you have any doubts. Symptoms may include flushing, swelling, itching, fever and, very rarely, difficulty in breathing.

Instructions for use

Our nurses will instruct you on how to take your medicine. Some couples prefer that the woman injects herself, while others prefer the male partner to do it for her. Our nurse will help you find the solution that suits you best. We cannot offer to help you with your injections at the clinic *inter alia* because the medication is to be taken outside our opening hours. Almost all couples will easily learn the technique, although it does, of course, take some effort the first few times. Most medications are injected into the skin of the abdomen with an injection pen similar to that used by diabetes patients.

The treatment

Starting treatment

Please call **+45 3834 9030** during the clinic's telephone hours from **9.30 am to 12 noon** or **1 to 3 pm** when you get your period, informing us of the first day of your period and of the treatment you will be starting (short or long protocol). You will then be given an appointment for an ultrasound scan. *Patient outside Denmark are requested to send an e-mail to Ursula@danfert.dk, as most treatments are long-distance with co-operation with your gynaecologist in your native country.*

Daily opening hours

The clinic is an out-patient clinic which is open to patients from 7.30 am to 5 pm, on Fridays until 3 pm. Treatments are conducted all days of the week, including bank holidays. However, during the weekends, we only perform procedures that cannot be deferred and the clinic is closed for patients on Sundays.

We know that it may be of inconvenience to you that the clinic is only open during normal working hours, especially since it is not always possible for us to predict when you need to come in for egg collection and embryo transfer.
For this reason, many couples choose to inform their employers of the treatment. Naturally, your partner is very welcome to be present at all examinations; however, for practical reasons, some couples choose to let the woman come alone to some of the scans. It should be noted that the partner should be present when the eggs are collected and transferred.

Long or short treatment?

In most cases, we use the **long protocol**. However, if you are experiencing severe side effects during the down regulation stage, we often use the **short protocol**. Both protocols have advantages and disadvantages. There are also different varieties of both protocols, which we naturally know and will use when required. The stimulation of the woman is the same, regardless of whether you are undergoing normal in-vitro fertilisation (IVF) or intra-cytoplasmic sperm injection (ICSI).

Long protocol

The principle of the long protocol means that you will begin pre-treatment two weeks before the actual stimulation of the ovaries begins. We call this the **down regulation stage**, as the pituitary gland is emptied of your own natural hormones and made redundant. This means that we are subsequently better able to control treatment. This treatment has proven to be very effective and has improved results worldwide in the past 16 years.

An ultrasound scan is performed at all consultations, and it is best done on an empty bladder.

After this time, all references to days are based on the first day of the menstrual period. If your period begins on a Monday, Monday will be cycle day 1. Wednesday will then be cycle day 3 and so on.

Patients from abroad will receive necessary prescriptions, a treatment plan and a covering letter for your assistant gynaecologist in advance, explaining what information we need each day in order to treat you according to gold standard. Please, make sure we receive the relevant information by e-mail the same day you went for an examination. Your treatment will not differ from patients visiting our clinic for all examinations. *Since we have experienced that some British pharmacies will not accept Danish prescriptions, please, ask your gynaecologist at home whether he or she will change ours into British prescriptions.*

Cycle day 21:
Approximately cycle day 21 an ultrasound scan is performed, and down regulation phase begins with three daily sprays of **Synarel** nasal spray at intervals of about every eight hours, or injection of 0.5 ml of **Suprefact** under the skin (subcutaneously) every evening.

Cycle day 35:
Two weeks after the beginning of the down regulation phase (most often a Wednesday or Thursday), you will be scanned again. You will usually have your menstrual period within 7-10 days from the beginning of the down regulation phase and not necessarily on the day when it would usually begin. There is no need to worry - this is quite normal. Your menstrual period may also be lighter or, what is more common, a bit heavier than usual. Often, the menstrual period does not stop altogether, but will continue with light spotting up to the time when you come in for your scan. About ten per cent of women have not had their period when they come in for a scan. In that case, we will do a pregnancy test and scan to check whether cysts have formed. About five per cent of the women treated needs one additional week of down regulation. You are allowed to take headache tablets if you have headaches (paracetamol) which may be necessary towards the end of the down regulation stage.

The following days refer to the stimulation day. The third day therefore refers to FSH day 3 with the medication stimulating follicle production.

FSH day 1:
Now, it is time to start the actual hormone stimulation. This involves daily injections of **Puregon**, **Gonal-F** or **Menopur**, which must be injected at the same time every night (preferably between 9 and 10 pm). These three drugs are almost identical, but are produced by different pharmaceutical companies. When hormone stimulation starts, the down regulation is reduced to two daily sprays of **Synarel** nasal spray every 12 hours or one daily injection of 0.2 ml of **Suprefact** It is very important that you continue this part of the treatment up to two days before egg collection. This means that you will be taking two kinds of medication from now on. You will normally be given an appointment for a scan on FSH day 6 and 9 again.

FSH day 6+9:
During this ultrasound scan, we will assess whether the stimulation produces an adequate number of follicles. We will adjust the dosage, if necessary, and make a new appointment for a scan. Most women will need another 1-4 days of stimulation before they are ready for the ovulation-triggering injection. If the follicles measure less than 14 mm, another ultrasound scan might be necessary for optimal timing of ovulation induction.

FSH day 10-?:
Injection of the ovulation-triggering hormone
We will let you know when to start taking **Ovitrelle in doses of 250 micrograms** or **Pregnyl 10.000 IU**. Ovitrelle or Pregnyl must be taken 36 hours before the egg collection,

normally between 9 and 10 pm, but you will receive further instructions from us. This will trigger ovulation about 40 hours later in order for the eggs to be released. **It is very important that you inject Ovitrelle/Pregnyl at the exact time prescribed.** The day before commencing the Ovitrelle injections, you will stop taking Synarel/Suprefact and Gonal-F/Puregon/Menopur. If you have many follicles, you may experience slight abdominal pain.

Short protocol

In the short protocol, you will not undergo down regulation before the treatment. This means that we will start hormone stimulation on the eggs on the second or third day of their menstrual period. Often, we plan a 3-week pre-treatment using contraceptive pills before the treatment begins or pre-treatment with Oestradiol tablets from 5 days before the expected day of menses.
With the long protocol, eggs are collected about seven weeks after the menstrual period and registration for treatment, while this is done about two weeks later in the short protocol (5-6 weeks later if you will be pre-treated with contraceptive pills).

Patients from abroad will receive necessary prescriptions, a treatment plan and a covering letter for your assistant gynaecologist in advance, explaining what information we need each day in order to treat you according to gold standard. Please, make sure we receive the relevant information by e-mail the same day you went for an examination. Your treatment will not differ from patients visiting our clinic for all examinations.

