



# **Treatment for infertility**

**Regionshospitalet** Skive *Fertilitetsklinikken* 



### WELCOME TO THE FERTILITY CLINIC

We look forward to meeting you for your first examination at our clinic. The Fertility Clinic at Skive Regional Hospital is a public clinic, subject to the legislation governing free choice of hospital. As a result, we receive patients from all over the country. We offer all kinds of modern fertility treatment and have no waiting list. We focus on the treatment of the individual patient and have experienced staff to take care of you. Research and development is central to the clinic, and our results have for many years been among the best, both nationally and internationally.

### Personnel

Consultant, Medical Director, M.D. Helle Olesen Elbæk and Laboratory Director, MSc. Betina Boel Povlsen are responsible for the day-to-day management of the clinic. Doctors, nurses, biomedical laboratory scientists, medical secretaries, cleaners and service personnel make up the remaining staff.

We offer professional treatment in a safe, inviting environment. It is important to us that your fertility treatment is a personal experience that you can look back on with joy.

### **Contact doctor**

Your contact doctor will usually be the doctor you meet at your first examination. Your contact doctor is the doctor responsible for the planning of your treatment, but not necessarily the doctor you will see for every examination at the clinic.

The Medical Director has overall responsibility for all patients.

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### **GENERAL INFORMATION**

Telephone contact with the Fertility Clinic

	Telephone no.	Telephone hours
The secretariat	7844 5760	08.00 – 10.00 10.30 – 12.30 13.00 – 14.30
The laboratory	7844 5768	09.15 – 09.45
Nurses	7844 5770	13.00 – 15.00 13.00 – 14.30 Friday 10.30 – 11.00 Saturday
Fax no.	7844 5765	

We recommend that you store the phone numbers on your mobile phones, as it will make it easier for you to contact us.

Website:www.fertiliThe Fertility Clinic's e-mail address:fertilitetskli

www.fertilitetsklinikkenskive.dk fertilitetsklinikken@midt.rm.dk

Please be aware when e-mailing us that, for reasons of security, we are unable to reply to emails containing personal information. E-mails should therefore be used for general enquiries only.

Please notify us if you change address, e-mail address, telephone number or physician.

### **BEFORE YOU START TREATMENT**

### Hepatitis, HIV, chlamydia, etc.

Before the actual treatment can begin, all test results must be available and approved. It is extremely important that you take responsibility for this, also if renewed tests are required later in the process.

If any test results are missing, the Fertility Clinic will obtain them. If you cannot accept this, please let the clinic know as soon as possible.

Fertility clinics are also required to demand testing for HIV and hepatitis (Hepatitis B and Hepatitis C) for both men and women.

### The woman

You must be tested for chlamydia because fertility treatment can worsen and, in the worst case, spread the infection.

The result of a smear test (routine testing for cervical cancer) must be available. Hormone blood tests are used to plan hormone treatment tailored to you specifically.

You must also have a blood test done to determine whether you are immune to German measles (rubella). This is because rubella during pregnancy can cause severe abnormalities or disability in the foetus. If you are not immune to rubella, and have not previously been vaccinated against this, you should be vaccinated by your physician. You must wait one month after vaccination before becoming pregnant. We also screen for metabolic disease and vitamin D deficiency.

### **HPV vaccination**

We recommend that you follow a planned vaccination programme. In the event of pregnancy, any outstanding vaccinations will be postponed. In other words, you do not need to start from the beginning again in the event of an interruption.

It is OK to become pregnant immediately after a vaccination.

With other types of vaccination: Talk to the staff.

If you work with children or have close contact with young children, it may be necessary to have additional blood tests done to determine whether you have formed antibodies against slapped cheek disease (parvovirus), for example.

If you have a cat/close contact with cats, it is a good idea to talk to your physician about toxoplasmosis.

### **First examination**

It is important that you both attend the first examination, which takes about an hour.

The first examination consists of a consultation with a doctor where your health and your chances of becoming pregnant will be discussed.

This brochure is given to you at the first examination, and we ask that you read it through carefully before starting treatment.

#### The woman

An ultrasound scan will be performed of your uterus and ovaries to examine your ovarian reserve. Even if you are fit and healthy and have regular periods, you may have a benign disorder such as a cyst on the ovary or a polyp, which is a small growth inside the uterus. You may also have fibroids (benign tumours from smooth muscle tissue), which can sit unfavourably in the uterus without you noticing it.

#### The man

You may be required to submit a semen sample in connection with the preliminary examination. In the event of significantly reduced semen quality, this may be supplemented with blood tests/chromosome analysis and scanning of the testes.

#### Consent

If you do not wish to give your consent to send letters to the referring physician about the treatment here at the clinic, please let us know about this as soon as possible.

By consenting to treatment at the clinic, you also consent to the use of semen samples and unusable unfertilised eggs or embryos for training of the staff at the Fertility Clinic before the destruction of these.

### Water scan/Fallopian tube examination (HSU)

The water scan is used to clarify whether there are any blockages in your fallopian tubes and to identify polyps or anything else that could impede pregnancy.

A condition for the examination is a negative chlamydia test.

Without this result, we will be unable to perform the examination, delaying treatment until the result is available.

After the first examination you will be informed about which treatments we can offer. In most cases, you can start treatment after an appointment with a nurse.

### **Treatment start**

You will have an appointment with a nurse where we go through the different stages and risks of the treatment. We will inform you about our current results and instruct you in injection technique.

#### Your rights and responsibilities as a patient

If you would like to read more about "rights and responsibilities as a patient", please consult the hospital's website.

