

INTRODUCTION

Dear Sir, Madam,

A detailed examination of your infertility file has led us, together with you, to consider recourse to egg donation.

You will certainly have many questions to ask about this technique. This brochure has been drawn up in order to explain to you exactly what is involved in egg donation. As you read this brochure, rest assured that the entire team is at your disposal to reply to any particular questions you may have.



1. WHAT IS EGG DONATION?

Egg donation is one of the techniques of reproductive medicine. Its basic principle consists of retrieving from a woman (called a donor) her reproductive cells or eggs, called oocytes or ova, which are situated in the ovary, in order to donate them to another woman (the patient, called the recipient) to be used in the latter's parenting project, through in vitro fertilisation (IVF) (Fig. 1).

This donation, regarded by some for as a donation of an organ or blood, is a donation of life, result of the fruit of great feminine solidarity, enabling certain women to allow others to become mothers. This exceptional donation without any doubt gives rise to questions at various levels: practical, genetic and ethical.



2. THE INDICATIONS FOR EGG DONATION

Originally intended to treat women suffering from early menopause or who were carriers of genetic anomalies, the indications for this technique have been extended to other fertility disorders, as well as to women beyond the normal age of menopause.

Egg donation is therefore practised to remedy many causes of infertility, classifiable in 5 categories:

1. Early menopause or ovarian dysgenesis
2. Genetic disease
3. Ovarian insufficiency
4. Insufficient egg quality during IVF
5. Late age for reproduction (physiological menopause)



3. CONDITIONS FOR EGG DONATION

The new Belgian Law "concerning medically assisted reproduction and the use of supernumerary embryos and gametes" was passed in the House of Representatives on 9/3/2007 and published officially Gazette on 17/7/2007; it has been in force since 27/7/2007.

This Law provides for limitations of age for the recipients:

- "**Request** for the implanting of embryos or insemination of gametes: for women having reached their majority, aged 45 years maximum", i.e. up to and including the day before their 45th birthday.
- "**Implantation** of embryos or insemination of gametes: for women having reached their majority, aged 47 years maximum", i.e. up to and including the day before their 47th birthday.

This Law also stipulates that the donor and the recipient couple be informed through an informed consent binding them to the ART centres.

Our department offers anonymous donations or **indirect donations**, as well as non-anonymous or **directed** donations.

Indirect donation means that the recipient couple who have recruited a donor will not benefit from the latter's eggs but from those of another donor whom they do not know. This anonymity ensures that the identity of the donor will never be revealed to the recipient couple and vice versa. The donor's eggs (around ten on average), obtained after ovarian stimulation and egg retrieval, will be divided up between two to three recipient couples who will then receive, in the best scenario, approximately three eggs per attempt.

Directed donations imply that the recipient couple who have recruited a donor will have the benefit of all the eggs of their own donor. In this case there is no anonymity: the recipient couple know the donor whom they have recruited.

Candidates for the donation of eggs (called donors) are rare, on the one hand because it is one of the assisted reproductive technology (ART) which is still little known and, on the other, because the treatment requires a demanding physical and organisational investment on the part of the donor. In addition it involves certain risks. These circumstances oblige us to create a waiting list for recipient couples. Waiting time before receiving a donation varies between 6 months and two years for indirect donations. Recipient couples who have been able to recruit a donor will have priority on the waiting list.



4. STEPS TO BE TAKEN TO HAVE THE BENEFIT OF AN EGG DONATION

From the medical point of view?

An initial consultation between the department's consultant gynaecologist and the recipient couple will be scheduled.

Following this consultation the following will have to be done:

On the female side:

- various examinations in order to exclude possible implantation failures: ultrasound scan, hystero-graphy or hysteroscopy.
- a hormone test, a screening examination of the cervix (smear test) or even a mammography will also be carried out.
- a blood test with a view to pregnancy to screen for toxoplasmosis, Rubella, HIV, syphilis, hepatitis B and C, cytomegalovirus and chickenpox.
- in patients over forty years of age, a medical check-up may be required and carried out by the family doctor.

On the male side:

- a blood test to screen for HIV, syphilis, hepatitis B and C, cytomegalovirus and Chlamydia..

- a karyotype and screening test for cystic fibrosis, as well as for certain other pathologies of genetic origin may be carried out according to the quality of the sperm and the ethnic origin of the father (thalassaemia, sickle-cell anaemia, Tay-Sachs disease etc).
- an appointment must be made with the secretariat of the andrology laboratory in order to carry out a semen analysis and possibly freeze a sample of semen.
- in patients aged over 55, a medical check-up may be required and carried out by the family doctor.