Our indications for short treatment will usually be:

- Difficult stimulation in the long protocol for some reason.
- Too few eggs (low responder) in the long protocol.
- Many side effects in the long protocol in connection with down regulation.
- Other special circumstances.

There are advantages and disadvantages of both protocols. For further information, please consult us.

The below days refer to the stimulation day and not the day after the start of the menstrual cycle.

FSH day 1 (second day of the menstrual period):
Ultrasound scan to check whether everything is in order. After the scan, FSH treatment begins as on day 1 in the long protocol.

FSH day 6 (seventh day of the menstrual period):
Ultrasound will be used to determine the number of follicles and their size. We will begin treatment with the medication preventing premature ovulation (**Cetrotide/Orgalutran**) from the evening of FSH day 5 or 6. This is necessary in order to prevent you from ovulating before egg collection. If that happens, we would miss our chance of retrieving eggs. You must therefore inject two different drugs from FSH day 5 or 6.

FSH day 9:
Ultrasound to check for mature follicles. We schedule the day for administration of the ovulation-triggering injection and the day of egg collection. In case the follicles measure

less than 14 mm, another ultrasound scan might be necessary for optimal timing of ovulation induction.

FSH day 10-?:
Injection of the ovulation-triggering hormone
This is exactly the same as in the long protocol. **250 micrograms of Ovitrelle** or **10.000 IU Pregnyl** must be taken 36 hours before egg collection, normally between 9 and 10 pm, but you will receive further instructions from us. This will trigger ovulation about 40 hours later in order for the eggs to be released. **It is very important that you inject Ovitrelle/Pregnyl at the exact time prescribed.** The day before starting on Ovitrelle, you must stop FSH stimulation and take Cetrotide/Orgalutran for the last time. *If you have injected Orgalutran or Cetrotide in the morning instead of evenings, you need the last injection in the morning of the ovulation triggering day.* If you have many follicles, you may experience slight abdominal pain.

The egg collection and embryo transfer procedures are exactly the same in the two protocols.

Egg collection

You will receive detailed instructions from our nurses or by e-mail.
It is important that you arrive at the clinic at the agreed time (usually between 9 and 11 am) and bring a sperm sample from home which may not be more than 1-1½ hours old (see below).
You are advised to eat only a light breakfast not containing dairy. One hour before the oocyte aspiration procedure, you are to take 1 gram of paracetamol. Please, empty your bladder when you arrive at the clinic. Immediately before collecting the oocytes, the nurse inserts a venflon, which is a small plastic cannula, into a vein, and an embryologist will come to check your identity (name and birthday) before the doctor arrives.
The nurse administers a quick-acting analgesic morphine drug (Rapifen/Alfentanyl) through the venflon, while the doctor washes the vagina and injects a local anaesthetic on both sides of the cervix.

The doctor performs the usual ultrasound scan and aspirates the oocytes from the follicles by inserting a small needle on both sides of the cervix. It is usually only necessary to insert the needle once on each side. In the adjoining room, the embryologist checks in a microscope that the oocyte has been retrieved. All follicles are emptied, regardless of whether only one or two embryos are to be transferred. Not all the follicles contain an oocyte, and not all oocytes are mature and will be fertilised. After the procedure, we will tell you how many oocytes we collected.

Your partner will sit next to you during the procedure. You will feel a bit drowsy, but will be awake during the entire procedure which usually takes 15-20 minutes. This depends on the number of follicles and on how easy they are to retrieve.
After the procedure, you will rest for about 20 minutes, after which time your partner may take you home. The woman is not allowed to drive herself, and you must be in the company of another adult for the next six hours.
Usually, you will experience slight bleeding after the procedure and are therefore provided with a sanitary towel. For this reason, it is recommended **not** to wear a G-string on the day of the procedure!!
You must be sure to drink plenty of fluids during the days following oocyte collection, preferably three litres of water, juice or tea/coffee, but not alcohol.

The sperm sample

The male partner may bring his sperm sample from home or choose to do it at the clinic, especially if you have a long drive to the clinic or very poor sperm quality. Preferably, the male partner should not have ejaculated for two-three days before the oocyte collection procedure. At your last visit before the procedure, a nurse will provide you with a sperm cup. Sometimes, the sperm sample may unexpectedly be poor or the male partner may not be able to do a sperm sample at home due to stress. In such situations, you do not need to bring one. Usually, the male partner finds it easier to deliver the sperm sample after the oocyte collection procedure, when things have calmed down a little. This is only normal.
You must tell the doctor if the male partner has had a temperature exceeding 38 degrees centigrade up to three month before oocyte collection, as the procedure may then have to be rescheduled. Sperm cells die at a high fever and fail to fertilise the oocytes, and it may take three months for the sperm quality to normalise.

Cultivation of the oocytes

All the oocytes retrieved in the oocyte aspiration procedure are placed in small dishes in our incubator at 37 degrees centigrade. We will add the sperm cells (50,000-100,000 sperm cells to each egg) or perform ICSI later. Then, the oocytes are suspended in a culture medium for two days, during which time we will monitor each oocyte closely. The next morning, after about twenty hours, we will check whether the oocytes have been fertilised, and later in the day, the embryologist will assess how and how quickly the embryos are developing. This is vital for determining which embryo or embryos will be recommended for transfer. You will receive detailed information on this aspect of the procedure.
About 48 hours, or two days, after oocyte collection, the embryologist checks how many embryos are available. You will be informed when you visit the clinic later that morning.

Embryo transfer

The embryos are usually transferred two days after having been collected. If your oocytes were collected on Friday, the embryos will be transferred Monday morning.

Unfortunately, about fifteen per cent of all women treated do not have any embryos suitable for transfer. This is either due to lack of fertilisation or poor fertilisation of the oocytes. If this is the case, we will try to contact you before you arrive at the fertility clinic, so as to not waste your time. Of course, you can make an appointment to speak to the doctor at the clinic later in the coming week.

The transfer procedure:

- **It is very important that you have a full bladder**. Therefore, it is a good idea to drink plenty of fluids on your way to the clinic and not use the toilet when you arrive at the clinic.
- Amount of embryos: The doctor and the embryologist will speak to you about the quality of the embryos and how many embryos will be transferred. We will normally transfer **one or two embryos**, depending on your age, the quality of the embryos and your wishes. It is important that your partner is present during the embryo transfer procedure, as it is preferable that you both hear what we have to tell you.

- **Hyperstimulation:** If there is an immediate risk of hyperstimulation, we suggest that only **one embryo** be transferred – or perhaps none at all. In that case, we can freeze the embryos instead and transfer them at a later time. This is to prevent you from becoming ill.
- As with insemination treatment, the embryo transfer procedure takes place on a gynaecological couch, and there is no pain involved. You will usually experience slight tenderness in the abdomen after the procedure, but that is all. The nurse scans your abdomen in order for the doctor to see where the embryo is being placed. You must therefore have a **full bladder**. This will also ensure that the uterus is straightened out which will make embryo transfer easier. You do not have to lie down after the procedure.
- The entire procedure usually takes 15 minutes.
- **You should still remember to drink plenty of fluids in the days following embryo transfer, i.e. three litres a day, but other than that, you do not have to take any special precautions. The nurse will tell you more about this.**
- We will schedule an appointment for a pregnancy test (a blood sample) two weeks after embryo transfer.