### **READY FOR TREATMENT**

### The term "cycle day"

When you are ready for treatment, you can call the clinic at the start of your period to obtain treatment dates. In this information material – and when we speak with you from now on – we will use the terms: "cycle day no. xx" or "day xx of your cycle". The first day of your cycle is the first day of your period, if your bleeding starts in the morning.

If you experience slight spotting a few days before your period really starts, these days do not count. If your cycle is controlled by the contraceptive pill, please let us know the day you take the first pill when you call.

### The contraceptive pill

If you experience irregular bleeding, we often recommend regulating your menstrual cycle with a low-dose contraceptive pill.

#### Side-effects

Side-effects of low-dose contraceptive pills are rare, but headaches, nausea, breast tenderness and spotting may occur.

### **IUI TREATMENT**

Intrauterine insemination (IUI) is one of the simplest forms of infertility treatment. For insemination to be a viable treatment option, the woman's fallopian tubes must be unblocked and the man's semen quality must be satisfactory. Hormone stimulation and insemination are used as ways of trying to improve the following conditions:

- To mature and release 1–3 eggs.
- To filter and select normal, motile sperm.
- To introduce sperm into the uterus.

Approximately 30–40% have a baby after 1–3 IUI treatment cycles. If this treatment does not work, usually we will proceed with in vitro fertilisation (IVF), if you wish to continue treatment.

### Who is offered IUI treatment?

- Couples where the man has a normal/slightly reduced semen quality and the woman has normal fallopian tube function.
- Single women with normal fallopian tube function.
- Lesbian couples where the woman being treated has normal fallopian tube function.

### **Registering for IUI**

On the first day of your period after having attended the kick-off meeting, please fill in the online-form with CPR number, date of the start of your period, and that you are due to have insemination treatment. For further information on starting treatment, please call the nurses at the clinic:

### Registration weekdays + Saturday

The registrations are checked on weekdays before 9.00. You will receive a letter in your eboks or an email regarding the treatment. If you have any questions regarding the treatment, you can contact the nurses during their telephone hours on: Tel.: 7844 5770 from 13.00 – 15.00, *Fridays until 14.30 only.* 

### **Registration Saturday**

If your period starts on a Saturday morning, you will not receive a letter in your e-boks or an email until Monday.

In rare cases, during holiday periods for example, it may be necessary to delay some treatments by one month.

### Insemination

We try to make the insemination process as relaxed and as comfortable as possible. The washed sperm are passed through your cervix by means of a thin catheter. Insemination is usually painless and takes 5–10 minutes.

### After insemination

After insemination, you can go about your daily business. Movement increases blood flow to all organs, including the uterus. You will not increase your chances of becoming pregnant by lying on the sofa for the next two weeks. However, we advise against horse riding, team sports and extreme sports.

### Side-effects of hormone treatment

Usually none. Some women may experience side-effects such as mood swings, nausea, hot flushes, breast tenderness and, on rare occasions, blurred vision. These side effects, however, will all pass.

### **Undesired effects**

A few patients (5–10%) react strongly to treatment and produce more than 3–4 follicles. This leads to a high risk of triplets. In these cases, insemination may be cancelled. It is also possible to aspirate the excess follicles with a thin needle under ultrasonographic guidance. Ultimately, you can switch to IVF treatment.

There is a small chance of twins (less than 3%) – and even lower for triplets – after IUI.

### Sex after insemination

It is perfectly OK, and sex increases blood circulation.

### **Pregnancy test**

The time you have to wait until you can take a pregnancy test may seem like an eternity, and it is natural to alternate between feeling negative and feeling positive.

The pregnancy test is taken at home, 17 days after insemination, and it is your responsibility to notify us of the result. After this, please contact the nurses to plan the next step.

### **Positive pregnancy test**

We look forward to being able to congratulate you.

We offer a pregnancy scan in the 7th–8th week of pregnancy, approximately five weeks after insemination. The scan shows the number of foetuses and their location. It is also possible to see whether the size corresponds to the length of the pregnancy, and if a heart beat can be detected.

Next you should contact your physician to make sure you are followed with scans and visits to the midwife until delivery.

There is always a risk that the pregnancy will not result in a birth. Around 20% of women with a positive pregnancy test result will go on to miscarry (the same risk as for spontaneous pregnancies).

### **Negative pregnancy test**

The clinic should be contacted with the result of the pregnancy test. Further treatment is agreed individually at the time of the insemination.

### **IVF TREATMENT**

### In vitro fertilisation

IVF is commonly known as test tube fertilisation. Mature eggs are retrieved from the ovaries and fertilised with sperm outside the body. Embryos which have begun to divide are then transferred to the uterus.

### Who is offered IVF treatment?

Couples with a medical reason to use IVF:

- The woman's fallopian tubes are blocked or not functioning
- PCO/PCOS (see "Specific factors affecting your chances of becoming pregnant")
- Endometriosis (see "Specific factors affecting your chances of becoming pregnant")
- Low semen quality and previous sterilisation
- Unexplained infertility
- Single women
- Lesbian couples

### How is IVF treatment carried out?

The IVF treatment is divided into seven stages:

- Pretreatment (down-regulation)
- Hormone stimulation
- Egg retrieval
- Semen sample
- Fertilisation in glass (In Vitro period)
- Embryo transfer
- Hormone treatment and pregnancy test

### **Stimulation methods**

IVF treatment is generally divided into two methods of stimulation:

- Long protocol Down-regulation and subsequent hormone stimulation
- Short Protocol Hormone Stimulation

We offer a variety of medical treatments, and these are always planned individually.

