IVF Patient Information

the Agora

You are about to commence your IVF/ICSI treatment with the Agora Gynaecology and Fertility Centre.

The Agora is the licensed centre where your scans, blood tests, egg collection and embryo transfer will take place.

All treatment cycles will be co-ordinated by our fertility nurse specialists, to whom all enquiries should be made.

Contact Telephone Numbers

The Agora Gynaecology and Fertility Centre Enquiries and Appointments	01273 229411
Urgent calls for out of hours emergencies	07912 341857
Or you can email enquiries to:	info@agoraclinic.co.uk

In the unlikely event you are unable to make contact with one of the above, your GP or local Accident and Emergency department will be able to provide assistance.

Screening

It is our policy to screen both partners for HIV, Syphilis and Hepatitis B and C. This is repeated annually. The results of these tests will be given to you at one of your appointments. If any of these tests are positive then treatment will be stopped and a referral made to a specialist clinic. If after counselling and appropriate medical management you wish to pursue fertility treatment then you can be referred to a specialist centre for fertility management.

Before treatment begins

Before you commence your proposed treatment cycle, please ensure you have been given the following information:

- The limitations and possible outcomes of the proposed treatment
- The possible side effects and risks of the treatment
- The techniques involved
- All alternative treatments
- Cost involved
- The possible disruption to your life
- The availability of counselling
- Details of the Human Fertilisation and Embryology Authority (HFEA)
- Our duty to consider the welfare of any child resulting from treatment with us

Counselling

The difficulties associated with trying to conceive and a diagnosis of infertility can often be a major life crisis. Many conflicting feelings and strong emotions arise and often their strength and intensity are greater than those we are used to dealing with.

Counselling starts with addressing immediate issues in your life, including fertility that may cause you confusion, uncertainty or anxiety. It is important to have the opportunity to ask questions, access information and generally feel prepared for whatever lies ahead. Counselling can provide you with time and a quiet space where you can explore and consider the things that are worrying you.

Rory Singer is our independent counsellor based in Brighton at:

28 New Road
Brighton
BN1 1UG

Appointments are made by contacting Rory or a member of his team directly on Brighton 681333 and are charged at a rate of approx £55 per session.

Patient Support Groups

Infertility Network UK

Charter House
43, St Leonards Road
Bexhill on Sea
TN40 1JA
Tel: 01424 732361
www.infertility.networkuk.com

Consent Forms

Prior to commencing your treatment cycle you will be required to read and sign forms consenting to the drug treatment, the egg collection, the number of embryos to be transferred or frozen and the HFEA consents. They will all be discussed at your nurse consultation but if you have any queries please contact the nurses.

All consents must be completed and returned prior to starting treatment.

Drugs

All the medication needed for treatment will be prescribed at the Agora and delivered to you, using our home delivery service.

What is IVF?

IVF (In Vitro Fertilisation) is a treatment by which fertilisation of eggs by sperm takes place outside the body in a dish in an IVF laboratory.

An ovary has a pool of immature eggs. In a woman's natural cycle, it is usual to produce one egg each month, which is released from the developing follicle (fluid filled sacs) two weeks before the next period starts. In IVF cycles the aim is to achieve the growth and development of several follicles in order to maximise the chance of collecting several eggs. Injections of follicle stimulating hormone (FSH) are taken from the start of the cycle to stimulate growth. and when the follicles are mature the eggs are collected. These are then put together with the sperm in the laboratory to allow fertilisation to take place. The fertilised eggs are allowed to grow in the laboratory for 2 or 3 days before being replaced in the woman's womb (uterus)

The main reasons for advising IVF in a couple are:

- Damaged or blocked fallopian tubes, which stop the sperm from reaching the egg
- Suboptimal sperm quantity or quality, which reduces the chance of fertilisation
- Antisperm antibodies present in sperm
- Anovulation (failure of the ovary to release an egg) resistant to conventional ovulation induction techniques
- Unexplained infertility

ICSI is a special form of IVF in which individual sperm are injected into the egg under microscopic vision (see separate information sheet). This is the treatment advised for couples where the sperm quantity or quality is very poor.