From the administrative and financial point of view?

A letter stating that the couple wish to benefit from an egg donation at the ART department of the hospital must be sent to the secretariat of the ART center, by registered letter (Ms C. GARNIER).

An egg donation informed consent form (agreement to receive gametes) will be given to you at the consultation. It must be signed by the two partners and returned to the ART center before you can benefit from the donation.

For Belgian female patients covered by a mutual insurance company and under 43 years of age, an application/applications for the covering of the laboratory expenses or even the drugs with a view to IVF must be submitted to the medical examiner of the mutual insurance company.

This form must be completed by the department's consultant gynaecologist. Once the agreements of the mutual company have been obtained they must be submitted to the ART secretariat.

An estimate, which will be based on the insurance situation of the individual patient (age, number of previous cycles, covered by mutual insurance or not, nationality), will be given to you by our administrative secretary (Ms C. GARNIER – 04/239.46.24). It must be approved and signed before treatment can commence. Payment is always in advance for the retrieval of eggs.

Explanations with regard to the number of cycles covered by these payments will be given to the couples on this occasion and these arrangements will be confirmed and signed after all questions have been asked.



5. WHO ARE THE EGG DONORS? RECRUITMENT, COMMITMENTS, EXAMINATIONS TO BE CARRIED OUT.

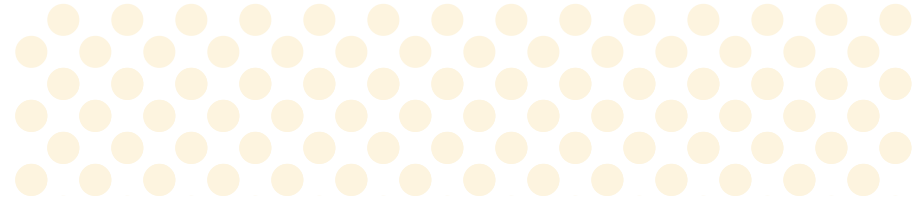
The donors are usually recruited among the family or social circle of the recipient couple, a sister or a friend for example who has become aware of these fertility problems and is prepared to make the effort to help the couple become parents. The donation proposed by a person of this circle then gives rise to a "donation by exchange or indirect donation" or to a "directed or direct donation".

There are therefore among the donors a great majority who are motivated by solidarity, the desire to give something of oneself to enable couples to realise their parental project. On the basis of friendship and of the understanding of a problem shared, that of infertility, women come together to promote a treatment during which they must nonetheless demonstrate a strong will to achieve the goal.

It is recommended to recruit donors who have already had at least one child and are under 36 years of age, essentially to limit the risks of Down's syndrome (the incidence of which increases after the age of 35), but also to increase the chances of pregnancy, which greatly depend on the age of the donor.

The candidate donor must be ready to undergo different preliminary examinations, attend several consultations with the ART center's gynaecologist and two interviews with the psychologist in charge of egg donations. She will also be asked to come to the information session about IVF (first Monday of the month at 7.30 PM at the "Polyclinelle").

The preliminary examinations requested of the donor are analyses aimed at excluding the transmission of any disease to the recipient and/or foetus. They also have the purpose of ensuring that the treatment which the donor is going to undergo for another person will not damage her health or put her in any danger. In the first instance this involves a questionnaire (anamnesis) concerning her medical history and that of her family, as well as her life style (smoking, exposure to toxic substances



etc). The gynaecologist will then carry out a gynaecological examination, including an endovaginal ultrasound scan, in order to explore the ovaries (position, absence of anomalies, egg reserve). He/she will ensure that the recommended screening examinations are carried out (cervix, breasts). Finally a blood test will explore the donor's ovarian reserve, the correct functioning of the glands which control the work of the ovaries (thyroid, adrenal, pituitary) and infectious disease serologies) hepatitis B and C, HIV, Syphilis, Chlamydia, CMV).

According to the ethnic origin of the donor, certain genetic diseases are screened for (cystic fibrosis, thalassaemia, sickle-cell anaemia, Tay-Sachs Disease etc). An analysis of the chromosome formula (karyotype) and her blood group will be required.

During the treatment, which will last for 2 to 3 weeks, the donor must be available for ultrasound scans and blood tests, which are difficult to schedule as they depend on the menstrual cycle.