### **Registering for IVF**

On the first day of your period after having attended the kick-off meeting, please fill in the online-form with CPR-number, date of the start of your period and that you are due to have IVF-treatment. If you need prescriptions remember to write the name of the preparation. The registrations are checked weekdays before 9 o'clock in the morning. Registrations received after this time will be checked the following day. You will receive a letter in your e-boks or an email regarding your treatment.

### Short protocol

After sending an email about the start of your period to <u>ivftilmeldingskive@midt.rm.dk</u> you will receive a letter in your e-boks or an email regarding the treatment.

If your period during the weekend you only get a letter in your e-boks Saturdays if you must come to a scan Monday. Mails received after 9 o'clock Saturday will not be read until Monday, if you need to come for a scan Monday you will be contacted by phone.

In rare cases, during holiday periods for example, it may be necessary to delay some treatments by one month.

The short protocol consists exclusively of a hormone stimulation which lasts 12-14 days and starts at the 2<sup>nd</sup> og 3<sup>rd</sup> day on your period. You will not be starting your treatment until you have a control-scan at the clinic.

On the 2nd or 3rd attempt (short protocol), you should contact the clinic to make an appointment with a nurse at least two weeks before your period is due where you will be informed about the treatment.

### Long protocol

After sending an email about the start of your period to <u>ivftilmeldingskive@midt.rm.dk</u> you will receive a letter or an email within a week outlining the treatment plan.

### Pretreatment

Pretreatment consists of Suprefact injections, which the woman should start on around day 21 of her cycle. We will let you know the date. Suprefact contains a hormone that blocks your own production of sex hormones, preventing spontaneous ovulation. So it is important to continue with Suprefact alongside the hormone stimulation.

The blocking of your own sex hormones with Suprefact may cause temporary side effects such as hot flushes, headaches, fatigue and dry mucous membranes. Some women may find that they are more irritable during treatment.

### **Hormone stimulation**

The next step of the treatment is hormone stimulation to stimulate your ovaries to produce eggs. To increase your chances of pregnancy, we aim to retrieve more than the one egg, which is matured in a natural cycle. Hormone stimulation is individually tailored to you. When your treatment starts, we will decide which hormone stimulation to choose in your case and a personal treatment schedule will be given.

Before starting the hormone stimulation, you will be given an ultrasound scan at the clinic to ensure that everything is in order to start stimulation. While undergoing hormone stimulation,

you will be closely monitored by ultrasound to check the development of eggs and to determine the right time for egg retrieval. A nurse will talk to you after each scan.

In most cases, the eggs are retrieved 10 to 16 days after initiation of hormone stimulation. You will be told the exact time of retrieval two to three days ahead.

In rare cases, follicular growth may be unsatisfactory, and the treatment may have to be dropped that month. As a consequence of this, in the next cycle, the hormone dosage may be changed or an alternative pretreatment/hormone stimulation may be selected.

Hormone stimulation may cause fluid retention, which may manifest itself in a slight weight gain. In addition, you may experience bloating and abdominal tenderness/pain, which can cause frequent urination. You may notice an increase in vaginal discharge.

The injections may cause minor bruising, pain or redness at the injection sites. If this is severe, you should contact the clinic.

### **Ovulation trigger injection**

At the last scan before egg retrieval, you will be told the exact time of the injection to help the eggs mature.

### Egg retrieval

On the day of egg retrieval, both you and your partner should come to the clinic. Egg retrieval is performed on an ambulant basis and takes approximately 10 minutes.

Using ultrasound guidance, the eggs are aspirated with a thin needle being passed through the vaginal wall into the ovary and gently sucking the follicular fluid containing the egg out. This is done in both ovaries, until all follicles are empty. You can follow the entire process on a TV screen and see the eggs that are found.

During retrieval, you will be offered two types of pain relief, acupuncture or traditional painkillers. Acupuncture consists of seven needles, which stimulate the body's own production of endorphins (pain relieving hormones). Research shows acupuncture to be as effective at relieving pain as medicine. Whatever you choose, a needle is always placed in a vein and you will be given a local anaesthetic in the vagina.

It is natural to feel both excited and apprehensive before the first egg retrieval. You wonder how it will go. How many eggs will there be? Will it hurt? Is the semen quality good enough? We try to make the egg retrieval process as comfortable as possible.

Your partner is with you the whole time. The room is dimly lit with music playing, and we talk about the treatment along the way.

Most women are ready to go home about an hour after the procedure. Before you leave the clinic, a nurse will let you know how many eggs were retrieved, the semen quality (if applicable) and what happens from there.

### Complications

It is normal to experience slight bleeding and menstrual-like pain after egg retrieval. The pain will usually disappear if you take paracetamol (e.g. Pamol, Pinex or Panodil).

If you were given pain medication during the procedure, your reaction ability may be impaired, so you should not drive for the rest of the day. If you begin to feel unwell or feverish, experience severe pain or start bleeding so heavily that you feel uneasy on your return home, please contact the clinic or the Emergency Doctor Service outside the clinic's opening hours.

### The eggs can be fertilised in two ways:

### 1. IVF (In vitro fertilisation)

With IVF, washed sperm is introduced to the eggs. A single sperm finds its way into the egg. Just as it would in nature – only in a petri dish.

### 2. ICSI (Microinsemination)

If the semen quality is extremely poor, or previous attempts at fertilisation with IVF have failed, ICSI treatment will be offered. Here, a single sperm is introduced into the egg using a thin glass pipette.

For couples undergoing ICSI, the treatment process is much the same as for IVF. The difference consists in the laboratory work.

The clinic's approach is to offer ICSI to couples for whom this treatment is necessary and thus interfere with "nature" as little as possible.

