FREQUENTLY ASKED QUESTIONS ABOUT IVF

Is there something we can do to improve our chances of succes?

Even though IVF treatment is a medical process on which you have no influence, there are a number of things connected to your lifestyle which you can change to increase your chances of benefiting from the treatment.

Stop smoking - for both partners - is the most important thing to do. Its positive effects cannot be equaled by any medical adjustment of your treatment!

Did you know - as various studies have shown - that women who smoke need about twice as many IVF attempts in order to achieve a pregnancy! Or that the residue products of nicotine lead to a faster decrease of the ovum reserve, which according to several researchers can cause smoking women to enter their menopause one to four years earlier? Or that smoking also has a negative influence on the fertility of man? A smokers' sperm is significantly poorer in quality than that of a non smoker.

If you really want to get pregnant, the first thing you both should do is stop smoking!

The best motivation for you as a woman to stop smoking when starting IVF treatment is the fact that the implantation rate of an embryo quickly gets back to normal, i.e. it is restored to that of a non smoker.

Does ovarian stimulation affect the store of eggs resulting in early menopause?

Definitely not. Ten or more follicles may be encouraged to ripen during stimulation, but this happens during a normal cycle too. The only difference is that most of the follicles die during a normal cycle, leaving only one or two survivors. With IVF they all ripen. In other words, ovarian stimulation saves many of the eggs which would otherwise be lost.

In the early part of her fertile years, a woman has more than 400,000 egg cells on average, most of which die spontaneously as the years pass. Stimulation draws on a large reserve of eggs which would otherwise remain almost completely unused.

Are the hormone treatments harmful for me or for our (future) child?

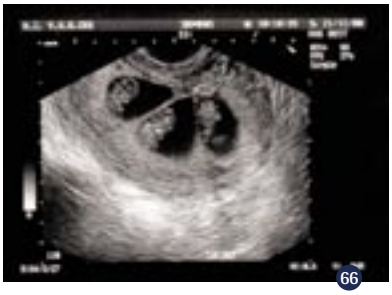
As stated in this guide, the hormones administered during IVF treatment may have some side-effects. Fortunately, they are not serious and are only temporary.

Claims that the hormones used in IVF treatment can be carcinogenic or have other 'harmful' effects are not founded on medical data. Moreover, these hormones were administered to women with infertility problems on a large scale long before IVF treatments were developed, without any harmful effects.

Also with regards to children born from IVF/ICSI up until now no study has proven that (certain) cancers would occur more frequently than with children who were conceived without hormonal stimulation.

Having said that, research regarding the effects of hormone treatments is still conducted worldwide in the interests of safety.

Does IVF significantly increase the chances of twins or triplets?



66| This ultrasound scan reveals triplets.

No, not anymore. The medical stance of the CRG has always been to transfer only a limited number of embryos, and the statutory rules as well have as principal goal to restrict the number of embryos that will be transferred.

Why is this so important? Well, if a woman who is under the age of 37 becomes pregnant through IVF, she has an almost 30% chance of producing twins if two embryos were transferred into her womb and nearly 40% if three embryos were transferred. In the latter case, there is a 5% chance of triplets.

Multiple pregnancies increase the risk of miscarriage, premature births and other medical problems for mother and/or child. The higher incidence of twins and triplets also explains the significantly higher perinatal mortality rate (i.e. number of deaths between the 28th week of pregnancy and the 7th day after birth) previously

associated with IVF. In other words, this higher perinatal mortality rate was completely unconnected with laboratory fertilization.
In order to meet these important health considerations the Belgian legislator has made the maximum allowed number of embryos that can be transferred dependant on the age of the woman and the number of treatments she has undergone (see Practical, Financial, p. 114). As a rule, maximum two embryos - but often one - are transferred when it concerns a woman under the age of 37.

Do we have to be extra careful after transfer of the embryo to ensure its implantation?

There is actually nothing you can do – medically nor practically – after the transfer of the embryo to aid its implantation. A good number of studies have researched whether bed rest (e.g. staying the night at the hospital) after the embryo transfer has a positive influence on the chances of success of the treatment. The outcome was unanimous – there is no indication that this would lead to an increased chance of pregnancy.
Regarding other activities as well (travel, sports, bathing, etc.) no study revealed any of those to have an adverse effect. So it makes no sense at all to feel guilty if the implantation doesn't occur: your behaviour certainly has nothing to do with it.