After-treatment with Progestan/Utrogestan suppositories/Crinone gel

- After the embryo transfer procedure, you are to insert **two 100 mg Progestan/Utrogestan suppositories three times a day or apply 90 mg of Crinone gel once or twice a day** for the two weeks up leading to the pregnancy test. This will help the uterine mucosa mature correctly. The suppositories must be placed deep inside the vagina using a finger or an applicator, and it is recommended that you rest for 15 minutes afterwards. Crinone gel must be applied in the morning. If you have to take it twice daily, we recommend morning and late afternoon. Some of the gel will probably run out, but you do not need to worry about this. For this reason, it is necessary to use a small panty-liner during the two weeks. **In the event that you need to travel by air, it is recommended that you use Progesterone suppositories, as the gel is affected by the low pressure in the flight cabin.** Please consult the nurse.
- In the event of spotting, you must continue using the suppositories/gel until we have taken a pregnancy test.
- If you become pregnant, you must continue with the Progestan/Crinone until the pregnancy scan three weeks later.

Progestan/Utrogestan/Crinone contains the natural hormone progesterone which the yellow body normally produces after ovulation. It stabilises the uterine mucosa which increases your chances of getting pregnant. In the oocyte aspiration procedure, the doctor retrieved the oocytes from the follicles, and thereby also all or part of the cells that would normally produce progesterone. This is a problem which we will then have to remedy.

Side effects: Progesterone may cause fluid retention, tender breasts and slight nausea. This may cause you to think that you are pregnant. There may be some irritation of the vagina. Some women become very mentally affected by progesterone (anxiety). Please contact the clinic if this happens to you.

Pregnancy test

You must always perform a pregnancy test, whether or not you think you are pregnant. Also if you have started bleeding because you may still be pregnant, even if you are bleeding a little.
If your menstrual period begins several days before the pregnancy test, you must tell the nurse when you come in for your blood test. We will take this into account in your next treatment. Always continue using the Progestan/Utrogestan suppositories/Crinone gel, also if you have started bleeding prematurely. *Patient from abroad most often make an appointment regarding the pregnancy test with the assistant gynaecologist.*

The blood test is taken in the morning about 14 days after embryo transfer. We will schedule an appointment for a blood test in connection with the embryo transfer. We will tell you when you can call us to get the result of your blood test. Please, e-mail us the result if you do not come to our clinic for the test.

- If you are **pregnant**, we will make an appointment for a pregnancy scan about three weeks later, and you must continue using Crinone/Progestan/Utrogestan until the pregnancy scan. If you have the pregnancy scan abroad, please, keep us informed of the result.
- If you are **not pregnant**, we will make an appointment for you to speak/e-mail to a doctor, who will review the treatment with you. During this consultation, you will talk about when you can register for treatment again, if you wish to have further treatment. This will usually be when your menstrual period begins again. You are, of course, allowed to wait longer, if you wish to do so. The length of time that couples wish to wait before they start treatment again varies greatly. It is unfortunate when the desired pregnancy is not achieved, and we know that it is hard on you. If no problems have occurred during your treatment, your chances of getting pregnant with your next treatment remain the same.
- With some women, we have to **repeat the blood test** in order to follow the development of the pregnancy.

Pregnancy scan

About three weeks after a positive pregnancy test, we will use ultrasound scan through the vagina to show:

- Whether you are pregnant with an embryo inside the uterus (ectopic pregnancy?).
- Whether the embryo is viable (heart rate).
- The size of the embryo (does it correspond to the expected size?).
- Whether there are one or two embryos (twins).

At this time, we **cannot** scan for deformities or tell the sex.

Conclusion: If everything is in order, you have a good chance of a successful pregnancy and of having a healthy child. The risk of abortion after a normal scan is between 5 -10%. Your case will be closed at the clinic, and you must now call your own GP to make an appointment, where you will make the necessary arrangements for your pregnancy and birth.
If you start bleeding shortly after your case has been closed at the clinic, you are welcome to have an additional ultrasound scan at the clinic. In the event of any pregnancy complications after week 12, we recommend that you contact the hospital where you are going to give birth.

If you are expecting **twins**, we will usually do another scan 2 weeks later.

If it turns out that the embryo is sadly not viable, you have three options:

- You may wait until you have your period (spontaneous abortion). This may take from one day to several weeks. Many couples prefer this option.
- You may be referred to the gynaecology clinic at the hospital for a medical abortion, which is, of course, not an induced abortion, as the pregnancy has ceased.
- You may also choose a D&C of the uterus during general anaesthesia at the gynaecology clinic at the hospital. Patients from abroad most often discuss the options with their assistant gynaecologist.

With all three options, you will usually have your period 4-6 weeks after the abortion, so you may have to wait a while. This is quite normal. Under normal circumstances, you can register for a new treatment after your first menstrual period.

Intra-Cytoplasmic Sperm Injection (ICSI)

In this procedure, the embryologist will help the individual sperm cells into the oocyte by injecting the sperm cell directly into the oocyte using a fine needle. This is where it differs from IVF, where the sperm cells are merely merged with the oocyte in a dish and have to penetrate the oocyte **themselves**. You could say that the embryologist looks at the sperm cells under the microscope and selects a sperm cell that swims straight ahead, preferably fast, and looks normal. Then, the embryologist draws up the sperm cell using a microneedle and inserts it into the oocyte, which replaces the otherwise natural process.

When will this treatment be offered?

- If your partner has very poor sperm quality, i.e. less than five million after sperm purification, of if the sperm cells have poor motility. In that case, the chance of fertilisation by IVF is very low.
- If the oocytes are not fertilised by IVF despite of an apparently normal sperm test. (This may of course also be due to defects in the oocyte). We will then offer you ICSI for the next treatment. This does not always help the situation, especially if the oocyte quality is poor.

Examination of the male partner:

If you are going to be treated by ICSI and have not been examined at home, we will usually first perform a thorough examination of the male partner. The consultation with the doctor will comprise:

- Your partner will be asked about previous illness, working conditions and incomplete descent of one or both testicles at birth.
- If the semen quality is severely reduced, the doctor will examine the testicles and the epididymis, examine for varicocele and finally scan the testicles. If the scan pattern is not completely regular, the male partner will be recommended a biopsy of the testicles. (This will mostly happen in your native country). The biopsy will show any preliminary stages of cancer.
- We will also recommend your partner a blood test in order to examine the male partner's chromosomes in the lab, if the sperm count is below two million. In this blood sample, the Y chromosome is examined for minor changes (micro-deficiencies), which are known to cause very poor sperm quality, but which may also

be hereditable if you have a boy. A son will probably inherit the same defect and have poor sperm quality. In the event of Y deletion, you will receive thorough counselling.