The best embryos are selected for transfer, regardless of whether they are fertilised by ICSI or IVF. Your chances of becoming pregnant are the same with ICSI as they are with IVF treatment.

### Fertilisation – and what happens from there

On average, approximately eight eggs are retrieved from each patient. The eggs are stored in an incubator at the laboratory under optimal conditions.

The day after egg retrieval, it is possible to see if the eggs are fertilised. A fertilised egg (zygote) will have two nuclei. One nucleus comes from the woman's egg, the other comes from the man's sperm. The nuclei, which contain genetic material, have not yet merged, but

they will in a few hours. When the two nuclei merge, the fertilisation process is over and the egg can now start dividing.

The day after egg retrieval, you will be told by the laboratory whether fertilisation has occurred and where you go from there. However, sometimes, despite being fertilised, the zygote does not divide. And occasionally, the embryo stops developing. In such cases, the embryo is not transferred.

Around 60–70% of eggs are fertilised on average.

### Embryo transfer

The best embryo/s is/are selected for transfer.

We try to make the embryo transfer process as relaxed and as comfortable as possible.

The clinic follows the Danish Health and Medicines Authority's guidelines on the number of embryo that can be transferred back into the uterus. If the woman is under the age of 37 and the embryo is of top quality, only one embryo will be transferred at the first attempt. In any case, a maximum of two embryos are transferred.

Embryo transfer takes place 2–5 days after egg retrieval. Usually we will inform you of the date and time of transfer on the day itself. The embryos for transfer are selected by the laboratory on the basis of strict quality requirements.

Embryo transfer usually takes place without any discomfort. The embryo is transferred into the uterus through the cervical canal using a thin plastic catheter. We ask you to come to the clinic with a full bladder as this facilitates the process.

### **INFORMATION ON EMBRYO TRANSFER**

### Pain following embryo transfer

After embryo transfer, it is quite normal to feel discomfort in the lower abdomen in the form of a pressing sensation and bloating. This is partly because the ovaries are still stimulated, even though they are no longer producing eggs, and partly the effects of the egg retrieval. This discomfort should normally disappear after about two weeks. If you are unsure about anything, please feel free to contact the nurses at the Fertility Clinic.

### Aftercare

From the day after egg retrieval and in the period leading up to the pregnancy test, you will be treated with the hormone progesterone. This hormone stabilises the lining of the uterus, increasing your chances of getting pregnant.

Some women experience nausea, breast tenderness, bloating, headaches and water retention. This may be confused with pregnancy symptoms.

#### Implantation

The embryo attaches itself to the lining of the uterus approximately 5–7 days after fertilisation. It is located in a tightly sealed junction between the front and rear wall of the uterus, and cannot fall out.

#### **Sick leave**

It is not necessary to take sick leave after embryo transfer. Women who have had multiple eggs retrieved and are experiencing symptoms of ovarian hyperstimulation syndrome are advised to stay at home and take it easy for a few days.

#### Sex after embryo transfer

We recommend that you abstain from sex/orgasm for two weeks after embryo transfer to avoid uterine contractions.

### **Exercise and swimming**

Exercise increases the flow of blood to the uterus.

Recent studies suggest, however, that high intensity sport may increase the risk of miscarriage. We advise against running, ball sports, working out in the gym, racquet sports, horse riding and skiing.

The Danish Health and Medicines Authority recommends that you avoid lifting more than 10–15 kg at a time.

Do not swim or take a bath (only showers) until you have stopped progesterone treatment. We also refer to the Danish Health and Medicines Authority's recommendations.

### **Caffeine and alcohol**

See the section "What you can do yourself"

#### Painkillers

Studies have shown that there may be a link between the use of painkillers, such as empirin with codeine (Kodimagnyl), and anti-inflammatory drugs (NSAIDs), such as Ipren, Ibuprofen, Naprosyn, and the embryo's ability to implant in the lining of the uterus. We therefore advise against taking the above mentioned medicines in the period leading up to the pregnancy test, but it is OK to take paracetamol (e.g. Pamol, Pinex or Panodil) for a brief period.

#### Vitamins

From the time you start planning your pregnancy, you are recommended to take a supplement of the Vitamin: folic acid (folinsyre) (400 mg a day) The Vitamin may reduce the already low risk of having a child with spina bifida (spinal hernia). If you become pregnant, you should continue taking folic acid throughout the pregnancy.

Vegetarians and women with bowel disorders (e.g. ulcerative colitis) should supplement their diet with vitamin B12 throughout their pregnancy.

If you do not drink milk or eat dairy products, you should take a calcium supplement.

### **Iron supplement**

You need 40–50 mg a day from the 10th week of pregnancy. For better absorption, take the iron supplement between meals with fruit or vegetable juice or a citrus fruit. Iron is important because your need for it increases as the child grows. Iron is used in the formation of the child's red blood cells and affects the central nervous system.

### PREGNANCY TEST AND WHAT HAPPENS FROM THERE

The time you have to wait until you can take a pregnancy test may seem like an eternity, and it is natural to alternate between feeling negative and feeling positive.

The pregnancy test is taken as a blood test 14–16 days after egg retrieval. During holiday periods at the clinic, the test may have to be taken as a dipstick test 19 days after egg retrieval.

If you choose to have the blood test done here, you will be given the result the same day. If the blood test is done by your own physician, you will receive the result the following day. The result is given over the phone, and we urge you to plan where you are when you make the call. It may be difficult to be in an open office environment, for example, when you receive the result and need to react.

It is important to take the pregnancy test at the given time otherwise you may obtain a false result, positive or negative.

