

# In Vitro Fertilisation (IVF) procedures



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# 1. In Vitro Fertilisation

In Vitro Fertilisation is also called IVF. In IVF, mature eggs are retrieved from the ovaries and fertilised with sperm outside the body in the laboratory. *In Vitro* is Latin for *in glass*. Once the eggs have been fertilised, they are transferred into the uterus.

IVF treatment is efficient: Within three periods of treatment, 70 percent of our patients are pregnant with at least one child if the women's age is below 40 years.

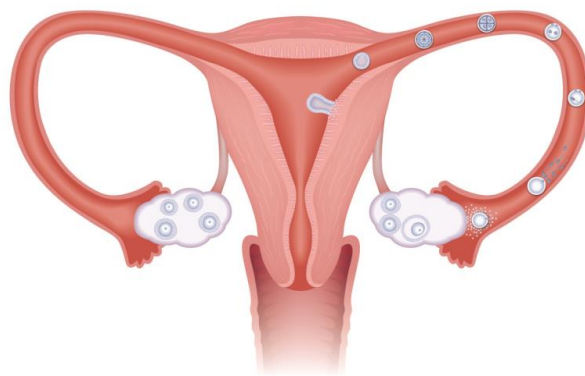
We recommend IVF if:

- the woman has blocked tubes
- the male has poor quality of semen
- unexplained infertility after failed IU
- single women can have IVF treatment in Denmark with donor semen as well as double donation (both donor sperm and donor egg)

## 1.2 Before IVF treatment the following aspects has to be controlled:

- that the woman has a normal uterus.
- that the woman is ovulating, either by herself or assisted by hormonal treatment.
- that the man is producing sperm cells. Or the sperm cells can be recovered from the testicle
- there is also the option of using donor semen.
- that both the woman and her partner have been tested for HIV and Hepatitis B and C prior to the treatment. The tests which need to be taken are: HbsAg, Anti-HBc, anti HCV and anti-HIV 1 + 2, Further test on the female partner are TSH,TPO, Rubella, AMH and prolactin.
- that the patient is fully aware of the consequences and side effect of the treatment

See the below illustration of a normally functioning uterus:



## 2. The female reproductive system

In this chapter you can read more about how the hormonal system interacts and the impact on the reproductive system. The chapter is meant as help to understand the treatment you are about to have.

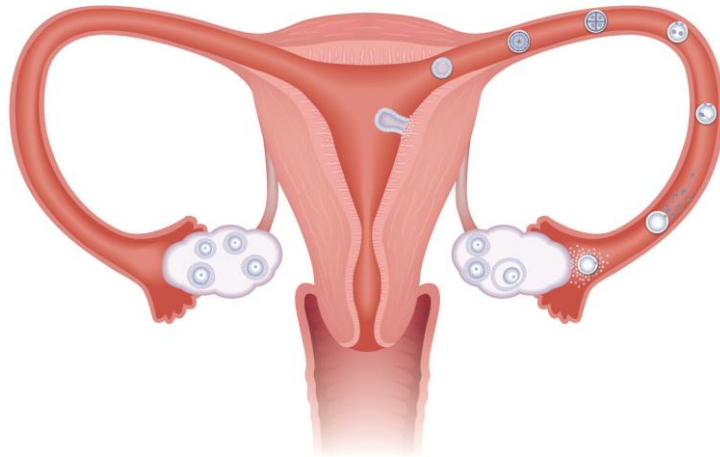
The female reproduction system is, somewhat simplified, constructed through the interplay of three elements:

- The hormonal interplay between the pituitary gland in the brain and the ovaries, where the eggs mature and the ovulation takes place.
- The uterine tubes, where the egg is fertilised and transported to the uterus.
- The uterus, where the fertilised egg adheres to the endometrium and becomes a pregnancy.

### 2.1 The development of the follicle

In the ovaries the egg is matured and fully developed prior to the ovulation. The egg is caught by the uterine tube, which leads the egg to the uterus. If the egg is fertilised, it will adhere to the endometrium in the uterus and develop further.