The egg donor will be informed, 48 hours in advance, of the day of the surgical intervention to retrieve the eggs ("oocyte pick-up" - OPU). This intervention will require day hospitalisation.

During the stimulation treatment and even after the eggs have been retrieved the donor may not have unprotected sexual intercourse because of the risk of non-programmed pregnancy. As the retrieval of the eggs is not always complete, a residual egg could be fertilized by sperm, the survival time of which ranges from 48 to 72 hours, which is why the contraception period must cover at least 3 weeks (condom or non-hormonal IUD).

All this treatment will require several visits to the Hospital (gynaecological consultations, consultation with the anaesthetist, psychological consultations), and will entail transport costs or possibly even loss of salary. This is why a fixed sum of €500 is allowed to cover the donor's costs, pursuant to the Law of July 2007.



6. PSYCHOLOGICAL SUPPORT

For the recipient couple:

As there will be many questions before the egg donation is received, the couple will have the opportunity to meet the psychologist for at least one interview.

Essential subjects will be discussed during these interviews, and particularly: the acceptance of the donation by both members of the couple, the concrete meaning for them of sterility, the idea of breaking biological kinship, the recourse to an third-party biological line etc.

The question of secrecy in the donation of eggs also gives rise to many questions: should the family/social circle and the child be told the history of his/her conception? At what time in the child's development is it preferable to talk about this? What might the consequences of this revelation be for the child, for the equilibrium of the family? What might the negative effects be of keeping it secret, of late or accidental revelation? etc.

The objective of these interviews is to help couples to engage in and develop a discussion of these different themes, each respecting the history and opinions of the other.

For the donor:

Where a indirect donation is involved, one obligatory interviews is provided for with the donor of the eggs (preferably accompanied by her partner). The interview will take place before any decision is taken about inclusion in the therapeutic protocol. The primary objective of this is to assess the reasons which motivate the person to make an egg donation and to ensure that she is acting in complete liberty and without any external constraint.

They will also provide the occasion to give specific information about the treatment (conditions, conduct, implications, constraints, risks etc) and make it possible to address essential questions: what is the nature of egg donation? What are its concrete forms? What is the position of the donor towards the child to be born? How to understand and accept the concept of anonymity and non-anonymity? To what extent does the idea of debt play a part? etc.

In the case of a directed donation, the two couples (the donor and her partner and the recipient and her partner) each have an interview with the psychologist. A third interview with the psychologist and the two couples is then organised. This provides the occasion to address common problems, to ensure that the treatment arrangements are clearly understood by each of the parties, to see that the project is transparent and that no member is taking part against his/her will or under any pressure whatsoever.

The couple, as well as the donor, may contact the psychologist at any moment in the process and ask for an additional interview.

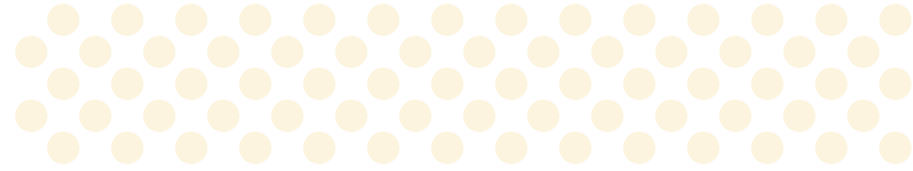
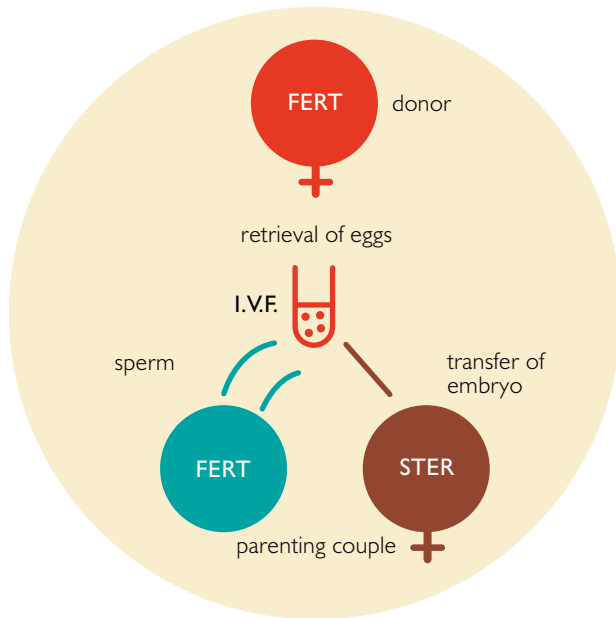


7. EGG DONATION AND TREATMENTS

Around the relatively simple principles of egg donation, the extremely developed technique of *in vitro* fertilisation has been elaborated.