The IVF cycle

The IVF cycle consists of five stages:

1. Stimulation of the ovary with fertility drugs to enhance egg production (superovulation)
2. Collection of mature eggs from the ovary (egg collection)
3. Preparation of motile sperm from the male
4. Mixing of eggs and sperm in the laboratory to allow fertilisation to occur
5. Selection of the one or two (occasionally three in some circumstances) best embryos and transferring these to the uterus (embryo transfer)

1 Stimulation of the ovary

The rationale behind using drugs in IVF is that the chances of pregnancy are increased if more than one egg is obtained. The aim is to obtain between 8 to 12 mature eggs by stimulating the ovary with fertility drugs. However the rate of growth of individual follicles varies and it is important that the eggs are collected when as many as possible are appropriately mature. In order to achieve this, we use a combination of drugs that take over from the body's natural hormone cycle. Injections of the hormone FSH are taken from day 2 or 3 of the cycle at a dose which allows several eggs to grow and mature in each ovary. The growth of the eggs is monitored using ultrasound scans which measure the size and number of the follicles. Once two or three follicles have reached 18mm in size or greater, the eggs inside them are mature and ready to be collected.

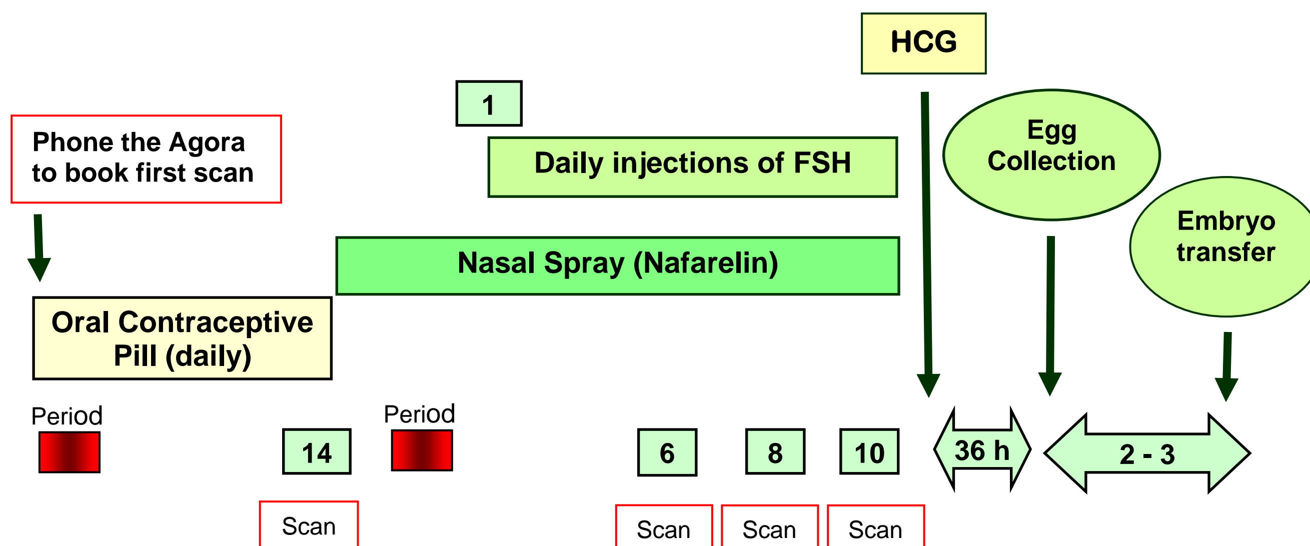
A number of different protocols are used to stimulate the ovaries to produce eggs. These are Long, Flare and Antagonist. The protocol chosen by your consultant will depend upon your age, day 2-5 FSH level and previous response (if applicable). In the majority of cases the first line approach is to use the long protocol.

2 The long protocol with oral contraceptive pill

In this protocol we generally start you taking the oral contraceptive pill on the first day of your natural cycle, prior to your treatment cycle. This is usually taken for up to 21 days. Your first scan is scheduled between days 14 and 21 of this pre-treatment cycle. The purpose of this scan is to check that your ovaries are quiet (i.e. no cysts present) and the lining of the womb is regular and not over-thickened.

If this is your first IVF cycle we will arrange for you to have a “trial” embryo transfer, performed at the time of the scan to check that the small catheter we use to transfer the embryos back can pass through the neck of the womb easily. This is a painless procedure performed by one of our doctors.