The development of the follicle and the embryo is illustrated below:



### The interplay of the hormones

Most of the superior sex hormones are formed in the pituitary gland, which is a gland in the brain. The hormone is transported via the blood to its destination (the organ), where a reaction takes place and a signal is sent back to the pituitary gland.

Below, the functions of the individual hormones are briefly described.

**GnRH (Gonadotropin Releasing Hormone).** GnRH causes release of FSH and LH in the pituitary gland.

**FSH (Follicle Stimulating Hormone)** - is formed in the pituitary gland and stimulates the growth of the follicles, which mature the eggs.

**LH (Luteinizing hormone)** - is formed in the pituitary gland and causes ovulation.

**Prolactin** is formed in the pituitary gland and is in interplay with the breasts and the ovaries. Prolactin causes growth of the mammary gland during pregnancy and stimulates the milk production after childbirth. A too high level of prolactin can restrain the ovulation.

**Estradiol** is formed in the ovaries. During a menstrual cycle estradiol causes growth of the endometrium in uterus. A high level of estradiol in the middle of the cycle results in an increase of LH, which leads to ovulation.

**Progesterone.** During the menstruation progesterone together with estradiol prepare the endometrium in the uterus to receive the fertilised eggs. During a pregnancy progesterone restrains the contractions of the uterus.

**HCG (human chorion gonadotropin)** is formed in the placenta and prevents that the follicles are destroyed during pregnancy. We analyse this hormone to find out if you are pregnant.

During the menstruation the ovaries contain several small follicles, each of them containing an egg. The pituitary gland releases the hormone FSH, which leads to development of one single follicle to be approximately 20 mm in size. When the follicle is mature, the ovulating hormone LH is released. The hormones are interdependent, and for some hormones the rule is that an increase in one hormone results in a decrease in another.

### 3. Treatment – the long down regulation protocol

Copenhagen Fertility Center's long course of treatment with test tube fertilisation normally takes 45-50 days. We divide the treatment into four phases:

1. **Down regulation** with Synarela® or Suprefact® takes approximately 16-19 days.
2. **Stimulation** with Puregon®, Gonal F® or Menopur® takes an average of 15 days.
3. **The laboratory work** with egg aspiration, fertilisation *in vitro* and transferral of the fertilised egg/eggs takes 2 days
4. **After-treatment** with Lutinus® for 14 days. The after-treatment is completed by a pregnancy test.

The hormones that normally regulate the function of the uterus are blocked. The ovaries come to a stop, no eggs are developed and therefore there is no ovulation.

Now the ovaries only react to the hormone that is supplied from the outside. The hormone FSH (follicle stimulating hormone) helps the follicles grow, and when a suitable number have reached a size of 18-20 mm, the maturation of the eggs is induced with another hormone hCG (human chorion gonadotrophin = ordinary pregnancy hormone).



After 36 hours, the eggs are aspirated from the follicles and fertilised in the laboratory. Two days later, 1 fertilised egg is transferred to the uterus (embryo transfer).

For the following 14 days a supplement of the hormone progesterone is given. This hormone stabilises the mucous membrane in the uterus and this helps the embryos to adhere. Finally, on day 14 a pregnancy test is done.

### **How to get started on the treatment**

On the first day of your menstrual cycle you should call the nurse at Copenhagen Fertility Centre and get the 1<sup>st</sup> appointment for day 19-23 in the cycle. The telephone number is +45 3325 7000, and the telephone is open on weekdays between 8 am and 6pm and weekends between 9am and 12pm.

#### **1<sup>st</sup> appointment on day 19-23 in the cycle – down regulation.**

We perform an ultrasound scan, and if everything is in order you can start the down regulation. The down regulation is carried out with either Synarela® nasal spray, 3 puffs 3 times daily, i.e. with an interval of 8 hours, or with Suprefact® injection, 0,5 mg subcutaneous once daily. The down regulation must be continued until the aspiration.

The nurse will explain the treatment in details and together you will discuss and make arrangements for possible egg donation and freezing of fertilised eggs. Should any questions arise, you should feel free to ask during this or future consultations. You will receive various forms, which we kindly ask you to read thoroughly and bring back signed for the next consultation. Also, you will get a written treatment schedule with all relevant information. Finally, we supply you with all medication, syringes and needles, and we keep a careful record of your medicine. Later on you will receive an invoice directly from the pharmacy.