### Results

The results of IVF treatment have improved considerably in recent years. Generally speaking, 70–80% of couples have a baby within 1–3 completed treatment cycles. The treatment will result in twins in approximately 10% of the cases.

In very rare cases, the transfer of two embryos may result in triplets or quadruplets.

On a worldwide scale, millions of children have been born as a result of IVF treatment. Studies from several countries suggest that there is no increase in the number of abnormalities after IVF treatment.

### If positive

We look forward to being able to congratulate you. We offer you a pregnancy scan in 7th–8th week of pregnancy = approximately five weeks after embryo transfer. The scan shows whether the pregnancy is developing as it should, the number of foetuses and their location. It also shows whether the size of the foetus corresponds to the length of the pregnancy, and if a heart beat can be detected.

Your treatment with us ends with another scan at around the 11th week of pregnancy. You should by now have contacted your own doctor to make sure you are followed with scans and visits to the midwife until delivery.

There is always a risk that the pregnancy will not result in a birth. Around 20% of women with a positive pregnancy test result will go on to miscarry (the same risk as for spontaneous pregnancies).

### If negative

For every embryo transfer, there is approximately a 48% chance of a positive pregnancy test. This means the result will be negative in a lot of cases. A negative result is a psychological blow, and it is natural to feel disappointment, sadness and anger.

We encourage you to talk about it, and you are always welcome to contact the clinic for this purpose.

Little is known about why pregnancy does not occur every time an embryo is transferred to the uterus. There can be many reasons for this, e.g.:

- Chromosome abnormality is the main cause. Many embryos do not develop properly, even though they look perfectly normal under the microscope when they are transferred.
- The lining of the uterus is not receptive to the embryos.
- The woman's age is a major factor. Women in their early 20s are, for example, twice as likely to become pregnant per treatment cycle as women in their late 30s.
- The cause of infertility can play a role.
- Uterine fibroids considerably reduce a woman's chance of pregnancy. Women with blocked and dilated fallopian tubes, which are shown to be filled with fluid during the course of treatment, also have a reduced chance. If this is the case, it helps to have the fallopian tubes removed after an unsuccessful IVF attempt.

Following a negative pregnancy test, we review your treatment to determine whether anything can be done differently the next time, if you have more attempts left. The next step is arranged with the nurse.

### FREEZING OF EMBRYOS/UNFERTILISED EGGS

Around half of IVF treatments will result in the possibility of freezing embryos.

Under Danish law, excess embryos may be frozen for up to five years, though only until the woman reaches the age of 45. The freezing period may be extended if, during the five years, the woman develops a serious illness.

Eggs/embryos to be frozen must be of a high quality as the freezing process is hard on the eggs/embryos. In 80% of cases where the eggs/embryos are thawed, they can be transferred.

If you have frozen eggs/embryos, you are personally responsible for ensuring that they are used before the expiry date.

In order to plan treatment with frozen/thawed embryos, please contact us no later than three months before expiry of the freezing period.

### Information on the freezing of excess embryos

Frozen embryos can only be used in your own treatment. The embryos may only be thawed and used with the written consent of both parties each time they are to be thawed.

In the event of the death of the woman or the break-up of the relationship, the embryos will be destroyed. Embryos may be used to establish pregnancy after the death of the husband, if the couple has agreed to this in writing with the clinic.

Under Danish law, the embryos may be frozen for up to five years. If the embryos are not used before this, they will be destroyed without further notice from the clinic.

If the freezing period is amended by law, the following will apply:

If the freezing period is shortened, the frozen embryos will be destroyed accordingly.

If the freezing period is extended, the frozen embryos will be stored accordingly, though only until the woman reaches the age of 45, after which they will be destroyed without further notice.

### **TRANSFER OF THAWED EMBRYOS (FET)**

As a rule, we recommend the transfer of two embryos after freezing if there is nothing in the woman's medical history to argue against this.

Make sure that you have a normal smear test (max. 3 years old) and submitted a signed consent to thaw the embryos.

In connection with the freezing cycle, the lining of the uterus must be prepared in the most natural way to receive the thawed embryos.

### **Natural FET**

If your menstrual cycle is regular, no medication will be given, but you will be checked at 1–3 scans before embryo transfer is planned.

### **Stimulated FET**

If your menstrual cycle is irregular, hormone stimulation will be necessary (in tablet form), and later on in the process, progesterone treatment. Your doctor will evaluate what is best for you.

### Results

We have had some excellent results from transferring frozen embryos. You have approximately a 40% chance of pregnancy after the transfer of two thawed embryos.

### **SEMEN SAMPLE**

The man's contribution of a semen sample is an essential part of the treatment.

The sperm cells are formed 6–8 weeks before submission of the semen sample. There are certain things you can do to optimise the quality of the semen sample. Above all, you should try to avoid smoking because it lowers the count of normal sperm as it has an adverse effect on the genetic material.

We also recommend that you avoid exposing the testicles to heat, as heat may damage the sperm. Febrile illness may also have a negative impact on semen quality. Please inform the staff if you have had a temperature of more than 38°C at any time in the 6–8 weeks before treatment. It may be a good idea to bring the fever down with antipyretics in the form of over the counter painkillers.

Certain medicines can impair semen quality, so please let us know if you have to start taking any new medication during the course of treatment.

You will be asked to make a semen sample at the clinic, where it is subsequently washed to select the best sperm. In certain cases, you can bring the sample in with you from home.

It may seem straightforward to deliver a semen sample, but some men feel under pressure and have difficulty producing the sample. We will gladly talk with you about it.