In the egg-donation process, **the donor** will donate her eggs to the patient or recipient. These eggs will be fertilised by the sperm of the recipient's husband. The embryos so obtained will be transferred into the recipient's uterus where they will implant and bring about the pregnancy hoped for by the recipient couple (Fig. 1).

Principle of egg donation (fig1)



The technique:

During egg donation, the donor's cycle and that of the recipient are synchronised by hormone "manipulation". The donor's cycle is hyper-stimulated in order to obtain several eggs, while that of the recipient is shut down. The maturation of the endometrium (the mucous membrane covering the wall of the uterine cavity) of the recipient is then induced by the administration of hormones at a pace that allows her to be in phase with the donor and obtains an endometrium ready for the implanting of embryos when these are obtained, this time being determined by the results of the stimulation of the donor.

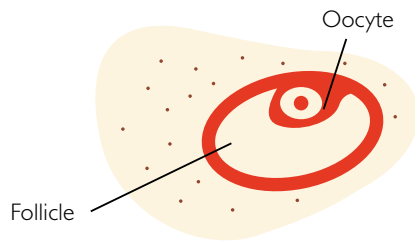
The donor's treatment:

The donor's treatment is an *in vitro* fertilisation treatment, comprising a first, medical, stage of ovarian stimulation and a second, surgical stage, the retrieval of the eggs.

The medical treatment sometimes consists, in the first instance, of down-regulation of the ovaries and pituitary gland with a pituitary inhibitor in the form of a nose spray or subcutaneous injections, for two to three weeks. The down-regulation phase is not always indispensable. Four days after this inhibition has been achieved, the ovarian stimulation phase begins; it consists of subcutaneous injections of hormones which induce the development of several follicles (liquid pouches containing the egg) (Fig.2). These hormones, called gonadotropins, are of human origin (Menopur®) or are manufactured artificially (Puregon®, GonalF®). They play the role that the pituitary gland plays in the natural cycle, but more powerfully, so that some ten follicles reach maturity instead of the one or two under natural conditions. This stimulation phase lasts about 12 days.

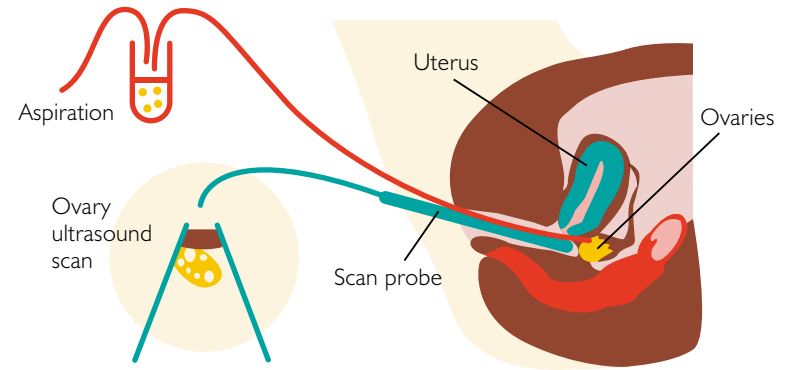
To avoid spontaneous ovulation, which consists of the rupturing of the follicle and the release of the egg into the abdomen, another hormone inhibiting the normal functioning of the pituitary gland may also be administered by subcutaneous injection or spray (Cetrotide®, Orgalutran®, Decapeptyl®, Suprefact®). This hormone is introduced during or just before stimulation. At the end of stimulation, the final maturation of the egg is achieved through the administration of a final molecule (Pregnyl® or Decapeptyl®). The retrieval of the oocytes (OPU) will be scheduled for 34 to 36 hours after this final injection, i.e. before the follicles have ruptured (Fig.3).

The follicle and the oocyte (fig2)



The surgical treatment enables the retrieval of the eggs. It takes place under local or general anaesthesia, according to the indications of pain risk factors and taking into account the desires of the donor. The intervention takes place in the operating theatre in order to comply with all the necessary aseptic measures. It is a "closed abdomen" procedure. The gynaecologist inserts a thin needle through the vagina; this reaches the ovary and penetrates the follicle, aspirating the follicular liquid containing the egg (Fig.3).