Please note that you inject the medicine yourself. After careful instructions from the nurse most patients are able to inject themselves, but of course you can attend the clinic for injections, if you wish.

### **Menstruation**

Your menstruation will typically begin 8-10 days after starting down regulation and will probably last a little longer than usually. In some cases, menstruation can be up to 8-14 days overdue. If the menstruation has not yet started on the date where the stimulation is scheduled to start, please contact the clinic.

### **Stimulation**

Stimulation with FSH starts after 16-19 days of down regulation and when you have had your menstruation. The injections are made daily. Be sure to continue using Synarela®/Suprefact®, but now it is only necessary to use the nasal spray twice a day: 1 puff 2 times daily, i.e. with an interval of 12 hours and Suprefact® 0,2 mm daily.

#### **2<sup>nd</sup> appointment after 8 days of stimulation**

Nine days later we perform another ultrasound scan. We measure the thickness of the mucous membrane in the uterus, the number and size of follicles. We often perform an extra scan a couple of days later.

When a suitable number of follicles have reached the size of 18-20 mm, we plan the egg aspiration and the time for the ovulating injection. We use 250 micrograms of Ovitrelle®.

The egg aspiration is performed 36 hours thereafter, and on average 15 days after the stimulation was started.

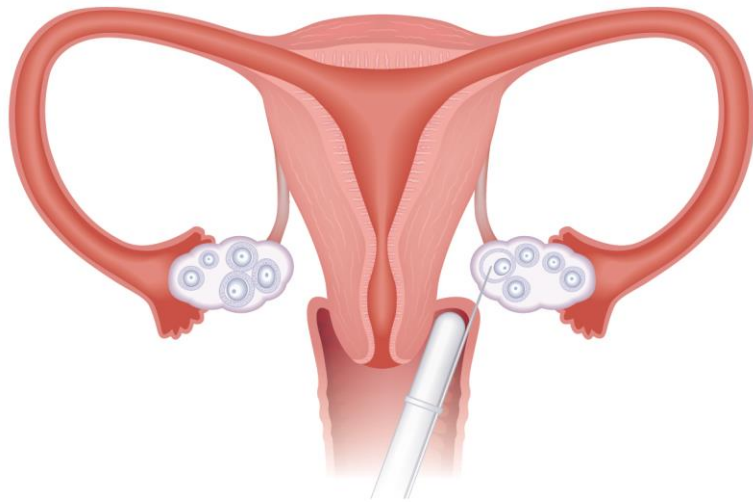


## Egg collection procedure

The aspiration takes place between 9 and 10am on weekdays and over the weekend. It will take about 10 minutes. You do not have to be fasting, but please refrain from eating anymore than a light meal before aspiration.

You can take two Panodil tablets one hour prior to your appointment at the clinic.

Immediately before the egg aspiration local analgetica is injected in the vaginal wall. The egg aspiration is performed through the vagina wall. Making use of ultrasound, a thin needle is inserted into the follicles. Each follicle is drained of fluid and at the same time the egg is sucked out. On our screen you are able to follow the whole procedure.



After the aspiration you will get something to drink and rest, if needed, at the clinic. The next couple of days there might be some minor bleeding from the vagina. There might also be some pain, and you can take some pain-killing Panodil tablets, but not more than 1 g = 2 tablets 4 times daily.

You are always welcome to call the clinic, should any problems occur or should you have further questions.

Finally, you need someone to escort you home and stay with you for the rest of the day, and you are still not allowed to drive a car yourself. Moreover, we advise you to rest that day.

## Sperm sample

When you attend for the aspiration you bring a sperm sample. It is important that the sample has your full name and d. o. b. on it. You can either make the sample at home or at the clinic. In either case, the sperm sample must not be more than four hours old, when you hand it in. After aspiration we will use the sperm sample to inseminate the egg.

## Fertilisation *in vitro*

Approximately 100.000 sperm cells are added to each egg. The next day the eggs are sorted and controlled, and we monitor whether the development is normal. During the next two days and nights the fertilised eggs (embryos) will develop from being 1 cell to being 2-6 cells. We follow this development daily, but it is only after 48 hours that we know for certain how many of the eggs that have developed satisfactorily.