### Retrieval of sperm from the epididymis (PESA) or testicle (TESA)

If there is no sperm in the semen sample, we can try to retrieve sperm from the epididymis or testicle.

Before retrieving sperm from the epididymis, a needle is inserted into a vein. This is in case you should need painkillers. You will also be given local anaesthetic, which is injected in a couple of places in the groin just above the scrotum. You are then anaesthetised, but you can still sense touch.

If it is possible to feel the epididymis (sometimes not possible if surgery has been performed there previously), we try to retrieve some small droplets of fluid, which often contain sperm.

If there is no sperm in the epididymis (PESA), we will try to extract sperm from the testicle itself (TESA). After the procedure, a loose bandage and an ice pack will be placed over the testicle.

You may feel some soreness in the testicle when the anaesthetic wears off. We recommend that you take it easy for the rest of the day (avoid heavy lifting, sport, etc.). Apart from this, there are no restrictions.

Over the counter painkillers should relieve any discomfort.

If you experience severe pain and severe swelling of the scrotum and/or a fever, please contact the clinic or the Emergency Doctor Service, if applicable.

At the last visit to the clinic before egg retrieval, you will be informed about the procedure, and you will have the opportunity to discuss the possible need for sedatives/painkillers. We should point out that you cannot drive for the rest of the day if you are given sedatives/painkillers.

If we are unable to find sperm, treatment with donor sperm may be an option. This will always be in agreement with you.

### Freezing and storage of semen

In special cases where the semen quality is very low, and in other special cases, it is possible to freeze and store semen.

A prerequisite for freezing semen is that your HIV and hepatitis tests must be no more than two years old.

The laboratory estimates how much of the frozen semen should be thawed before the treatment. In a few cases, there is no viable sperm after thawing.

If, at the end of the treatment with us, you wish to transfer the semen to another clinic/storage facility, please talk to us about it. We will guide you in how such a transfer takes place.

If you would like your partner to be able to use your semen in the event of your death, you must inform the clinic of this in writing.

You are responsible for ensuring that the address on your storage certificate is correct. Please notify the secretary of any changes. The address is used if the clinic wishes to terminate the storage.

The clinic will send a letter to the last address given regarding possible destruction. If we do not receive notification from you within three months of us writing to you that you would like to transfer the semen to another clinic or storage facility, it will be destroyed without further notice.

### Donor sperm

### Treatment with donor sperm

Treatment with donor sperm may be a solution to a couple's infertility if the man's semen quality is so low that the chances of achieving pregnancy are virtually zero.

There are also other reasons for using donor sperm, including serious hereditary diseases.

Furthermore, donor sperm is used in the treatment of lesbian couples and for artificial insemination of single women.

When you are considering using donor sperm, you may have many questions, such as: Should we be open about the use of a donor? When and how should we tell our child about its origins? Who is the father if we have a child?

We are more than happy to talk to you about your concerns. However, experience shows that once you have the baby, such concerns tend to disappear.

You have the option of choosing an anonymous or a non-anonymous donor. If you are to be treated with donor sperm, you will be given further information orally and in writing at the clinic.

### EGG DONATION

For some women, egg donation is the only way to achieve pregnancy.

Who can be helped with egg donation? Women:

- who have gone into early menopause.
- who for genetic reasons do not have functioning ovaries.
- who have had their ovaries removed due to infection, endometriosis or cancer.
- who have had poor embryo quality on several occasions.

Legislation requires that the partner of the woman receiving the donated eggs is the biological father.

You have the option of choosing an anonymous or a non-anonymous donor. If you require donor eggs, you will be given further information both orally and in writing at the clinic.

Who can donate eggs?

- Women who are themselves undergoing fertility treatment, and who would like to help others.
- Women who are not undergoing fertility treatment, but who approach the clinic.

If you would like to donate eggs, please contact the staff.

### WHAT YOU CAN DO YOURSELF

The biggest known risk factors are lifestyle factors such as smoking, alcohol, caffeine and being overweight.

Lifestyle-related problems are important because these are in fact the relatively few things you actively have an influence on to increase your chances of pregnancy.

The clinic offers help with lifestyle changes. If you require our help, please contact the clinic's secretary.

### SMOKING

We recommend that you give up smoking completely before starting treatment.

### Women

Studies show that smoking reduces fertility. It takes longer to become pregnant – in fact 50% longer than for non-smokers. Most women stop smoking once pregnant, but as the toxins from smoking also affect the eggs and early pregnancy, it is much better to stop smoking before treatment begins.

Smoking also has negative effects on the child, both before and after it is born.

Research suggests that women who smoke while pregnant have children who are themselves at a greater risk of impaired fertility in adulthood. The effect of this kind of passive smoking seems to correspond more or less to being a smoker. It also increases the risk of placental abruption (abruptio placentae), premature birth, low birth weight, sudden infant death syndrome, asthma and allergies.

### Men

Calculations from studies and population surveys suggest that infertility is twice as high in smokers as in non-smokers. This suggests that sperm production is impaired, and the genetic material in the sperm can be damaged by toxins from tobacco smoke.

To avoid this, you should stop smoking six weeks before the semen sample is to be used.

### ALCOHOL

We recommend that you follow the Danish Health and Medicines Authority's guidelines on alcohol.

### Women

Women with a high daily consumption of alcohol are known to have a greater risk of missing ovulation, irregular periods and impaired menstrual cycle after ovulation than women with lower consumption.

For women undergoing fertility treatment, there are relatively few studies regarding the impact of alcohol on the chances of pregnancy. A small weekly consumption does not seem to affect the results of insemination or in vitro fertilisation.