- We will often require a new sperm sample which will then be analysed in our lab. This will supplement the previous sperm sample and give us new information which will all help us reach a final conclusion.

Will the children be normal?
We do not know all the changes in the genes which may lead to poor sperm quality. We are also not completely sure whether girls will experience such changes, but there is no evidence pointing in that direction.
In Denmark, not as many children have been born following ICSI as with IVF. Both in Denmark and the rest of Europe, thorough follow-ups are being carried out on children born following both IVF and ICSI. It may not be excluded that there may be a slightly increased incidence of chromosome aberrations in foetuses following ICSI treatment (reference is however made to the description of TESE below). These studies will probably continue for many years, also assessing the general development of the children.

What are the chances of pregnancy with ICSI?
The chances are the same or even slightly higher than with IVF treatment, provided that you are normally fertile, and two good quality embryos are transferred. Extremely poor sperm quality reduces the chances of pregnancy.

Use of donor sperm vs. ICSI:

When you come in for a consultation, we will always tell you about the option of donor insemination, if you are normally fertile. This requires much less hormone and is therefore significantly less straining on you.
Sometimes, there are no live sperm cells in the sperm sample on the day when the sperm cells are to be used for ICSI. This is often the case with very poor sperm quality. We warn you that this may happen and ask you to consider beforehand whether you then wish us to inject the oocytes with donor sperm instead. (We are unfortunately not able to freeze the oocytes; they have to be destroyed). You now have two days, while fertilisation is taking place, to consider whether you want to use the embryos or perhaps to freeze them in order to give you more time to consider. This is, of course, a difficult decision, and one that should not be taken in haste; instead it should be considered before the day when it may become necessary.

We will counsel you on the use of a sperm donor, as there are, of course, various ethical and personal considerations to be made in connection with such a decision.

Very poor sperm quality (TESE)

Some men do not have a single live sperm cell in their sperm sample (azoospermia), but may have live, mature sperm cells in the testicles. The classic example is sterilised men.
After thorough examinations (see the section on ICSI above), other men may be offered TESE (**T**esticular **S**perm **E**xtraction), where we operatively retrieve live sperm cells from the testicles by means of a small biopsy. This is done on the day of oocyte collection.
Then, we carry out ICSI in the lab, as described above, provided that we retrieve live sperm cells.

The male partner is examined in the same way as with ICSI. In this group of men, we will find a slightly increased incidence of the gene defect in the Y chromosome which the male partner may pass down to his son. Statistics show that there is a slightly increased incidence of chromosomal aberrations and deformities in children born following TESE.
There is an increased incidence of men with preliminary stages of testicular cancer in this group, for which reason it is necessary to perform a biopsy, unless it is due to the male partner previously having been sterilised.

TESE procedure
The male partner is placed on a couch, and his genitalia are washed with spirit. Then, the doctor will inject a local anaesthetic upwards in the scrotum and locally in the testicle from which we will extract sperm cells. We will wait for five minutes and then perform a biopsy using a biopsy needle, which the embryologist will examine under the microscope in the lab immediately. The embryologist will then let us know whether there are any live sperm cells, or whether we should try again.
After the procedure, an ice bag will be placed on the biopsy site to avoid bruising, which will easily occur in the scrotum (loose skin). The male partner will be able to leave the clinic after about an hour.
If you are undergoing an oocyte collection procedure on the same day, your partner will usually be able to drive you home.
Few patients experience heavy bruising with swelling, pain and perhaps fever, which will require penicillin treatment. In the event of fever, you should contact us or, after 3 pm, your local emergency unit or your GP.

What if there are no sperm cells?
There will always be a risk that there are no live sperm cells to use for ICSI. For this reason, you should consider the option of using donor sperm (donor backup) beforehand. We will counsel you on this and will be happy to talk to you about this option beforehand (see above).

Treatment using frozen, thawed embryos

How many have their embryos frozen?
In about 30-40 per cent of treatments, there are so many high-quality **embryos** left over from embryo transfer that they may be frozen. This requires both your signatures (only one for singles, of course). We will need your signatures again if the embryos are to be thawed and replaced in the uterus.

Why only freeze the <u>embryos</u>?
It is possible to freeze sperm cells; however, the attempts made with freezing unfertilised oocytes still demonstrate poor results. The oocyte is a very big cell, for which reason it has proved to be complicated. On the other hand, the freezing of embryos, where the individual cells are smaller, has been carried out for many years.

Why freeze embryos?
- In order to reduce the number of transferred embryos and thus multiple pregnancies.
- The frozen embryos may be used in a subsequent artificial cycle.
- In order to reduce the need for hormone stimulation of the woman.

Legislation

- Both partners have to sign the permission for thawing and replacing the embryos into the uterus.
- In case of divorce or death of one partner, the embryos have to be discarded.
- Embryos can be stored for 5 years.
- Embryos cannot be used after the woman's 46th birthday, but will be discarded.
- According to Danish law, embryos cannot be exported outside Denmark.

How many survive?

- About 50-60 per cent of the embryos survive freezing and thawing. For this reason, you should preferably have 2-3 embryos frozen, before we commence treatment with frozen embryos. However, this field is developing fast, so things may change.
- This means that about 15-20 per cent of our patients will have the unfortunate news that there are **no** surviving embryos for transfer. However, on a positive note, this treatment has been less straining on the woman.

The treatment:

You must have undergone a normal menstrual cycle after the last IVF/ICSI treatment.
As with the other treatments, you are to call us when your period begins:

- **Artificial cycle:** The treatment will take place in an artificial cycle, where 6 mg of **Progynon or Oestradiol** (three tablets daily) are administered daily from cycle day 2. In the scan on day 10-14, we will check whether the uterine mucosa is sufficiently thick. Otherwise, 6 mg will be administered daily for a few more days. When the uterine mucosa is sufficiently thick, we will schedule the day when the embryos will be thawed and subsequently transferred to the uterus. In the intervening four days, both **Oestradiol tablets** and **Progestan suppositories/Crinone gel** (in the vagina) will be administered to fully prepare the uterine mucosa. You must continue using both these medications after the embryo transfer, until you know whether you are pregnant. If your partner does not accompany you to the consultation, you must remember to take home the document on which you must both give your consent to us thawing the embryos and transferring them to the uterus.
- If you become pregnant, the hormone treatment must **continue** until the pregnancy scan and then up to the end of week 10.
- **In the event that you need to travel by air, it is recommended that you use Progesterone suppositories, as the Crinone gel is affected by the low pressure in the flight cabin.** Please consult our nurses.