### **Aspiration of sperm from the testicle – TESA**

We use TESA if the man cannot produce sperm cells naturally. The procedure is performed under local anaesthesia. A fine needle is introduced directly into the testicle, and suck out a tissue sample containing sperm cells. The sperm cells of which there are only few, are at first completely immobile, but after 3-4 hours they can be used for fertilisation by microinsemination (ICSI).

### **Fertilisation by microinsemination – ICSI**

At microinsemination the sperm cell is injected directly into the egg. This method is used when only very few sperm cells are available or when the sperm cells are quite immobile. Microinsemination does not reduce the chance of pregnancy.

### **Embryo transfer**

The next day, i.e. 2 days after the egg aspiration, the fertilised eggs (embryos) are transferred to the uterus. Routinely, only one (maybe two) fertilised egg is transferred. The fertilised egg is transferred to the uterus through a thin plastic catheter, which is inserted into the cervix. The embryo transfer is usually a quite simple procedure and completely painless; you will probably feel nothing at all. We normally recommend that the women has a full urinary bladder during the procedure.

### **Freezing of surplus embryos**

After the embryo transfer, surplus embryos might be frozen and later on be transferred to the uterus. Of course, this only applies for embryos that are considered suitable for freezing.

### **After-treatment**

For the following 14 days you will take Lutinus® vaginal suppositories 3 times daily. Lutinus® contains the hormone progesterone, which stabilises the mucous membrane in the uterus. You will not need any time off from work. If you use your common sense, you can live quite normal.

### **The pregnancy test**

14 days after the embryo transfer you should take a pregnancy test. The pregnancy test has to be performed, also if you have started to bleed. If the test is positive, we will offer you a pregnancy scan three weeks later (the 7th week of pregnancy). If the test is negative, we recommend you to make an appointment with the doctor, where we can evaluate your course of treatment and maybe reschedule. If you live far away from the clinic, your general practitioner can do the pregnancy test or you can do a sample of morning urine with a test supplied by us. We kindly ask you to telephone the result to Copenhagen Fertility Center.

## **4. Treatment - Short down regulation**

Copenhagen Fertility Centre's short course of treatment normally takes 30 days, and can be divided into three phases:

- **FSH Stimulation** with Puregon®, Gonal-F® or Menopur®. Approx.10-15 days.
  - **Preventing ovulation** with Orgalutran® 0,25 mg daily from the 7th day for 3-8 days.
- **The laboratory phase** with aspiration, fertilisation *in vitro* and transfer takes 2 days.
- **After-treatment** with Lutinus® for 14 days and finally a pregnancy test.





We use FSH (follicle stimulating hormone) that helps the follicles grow. When the follicles have reached a size of about 12-14 mm, (around day 7), you must also take Orgalutran®, which prevents ovulation. When a suitable amount of follicles have reached the size of 18-20 mm, the maturation of the eggs is induced with ordinary pregnancy hormone hCG, called Ovitrelle®.

After 36 hours, the eggs are aspirated from the follicles (aspiration) and become fertilised in the laboratory. Two days later 1 of the best fertilised eggs (embryos) is transferred to the uterus (embryo transfer).

For the following 14 days a supplement of the hormone progesterone is given. This hormone stabilises the mucous membrane in the uterus and this helps the embryos to adhere. Finally, on day 14, a pregnancy test is done, and this is hopefully positive.

### **How to get started on the treatment**

On the first day of your menstrual cycle you call our nurse and schedule an appointment for the second or the third day.

#### **1<sup>st</sup> appointment on day 2 in the cycle**

We perform an ultrasound scan, and if everything is in order you can start stimulation with Gonal-F or Puregon. You must take the injections daily at the same time.

The nurse will explain the treatment in details and together you will discuss and make arrangement for possible egg donation and freezing of fertilised eggs. Should any questions arise, you should feel free to ask during this or future consultations. You will receive various documents, which we kindly ask you to read thoroughly and bring back signed for the next consultation. Also, you will get a written treatment schedule with all relevant information. Finally, we supply you with all medication, syringes and needles, and we keep a careful record of your medicine. You will pay for the medicine here at the clinic.