However, consumption of 1–2 drinks per day seems to increase the risk of miscarriage – in early pregnancy at any rate.

### Men

Men with a high daily consumption of alcohol are at increased risk of having small testes and reduced semen quality. Moderate alcohol intake does not appear to be detrimental to semen quality.

### CAFFEINE

### Women

Large amounts of caffeine reduce the chances of achieving pregnancy. Caffeine is a major ingredient in coffee, but is also found in tea, iced tea, cola, energy drinks, cocoa and dark chocolate. Drinking around five cups a day halves the chances of pregnancy and increases the risk of early miscarriage.

We therefore recommend that you stick to a maximum of 2–3 cups of coffee a day and avoid caffeinated drinks entirely for a few days after embryo transfer.

### Men

There is no evidence to suggest a link between caffeine and reduced semen quality.

### **BEING OVERWEIGHT**

Being overweight increases the risk of it taking a long time for you to get pregnant. Similarly, it increases the risk of miscarriage, high blood pressure, diabetes, pre-eclampsia and birth complications.

Our assessment of weight is based on WHO's definition, which uses BMI to classify weight categories:

BMI < 20	=	underweight
BMI 20 – 25	=	normal weight
BMI 25 – 29	=	overweight
BMI 29 – 35	=	obese
BMI > 35	=	morbidly obese

Our goal is that your BMI should not be higher than 29 at the start of treatment. In some cases, a higher BMI may be accepted – preceded by an agreed weight loss, usually around 10%. However, treatment will not be started at a BMI > 34.

### ALTERNATIVE TREATMENT

### Acupuncture

Many people wish to supplement their treatment with acupuncture or other alternative therapies.

This is entirely up to you. There is no scientific evidence that acupuncture increases the chances of pregnancy. However, acupuncture has been proven to increase blood flow to the uterus.

### **Dietary supplements**

If either of you take any supplements, we recommend that you bring them with you to the clinic for evaluation in relation to treatment.

### THE EMOTIONAL ASPECTS

For many people, trying to get pregnant is perceived as a special time filled with wishes, hopes and dreams. But however fit and healthy you are, there is no guarantee of pregnancy after the first treatment cycle.

Some people may find it helpful to talk to others about it.

Acknowledge your feelings, but try also to be open to other exciting things in life besides your menstrual cycle, ovulation, hormones and waiting time.

The staff at the Fertility Clinic always strive to be there for you if you need a chat. It is an important part of the treatment, so please let us know if you do.

### **RISKS ASSOCIATED WITH THE TREATMENT**

### Hormone treatment

There is no evidence that hormone treatment increases the risk of ovarian cancer or breast cancer.

### Egg retrieval

There is a very small chance of bleeding or infection around the ovaries after egg retrieval. The risk is less than 0.1%.

### **Ovarian hyperstimulation syndrome**

If you have many eggs/follicles, there is a small risk of developing ovarian hyperstimulation syndrome in connection with egg retrieval. Around 1% of women require treatment. It is a transient condition that can usually be treated on an ambulant basis.

It usually manifests itself 5–10 days after the ovulation trigger injection. Symptoms include severe bloating, discomfort, possible pain, nausea, vomiting and/or diarrhoea.

Most hyperstimulation is mild to moderate and is harmless despite the discomfort experienced by the woman.

If you experience symptoms, please call the Fertility Clinic.

Outside the clinic's opening hours, please contact the Emergency Doctor Service.

### SPECIFIC FACTORS AFFECTING YOUR CHANCES OF BECOMING PREGNANT

### Age

Women's eggs are affected by age. Unlike men, who produce new sperm all the time, women's eggs are formed before they are born. For women, fertility is relatively constant up until the age of around 30, when a drop in their natural fertility occurs.

This decline in fertility as you get older is due, among other things, to the fact that a woman has fewer and fewer eggs left, the older she gets. In addition, older women have more chromosomal abnormalities in their eggs than younger women.

So the chances of pregnancy by artificial insemination also decrease with age.

### PCOS – Polycystic ovary syndrome

Up to 20–30% of all women suffer from PCOS, with an increased tendency in women who are overweight.

The symptoms of PCOS are irregular periods, lack of ovulation, hormonal imbalances, excessive hair growth and acne.

If you belong to the group of overweight PCOS patients, it is important to lose weight. In some cases, this can lead to a normalisation of the symptoms.

Please also refer to www.pcoinfo.dk.

### Endometriosis

Endometriosis is a painful, chronic condition affecting 4–7% of all women. The condition occurs when tissue similar to the uterine lining is found outside the uterus.

Endometrial tissue reacts in the same way as the uterine lining, i.e. the tissue grows with the lining, but unlike menstrual blood, bleeding from the endometriosis cannot escape. Instead, it bleeds into the abdominal cavity, where an infection-like condition may occur and adhesions and scar tissue may form.

Please also refer to www.endometrioseforeningen.dk.

### **GENERAL QUESTIONS**

### What is AHA?

In Assisted Hatching (AHA), a small hole is made in the outer protein coating (zona pellucida) of the embryo before it is transferred to the woman's uterus to help the egg to hatch. In most cases, embryos hatch by themselves, so Assisted Hatching is only relevant for a few women. Assisted Hatching is suggested if:

- two seemingly perfect IVF/ICSI treatment cycles have not resulted in pregnancy.
- the woman is of a high maternal age.
- the embryo has a thick zona pellucida.

The results of this method are good, but experience is limited in a scientific context. The method is part of the clinic's standard procedure, but it is only carried out in the above cases.

### What is a biochemical pregnancy?

A biochemical pregnancy is when a blood test has detected an increase in the pregnancy hormone, without it leading to a visible pregnancy.