Retrieval of eggs (fig3)



At this point, the work of the biologists becomes necessary; they examine the follicular liquid under the microscope and isolate the egg, which is not visible to the naked eye. The egg is preserved in a culture medium and in an appropriate environment (incubator) before being fertilised.

Risks linked to the treatment

Apart from very rare serious complications (less than 1% for the donors) requiring active treatment, patients presented few complaints related to treatment due to the procedure. Abdominal discomfort and pain, which are nonetheless what is most frequently encountered, rarely constitute a complaint requiring a consultation.

Complications linked to stimulation:

Discomfort linked to stimulation:

The hormone injections are carried out subcutaneously using ever finer needles, which limits pain at the injection site. Allergies to the products used are very rare and can be avoided by changing the drug for another in the same treatment range. At the end of stimulation, a certain abdominal discomfort may be felt, because around ten follicles are present instead of the one or two found without stimulation.

In the same way, the discomforts felt at the approach of one's period, called the "premenstrual syndrome" (bloating, mood disorders, breast pain), sometimes occur more intensely a week after the retrieval of the eggs.

Ovarian hyperstimulation syndrome (OHSS):

OHSS is a rare complication, presenting different degrees of gravity and occurring around a week after egg retrieval. The first symptoms are abdominal discomfort, accompanied by digestive disorders. The ovaries increase in size because of the presence of corpus luteum cysts and fluid may appear around the intestines (ascites). This is a syndrome of progressive gravity, the severe form of which is almost non-existent in donors as the aggravating factor par is pregnancy, which by definition will not occur in the stimulated donor but in the non-stimulated recipient.

The principal risk factor is the presence of micropolycystic ovaries. By close monitoring of their ovarian response to stimulation, certain at-risk patients may also be detected. Moderate OHSS requires only outpatient monitoring by means of blood tests and ultrasound scans.

Ovarian torsion:

This complication is a torsion of the blood vessels which supply the ovary, caused by the rotation of the heavier ovary on itself. The ovary is no longer vascularised and if this situation continued, it could become necrosed. The patient will experience abdominal pain and nausea following egg retrieval. Incidences of torsion are rare in donors. Caution is observed in stimulation and the ovaries recover a normal structure at menstruation, again because the donor is not subject to the effect of the pregnancy hormone. The treatment recommended for this kind of complication is the uncoiling of the torted ovary using laparoscopy, enabling proper functioning to be restored to the affected ovary.

Complications linked to egg retrieval:

These complications are related to the vaginal approach (passage of the aspirating needle through the vagina into the abdomen) and the indirect monitoring of operations under ultrasound scanning.

The eggs may be retrieved under local anesthesia with slight sedation or under general anesthesia. In the latter case, the risks involved in this type of anaesthesia must also be considered.

Haemorrhage:

Loss of blood from the vagina is the most frequent haemorrhage (8.6%) but it is moderate and without consequence.

Slight abdominal bleeding is common during ovarian puncture. It is mostly moderate and is usually without medical consequence. Abdominal discomfort may be observed for two to three days following egg retrieval. This symptom responds easily to the traditional painkillers (paracetamol etc.).

Significant bleeding around the intestines (haemoperitoneum) is rare after egg retrieval (0.08 % to 0.2%). It usually appears following 48 hours by abdominal pain and signs of low blood pressure, rarely by fainting. The treatment is usually limited to observation of the patient in hospital to ensure that the bleeding stops spontaneously and is not a cause of any danger to her. Very rarely, a procedure to carry out haemostasis (stopping of bleeding) is required.

Lesions of the pelvic organs:

The ultrasound-guided vaginal approach theoretically exposes the patient to lesions of the intestine and ureter, but the cases described are very rare, around 0,04% .

Infection:

These complications are related to the vaginal approach which can lead to infection of the abdomen by germs carried from the vagina on the aspirating needle. Their frequency is 0.3%. The symptoms generally are fever and abdominal pain that occur during the week following eggs retrieval.

The accidental puncturing of the bladder by the aspirating needle is usually without consequence; however the complication of a urinary infection can occur, and the presence of blood in the urine (haematuria).

In these two situations, antibiotic treatment must be administered to the donor.

Treatment of the recipient:

Medical treatment consists of taking hormone treatment throughout the period of waiting for the egg donation.