Please note that you inject the medicine yourself. After careful instructions from the nurse most patients are able to inject themselves, but of course you can attend the clinic for injections, if you wish.

#### **2<sup>nd</sup> appointment on day 7 or 8 of your cycle**

We perform an ultrasound scan on the 7th day in your cycle. We measure the thickness of the mucous membrane in the uterus, the number of follicles and their size. You must begin taking injections with Orgalutran® whilst continuing with FSH, when the follicles have reached the size of 12-14 mm.

#### **3<sup>rd</sup> appointment**

When a suitable number of follicles have reached a size of 18-20 mm, we plan the egg aspiration and the time for the ovulating injection. We use 250 micrograms of Ovitrelle®. The egg aspiration is performed 36 hours after you have taken the injection and on average 15 days after the stimulation was started.

### **Egg aspiration**

This takes place as mentioned in the chapter for the long protocol, see page 6.



## 5. Treatment - Mild Stimulation

With this treatment, only a few eggs are matured.

### The treatment

Mild hormone stimulation is given with Tamoxifen 2 tablets daily or Clomifen tablets daily starting on the 3<sup>rd</sup> day of the menstrual cycle. In addition, 150 units of Gonal F® is given every other day. With this treatment, 1-5 eggs will mature. When the follicles are 17-18 mm in diameter, you must take Ovitrelle injection to provoke ovulation. 34 hours later, the eggs are aspirated from the follicles.

The eggs are fertilized in the laboratory and 2 days hereafter, the best fertilized eggs are transferred to the uterus. Any surplus eggs can eventually be cryo preserved.

### The treatment day by day

Call Copenhagen Fertility Center when you start your menstruation. Our number is +45 3325 7000. Then you will have an ultrasound scanning on the 2-3 day in the cycle, and if there is no cysts and the endometrium is discarded, you can start the treatment. When the follicles have reached 17-18 mm the Ovitrelle injection will ensure ovulation and you should have the eggs aspirated 34 hours later. 2-3 days later the eggs will be transferred to the uterus.

### Egg aspiration

This takes place as mentioned in the chapter for the long protocol, see page 6.

## 6. Crash

*Crash* treatment combines *the short protocol* and *the long protocol*. Treatment normally takes 45-50 days and can be divided into four phases:

1. **Injection** with 3 mg of Cetrotide® on the 21<sup>st</sup> day of your cycle.
2. **FSH Stimulation** with Puregon®, Gonal F® or Menopur® from day 2 or 3 in your cycle for an average of 15 days. **Preventing ovulation** with Orgalutran®, 0,25 mg, once daily for 3-8 days from day 7.
3. **The laboratory phase** with egg aspiration, fertilisation *in vitro* and transferral of the fertilised egg/eggs takes 2 days.
4. **After-treatment** with Progesteron® for 14 days. The after-treatment is completed by a pregnancy test.

We give an injection Cetrotide® 3 mg approx. the 21<sup>st</sup> day of the cycle. By suppressing the ovulating hormone (LH) we expect the egg-stimulating hormone (FSH) to have a stronger effect.

We use the hormone FSH (follicle stimulating hormone) that helps the follicles grow. When the follicles have reached a size of about 12-14 mm, (around day 7), you must also take Orgalutran®, which prevents ovulation. When a suitable amount of follicles have reached the size of 18-20 mm, the maturation of the eggs is induced with ordinary pregnancy hormone hCG, called Ovitrelle®.

After 36 hours, the eggs are aspirated from the follicles (aspiration) and become fertilised in the laboratory. Two days later 2-3 of the best fertilised eggs (embryos) are transferred to the uterus (embryo transfer).



For the following 14 days a supplement of the hormone progesterone is given. This hormone stabilises the mucous membrane in the uterus and this helps the embryos to adhere. Finally, on day 14, a pregnancy test is done, and this is hopefully positive.

### **How to get started on the treatment**

At the first day of your menstrual cycle you call the nurse at Copenhagen Fertility Center and get the 1<sup>st</sup> appointment for day 19-23 in the cycle. The telephone number is +45 3325 7000.