Provided the first scan is normal you will be advised to stop taking the pill and will be started on a nasal spray called Nafarelin or “gonadotrophin releasing hormone analogue GnRHa” twice daily. Nafarelin suppresses FSH and LH hormone signals from the pituitary gland and prevents the ovary from naturally producing and releasing eggs. In this way we gain the control over the development and release of eggs during your IVF cycle. This is called down regulation. This drug can also be taken once daily in subcutaneous injection form.



You should then expect a period within one week of stopping the oral contraceptive pill. You may require a second scan (down regulation scan) scheduled during the following one to two weeks, usually on day 3 or 4 of bleeding. The lining of the womb is measured and provided it is thin, FSH injections are commenced to stimulate your ovaries. FSH is commercially known as Gonal-F, Puregon or Menopur, if given in combination with LH. At this stage you may be asked to reduce your nasal spray to half the amount you were taking.

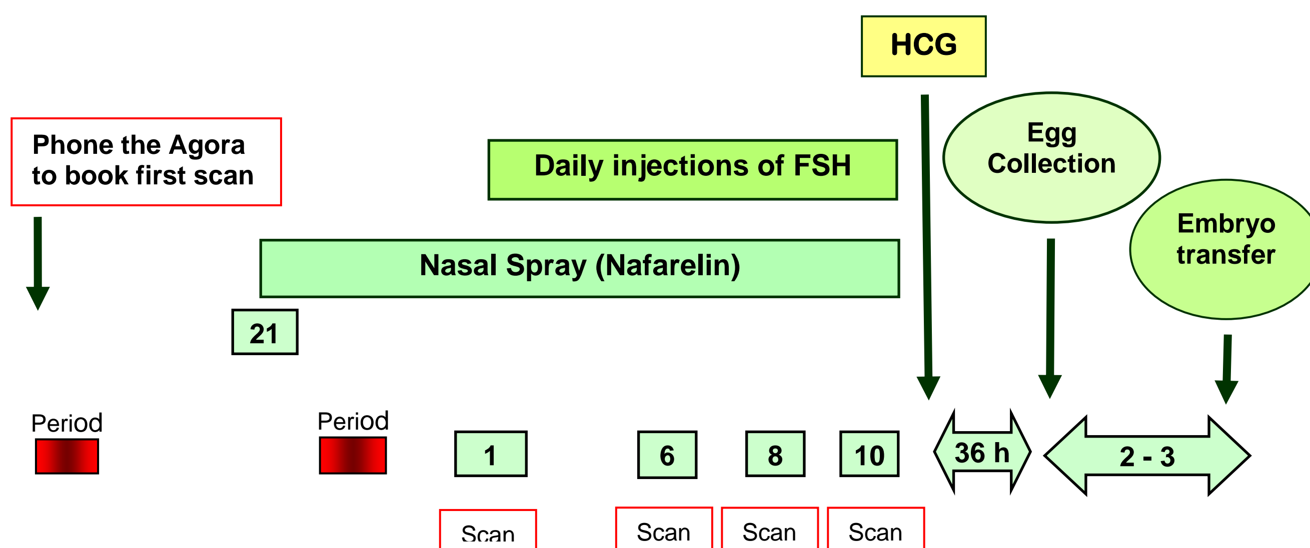
A third scan is booked for 5 days after starting stimulation during which the size of the growing follicles are measured. It is usual to also take a blood test for Oestrogen at this time. The dose of FSH may be adjusted up or down depending on the scan and blood test results.

Scans are then repeated every 2 or 3 days until there are 3 or more follicles greater than 18 mm in size. The time it takes for FSH injections to grow follicles to this size varies between women, but is on average 10 to 16 days. Once two or three follicles have reached 18 mm in diameter or greater, you will be given an injection of HCG called Ovitrelle. This is more commonly known as the "trigger" injection. This drug mimics the action of LH, the hormone a woman naturally produces mid-cycle to mature and release the egg. The injection is usually given at 10 or 11pm and your egg collection will be timed to take place 35 to 36 hours later, corresponding to the time it takes for the drug to mature the eggs ready for fertilisation.