How do we know whether there are any embryos available for transfer?

We will contact you if there are no embryos available for transfer before your appointment at the clinic.
Please note: You must remember to bring the document on which you have both given your consent to us thawing your embryos. We will not transfer them to the uterus, if the formalities are not in order.

Will the children be healthy?

All statistics show that the children will be just as healthy as after IVF or ICSI.

How long may the embryos be frozen?

Under Danish law, embryos may be frozen for five years.

What are the chances of pregnancy?
The chances of pregnancy are unfortunately not as good as with a fresh cycle. They are about 15-20 per cent per transfer, depending on the number of embryos transferred. When using frozen, thawed embryos, we are allowed to transfer three embryos, provided that we consider this to be reasonable. We will discuss this with you. The **general** chances of pregnancy will, of course, improve with each hormone stimulation treatment, if thawed frozen embryos are subsequently transferred, and you then become pregnant.

Part 2: Problems, side effects, risks

Cancellation before egg collection:

Some cycles are cancelled before egg collection: This may be caused by:

- **Hormone under-stimulation**, which means that an insufficient number of follicles is matured. Women over 38 years of age and women who have previously had ovary surgery or endometriosis are especially at risk of producing an insufficient number of eggs.
- **Hormone hyperstimulation**: Some women react very strongly to the hormones. If there is a serious risk of hyperstimulation, we will cancel. We will then have to start with a smaller hormone dosage the next time. Women with polycystic ovaries (PCO), young women, tall and slim women have a particularly high risk of hyperstimulation, and we will, of course, endeavour to factor this into the planning of your treatment.
- Sometimes, cysts may develop after down regulation, which we cannot remove, for which reason we have to stop the treatment and plan another strategy. Women who have previously experienced problems with cyst formation will have a particularly high risk of this. We are not quite sure why this is the case.
- **Illness**. If you or your male partner catches a fever (e.g. the flu), it may be best to cancel the treatment, since fever above 38^0C reduces semen quality significantly.
- **Holiday, seminars, parties**. Of course, you should live your life as usual. However, you should still seek to plan your treatment so that it does not collide with big family gatherings, parties, holidays etc. **If in doubt**, please call us and ask about the timing. We will tell you if it is best that you wait a month before registering for treatment. It is very unfortunate if you have to undergo a less optimal treatment due to pressure of time.

Failed fertilisation of the eggs:

- For almost 10-15 per cent of all women who undergo egg collection, the eggs unfortunately do not fertilise or divide. This means that there are no embryos to transfer to the uterus. Usually, we do not know what the cause is. In some cases, we can offer ICSI treatment the next time; however, it is not entirely certain that this will improve the situation. We may change the treatment the next time. If it turns out to be the case for you, we will call you before the planned embryo transfer. You are of course welcome to schedule an appointment during the following days, where we can discuss further treatment.
- Couples with unexplained childlessness have a slightly higher risk of failed fertilisation of the eggs. Such couples should view the first treatment as an extended diagnosis, in addition to it being additional treatment after the insemination treatment. It may be revealed that no fertilisation is taking place at all. You will be offered ICSI for your next treatment; however, this is not a full-proof solution to the problem.

Failure to become pregnant:

- Sometimes, you will not become pregnant, although one or two fertilised good quality embryos have been transferred. On average, the chances of a positive pregnancy test are about 25-45 per cent, depending on various factors. The chances of becoming pregnant in subsequent treatments are **just as high**, provided that there are good quality embryos available for transfer. The chances of becoming pregnant will only decrease after at least 4-5 treatments.
- There are several factors that will explain why you do not become pregnant; however, most of them are unknown: (1) The older the woman is, the more chromosomal aberrations are in the embryos and consequently in the embryo, which often means that they stop developing. (2) Due to the stimulation treatment, the uterine mucosa may not be receptive at the right time. However, other factors clearly also come into play. (3) Fibroids in the uterus or (4) polypi in the uterine mucosa (both may be removed). (5) Blocked fallopian tubes containing water (hydrosalpinges) which disrupts the mucosa. In this case, we know that removing the fallopian tube will increase the chances of pregnancy by 50%. Sometimes, we will not discover the changes in question before starting treatment, as they do not occur at all stages of the cycle.

Side effects of IVF/ICSI treatment

Fortunately, serious side effects are rare. However, even minor side effects may be hard to tolerate in this process, as there are many feelings involved.

- Side effects from the **medication**: Please see the section on medication and side effects on page 3. The most common side effects caused by down regulation are bloating, a bearing-down feeling in the abdomen as the ovaries grow and mood swings.
- **Ovarian Hyperstimulation Syndrome (OHSS):** The most predominant risk is that of hyperstimulation, which may be very serious. We are therefore very attentive towards associated factors, and during the actual treatment, we continuously assess whether you are becoming hyperstimulated. In that case, we will consider cancelling the treatment in order not to take any risks. During the process, we have different options for **reducing the risk**, if it has arisen. We will inform you of these options, if necessary. Unfortunately, all clinics have women who are hyperstimulated, as this is difficult to avoid. A lot of effort is being made to introduce new treatments minimising this risk. The symptoms are bloating with an increased waist measurement (you are unable to zip up her trousers), nausea, diarrhoea, fluid retention in the abdomen, legs and labia. Later on in the process, the woman may experience weight gain (1 kg a day) and difficulty breathing (shortness of breath). A pronounced symptom may be pain in the enlarged ovaries, especially at night. The treatment includes everything from out-patient check-ups here at the clinic to hospitalisation. It would comprise respite care, plenty of fluids, drop, analgesic, anti-nausea medication and you will need **prophylactic treatment against thrombosis**. In serious cases, it will be necessary to insert a drain in the abdomen and draw out the fluid (ascites tapping).
- **Torsion of the ovary**: in very seldom cases, one or both ovaries can rotate and thereby constrict the normal blood supply. This results in constant, mostly unilateral pain. If the pain does not disappear by changing your position, you need to seek medical advice. Ovarian torsion can also happen before oocyte collection.