### How long does the fertility treatment take?

#### Preliminary examination:

The consultation takes approximately an hour. If a semen sample is to be examined, this should be submitted 1–2 hours before the consultation.

The kick-off meeting for IVF takes approximately 2.5 hours, and for IUI about an hour.

### Start of treatment:

The consultation takes around 30 minutes.

### Ultrasound scan:

The number of scans you will be given during your treatment varies according to your individual needs. The scan itself takes 5–10 minutes, followed by a brief chat with the nurse. You will be given an appointment for the scan from one time to the next, and often with just a few days in between during hormone stimulation.

### Egg retrieval:

The woman should take the whole day off work and should not be alone.

### Embryo transfer:

The consultation takes around 15 minutes.

The time specified indicates the time needed for the procedure, but some days we are very busy, and there may be a waiting time.

We ask for your understanding and that you allow for this when calculating how long you will be here.

### Section 56 (The Danish Act on Sickness Benefits)

An agreement which allows you to claim for sickness benefits during absence for fertility treatment, if the condition is likely to cause at least 10 sick days in one year. The agreement only applies to the party with the chronic illness (it does not apply to the man, for example, if the infertility is due solely to chronic illness in the woman). The agreement applies for a maximum of two years at a time. Please contact your physician or municipality about this. Refer to the website of your municipality.

### Who can we contact in the event of problems?

On weekdays, you are always welcome to call the Fertility Clinic directly during telephone hours. In the event of acute problems during the day, please contact the Fertility Clinic on 7844 5770/7844 5760.

Outside normal working hours, please contact the nearest Emergency Doctor Service.

Always remember to bring your treatment folder with you.

### How many times can you undergo treatment?

At public IVF clinics, three cycles of treatment with embryo transfer are offered as standard. Additionally, the transfer of any frozen/thawed embryos. However, you are not guaranteed to receive three complete cycles. The treatment may be stopped if the doctors feel that it is futile. When a treatment cycle leads to pregnancy and the birth of one or more children, the treatment comes to an end. However, it is possible to have frozen, thawed embryo transferred in the future, even if you have had a child by previous treatment.

### Security

The Fertility Clinic attaches great importance to security. A number of measures are taken to ensure that biological material cannot be mixed up. All biological material such as eggs and sperm are labelled with your name and CPR number. In addition to this, each couple has a colour code, which helps to ensure that the material is not mixed up. At egg retrieval and embryo transfer, your identity will be checked by name, CPR number and photo in the medical record. This way, you can be absolutely sure that the embryos belong to you.

### **Change of address**

If you move, please notify the clinic immediately so we can adjust your address where necessary.

Please be aware that if you move abroad, you will have to pay in advance for the full course of treatment.

### Mileage allowance

For further information on the conditions for payment of mileage allowance, please refer to the clinic's website. If you do not live in Central Jutland Region, please call your nearest hospital and ask if you are entitled to mileage allowance. Ask the secretary for a form for this if you believe you are entitled.

### Free choice of hospital

Fertility treatment is covered by the Danish act on free choice of hospital. This means that, as a patient, you are free to choose from the public fertility clinics in Denmark.

### Copy of your medical record at the Fertility Clinic

All patients under the Danish health service have access to their medical records at www.sundhed.dk. If you would like a copy of your medical record, you can find it here. Log in using your Nem-ID and select the "Min e-journal" link, which shows you the various treatments you have received at public hospitals.

### If the treatment is unsuccessful

We recommend that you consider early on what you will do if the treatment does not produce the desired result. It is always best to be prepared for this situation, and we believe it can help you, even during your treatment. Such considerations might be:

- to continue treatment at a private clinic.
- to apply for adoption.
- to choose a life without children.

If you find yourselves in one of the above situations, we offer a final meeting with your contact doctor at the clinic.

## The National Association for the Involuntarily Childless (Landsforeningen for Ufrivillige Barnløse)

'The National Association for the Involuntarily Childless' (LFUB) was founded in 1990. The association has a number of different functions. It gives advice and guidance to couples who have problems; it publishes a magazine, and it works for better treatment options for the childless.

Names and addresses of contacts are available from us. The membership magazine "Kimen" can be found in our waiting room – website: www.lfub.dk.

### RESEARCH

Since the birth of the world's first test tube baby in 1978, a great deal of work has been done to improve IVF methods, with a view to offering even more reliable treatment and to improve results.

Intensive research is still conducted in the field, both internationally and nationally, also at the Fertility Clinic in Skive.

The goal is the same: that as many people as possible can take a healthy baby home with them.

Even though the pregnancy rate at our clinic has been one of the highest in Denmark for many years, it is in the interests of you and future patients to further improve our results.

During your course of treatment at the clinic, you will be asked whether you wish to participate in local research, colloquially known as studies.

### Important information about studies at the clinic

We feel we should point out that:

- the studies should not be considered as an "experiment", but the development of current treatment.
- participation is voluntary.
- your undertaking to participate can be withdrawn at any time.
- not all studies will have an immediate impact on your treatment.

We hope you will view it positively if you have the opportunity to participate in a study. The good results we are able to demonstrate at the clinic are thanks to the participation of patients before you, which has helped develop and improve IVF treatment. In order to be able to offer future patients advanced, state-of-the-art treatment, we depend on new contributions to research.

Before accepting to participate in a research project, you will receive information both orally and in writing.

We also recommend that you read The National Committee on Health Research Ethics's publication: "Before making a decision about being a test subject in a health science trial".

Prepared by: Fertilitetsklinikken, Regionshospitalet Skive • Last revised Februar 2017.