3 The long protocol without the oral contraceptive

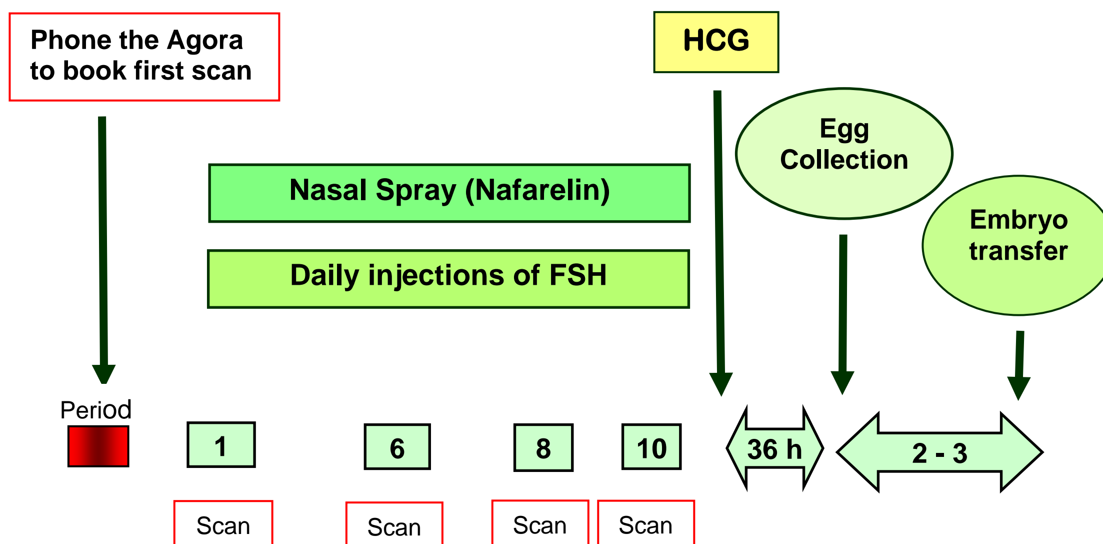
In this protocol we start you taking the GnRHa nasal spray twice daily from day 21 of your natural cycle. This drug can also be taken once daily in subcutaneous injection form. Nafarelin is generally taken on its own for 12 to 21 days during which time your next period will occur as usual. Your first scan or 'down regulation' scan is scheduled following this bleed from day 3 onwards. The lining of the womb is measured and provided it is thin and both ovaries are quiet, FSH injections are commenced to stimulate your ovaries. At this stage you may be asked to reduce your nasal spray to half the amount you were taking. If this is your first cycle a trial ET will be performed at the time of your scan.

All further scans and treatment then follow the same pattern as the long protocol with oral contraceptive pill.



4 The Flare protocol

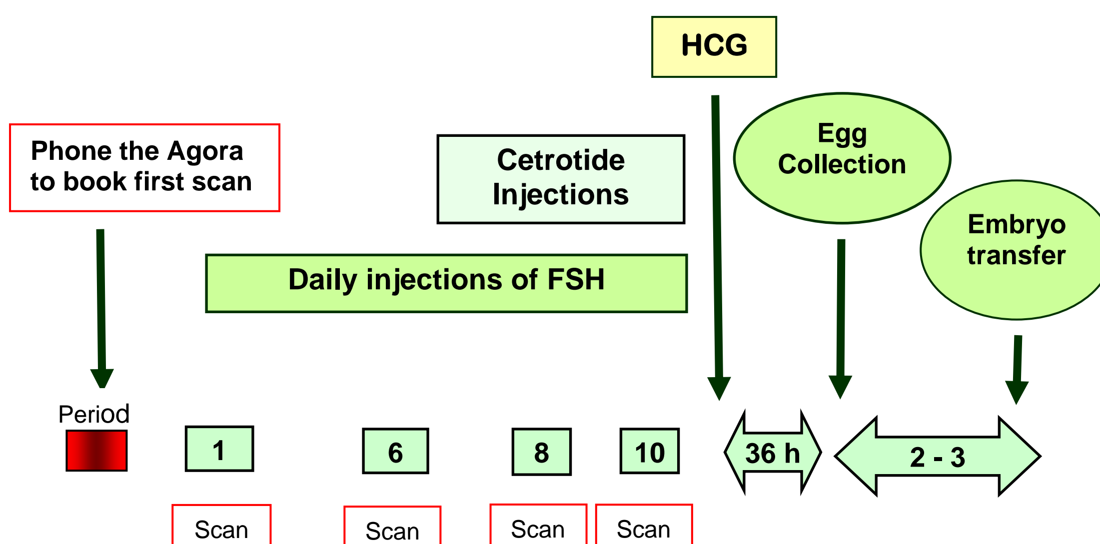
With this protocol you start the GnRHa nasal spray at the same time as the FSH injections on day 2 or 3 of your natural cycle. Again a scan is performed prior to starting the injections to check the ovaries and lining of the womb. If you have previously had a high FSH level a blood test to re-check this may also be done to see whether it is a good month in which to start treatment.