- **Pain following egg collection**: Hyperstimulation must not be confused with the normal discomfort following egg collection. You may experience pain, particularly during the first day following the procedure, but this pain may often be relieved with paracetamol. Sometimes, you may experience pain at the injection sites, other times in the ovaries, because they are bleeding a little. This will pass, usually within the first two days. There may be slight discomfort for up to a week afterwards.
- **Bleeding**: There will always be some bleeding following egg collection, both from the vagina and in the abdomen. There is ample blood supply to these areas, especially following hormone treatment. The bleeding will usually stop quickly, but sometimes the doctor will have to apply compression at the top of the vagina using a gauze pad after egg collection.
- **Pelvic infection or ovarian infection** is very rare, since the women undergoing egg collection are healthy. However, you may be predisposed, in which case we will administer penicillin during the procedure. In the event of fever or pain after the procedure, you must call us here at the clinic or contact the emergency call service.
- **Lesion of other abdominal organs** during oocyte pick-up is theoretically possible; however, we have never experienced this.
- **Risk of subsequent development of ovarian cancer**: Some years ago, an Australian study showed that there may be a risk of ovarian cancer. This has since been repudiated, and so far, no certain correlation between hormone treatment and ovarian cancer or breast cancer has been demonstrated. Statistics are continuously being compiled worldwide. If the woman never gives birth, she will have a slightly increased risk, as she has never completed a pregnancy (pregnancy protects against ovarian cancer, breast feeding against breast cancer). Consequently, if the woman becomes pregnant, she is believed to have the same low risk as other women who have given birth.
- **Will the children be healthy? One child (singleton)**: Yes, they almost always will. There are now many statistics available in Denmark, the Nordic countries, Europe, Australia and the USA showing that singleton children born following IVF treatment have no more deformities than children conceived naturally. However, on average, they weigh 150 g less than children born after a spontaneous pregnancy. The children's psychological development has been followed all the way up to the school age. The reason behind the mother's or the father's childlessness may in itself be the cause of the lower birth weight.
- **Twins** are different however. There will always be an increased risk of premature birth and the related problems, if the woman is pregnant with twins. Since IVF treatment almost always provides **fraternal** twins, the risk is lower than for monozygotic twins, which are more normal in spontaneous twin pregnancies.
- Special circumstances apply to pregnancies following TESE, please see the relevant section.
- An amniocentesis is no longer indicated for pregnancies following IVF/ICSI. Many countries have decided to offer all women screening comprising a **nuchal scan (NT scan)** of the child, regardless of the woman's age. This scan is performed during week 11-13 and is combined with a blood test from the mother. The scan and the blood test should show whether there is an increased risk of having a baby with a chromosomal aberration (Downs syndrome), which means that an amniocentesis will be offered. It is, of course, up to you whether you wish to have a nuchal scan and, if necessary, an amniocentesis. At present, it is not possible to have a nuchal scan everywhere. Please consult your GP regarding your options of having a NT scan.

Part 3: The chances of pregnancy following IVF/ICSI treatment

The chances of getting pregnant depend on several factors, especially (1) the **woman's age** and (2) the **quality of the embryos**.

- **Age**: The younger the woman, the higher the chances of getting pregnant and giving birth. A 20-year-old woman is twice as likely to become pregnant spontaneously as a 35-year-old woman. For each additional year, the ability to get pregnant spontaneously and complete the pregnancy is thus reduced.
- **The quality of the embryos**: We only keep embryos that we know could produce a pregnancy. If the woman has **one** top-quality embryo transferred, the chances are about the same as after having **two** embryos transferred, where one or both of the embryos are of a slightly lower quality. On the other hand, transfer of two embryos would mean an increased risk of twins.

The above two things thus affect the information below, which are average figures:

- The chances of pregnancy following IVF/ICSI after transfer of **one top-quality embryo** are about 40 per cent for women under the age of 40, and the risk of twins is almost non-existing.
- The chances of pregnancy following IVF/ICSI after transfer of **two embryos** are about 40-50 per cent for women under the age of 40, depending on the quality; however, the risk of twins, if the woman becomes pregnant, will be about 25 per cent.
- If **three embryos** are transferred (which is very rare), the chances of pregnancy are increased by a few per cent, while the risk of twins is increased considerably, and, of course, there is also a risk of triplets.
- For women over the age of 40, the figures are slightly lower, for which reason we usually offer to transfer two or three embryos.
- The **Danish National Board of Health's guidance** says that women below 37 years with two top-quality embryos present in their first two cycles should have only one transferred and the other frozen. Women over 37 years can be offered two embryos after counselling.

Our target is **one child per birth**.

What happens if my pregnancy test is positive?

- 75 per cent of the women who become pregnant have one or more children.
- 15 per cent have a biochemical pregnancy (early pregnancy loss).
- 10 per cent miscarry (as is also the case with spontaneous pregnancies).
- 1-2 per cent unfortunately have a pregnancy outside the uterus (ectopic pregnancy). Women with damaged fallopian tubes have an increased risk of this.

The figures are the same as for "natural" pregnancies. The risk of abortion is not higher after IVF/ICSI treatment.

You can find additional information at our homepage www.danfert.dk

Part 4: Frequently Asked Questions – FAQ

How much do we have to be absent from work?
Of course, this depends on your job. Unfortunately, we are only able to offer scans between 7.30 and 17. Egg collection and embryo transfer take place in the **morning**, and your male partner should preferably be present. You may also choose to come alone to some of the scans, so that your partner does not have to be too much away from work.
If you have your scans in your home-country, please, make sure that we obtain the results immediately after the examinations, preferably by e-mail and before noon.

Are we allowed to have intercourse while we are undergoing treatment?

- We are not completely sure whether sexual intercourse affects the treatment, but presumably not during the actual stimulation. However, please remember that the male partner should not have ejaculated for two days **before** egg collection, especially if you are undergoing ICSI treatment. This means that when we notify you of the day of egg collection, you should stop having intercourse. **After** egg collection, most women do not feel like having intercourse, and we advise you against it during the first week due to the risk of infection.

Who do we call if there is a problem?

- You are of course welcome to call the clinic during our telephone hours (see page 4). On Saturdays and bank holidays, when only a nurse and a doctor are here, we are not able to answer the telephone all the time, and we may be difficult to reach. You could leave a message on the answering machine, and we will call you back.
- You can send us an e-mail. We aim at answering all mails every day, but if it is very important, please, phone us.
- You could look for an answer in this guide.
- If you have an emergency outside of the clinic's opening hours, you may try to contact the doctor on +45 20 63 62 62 or your accompanying gynaecologist at home. In case of an emergency occurring during the evening or the night, you should call the emergency call service and perhaps ask for the doctor on duty at the gynaecology clinic at your nearest hospital.
- If you experience any problems after egg collection, or if you are feeling ill, you should contact the nearest emergency gynaecology clinic.

Are we allowed to bring our children to the clinic?

- This is a somewhat difficult issue. Some women undergoing down regulation or their last treatment are considerably thin-skinned and vulnerable. It may be very difficult for them to see that others have been more fortunate and are maybe already undergoing treatment to have their second child. It is not possible to tell whether the children are a couple's own children or stepchildren, and some women require peace and quiet during their treatment. On the other hand, it may be difficult to get someone to look after your child, especially at weekends, and you may argue that you constantly come into contact with other children everywhere else. Consider that it may be a positive thing for you to see that it can happen and that it may also happen to you. This issue probably has no right answer, as different couples have different interests. Please just remember to consider other people's feelings.
- Naturally, the staff at the clinic enjoys meeting the children who have been conceived at the clinic, but this is a different matter.