#### **1<sup>st</sup> appointment on day 19-23 in the cycle – down regulation**

We perform an ultrasound scan, and if everything is in order you get an injection with 3 mg of Cetrotide®. This will suppress the ovulating hormone endemic to the female body. If the menstruation has not occurred within 5 days, the Cetrotide® injection is repeated.

The nurse will explain the treatment in details and together you will discuss and make arrangements for possible egg donation and freezing of fertilised eggs. Should any questions arise, you should feel free to ask during this or future consultations. You will receive various documents, which we kindly ask you to read thoroughly and bring back signed for the next consultation. Also, you will get a written treatment schedule with all relevant information. Finally, we supply you with all medication, syringes and needles, and we keep a careful record of your medicine. You will pay for the medicine here at the clinic. Please note that you inject the medicine yourself. After careful instructions from the nurse most patients are able to inject themselves, but of course you can attend the clinic for injections, if you wish.

### **Menstruation**

Your menstruation should begin 1-5 days after the injection with Cetrotide®. If menstruation doesn't occur within 5 days, please contact the clinic and reschedule a new appointment. If you do get your menstruation within the 5 days, please also contact the clinic. Our phone number is +45 3325 7000 and you can call any weekday. We will then tell you when to start Puregon® and FSH and when your next appointment at the clinic should be (approx. day 7-8 in your cycle).

#### **2<sup>nd</sup> appointment on day 7-8 of your cycle**

On day 7-8 in your cycle we perform another ultrasound scan. We measure the thickness of the mucous membrane in the uterus, the number of follicles and their size. When the follicles have reached 12-14 mm in diameter, you will get injections with Orgalutran®.

### **Third appointment**

When a suitable number of follicles have reached a size of 18-20 mm, we plan the egg aspiration and the time for the ovulating injection. We use 250 micrograms of Ovitrelle®. The egg aspiration is performed 36 hours after you have taken Ovitrelle® and on average 10-15 days after the beginning of menstruation.

### **Egg aspiration**

This takes place as mentioned in the chapter for the long protocol, see page 6.



## 7. Treatment with frozen/thawed fertilised eggs

Before starting the treatment, you should have a consultation with the doctor and plan the transfer of the thawed eggs. Normally we use a hormone stimulation in the form of pills. The mucous membrane in the uterus is thus stimulated with hormones. The frozen eggs are thawed, and a maximum of 1-2 thawed eggs are transferred to the uterus.

Please note the following:

- According to prevailing law frozen eggs must be destroyed after 5 years.
- Frozen eggs will only be thawed if we have your permission in writing.
- Approx. 40 % of frozen eggs do not survive the thawing, but we will not know with certainty until the day after the thawing.
- 90% of frozen blastocysts survive thawing.

### The treatment day by day

You call the clinic and get an appointment for an ultrasound scan on the 2<sup>th</sup> day of the cycle. Our phone number is +45 3325 7000.

You take Estradiol® 2 mg, following your own specific schedule made by the doctor.

After the embryo transfer you continue with Estradiol® and Lutinus®.

14 days after the embryo transfer, you make a pregnancy test. If the test is positive, it is important that you continue with Estradiol® and Lutinus® until the 12th week of your pregnancy.

## 8. Laser assisted hatching

Assisted hatching is a technology that helps embryos to attach to the womb of the woman. Pregnancy cannot occur unless the human embryo hatches.

The unfertilised egg is surrounded by a shell called zona pellucida. The zona pellucida ensures that only one sperm cell enters and thus fertilises the egg. After fertilisation of the egg, zona pellucida keeps the cells of the embryo together. Now the cell begins to cleave into a two-cell, then a four-cell and so on.

During the cleavage of the early foetus, zona pellucida hardens. This development is normal and the purpose is to keep the cells in the egg together. Removing the egg for in vitro fertilisation and micro insemination takes it out of its natural environment. This procedure tends to lead to egg shells that harden faster than those of normally fertilised eggs.