All further scans and treatment then follow the same pattern as with the long protocol.

5 The Antagonist protocol

This protocol is an alternative approach used in some women. It does not involve taking a GnRH analogue. Instead you will start FSH injections only, on day 2 or 3 of your natural cycle (following a scan). Regular scans will again monitor the development of the follicles and once the largest one is 12-14mm in diameter, you will start injections of a GnRH antagonist called Cetrotide, the effect of which is to block spontaneous ovulation. HCG is given in the same way once two or three follicles are 18mm in size or greater.



Unfortunately FSH and Ovitrelle have to be taken as injections otherwise they would be destroyed in the stomach if they were taken orally. Whilst the idea of taking injections may seem daunting, in practice most women cope very well and either learn to do their own injections or ask their partner or a friend to help. You will have a nurse consultation before commencing a treatment cycle during which you will be shown how to do your injections. If you feel that you cannot do your own injections you can come to the Agora every day or enlist the help of your GP (often a nurse practitioner is able to do the injections for you at your surgery). You can get your drugs through our home delivery service.

During each ultrasound scan the number and size of the follicles is measured. You will be seen by a nurse or doctor after each scan and given clear instructions on what to do next.

6 Possible side effects of drugs

All medication has potential side effects, we hope you do not experience any at all but you should be aware of the possible ones associated with fertility drugs:

- Headaches
- Tiredness
- Mood swings
- Hot flushes
- Nausea
- Nasal irritation
- Discomfort and redness at injection site
- Vaginal bleeding
- Allergy
- Pelvic discomfort

If you experience any other side effects of the drugs and you are concerned then speak with one of the nurses for advice.

7 Collection of mature eggs from the ovaries

Egg collections are routinely performed at the Agora. However if you have a serious medical condition or are overweight with a body mass index (BMI) more than 35, the procedure will be performed at the Lister Fertility Clinic in Chelsea and an extra charge will be incurred. The Lister Fertility Clinic will also perform your egg collection if you are on the Pre-genetic Screening (PGS) Program. You will be seen at a pre-operative appointment when our nursing team will carefully assess your general health and any pre-existing medical conditions to determine your individual requirements.

Egg collection takes place between 35 and 36 hours after taking the trigger injection of HCG. The eggs are collected vaginally under ultrasound guidance. As with all scans during treatment, a vaginal ultrasound probe is introduced into your vagina. A fine aspiration needle is passed along a guide attached to the probe and passes gently through the top of your vagina into each ovary. The follicles and tip of the needle can be clearly seen on the ultrasound screen. As the tip of the needle passes into each follicle, the fluid gets sucked out, and the follicle collapses. The fluid is collected in test tubes which are passed to the embryologist in the IVF laboratory. The fluid is then examined under a microscope to look for the eggs (eggs are tiny 0.1mm in diameter, smaller than a full stop on a sheet of paper). The needle is passed from one follicle to the next until all are emptied. Sometimes if there are only a few follicles it is necessary to flush the follicle with some culture fluid to tease out the egg. The procedure should take between 30 and 60 minutes, depending on the number of follicles. Most, but not all follicles should contain an egg. Very occasionally it is not possible to reach the ovary with the vaginal probe so an

abdominal scanning approach or laparoscopic method of collecting your eggs will be used. This will have been identified during treatment and your egg collection will take place at the Lister.

Once identified, the eggs are put in a dish clearly labelled with your name and Agora clinic number and placed in an incubator to keep warm.

At the Agora we perform egg collections under intravenous sedation, not general anaesthesia. It is highly effective in controlling pain and anxiety and is safer than anaesthesia. You will be sleepy and comfortable throughout the procedure and recover very quickly. You will be able to go home around 2 hours later but must have a responsible adult to accompany you. If you require or request a general anaesthetic you will have your egg collection at the Lister for which there will be an extra charge.

After the egg collection you may feel drowsy on and off throughout the day. You should take the following day off work as you should not drive or operate any form of machinery, sign any legal documentation or be left alone during this time.