When the donor begins her treatment, the hormone treatment is stopped and this results in menstruation. From the beginning of menstruation, oestrogens are administered orally (tablets) or transcutaneously (patch or gel).

An endovaginal ultrasound scan and a blood test are carried out on the recipient a few days before the retrieval of the eggs from the donor in order to check the "correct maturation" of the endometrium (mucous membrane covering the wall of the uterus where the embryo implants). If it is well developed, progesterone (Utrogestan®) is administered by the vaginal route.

Embryo transfer takes place 3 to 5 days after commencement of the administration of progesterone.

The administration of the oestrogens and progesterone continues up to the day of the pregnancy test, i.e. 12 days after embryo transfer. If the test is positive, the treatment continues for the first three months of pregnancy. If the test is negative, the treatment must be stopped.

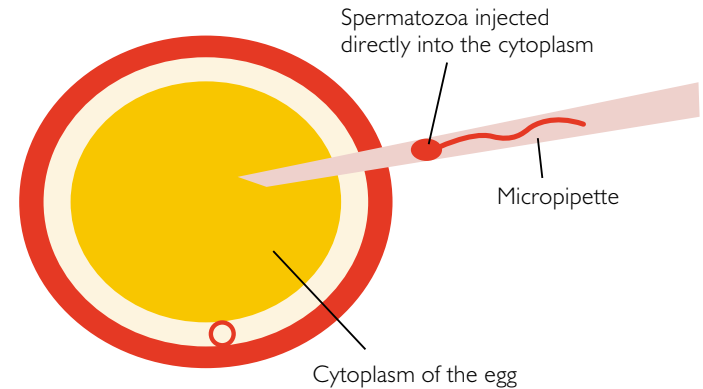
The administration of oestrogens may cause a sensation of tenderness in the breasts and, in very rare cases, gastro-intestinal disorders and headaches. When progesterone is administered orally, it may cause sleepiness and fatigue. These effects are greatly reduced when the progesterone is administered by the vaginal route.

Le travail de laboratoire :

The day of the donor's eggs retrieval, the semen of the recipient's partner is defrosted or deposited fresh at the laboratory of the ART center. The capacitation of the sperm which consists of making the sperm competent to fertilise, is carried out by the biologists. If the quality of the spermatozoa is insufficient, a single spermatozoa is injected directly into the egg with a micropipette in order to facilitate fertilisation: this technique is called "intracytoplasmic sperm injection" (ICSI) (Fig.4).

The day following the uniting of the sperm and eggs, the biologist deter-

ICSI (fig4)



mines the number of eggs that have been fertilised; this is generally 60% of the eggs retrieved.

For 2 to 5 days, the embryos will stay in the incubator and their progress will be carefully followed by the biologists (Fig.5). This progress will enable the embryos to be classed according to their quality, i.e. their ability to implant in the uterus.

The transfer of the embryo(s):

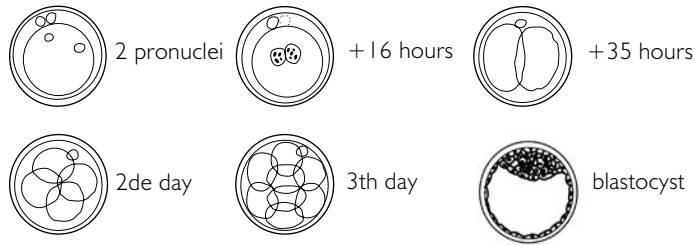
After 2 to 5 days of culture, the embryo(s) will be transferred into the recipient's uterus.

The number of embryos transferred varies from 1 to 3 and depends on several factors: the age of the donor, the age of the recipient, the number and quality of the embryos available, the nature of the embryos (fresh or frozen), the number of previous implantation attempts. Well developed embryos not transferred immediately will be frozen with a view to embryo transfer in a later cycle.