Part 5: Lifestyle

It is far from all lifestyle factors that have been scientifically studied adequately, and it may be very difficult to carry out such studies. However, a number of extensive studies have been published, some of them Danish and our recommendations are based on them.

Vitamins and folic acid:

Take a vitamin tablet daily. Folic acid reduces the risk of having a baby with neural tube defects.
We recommend: That the woman take 0.4 mg of folic acid daily from three months before treatment and during her pregnancy. In case the woman has had a child with neural tube defect or is taking medication against epilepsy, 5 mg folic acid might be recommended. Please, consult your GP.

Medication:

Our knowledge about the influence of medications on the developing foetus is very limited.
We recommend: That the woman reduces her intake of medication during the stimulation and pregnancy to a minimum. If you are to take daily medication, please, consult your doctor *before* you become pregnant and ask whether you should change your prescribed medicine. We cannot recommend naturopathic medications, since their influence on the foetus is mostly unknown. If you need pain killers, we recommend paracetamol. Pain killers belonging to the group of non-steroid anti-inflammatory drugs should be omitted during stimulation and the second half of pregnancy.

Smoking:

Fertility is generally reduced if the *woman* smokes. This means that you can become pregnant, but it will take longer. We all know women smokers who have become pregnant. However, this does not change the fact that they may not have had any fertility problems, and thus not a limited amount of attempts as you have. In addition, it is a lot more fun to get pregnant naturally than having treatments at the fertility clinic. The risk of pregnancy outside of the uterus is increased for women smokers, also in connection with IVF treatment. The combination of advanced age and smoking clearly reduces the chances of pregnancy.

If you become pregnant, the chances of having a normal pregnancy ending in the birth of a healthy child are higher if you quit smoking. In addition, the child has a lower risk of developing asthma, allergy etc. if it lives in a smoke-free environment.
Whether or not your *male partner* smokes is of less importance for your fertility, provided that his sperm quality is normal. In case his semen quality is reduced, tar and cadmium in the smoke affect the DNA quality of the sperm cells. For the above reasons, the male partner should also quit, particularly also to show solidarity to you. Experience shows that it is difficult to quit smoking if the other party continues.
We recommend: There are many good reasons for us to **strongly recommend everyone to quit** smoking before and during treatment.

Alcohol:

Experts do not agree on the impact of alcohol consumption on fertility. It has not previously been possible to demonstrate that consumption of less than five units a week has a negative effect. However, a recent Danish study called this into question and demonstrated that even small amounts of alcohol reduce the chances of pregnancy.
If a woman consumes 1-10 units a week, the chances of pregnancy are reduced by 30-40 per cent. If she drinks more than fifteen units a week, the chances of pregnancy are reduced to a third relative to a woman who does not drink alcohol. Alcohol is a poinson for cells and affects foetal development during pregnancy.
We recommend: The woman should not get drunk, which means that she should not drink the week's entire ration on Saturday night. She should preferably refrain from drinking and not drink more than a couple of units a week. This means that you are allowed to have a couple of drinks at a party.

Coffee:

Your fertility will be affected if you drink more than three cups of strong coffee each day.

Weight:

The body mass index (BMI) is used as a measure of your weight in relation to your height (kg/m^2). A BMI of 18.5-24.9 is classed as normal. A BMI of 25-29.9 is classed as overweight. If your BMI is above 30, you are classed as obese, and we prefer not to start treatment before you have lost weight.

- Examples:
- Height 1.70 m, weight 58 kg: BMI 20
- Height 1.70 m, weight 72 kg: BMI 25
- Height 1.70 m, weight 87 kg: BMI 30
- Height 1.70 m, weight 101 kg: BMI 35

A lot of overweight women have reduced fertility due to the influence of the fatty tissue and disruptions to the hormonal system. Many obese women have no or very rare menstrual periods and do thus not ovulate normally. Of course, this means that the woman does not become pregnant. Often, she will have what we call polycystic ovaries (PCO), which we will not describe in detail here.
It may help the woman to know that her weight may be the cause of her PCO; however, the vicious circle should be broken. If obese women become pregnant, they have:

- A higher risk of **abortion**.
- A higher risk of developing **diabetes during pregnancy**.
- A higher risk of having a **complicated birth**.
- During the fertility treatment, an obese woman must be given **more hormones** (and they are expensive), and egg collection is often much more difficult. The reason for this is that the woman has a lot of fat on her intestines, which makes it difficult to see the ovaries and is sometimes in the way.

Consequently, obese women have a smaller chance of having a living, healthy child. To us, it is not just about getting the woman pregnant, but also about her having a living, healthy baby.

We recommend: That women with a BMI over 30 lose at least five to ten per cent of their weight. They should preferably reach a BMI below 30. This will often trigger ovulation and provide a better chance of good hormone stimulation with an adequate number of eggs. If you are extremely obese, you must lose more than ten per cent. Our nurses are happy to counsel you. Some will benefit from more exercise, using a gym, Weight Watchers, consulting their GP or joining a group.

Hormone disturbing substances:

New research results indicate, that many additives contained in cosmetics, hair dyes, plastic goods etc. demonstrate hormone disturbing effects that might affect the foetus, especially the developing testicles. The effect is most pronounced within the first 3 months of pregnancy.
We recommend: Be careful and do not use unnecessary cosmetics. Read the declaration of contents and ask your pharmacy.

Working environment:

Most workplaces, including staggered working hours, seem not to influence on your chance of becoming pregnant. However, you should omit any contact with organic solvents, toxic substances or radioactive substances during pregnancy.
We recommend: Talk to your employer or physician before you become pregnant and examine whether your should be given other tasks during your pregnancy.

Exercise:

Generally, exercise is a good thing – also for your general health.
We recommend: That women continue doing the exercise they are used to doing. It is good to walk a lot, run (if you are used to it), swim, ride or go to the gym. However, it may be that we recommend that you take it easy for a few days after egg collection. Women who are used to intensive exercise might benefit from reducing the load.
We are all different, and the need for exercise may thus vary from woman to woman. Pregnancy and birth and the subsequent weight loss will be a lot easier if you are fit.

Especially for the man:

Sweeteners, hot baths, sauna, close-fitting pants and heat in your car seat impairs semen quality.

Links to websites

Infertility treatment	www.ivf.com
International Council on Infertility	www.inciid.org
NetDoctor	www.netdoctor.co.uk
Fertility treatments (sponsored by Serono)	www.fertilitylifelines.com

Who will you meet at the clinic?