It is not uncommon following egg collection to feel some lower abdominal discomfort lasting for a few days, for which take Paracetamol. A small amount of vaginal bleeding is also normal. Complications are rare; however every operative procedure is associated with a small risk of infection and bleeding.

You will be prescribed hormone pessaries of progesterone (Cyclogest) to take every day, morning and evening. These are put into the vagina or can be taken as a suppository in the rectum. You should take these from the day of egg collection to support the hormone level in the second half of the cycle. You may need to continue taking them until 12 weeks of pregnancy

8 Sperm preparation

Your partner will need to produce a fresh sample of sperm on the morning of egg collection. We advise 2 to 3 days (no more) abstinence from sexual intercourse or masturbation prior to this day. We prefer it if he can produce a sample here at the Agora. There is a private room designated for this purpose in a quiet area within the clinic. If he anticipates any difficulty with this it is important to mention it to a doctor or nurse well ahead of the day of egg collection as it may be advisable to freeze a sample of sperm as a back up. If the sample is poor on the day of collection we may ask for a second sample. The sample is then processed in the laboratory to separate the health fast swimming sperm from the fluid.

9 Fertilisation

After egg collection each egg is incubated for a short time and then placed in a dish with an aliquot of prepared sperm and left overnight in the incubator. Fertilisation should take place in the next 12 to 18 hours. We anticipate that about 70% of the eggs will fertilise. On the morning after egg collection the embryologist will examine the eggs to see which ones have fertilised and call you to let you know the outcome. A fertilised egg or embryo has a characteristic appearance showing two pronuclei. It then goes on to divide into 2 cells then 4 cells and 6-8 cells over the next 24 to 48 hours. The embryos are transferred back to the uterus 2 to 3 days after the egg collection. Occasionally none of the eggs fertilise which can be extremely upsetting. We will always arrange for you to see one of our doctors if this is the case.

10 Embryo transfer

Embryo transfer is a simple procedure which should be pain free and similar to having a smear test. It only takes a few minutes and you can go home immediately afterwards. We do embryo transfer under ultrasound scan

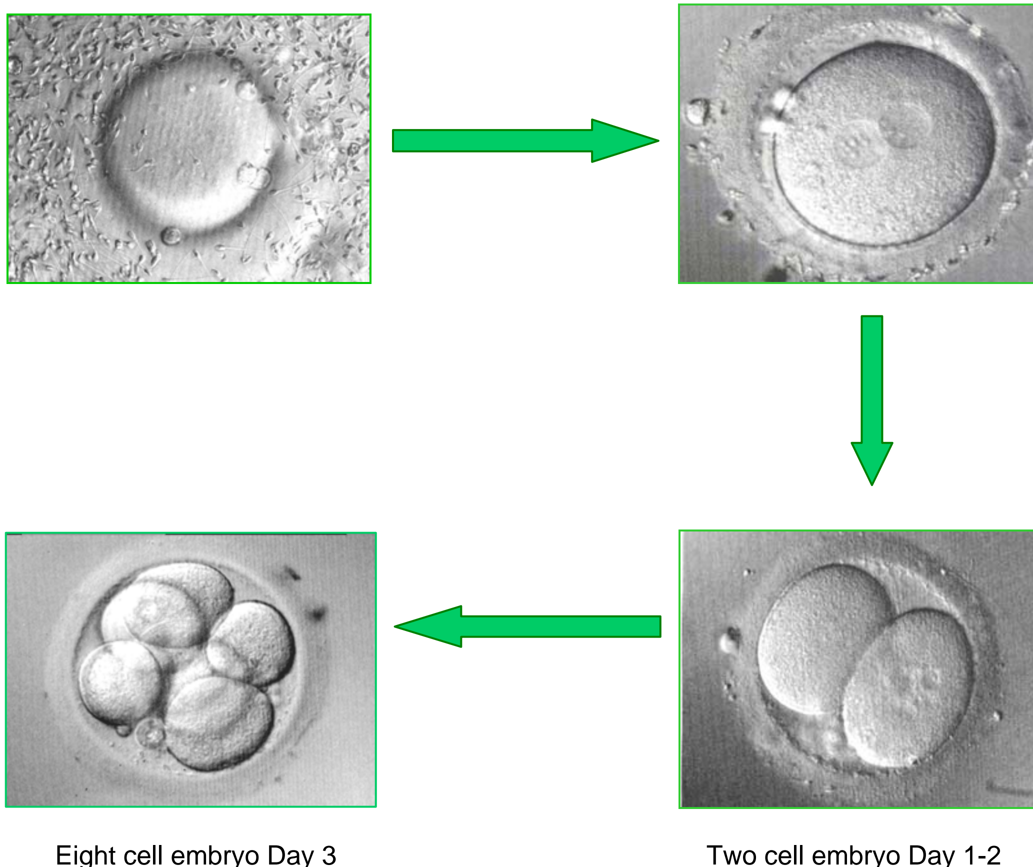
guidance so you will need to have a full bladder. The embryologist will first discuss the number and grade of your embryos with you and which 1 or 2 are to be transferred. Under recent HFEA guidelines we will only put 3 embryos back in exceptional circumstances in women over 40 years of age.