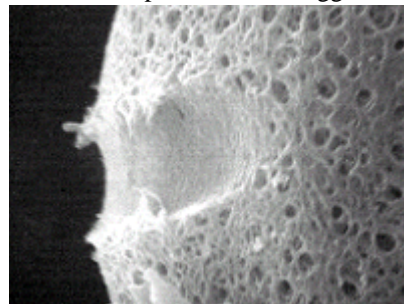
Especially women older than 37 years of age have a tendency to produce eggs with a harder zona pellucida than younger women. The same goes for women with a high level of follicle stimulating hormone (FSH). This can be diagnosed from a blood sample.

The problem of a harder zona pellucida is that the egg may not hatch and thus not attach to the woman's womb. Hatching of the egg is necessary to become pregnant.



We know that eggs from older women have problems hatching, explaining why some older women have problems with becoming pregnant.

Laser assisted hatching is one out of several methods to help the fertilised egg hatch and attach to the womb. Other methods are acid or mechanical hatching of one as a part of zona pellucida. At Copenhagen Fertility Center we offer laser assisted hatching, which is a gentle and safe way to weaken a part of zona pellucida. After treating the fertilised egg with laser assisted hatching, we transfer the embryo into the woman's womb. In most cases the embryo will attach for normal growth and development.



Scientific experiments have shown that one method of assisted hatching is not superior to another. Nor does assisted hatching damage the eggs. On the contrary, different studies on assisted hatching show better pregnancy results, mainly among women over 37 years of age. Other studies do not report significantly better results using assisted hatching on "normal" IVF patients or patients treated with micro insemination. At Copenhagen Fertility Center we offer laser assisted hatching for patients who have undergone repeated treatments without conceiving, and/or in cases where the woman is over 37 years of age.

We also recommend that thawed embryos are treated with laser assisted hatching. It is our experience that thawed embryos have difficulty attaching to the womb. The likelihood of improved chances for pregnancy is assessed medically before recommending laser assisted hatching.

## 9. Possible adverse effects of IVF

The patient as well as the doctor can cancel the treatment. Before the aspiration there are three reasons for cancelling the treatment:

1. development of few or no follicles, i.e. under- stimulation/*low response*.
2. development of too many follicles, i.e. over-stimulation.
3. one of the parties becomes ill.

After the aspiration there are also three reasons for cancelling the treatment:

1. no eggs at the aspiration.
2. none of the eggs are fertilised.
3. none of the fertilised eggs cleave.

### Over stimulation

The primary adverse effect of the treatment is over stimulation of the ovaries, i.e. too many follicles are developed. The probability of over stimulation is 0.5 percent. Over stimulation will occur 2-14 days after injection of Ovitrelle®. The symptoms are abdominal pain and abdominal distension, which in the worst case can result in hospital admission.

If there is a risk of over stimulation we usually stop the stimulation with Gonal-F® / Puregon® but continue the down regulation with Synarela®/Suprefact®, and



control the level of the female sex hormone daily. We give Ovitrelle® when the female sex hormone level has fallen again. This might take a few days.

### **Bleeding**

Usually there is a minor bleeding or a bloodstained discharge from the vagina after the aspiration. A heavy bleeding during and right after the aspiration is caused by a ruptured blood vessel in the vagina wall. The bleeding will stop after compression with a pad of gauze for 5 minutes. Should heavy bleeding occur after you have returned home, please contact the clinic or the nearest doctor or hospital.

### **Pain**

There might be some abdominal pain, especially the day after the aspiration. The pain will disappear within a few days. You can take Panodil, 2 tablets 4 times a day, if necessary.

### **Infection**

Infection as a consequence of the treatment is very rare. It could be infection in one of the ovaries following the aspiration or infection in a collection of blood (haematoma) in the vagina wall. The symptoms would be fever and some soreness or pain.

### **Ectopic pregnancy**

A pregnancy outside uterus occurs if the fertilised egg adheres in the uterine tube. It is a serious condition and involves hospital admission. In the worst case an operation is necessary. In case of extra-uterine pregnancy, the uterine tube is often removed.

## **10. Medicine**

### **Rules of medicine subsidy**

Copenhagen Fertility Center always applies to The Danish Medicines Agency for the so-called *kronikertilskud* (State-subsidized grants) for medicine. This means that the subsidies for the medicine mentioned below amount to 100% of expenditures exceeding 3.600 kroner. With *kronikertilskud*, therefore, the cost of medicine will amount to no more than 3.600 annually. The *kronikertilskud* is valid for two years. 85% subsidy at expenditure above 3.600 DKK.