Doctors:

Specialist	Hans Krog	hans@danfert.dk
Specialist	Ursula Bentin-Ley	ursula@danfert.dk

On the telephone and in reception:

Secretary	Birgit Bøwig	birgit@danfert.dk
Secretary	Susanne Engel	

On the telephone and as therapists:

Nurse	Mie Varming
Nurse	Kirsten Funder
Nurse	Christine von Müllen
Nurse	Jeanette Crone

At your egg collection procedure and embryo transfer:

Embryologist	Susanne van der Jagt
Embryologist	Merete Kristensen
Embryologist	Dorthe Brynningsen

Head of the laboratory:

MSc. PhD	Thomas Høst

Permanent substitutes:
Doctors: Lars Franch Andersen, Anne Lis Mikkelsen, Stine Fürst
Nurses: Dorthe Lundmark, Malene Røpke-Gleerup, Birgit Olkjær, Line Dessing
Embryologists: Anette Sellmer Lorentsen, Louise Greisen, Tina Christensen, Stine Ravn, Birgitte Lindsey

Research

The Danish Fertility Clinic is a private fertility clinic, and we participate in research and development as well as quality control to ensure that our treatments are optimal and continuously improved.

- Naturally, projects are continuously changing.
- A lot of the projects are carried out in cooperation with other Danish clinics, as this is one of our strengths in Denmark,
- or in cooperation with selected clinics, depending on the subject.

Before participating in a project, you will be asked specifically whether you wish to participate. No one will take part in a project without being given detailed information, and you are free to opt out of a project at any time.

Your participation in a project will not affect your treatment as your best interests will always be considered.

We hope that you will be open to participating in one of our projects.

Summary – *long* protocol – IVF/ICSI

Cycle day 1: You will call us to register for treatment on +45 38 34 90 30 during the clinic's telephone hours: Monday to Friday 9 am. to 12 or 1 to 3 pm.
You will speak to the secretary who will make an appointment for your first scan.
If you have planned to have the ultrasound scans in your home-country, please, send an email to one of the doctors in order to plan the next steps.

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Cycle days 18-21: Scanning performed by a doctor, treatment plan and commencement of down regulation with ***Synarel*** or ***Suprefact or Profact.***
Instructions provided by a nurse in house or doctor by e-mail.

↓

Cycle days 28-35: 90 per cent will get their menstrual period. If you do not, please call or e-mail us the day before your scheduled scan on day 35.

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FSH day 1: Scanning performed by a doctor and commencement of stimulation using ***Puregon***, ***Gonal-F*** or ***Menopur***, if everything is in order. This day is the first stimulation day (FSH day 1). Instructions provided by a nurse in the clinic or doctor by e-mail.

↓

FSH day 6: Scanning performed by a doctor and adjustment of hormone dosage, if necessary.
Instructions provided by a nurse in the clinic or doctor by e-mail.

↓

FSH days 9-14: Scanning performed by a doctor, scheduling of date for egg collection, planning of ovulation-triggering drug hCG in the form of ***Ovitrelle*** or ***Pregnyl*** at 9-10 pm.
Instructions provided by a nurse regarding the sperm sample or by doctor by e-mail. Discontinuation of all other medication following hCG.

↓

Egg collection: You will come in at the appointed time and bring a sperm sample (or deliver one at the clinic).
Remember to take paracetamol one hour before coming in. A nurse will insert a venflon.
An embryologist will ask for your name and birthday.
The doctor will carry out the egg collection procedure.
Rest for about 30 minutes. You will be attended by a nurse who will send you home.

↓

Embryo transfer: Two days later from 10 am.
Requires only a **full bladder** (do not use the toilet).
An embryologist will inform you of the quality of your embryos.
You will agree with the doctor on the number of embryos to be transferred.
Commencement of ***Progestan/Utrogest/Crinone*** treatment.
You will be instructed on how to inject ***Pregnyl*** 2500 IU, if required.

Day 14 after embryo transfer:

Pregnancy test in the form of a blood test taken in the morning.
Result over the telephone on the same day.

Positive: Appointment for pregnancy scan about three weeks later.

Negative: May start new treatment when the next menstrual period begins. If required, a brief telephone or e-mail consultation with a doctor with a view to setting up a new treatment plan.
Patients from abroad are requested to send us the information regarding the pregnancy test and ultrasound scan by e-mail.

Summary – *short* protocol – IVF/ICSI

Cycle day 1: You will call us to register for treatment on +45 38 34 90 30 during the clinic's telephone hours: Monday to Friday 9-12 or 1-3 pm.
You will speak to the secretary who will give you an appointment for your first check-up on cycle day 2 or 3.
Often, you will be pre-treated with contraceptive pills for 3-4 weeks or Oestradiol tablets from cycle day 23.

If you have planned to have the ultrasound scans in your home-country, please, send an email to one of the doctors in order to plan the next steps according to the treatment plan we have sent to you ahead of start of treatment.

Cycle days 2-3: FSH day 1:

Scanning performed by a doctor, treatment plan and commencement of stimulation using ***Puregon***, ***Gonal-F*** or ***Menopur***, if everything is in order.
Instructions provided by a nurse in the clinic or doctor by e-mail.

FSH day 6: Scanning performed by a doctor after five stimulation days. Adjustment of dosage. From FSH day 5 or 6, it is time to begin injecting a hormone that prevents ovulation (***Cetrotide*** or ***Orgalutran***). You are to inject yourself **with tow medications** every evening for the next 3-5 days. Instructions provided by a nurse in the clinic or doctor by e-mail.

FSH day 9-12: Scanning performed by a doctor and adjustment of hormone dosage, if necessary. Usually, scheduling of the day for the ovulation-triggering drug hCG in the form of ***Ovitrelle*** or ***Pregnyl*** at 9-10 pm. Instructions provided by a nurse regarding the sperm sample or doctor by e-mail.
Discontinuation of all other medication following the hCG injection.

Egg collection: You will arrive at the clinic at the agreed time and bring a sperm sample (or deliver one at the clinic).
Remember to take paracetamol one hour before arriving at the clinic. A nurse will insert a venflon.
An embryologist will ask for your name and birthday.
A doctor will perform the egg collection procedure.

Rest for 30 minutes. You will be attended by a nurse who will send you home.

↓

Embryo transfer: Two days later from 10 am.
Requires only a **full bladder** (do not use the toilet).
An embryologist will inform you of the quality of your embryos.
You will agree with the doctor on the number of embryos to be transferred.
Commencement of ***Progestan/Utrogest/Crinone*** treatment.
You will be instructed on how to inject ***Pregnyl*** 2500 IU, if required.

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Day 14 after embryo transfer:
Pregnancy test in the form of a blood test taken in the morning.
Result over the telephone on the same day.

Positive: Appointment for pregnancy scan about three weeks later.

Negative: May start new treatment when the next menstrual period begins. If required, a brief telephone or e-mail consultation with a doctor with a view to setting up a new treatment plan.
Patients from abroad are requested to send us the information regarding the pregnancy test and ultrasound scan by e-mail.