Even when only two embryos are transferred there is significant risk of twins (up to 20%). Multiple pregnancies are associated with increased risk of premature delivery and cerebral palsy as well as most of the complications of pregnancy itself such as diabetes and high blood pressure. In addition once they are born, bringing up twins or triplets has financial, emotional and physical implications for the parents. By adopting a strict policy on numbers of embryos transferred we aim to keep multiple pregnancies to a minimum.

The embryos are quite safe within the uterus and you can walk about, bathe, shower and undertake normal daily activities. It is best to avoid strenuous exercise until your abdomen feels less tender and back to normal. Sexual intercourse can be resumed whenever you feel like it.

If you do not have a period 2 weeks after embryo transfer, a pregnancy test should be done. This can be a standard home pregnancy test or you may choose to come to the clinic for a blood test. If the test result is positive we can arrange for you to come in for an early pregnancy scan 3 weeks later (you will be 7 weeks pregnant at this stage). If the test result is negative you can stop the progesterone pessaries and should come for a follow up consultation with one of the doctors.

11 Embryo Formation



Eight cell embryo Day 3

Two cell embryo Day 1-2

12 Freezing embryos

If there are any surplus embryos of sufficiently good quality, you may be able to have them frozen for future use. The embryologist will advise you on this. However, even good quality embryos may nor survive the freezing process and the pregnancy rate is a little lower than with fresh embryos. Embryos can be replaced either during a natural cycle or a cycle where hormone therapy is used. This will be discussed by your doctor at the appropriate time.

13 Response to treatment

Although we try to determine the dose of drugs based on each woman's individual needs, considering their age, hormone levels, BMI and ovaries, in 5 to 10% of patients the initial dose of drugs given to stimulate their ovaries is either too high or too low and the cycle occasionally has to be abandoned. If the response is too low this is usually apparent at the second or third scan and the dose of FSH can be increased. If there is still no improvement in response, we usually advise cancelling the cycle and restarting on a higher dose of FSH to optimise the chance of IVF working.

In some women, particularly those with polycystic ovaries, the ovaries can be very sensitive to FSH and they may produce too many follicles. We will start to measure oestrodiol levels in the blood once more than twenty follicles are seen on scan and occasionally have to either cancel the cycle or stop the FSH injections to "coast" the ovaries until the blood level of oestrodiol has fallen and we can proceed to egg collection. This is to avoid Ovarian Hyperstimulation Syndrome (OHSS) which is a rare but potentially serious complication of stimulating the ovaries.

14 Ovarian Hyperstimulation Syndrome

OHSS occurs in about 1% of women on IVF treatment despite all possible precautions being taken. The risk is higher if conception occurs as symptoms are triggered by the hormone of pregnancy. Symptoms include:

- Abdominal bloating and associated discomfort
- Nausea
- Shortness of breath
- Dehydration

The ovaries become very large and surrounded by fluid. In severe cases this causes dehydration and thickening of the blood which may lead to the formation of clots. We therefore closely monitor all women at risk of OHSS and admit them to hospital if this becomes necessary. Provided OHSS is diagnosed early and managed correctly, symptoms resolve spontaneously with very little medical intervention. Occasionally intravenous fluids and anti-sickness drugs are required and in rare cases the excess fluid around the ovaries needs to be drained. It is important to drink plenty of fluids and if you are worried that you may be developing symptoms, you must contact the nurses at the Agora.

15 Contacting the nurses

The telephone number for the fertility nurses at the Agora is 01273 229411. Out of hours there is an answer phone to leave non-urgent messages. In an emergency you can speak with the on-call doctor or nurse on 07912 341857