How can we be sure that the embryos transferred to the womb are really our own?

The CRG follows very strict and highly reliable procedures to identify eggs, sperm and embryos. We take no risks whatsoever. In our laboratory, the precise source identities of all eggs, sperm and embryos are tested carefully by two people, separately from each other. Also, during treatment your name will be asked for repeatedly; now you know the reason why.
In practice, errors (read switches) are excluded.

Is it a sensible idea to freeze embryos for use at a later date?

The new legislation regarding assisted fertilization and everything related specifies that prior to commencing your treatment you must decide what needs to be done with surplus embryos. These are embryos that originated from your treatment, but that you didn't need for transfer. You need to stipulate in the consent form that you sign prior to your treatment whether you want to have those frozen or not.
If you chose to have them frozen, you will first have to use the frozen material at the next IVF attempt or if you wish another child, unless there is a good medical reason to use fresh embryos again and thus to start over the whole IVF treatment.

67| IVF and ICSI treatments are permanent subjects of scientific investigation.

From a **health perspective of the baby** that possibly ensues from the embryo there is no objection against freezing. The misconception that thawed embryos produce more babies with abnormalities is not supported by any medical or scientific evidence.

But from a viewpoint of **efficiency of the treatment** we must note that not all embryos survive the freezing process, whilst thawed embryos have a smaller chance than fresh ones of implanting and developing successfully in the womb. Therefore the chances of success of a treatment with frozen embryos are less than one with fresh embryos, and this could be an argument against freezing.

Furthermore there also is an **emotional-psychological aspect** to consider, because you also need to stipulate in the contract what needs to be done with the frozen embryos once you have no (further) need for them: donation, destruction or releasing them for scientific research. You might have moral difficulties subsequently, especially if the IVF treatment would have resulted in the fulfillment of your child wish.

Does IVF produce a higher incidence of ectopic pregnancy (implantation outside the womb)?

A woman who is pregnant through natural fertilization has a 1% chance of an ectopic pregnancy. Chances are no higher for an IVF pregnancy unless the woman concerned already has damage to one or both of her fallopian tubes.

However, IVF treatment may produce an ectopic pregnancy. Even though the transfer involves very careful insertion of the embryo(s) into the womb, the embryo does not immediately attach itself to the wall of the womb. This explains why it sometimes still migrates to the fallopian tube and develops there.

Do children born as a result of IVF have more abnormalities than children born following natural fertilization?

All children born following an IVF or ICSI treatment at the CRG are examined by the Centrum voor Medische Genetica (CMG or Centre for Medical Genetics) of UZ Brussel at the ages of two months and one year. Abnormalities are found in around three percent of the children, which corresponds not only with the figures of other renowned IVF centres but also with the general population of children born following natural fertilization. There are no indications of increased risk.

However, it is still too early to draw clear conclusions in respect of some of the new techniques developed in the wake of IVF, owing to insufficient statistical data. For example, ICSI appears not to involve any greater risk of abnormalities, but it is still too early to be absolutely certain.

What happens to our frozen genetic material if our personal life situation changes?

As mentioned above you have to sign a form prior to commencing your fertility treatment where you stipulate what needs to be done with your frozen genetic material once you have no (further) need for it. This concerns you – the man – as well if you had (sperm) cells frozen that were harvested through surgery as part of the treatment.

If your child wish is fulfilled or if you abandon further treatment you have the choice to donate the material, to have it destroyed or to release it for scientific research.

However, if your personal life situation changes while you might in principle still have need for the genetic material a different set of rules apply. The new legislation (2007) regarding assisted fertilization and everything related stipulates that you have to consider this possibility as well and make your decision known in a permission form. So should you divorce during the treatment or should one of the partners pass away, it will depend on your contractual decision what happens with the stored material and if one partner still can claim it after the other partner has passed away. As long as the agreed upon storage period is in effect your decision can be revised, but this needs to be done unanimously: each and every revision needs to be signed by both original partners.

68| Preimplantation genetic diagnosis is only performed to detect possible congenital disorders.

Can we choose whether we have a son or a daughter?

The sex of embryos used in IVF can be determined before they are transferred to the womb. However, selection based on the embryo's sex is only made on valid medical grounds. For example, when we know that sons of a couple will suffer from a congenital disorder while daughters are likely to be healthy, clearly only female embryos will be selected for transfer. Howerver for ethical reasons we are unable to accommodate purely personal preferences for a boy or a girl.

CENTRE FOR MEDICAL GENETICS

Every couple who dream of parenthood hope and pray their child or children will be perfect in every respect. The Centrum voor Medische Genetica (CMG or Centre for Medical Genetics) of UZ Brussel is specialized in detecting congenital disorders and wants to help couples make this dream come true. Whereas many abnormalities are still unpredictable and unavoidable, an increasing number can now be diagnosed.

CALCULATING THE RISKS IN ADVANCE

If a couple suffers a congenital disorder or has a history of any such condition, the CMG can calculate what the risk is for the child even before a pregnancy is attempted. Also, if the woman is over 35, she and her partner should know the risks associated with a(nother) pregnancy. The chances of the baby having Down's syndrome increase sharply with age.

Based on the figures and calculations of the CMG, you will be able to better weigh up the pros and cons of trying for a baby. You might decide not to take the risk, or perhaps go ahead with donor sperm, donor eggs or donor embryos. Or you may accept the risk and the potential consequences for your child and yourselves. Or you might decide to have the pregnancy terminated if prenatal diagnosis shows an abnormality.

NO TOTAL CERTAINTY

Nobody - not even the CMG - can guarantee that your child will be healthy and sound in all respects. Our tests can only detect a certain number of abnormalities. Whereas a prenatal or preimplantation diagnosis (PGS/PGD, see paragraph below) provide a greater degree of certainty, it is never a 100% certainty.

The CMG does not oblige you to do anything. Its role is purely informative and advisory. For example, if a flake test shows that a foetus has a serious disorder, we shall provide you with information about the precise nature and consequences of the abnormality. The final decision to terminate a pregnancy or not is yours alone. We always respect your decision, within legal limits and the bounds of medical ethics.

PREIMPLANTATION GENETIC SCREENING OR DIAGNOSIS (PGS/PGD)

Initial testing can now be carried out very early during IVF treatment, i.e. after fertilization in the laboratory and before the embryo transfer. This is known as 'pre-implantation genetic screening' (PGS) or 'pre-implantation genetic diagnosis' (PGD): the examination of embryos before they are placed in the womb.

This research possibility is offered in the Universitair Ziekenhuis Brussel – in a close collaboration between the CRG and the CMG – to patients wishing to undergo a fertility treatment but who have a history of congenital disorders or run a higher risk for having abnormal embryos.

Thanks to PGS/PGD these patients who previously only could rely on prenatal examinations to assess their embryo can avoid a potential abortion: the defect in the embryo is tracked before it is replaced in the womb.

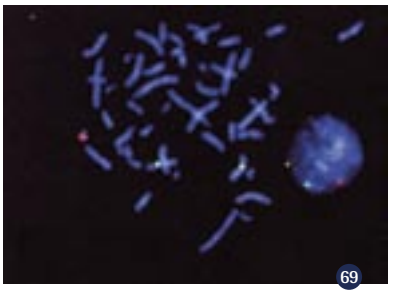
For the costs of a PGS or a PGD, which also comprise a preceding genetic examination of both parents, we refer to p. 74 for foreign patients and to p. 114 for Belgian ones.

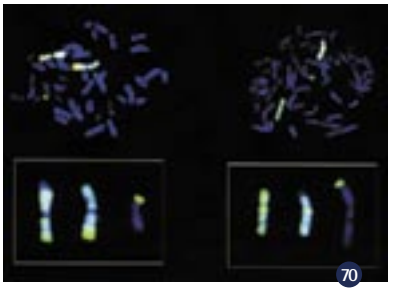
In the laboratory

Once several eggs from the same woman have been fertilized in the laboratory via ICSI, the embryos are allowed to grow until they have eight cells (day three). One or two cells are then very carefully removed from each embryo and genetically tested.

During the screening (PGS) certain chromosomes are checked to make sure they are normal; PGD does make an explicit diagnosis: does this gene carry the illness we are trying to detect or not?

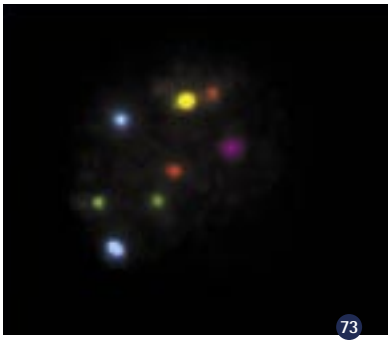
The results are known on day five. Embryos with signs of abnormality are not used, normal embryos are kept for possible





69| Chromosome investigation can reveal certain disorders. In this particular case 47, XXY or Klinefelter's syndrome...

70| ... and in this case an abnormal exchange between the genetic carriers (translocation).



71| Set up in the laboratory for PGD test (preimplantation diagnosis).

72| One cell is taken from an embryo with eight cells.

73| Reproduction of the cell with the signals of the different chromosomes.

The CMG carries out gender testing of embryos before transfer for medical reasons only.

transfer. If there are more than needed for transfer any surplus embryos can be frozen. The others are not used unless for scientific research purposes or to confirm the diagnosis.

Which applications and for whom?

PGS/PGD is used only for couples running an higher risk for their baby to suffer a congenital disorder.

Moreover, a PGD can only be performed with IVF treatment in combination with ICSI, to allow working with as many good quality embryos as possible.

During their treatment patients are counseled by a clinical geneticist and a CMG psychologist. Making a diagnosis on the basis of one single cell of an embryo is indeed only possible if intensive research was conducted beforehand. Each disorder requires a separate, often individualized test. That is why you may be confronted with a long waiting period, sometimes up to one year.

Nowadays a good number of congenital disorders can already be tracked via PGS/PGD. Let's take a look at two examples.

Cystic fibrosis (mucoviscidosis)

Cystic fibrosis (mucoviscidosis) is a severe congenital disorder that produces abnormally thick mucous in the lungs causing many infections.

About one in 2,000 children is affected by mucoviscidosis and one person in 22 is a carrier. If both partners are carriers, their child has a 25% risk of developing the condition. Preimplantation diagnosis allows healthy embryos to be separated from those carrying the disorder.

Gender-related disorders

Preimplantation diagnosis allows the sex of the embryos to be determined, thus providing a useful means of avoiding gender-related disorders.

An example is haemophilia A, a congenital disorder in which the blood clots very slowly and even the slightest injury can cause prolonged and life-threatening bleeding. The disease is passed on by the woman but only affects men. Male babies of a female carrier run a 50% risk of inheriting the disorder.

Preimplantation diagnosis allows for a selection of embryos based on their sex and thus for female embryos only to be transferred to the womb of a woman carrying haemophilia A.

How safe is preimplantation diagnosis?

Removing one or two cells from an embryo at the eight-cell stage produces one of two possible outcomes, i.e. the embryo either survives or dies. The great majority survive and very few die. There

is no evidence to suggest that preimplantation diagnosis damages an embryo that nevertheless survives, although experience with this new technique is still limited.

Extra tests

The success rate of PGS/PGD is estimated at 95%. Whereas a five percent chance of a wrong conclusion may be small, more tests are advisable. To cover this possibility, the CMG carries out a prenatal diagnosis provided the woman becomes pregnant.

Frequently asked question
Do children born as a result of IVF have more abnormalities than children born following natural fertilization?
Find the answer on p. 82.

PRENATAL DIAGNOSIS: TESTS BEFORE BIRTH

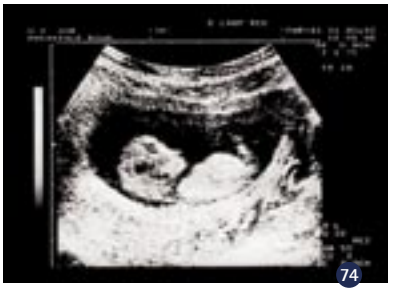
To a certain extent, tests during pregnancy can help to determine whether an embryo will develop into a healthy fetus. An ultrasound scan is an invaluable means of prenatal diagnosis, but sometimes more specialized examinations may be required: a flake test, an amniocentesis or an umbilical puncture. These three tests can be used to detect practically all the same abnormalities.

Indications

We recommend prenatal diagnosis
> to all couples with a history of congenital disorders;
> to couples where the woman is 35 or older; and
> to couples who have opted for IVF in combination with ICSI, i.e. the laboratory fertilization has taken place by injecting one sperm into each egg. IVF has become a well-known technique, ICSI is not that popular yet. Although the technique does not seem to produce extra abnormalities in children, prenatal diagnosis is recommended until further notice.

Ultrasound scan

Ultrasound scans are current practice in the monitoring of a pregnancy. But they are also used to detect fetal abnormalities. Ultrasound scans are a safe and painless method to visualize the womb, the placenta and the fetus by means of sound waves.
In contrast with the vaginal ultrasound scan, which is conducted with a probe in the vagina, pregnancy is shown with a scanner device going over the abdomen. For this examination it is preferable that you have a full bladder.



74| Ultrasound scan at seven weeks.

Blood analysis for Down's syndrome

A flake test, amniocentesis or umbilical puncture may not be needed immediately to check whether the fetus shows signs of Down's syndrome. Initial blood tests can indicate whether the risk is high. If so, a detailed diagnostic test can be performed to be sure.

Blood analysis is useful only as an aid. Although it can indicate potential problems, it is not conclusive. The result may show that everything is normal even though the fetus does have Down's syndrome.

Flake test

This test is carried out in the tenth week of pregnancy, and involves the removal of a small sample of tissue (a biopsy) from the placenta for examination. The tissue is removed using a thin tube that is passed into the womb via the vagina, or a needle that is inserted carefully through the abdominal wall. The biopsy procedure is guided by an ultrasound scan.

The flake test derives its name from the flake-like appearance of the placenta, and produces definite results by the twelfth week of pregnancy.

Amniocentesis

Amniocentesis is carried out around the fourteenth week of pregnancy. The amniotic fluid surrounding a fetus in the womb contains cells shed from the embryo's skin. In amniocentesis, a sample of the fluid is taken by piercing the amniotic sac through the abdominal wall, using a very fine needle.

The results of this test are usually available around the eighteenth week of pregnancy.

A carefully considered choice

The flake test can be carried out earlier than amniocentesis, although the chances of triggering a miscarriage are higher, i.e. 1% compared to 0.5%.

The choice of test is determined in each individual case by consultation between our medical specialists and the couple concerned. Generally speaking, amniocentesis is used for single pregnancies and the flake test for twins.

Umbilical puncture

An umbilical puncture is sometimes preferred to a flake test or amniocentesis. This procedure differs from amniocentesis in that blood from the fetus' umbilical cord is analysed, rather than amniotic fluid.

An umbilical puncture is not performed before the eighteenth week of pregnancy at least. If a physical deformity is detected, ultrasound scanning is used to determine whether this is coincidental or congenital.

Umbilical punctures are also used in cases where prenatal diagnosis is called for when a woman is already eighteen or more weeks pregnant.

75-76| Postnatal check up, two months and one year after birth.

POSTNATAL ANALYSIS: TESTS AFTER BIRTH

All couples who have a child through the CRG at UZ Brussel are strongly advised to have their children examined by one of the specialists at the CMG at the ages of two months and one year.
Why is postnatal analysis important? Some disorders do not become evident until after the child is born. The data that are currently available suggest that IVF and related techniques (ICSI, preimplantation diagnosis, etc.) carry no increased risk of abnormalities. UZ Brussel believes it is important to verify this data through consistent testing.

Follow-up of pregnancy and birth for scientific purposes

As soon as you are pregnant you will – as mentioned previously – be followed up and assisted by your own gynaecologist. Nevertheless you will receive two questionnaires from us concerning the course of your pregnancy and the delivery. Those fit in with the scientific research regarding the consequences of fertility treatments for the baby and the mother which is permanently conducted by the CRG.
That is why we request all our patients to return to us the filled-out questionnaires. Not only will you help further scientific research, but you will also serve numerous future patients by doing so.