- **This is only applying for Danish citizens.**

### **Down regulation**

#### **Cetrotide® (cetorelix) injection**

*Effect:* Prevents ovulation by inhibiting the excretion of the luteinizing hormone (LH) from the pituitary gland. Is injected in the subcutis on the abdominal wall,  
*Adverse effects:* Local irritation on the injection site is normal and completely harmless.

#### **Orgalutran® (ganirelix) injection; Suprefact (buserelin) injection; Synarela® (nafarelin) nasal spray**

*Effect:* Down regulates the superior sex hormones by inhibiting their excretion in the pituitary gland. Ovulation at the wrong moment is thus prevented. Is injected in the subcutis on the abdominal wall 0.25 mg = ½ ml once daily.  
*Adverse effects:* Induces a short false menopause, and slight hot flushes, sweats and headache might occur.



## **Stimulation**

### **Gonal F®; Puregon® ;Menopur®**

*Effect:* Stimulates the ovaries and causes the largest follicles to grow further. Is injected in the subcutis on the abdominal wall. Dosage varies.

*Adverse effects:* Local irritation on the injection site. Can cause over stimulation.

### **Ovitrelle®**

*Effect:* Stimulates the ovaries and cause the largest follicles to ovulate. Is injected in the subcutis on the abdominal wall.

*Adverse effects:* Over stimulation can be caused by hCG after over stimulation by FSH. Local irritation on the injection site, headache, tiredness, vomiting, abdominal pain and nausea.

### **Rapifen® injection**

*Effect:* A morphine-like drug, which has a strong pain-killing effect. During the aspiration 50 mg = 1 ml Rapifen is administered as an intravenous injection.

*Adverse effects:* nausea and tiredness.

### **After-treatment Progestan (progesterone)**

*Effect:* Stabilises the mucosa membrane in uterus and creates optimal conditions for the fertilised egg to adhere is available.

*Adverse effects:* mild nausea, bloating and tautness of the breasts

### **Treatment with thawed fertilised eggs**

#### **Estrofem® (oestradiol) tablets**

*Effect:* Stimulates the growth of the mucosa membrane in the uterus.

*Adverse effects:* mild nausea, tautness of the breasts, and a tendency to oedema.

### **“Mild stimulation” IVF-treatment**

#### **Tamoxifen® tablets 40mg**

*Effect:* Stimulates the ovaries and causes the largest follicles to grow further and mature the eggs.

*Adverse effect:* Nausea.



## 11. Prices and treatments

Prices we refer to our website [www.copenhagenfertilitycenter.com](http://www.copenhagenfertilitycenter.com)

## 12. Midwife consultation.

When you have had a successful IVF treatment in our clinic, we can offer you a free consultation with one of our midwives. For patients, who have had treatment covered by a referral (insemination), you can choose to pay for this consultation.

The consultation is based in your/yours individually needs, questions, thoughts and worries.

This can among other things be subjects as diet, smoking, alcohol, exercise, physical and mental changes in the body during pregnancy and the process in family planning.





## 13. Blood test before treatment

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According to present Danish law concerning in vitro fertilisation, all patients (male and female) treated in a Danish fertility clinic must have the following tests taken by their own doctor:

Blood tests for the following less than 3 month old:

Hepatitis B and C, i.e.: HbsAg, Anti-HBc and anti HCV from the woman and her partner.

HIV tests which is the following: anti-HIV 1+2.

For women: TSH, TPO, Prolactin, AMH and Rubella. A cell-sample (ex. PAP smear) from the cervix which is not more than 3 years old at the start of the treatment.

These tests cannot be more that 3 months old at the start of the treatment and are to be renewed every 24 months when in treatment.

This note is supposed to be given to your doctor if you have not had these tests taken already. The doctor can send the results directly to the fertility clinic or you can bring them with you.

According to European rules of analysis of human tissue, it must be very clear in which lab the tests have been analysed.

Kindest regards

Svend Lindenberg  
Professor. Dr. med.