8. TREATMENT RESULTS AND PREGNANCY AFTER EGG DONATION

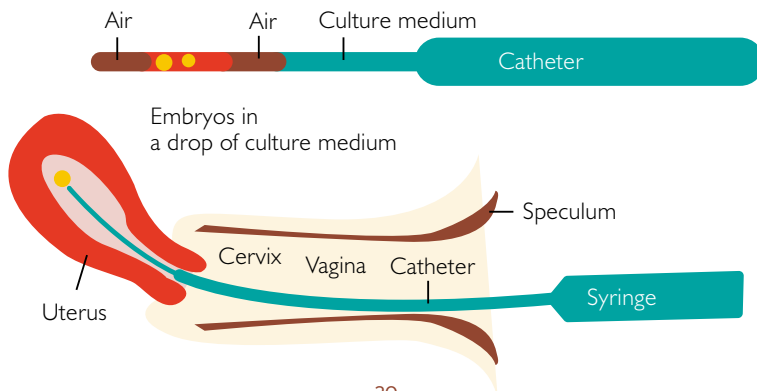
Development of embryos (fig5)



In certain situations, the transfer cannot be carried out, for example in the case of poor donor/recipient synchronisation. The embryos can then be frozen to be transfer after thawing in one of the recipient's later cycles.

The transfer is a simple medical procedure. After the speculum has been positioned, the gynaecologist inserts a fine catheter into the uterus through the opening of the cervix and delicately deposits the embryo(s), often under ultrasound guidance (Fig.6).

The transfer of the embryos (fig6)



The results of egg donation mainly depend on the **age of the donor**. On average, it is legitimate to expect that more than 60% of recipients will be pregnant at the end of their second transfer.

Most studies report worse prognosis for the progress of pregnancies obtained following egg donation. A higher rate of pregnancy hypertensive disorders, of preeclampsia (serious complication associating high blood pressure, oedema and proteins in the urine), growth retardation of the foetus and diabetes is observed.

The older the mother the higher the incidence of these disorders, with a rate of preeclampsia of 35% (5% to 10% in the general population) and a diabetes rate of 20% in mothers of 50 to 63 years of age.

The prognosis is better when the mothers are young but nonetheless seems compromised by egg donation, with the complications remaining 4 to 5 times more frequent.

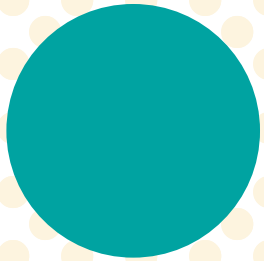
This is probably the result of an aberrant immunological response, reflecting greater adaptation difficulties of the maternal organism to this graft which is completely foreign as it is not constituted with maternal gametes. The phenomenon is also observed in the donation of embryos.

A greater rate of multiple pregnancies is found, which combined with the complications would explain the rate of 50% to 75% of caesarean deliveries.

Certain indications have a less good prognosis in terms of fertility or pregnancy pathology. For example, patients suffering from Turner Syndrome (ovarian insufficiency of genetic origin) may have associated uterine anomalies which are accompanied by endometrial maturation difficulties and a higher rate of miscarriage. This high rate of miscarriage has also been observed in ovarian insufficiency linked to chemotherapy.

Patients suffering from Turner Syndrome have more cardiovascular diseases during their pregnancies (high blood pressure) because of a poor vascular situation, more caesareans because of their small size and the disproportion between the size of their pelvis and that of the fetus.

In view of all these clinical data, obstetricians are extremely vigilant in the management of pregnancies arising from egg donations and are often obliged to make a closer monitoring of the course of pregnancy in order to prevent these complications.



IN CONCLUSION

Egg donation is one of the in vitro fertilisation techniques which enable women suffering from infertility to achieve pregnancy and become mothers. It requires an egg donor and is one of those actions inspired by human solidarity.

We hope that all couples waiting to receive an egg donation will become parents as soon as possible and thank all the women who have already donated their eggs or who are considering doing so.

THE REPRODUCTIVE MEDICINE TEAM

If you would like to have more information, do not hesitate to contact a member of the team:

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Head of Department
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- **Dr Pierre-Arnaud GODIN** / 0496 86 63 01
- **Dr Yves LEBRUN** / 0471 82 88 03

Administrative secretaries

- **Ms Carine GARNIER** / 04 239 46 24
Donation administrative coordinator
- **Ms Chantal SCHUGENS** / 04 239 46 22

Secretaries in ART department / 04 239 47 75

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- **Ms Martine LAURENT**
- **Ms Ilse ORY**
- **Ms Claudine JACQUE**

Psychologists / 04 239 47 75

- **Ms Marie FAFCHAMPS**
- **Ms Catherine MOTTE**



EGG DONATIONS

WANTED

The egg donation, likened by some to an organ donation or to a gift of blood is a gift of life, fruit of a big allowing feminine solidarity which allows to certain women to give the luck to others to become mothers.



This brochure was realized
with the support of:

