Creando Familias



Reproduction International Group





Editorial

Dr. José Jesús López Gálvez CEO of the UR Group



We begin a new year, this 2023, with the same objectives of quality, work, service, innovation, training and growth that have accompanied each Reproduction Unit since our beginnings.

I would like to take advantage of this magnificent window provided by the initiative of our magazine "Creando Familias" to share my impressions and expectations for this year with the whole UR Group and all the people who are part of the project.

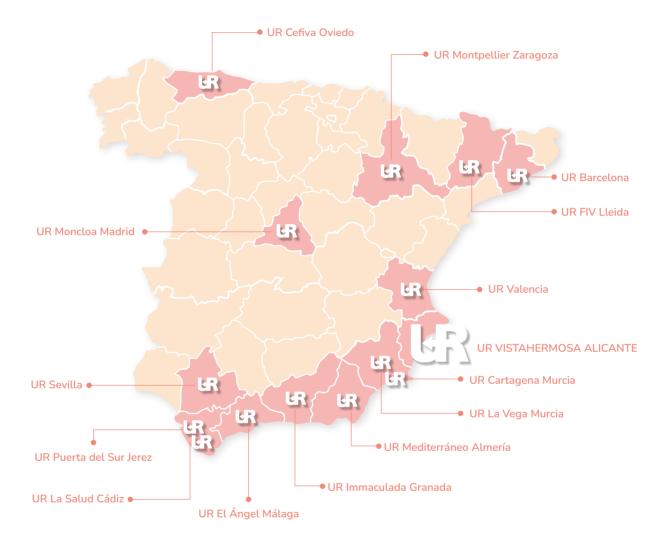
We have begun a 2023 that looks set to be complicated and is already marked by a significant drop in the birth rate in 2022. We must remember that Spain occupies, together with Italy, the lowest birth rate, while the European average is 9.3 per thousand inhabitants in Spain is 7.1 per thousand. This drop in such considerable numbers, which is logically conditioned as we all know by cultural, economic and social causes, will be aggravated this year by inflation, food costs, the energy crisis and geopolitical problems related to security in the countries.

Therefore we have to be prepared for this challenge, one more that the UR Group has already overcome, being as professional as possible, giving the best service and attention, applying the latest advances in reproduction techniques, looking for maximum efficiency as the Group has designed, trying to improve our results even more..... An example of this can be found in the application of a new technology for embryo selection such as the non-invasive PGTA.

For that reason, we should not let ourselves be discouraged, but rather work harder to transmit more security and confidence to our patients. Let them see and feel that we are their best solution to achieve the pregnancy they desire.

WE ARE SURE OF IT. AND OUR PATIENTS WILL NOTICE IT TOO, AS WE PASS IT ON TO THEM IN EACH OF OUR UNITS.

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SPERM/ FREEZING, when should it be done?

Alicia Armiñana Roca Embryologist - UR HLA La Vega

> Nowadays, an increasing number of couples need Assisted Reproduction treatments in order to become parents.

In many of these cases, freezing of the sperm sample will be necessary in order to be able to perform the technique.

Sperm freezing is a routine procedure in most assisted reproduction centres.

After a few days of abstinence, specified by the laboratory, the patient must collect his sample by ejaculation, and it is then frozen in liquid nitrogen for as long as the patient needs until he wishes to have offspring.

There are several reasons why a semen sample may be frozen, and the timing is also important. One of the most serious ones, and in which it is not necessary for an assisted reproduction technique to be considered at the time of freezing, is in the case of a man suffering from cancer or having to undergo gonadotoxic treatment or surgery in which his reproductive organs are affected. In this situation, it is advisable to freeze a semen sample before starting treatment, since after treatment the fertility of the male will be greatly compromised.

Another reason why freezing is recommended is low sperm quality.

In recent decades, the World Health Organisation (WHO) has warned of a **reduction in average sperm quality**, so freezing is often necessary to ensure that sperm are available at the time of follicular puncture.

On the other hand, there are men who, for personal reasons or circumstances, do not want to have children and decide to undergo a vasectomy. This procedure consists of a section and ligation of the male vas deferens to permanently prevent the release of spermatozoa in the ejaculate. For this reason, seminal freezing could be considered prior to vasectomy, in case the patient changes his mind in the future and wants to become a father. If the sample is not frozen prior to vasectomy, testicular biopsy or similar interventions would have to be used to obtain spermatozoa. Although vasovasostomy, a surgical intervention to reverse vasectomy, is available, it is a technique that may not be successful in all cases.

We also find men who, due to the pressure of the moment and stress on the day of the follicular puncture or insemination, are unable to obtain the sample. In this situation, it is essential to freeze the sperm prior to treatment. since. if this is not done. in In Vitro Fertilisation (IVF), the oocytes must be frozen to be used at another time when the man can collect the sample.

Similarly, when the man cannot be present on the day of the oocyte retrieval, with the frozen sample it is not necessary to postpone the puncture, as in many cases there is **no margin for doing so**.

For all these reasons, a good study of the male factor is of vital importance, both in terms of semen quality and psychologically, in order to solve problems that we may encounter during Assisted Reproduction treatment. But it is also important to properly advise the man who is going to undergo any treatment that may affect his reproductive life, in order to preserve his fertility, because the intention and the necessary means are sometimes not enough without the right moment.

Freeze your FERTILITY

Dr. Rocío López Rodríguez Gynaecologist - UR HLA Puerta del Sur

More and more women vitrify their eggs

As the age of motherhood is delayed, the number of women who decide to freeze their eggs for subsequent in vitro fertilisation is growing. Vitrification of eggs and embryos is now a routine technique in reproductive laboratories, an **ultra-rapid freezing process**, which avoids the formation of crystals in the cells. Once vitrified, they are preserved in nitrogen tanks at a temperature of -196° C for an indefinite period of time, without losing the characteristics they maintained at the time of vitrification.

Oocytes are vitrified when:

- The woman decides to postpone childbearing;
- If she has to undergo ovarian surgery;
- If gonadotoxic treatments have to be administered;
- When the accumulation of oocytes is necessary in a treatment due to low ovarian reserve;
- If in an oocyte donation treatment there is no synchronisation with the recipient.

This technique has made it possible to increase the cumulative pregnancy rate of each puncture and, at the same time, reduce the rate of multiple pregnancies. This is due to the fact that in IVF cycles, where several embryos suitable for transfer are obtained, an attempt is made to transfer only one embryo. Since, thanks to all the current embryo selection techniques, we can select the embryo to be transferred more accurately and the rest are vitrified, so that they can be counted on for future transfers.

Therefore, as long as embryos can be vitrified, it will not be necessary for the woman to be stimulated and enter the operating theatre again. Achieving pregnancy with a vitrified embryo will depend on the survival of the embryos after freezing, the embryo quality and developmental capacity, and the receptivity of the endometrium at the time of transfer.





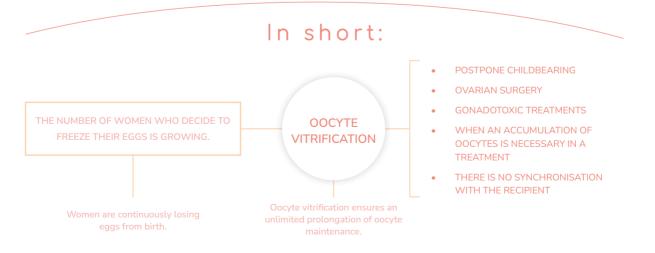
Although there are oocytes and embryos that do not survive this vitrification- devitrification process, the pregnancy rate after these techniques is similar to that of fresh oocytes and embryos (both D+3 and D+5), according to the statistical report of the **Spanish Fertility Soci**ety. Therefore, we can confirm that this technique provides a great number of advantages and opportunities for women.

AGE, the key factor

Women are continuously losing eggs from birth. To understand why age is a key factor in female fertility, we need to talk about ovarian reserve. In women, unlike in men, the loss of eggs is an irreversible process.

When a girl is born she has around **2,000,000 oocytes**, with the first menstruation we are at 500,000, at the age of 20 this figure drops to around 100,000, at the age of 30 we are talking about 40,000 and at the age of 40 it decreases to **8,000**. According to this, the ideal is to freeze eggs between the ages of 30 and 35. A frozen egg at the age of 33 has a much better quality than a "natural" one at the age of 40. The lower the age and the higher the number of oocytes obtained, the better the chances of a successful pregnancy.

Oocyte vitrification ensures an unlimited prolongation of oocyte maintenance. In fact, it has been proven that vitrified oocytes, once removed from the nitrogen tank and devitrified, achieve **a similar pregnancy rate to fresh**, i.e. non-vitrified, oocytes.



Comprehensive PARAMEDICAL TEAM CARE optimises REPRODUCTIVE OUTCOMES

Bernardo Fernández Martos Nurse - UR HLA Vistahermosa

> Assisted human reproduction is an extremely complex field, and it is difficult for a single discipline to solve the controversies it presents.

Advances in Reproductive Medicine have allowed the development of sophisticated assisted reproductive techniques (ART) that solve most of the reproductive problems of many couples.

The creation of a new life through the application of ART has brought with it numerous ethical dilemmas. The conception of a new being should not be limited to the performance of reproductive techniques, but involves other factors such as **psychological, social or emotional factors of the patients**.

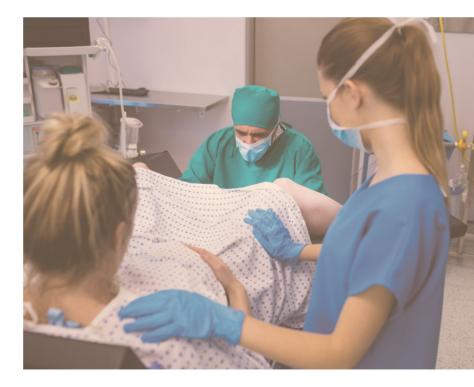
To make it possible for infertile couples to have a child, a **medical team of gynaecologists, biologists and geneticists,** among others, must work together, complemented by psychological and emotional support professionals, and health personnel qualified in management, organisation and coordination tasks.

The main objective of fertility centers is that couples feel helped and cared for, and to achieve this, all the professionals on the team join forces to develop their skills and abilities to the maximum, with mutual respect and transmitting positivity and confidence to the patients.

The nursing team has always stood out as a relevant figure in human reproduction, caring for and assisting mothers during pregnancy, childbirth and the newborn. This presence must continue in today's reproductive systems, adapting to new technologies and offering the speciality of the nursing discipline.

The complexity of the care required by couples with fertility problems requires in-depth and specific training in this field, making it essential for all nursing professionals working in assisted reproduction teams to have this training. This acquired knowledge and attitudes must be transferred in an appropriate manner to the rest of the professionals that make up the Paramedical Team led by Nursing, so that the way of working and acting of all its members is as uniform and coherent as possible with the work philosophy of the reproduction unit and the needs presented by each individual patient/couple.

Therefore, the main objective and responsibility of the Paramedical professional directed by a nurse working in an assisted reproduction unit is to **offer continuous care** to the couples who come to our centers throughout the entire process, in terms of reception, information, counselling, coordination of procedures, health education and emotional support, as well as the administrative management of all processes and oth-



er delegated activities. It should be noted that these professionals, due to their more continuous presence, can dedicate more time to the patients, getting to know them in greater depth than other members of the team.

This continuous contact facilitates continuous information and education for the couple, favouring the reduction of anxiety levels, which is very useful when applying assisted reproduction treatments and interventions.

It can be considered that the history of reproduction units is relatively short, if compared with other medical specialities, and the incorporation of Paramedical Professionals into them is even more recent in our country. This incorporation has been driven by technological advances and changes in social values that have forced the units to rethink their operation. With our knowledge and training, we have become a fundamental element in offering comprehensive care appropriate to the needs of today's users of reproductive techniques.

The work of the Paramedical Team is the ideal framework for providing comprehensive care to patients with active patient participation, responding to their individual needs and providing the highest levels of autonomy to follow treatments. It enables the establishment of effective clinical communication based on trust and respect, which will have a decisive influence on adherence to treatment and thus on clinical outcomes. It facilitates the **provision of patient-centred care**, meeting patients' expectations and preferences, and conveying the idea that together WE ADD. All of this will have an impact on the higher quality perceived by patients, regardless of the successful or unsuccessful outcome in terms of achieving a pregnancy.

The Paramedical Professionals who work in assisted reproduction, in addition to applying and controlling certain techniques and carrying out work specific to our disciplines, can help couples through counselling (psychological advice) to cover their needs and resolve any fears that may arise, using our skills of empathy and active listening, with the aim that the future parents can properly integrate the new being into their lives.

On the other hand, we will be responsible for the organization and management of the Unit's daily work, and for guiding patients through the different diagnostic tests and treatments, ensuring that the multidisciplinary team functions as smoothly as possible.

I would therefore like to emphasise the importance of the work of the Paramedic Teams in implementing strategies that enable each member of the team to cover their competencies in the best possible way.

ENSURING THE PROVISION OF COMPREHENSIVE AND HIGH QUALITY CARE TO THE PATIENTS WHO COME TO THE REPRODUCTIVE UNITS.

MILD AND MINIMAL Ovarian Stimulation Protocols

Dr. Manuel Lloret Ferrándiz Head of the HLA La Vega Reproduction Unit

In vitro fertilisation (IVF) began with the capture of the egg from the physiological monofollicular development of our own species, to be fertilised outside the maternal body and subsequently transferred to the uterus. The low success rate per cycle at the beginning led to **controlled ovarian stimulation (COS)**, using drugs called **Gonadotropins**, increasing the number of oocytes obtained, which allows us to carry out embryo selection to improve the results. The pregnancy rate in an IVF cycle is significantly related to the number of oocytes recovered in the puncture, which led to an increase in the doses of Gonadotropins to be used to "ensure" the ovarian response in each cycle. This has been the procedure for years and has had undesirable effects, both on the patients and on the results of the cycle itself, such as long and uncomfortable cycles, sometimes causing psychological and physical stress and the abandonment of the treatment, leading to the complication to be prevented: **Ovarian Hyperstimulation Syndrome (OHSS).**

Different strategies have perfected ovarian stimulation protocols aimed at obtaining an optimal number of oocytes in each treatment while avoiding risks. The current variety of ovarian stimulation drugs allows combinations in very different forms, which allows for a totally individualised approach for each patient, which is how ovarian stimulation is understood today.

The study of ovarian reserve, which predicts the capacity of the ovaries to continue functioning over time, and the degree of response to the drugs used in stimulation, is nowadays imperative. It is based on a direct study of the ovary by means of an ultrasound scan carried out in the first days of the cycle and the determination, among others, of the **Antimullerian Hormone**, which can be carried out at any stage of the cycle.

The introduction of **vitrification** as a method of preserving oocytes and embryos has allowed us to have very similar results in deferred transfers to when they are carried out fresh, which has contributed significantly to avoiding Hyperstimulation Syndrome.

Personalised stimulation

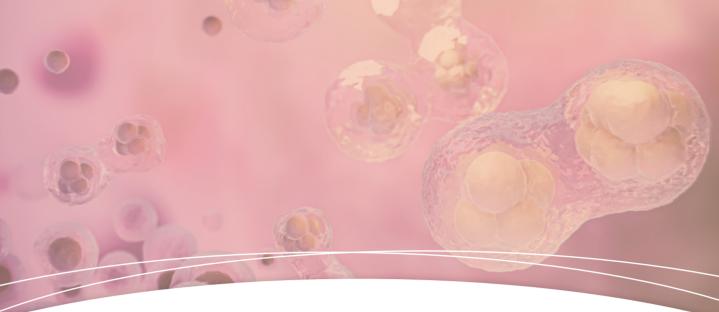
The ideal objective of an In Vitro Fertilisation cycle should be to achieve a single, healthy pregnancy, with minimum risk for mother and child, with the greatest comfort during the process, and at the lowest possi-



ble cost. In order to apply a protocol and personalise the stimulation, we must predict the ovarian response, decide on the appropriate medication according to the patient's profile, and choose the day of the cycle on which the stimulation is to begin.

THE MILD STIMULATION PROTOCOL contemplates the administration of Gonadotrophins in low doses of medication and/or for less time in the cycle to obtain less than 8 oocytes. Stimulation can be started on the 5th day of the cycle. With this delay a cohort of follicles is started in a more physiological way and a more natural follicular selection is carried out, leading to the development of follicles with a greater number of receptors to the concentration of FSH (follicle stimulating hormone). Stimulation in the mid and late follicular phase can lead to the production of higher quality embryos.

THE MINIMAL STIMULATION PROTOCOL is started on the **3rd day of the cycle**. In this procedure, oral medications are administered, which are less potent than gonadotrophins. It is clearly a simpler and better tolerated IVF due to the lower number of medications. It is usually accompanied by vitrification of the embryos with selective delayed embryo transfer, and allows for consecutive stimulations without cycle breaks.



What quality are my EMBRYOS OF?

Inmaculada Barros Embryologist - UR Cefiva Oviedo

One of the most important stages during the in vitro fertilisation cycle is embryo development. To evaluate embryonic development it is necessary to follow morphological parameters established by ASEBIR (Association for the Study of Reproductive Biology). With these parameters we observe the morphokinetics of the embryos, that is, the number and rate of cell division from day 2 to day 5 or 6 of development. It is a tool that helps us to select the best quality embryos, related to the probability of implantation. Embryo quality is related to various factors, one of the main ones being oocyte quality, which decreases as maternal age increases.

Embryo transfer can be performed at any stage of development. However, the most common is to perform the embryo transfer on day 3, or on day 5, at the blastocyst stage. The embryo quality on day 3 of development will depend on different parameters:

Cell number and rate of division.

A good quality embryo should divide into an adequate number of cells corresponding to its stage, and at the right time.

Cell size.

An embryo with symmetrical cells is related to better quality.

Fragmentation (cytoplasmic debris).

An embryo can have between 0%-35% fragmentation. In most cases, when it presents a high percentage of fragmentation, it alters the rhythm of cell division and embryonic development.

Multinucleation

(more than one nucleus per cell).

This is a sign of poor prognosis, as it may be related to genetic alterations.

Dimensions of the zona pellucida (outer layer surrounding the embryo). As embryonic development progresses, the thickness of the zona pellucida decreases.

Vacuoles ("sacs" filled with liquid).

Their presence has a negative influence on the quality of the embryo. A distinction must be made between vacuolar size and number of vacuolated cells.

With these criteria we can assign a quality to the embryo on the same day of the transfer or vitrification, taking into account the embryonic development throughout the culture.

GRADE A

Embryos of better quality and maximum probability of pregnancy.

GRADE B

Embryos of good quality and high probability of pregnancy.

GRADE C

Embryos of a lower quality and a lower probability of pregnancy.

GRADE D

Embryos of low quality and a low probability of pregnancy.

The parameters for morphological classification at day 5 or blastocyst stage are:

DEGREE OF EXPANSION

The embryo begins to expand in order to break through the zona pellucida. This favours implantation, as it allows it to adhere to the uterus in an optimal manner.

SIZE AND COMPACTNESS OF THE INNER CELL MASS

This is the part of the embryo that will give rise to the foetus.

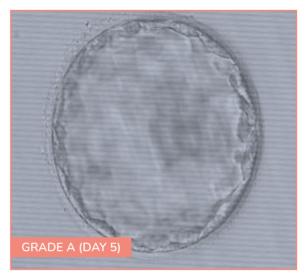
NUMBER AND ORGANISATION OF THE CELLS OF THE TROPHOECTODERM

The part of the blastocyst that will give rise to the formation of the placenta.

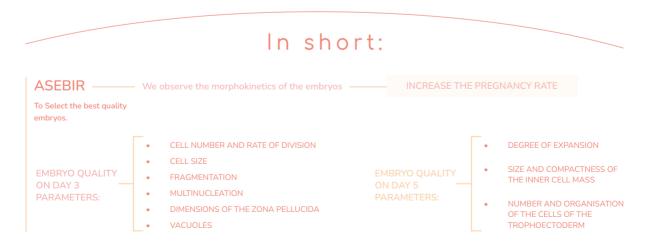
The blastocyst is assigned an embryonic quality (A, B, C and/or D), taking into account the history of evolution of the embryo throughout the days in culture and the different morphological structures that constitute it.



Our objective when assigning embryo quality is to be able to select the embryos with the best chance of implantation, and therefore increase the pregnancy rate. One of the main causes that limit the probability of success are **aneuploidies** (presence of an abnormal number of chromosomes), since morphokinetic parameters are not sufficient to detect these chromosomal abnormalities in embryos.



In order to make an accurate diagnosis, a pre-implantation genetic test is recommended. In short, neither a type A embryo guarantees pregnancy, nor a type D embryo ensures implantation failure. Because the success of embryo implantation is not only related to embryo quality and development, but there are many factors that influence it, such as maternal age, chromosomal abnormalities, immunological factors or endometrial receptivity.



THE EMBRYO bonk

Sónia Gili Embryologist - UR Lleida

Assisted reproduction techniques (ART) are the set of processes aimed at treating fertility problems in couples with gestational desire, who have difficulties in conceiving through natural processes.

Of the different techniques that exist today, the world's pioneer, as it is the most effective and capable of solving a wide range of problems, is in **vitro fertilisation (IVF**), either with the patient's own eggs or donor eggs.

In this technique, the patient is subjected to a hormonal treatment, by means of which the growth of several follicles in the ovary (vesicles containing the oocyte) is achieved. After the stimulation, which lasts between 10 and 15 days, follicular puncture



is carried out, a simple technique in which the oocytes are extracted from the ovary.

The gametes obtained are transferred to the laboratory to be fertilised with the sperm sample of the couple or a donor and, after a period of between 3 and 5 days of culture, necessary to observe the evolution of the different embryonic stages, the best embryos are transferred to the patient (in Spain the current legislation allows the transfer of a maximum of three).

It should be noted as a curiosity that the human species is one of the most infertile by nature, "only 47% of fertilised eggs are likely to come into contact with the endometrium and eventually implant", as indicated by the bioethicist Germán Zurriaráin. This is applicable to both natural and artificial procedures. This situation, together with many other factors such as fertilisation failure of some oocytes or poor quality embryos with less implantation potential, mean that the overall success rate of the in vitro fertilisation technique varies, reaching its maximum value when all the conditions are optimal, around **40-45%** if we are talking about IVF with the patient's own oocytes and when the patient is under 35 years of age.

As a result of the desire to optimise these procedures, the freezing of embryos through the vitrification process was born. This technique allows the conservation of embryos of optimum quality, generated after IVF treatments in which a high number of oocytes and embryos have been obtained. This process manages to maintain the metabolism of the embryo inactive and without modifying its structure, in order to be able to store it for an indefinite period of time at very low temperatures (between -80 and -196° C), thanks to the use of liquid nitrogen.

Like other techniques, this one has also evolved in recent years, going from what is known as slow freezing, with a more limited post-thawing success rate, to the vitrification used today, which allows better embryo survival, reaching rates of up to **95%**, and allowing the freezing of embryos in any of their evolutionary stages.

This technology allows patients to keep their embryos stored in the center's bank so that they can be used in future frozen embryo transfer cycles, thus improving the chances of pregnancy. This is done by thawing and then transferring the embryos, which avoids going back into the operating theatre or hormonally stimulating the patient's ovary again.

In some situations, couples who have already achieved their gestational desire, or who for personal reasons do not wish to continue with this project, the Spanish legislation gives the possibility of choosing different options for the future of these embryos, thus avoiding that they remain accumulated in the **banks of the centres**, a situation that currently represents a great problem for fertility clinics.

It is estimated that in Spain alone, according to the latest register of the Spanish Fertility Society (SEF), dated 2016, there are **485,482 embryos** stored in clinic banks.

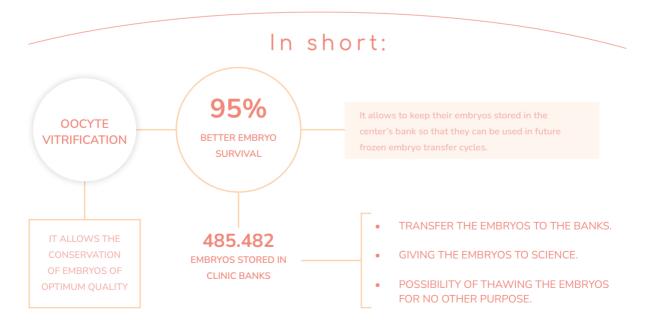
These options are: 1. To transfer the embryos to the banks of the centers on a confidential basis so that they can be adopted by patients with serious fertility problems. In this case, the embryos remain under the guardianship of the clinic, which can assign them to other couples in need. The allocation is made on the basis of physical characteristics between recipients and donors.

2. Giving the embryos to science, so that they can be assigned to different research projects. Work is currently being done with stem cell lines.

5. Possibility of thawing the embryos for no other purpose,

a situation that according to the current regulations in force can be chosen as long as the reproductive stage of the patient has ended, and that this fact can be confirmed by means of a report from two independent health professionals.

> Whatever choice the patient chooses is respectable, although both the embryo bank and the alternative of giving them a scientific outlet are of great value to scientific professionals as they allow us to continue researching and innovating in science and technology, as well as helping other couples with complex fertility problems to achieve their reproductive desire.



Egg donation: DONOR-RECIPIENT synchronisation

Vicente Llosa Embryologist - UR Cartagena

In our assisted reproduction centers it is increasingly common to see patients who, due to different factors, require treatments where the selection and preparation of egg donors is necessary for reproductive success.

These egg donation treatments are indicated in the following cases:

- Advanced maternal age
- Early ovarian failure
- Gonadal dysgenesis
- Severe maternal genetic diseases
- Previous failure of reproductive techniques due to low ovarian response
 - Repeated failure of embryo implantation

This selection of donors is carried out under the following criteria:

- Age between 18 and under 35 years of age
- Good psychophysical health which will be evaluated by a health professional.
- Absence of hereditary and infectious genetic diseases that can be transmitted to the offspring through blood studies.
- Gynaecological examination with ultrasound performed at the center.

How do we select the donor?

Once the oocyte donation treatment has been confirmed, we start looking for the most compatible donor, following different criteria:

- BLOOD GROUP AND RH
- WEIGHT
- HEIGHT
- COLOUR AND TEXTURE OF COAT
- EYE COLOUR
- BREED

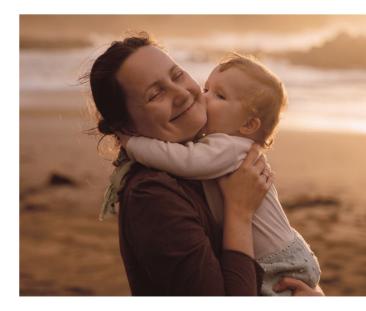
The compatibility between donor and recipient is also studied by means of **genetic matching** to rule out mutations and avoid possible recessive genetic diseases in the offspring.

Once the donor has been selected, we synchronise the donor's ovarian stimulation cycle with the recipient's endometrial preparation cycle in order to transfer embryos without the need for them to undergo a vitrification/devitrification process. We will perform the endometrial preparation of the recipient patient, observing the endometrial thickness and its trilaminar aspect by ultrasound, that is, that the endometrium presents optimal conditions at the time of transfer to maximise the chances of implantation.

The donor is stimulated by hormone administration for follicular development and growth, which is guided by vaginal ultrasound. Once the follicles are the right size, follicular puncture is performed to obtain the mature oocytes.

Generally, donors usually respond very well to stimulation with high numbers of follicles, and consequently, a good number of embryos can be fertilised, which allows us to take the embryos to the **blastocyst stage** (5 or 6 days development) in our Time Lapse incubators for a better selection of the most optimal embryo to transfer.

Ovodonation in vitro techniques provide higher pregnancy rates than in cycles with own oocytes, and there is a lower probability of miscarriages due precisely to the oocyte quality of the donors, as well as the convenience of avoiding surgery in the case of the recipient patient, which is a very suitable option to be taken into account for couples who need it.



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Inmaculada Barros Embryologist



Sónia Gili Embryologist



Vicente LLosá Embryologist

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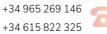
Carrer del Bisbe Messeguer, 3 - 25003 Lleida



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UR HLA VISTAHERMOSA

Hospital HLA Vistahermosa Avda, de Denia, 103, Alicante, 03015, España



+34 615 822 325

INTERNATIONAL DEPARTMENT



Hospital HLA Vistahermosa Avda. de Denia, 103, Alicante, 03015, España



+34 672 272 961

www.grupointernacionalur.com