

Creando

FAMILIAS



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Group



Editorial

Dr. José Jesús López Gálvez
CEO of the UR Group



Dear colleagues and readers,
we would like to greet you in this
new issue of Grupo UR's magazine.

We look back and we realize that it has been **4 years** since the first issue of Creando Familias was born. And we are very proud of the road we have traveled and to see that we have become a good initiative that allows us to bring to our patients the main advances and problems of assisted reproduction as well as to make known its major challenges. And all this at a national and international level.

During these last months, as it has always been our philosophy, we have been present in all the most important fertility congresses and events around the world: Amsterdam, London, Copenhagen, Mexico City, Central America...taking part and showing the **good work** of our team, following and reinforcing our commitment to **training** and continuous **innovation**.

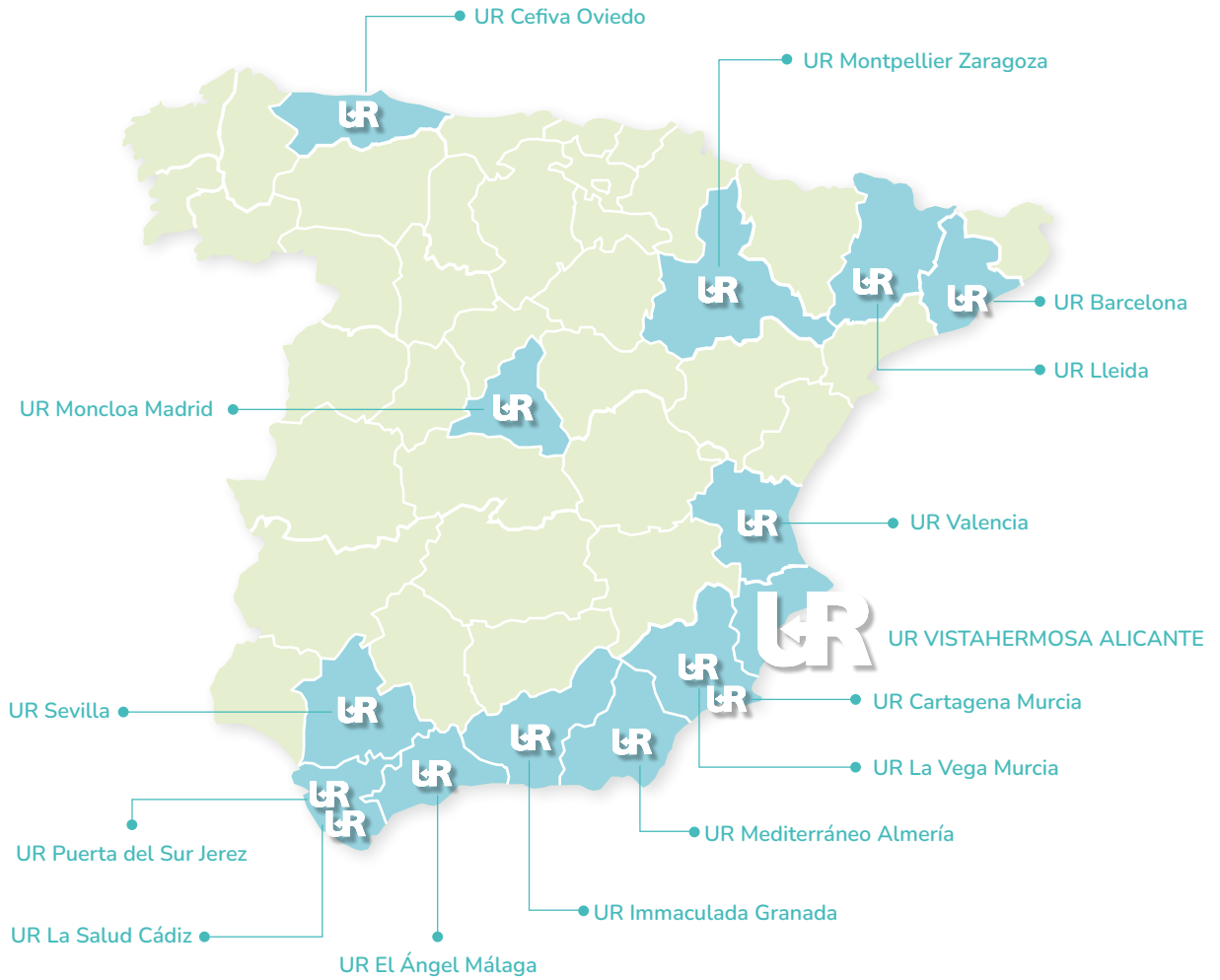
Also tell you that a month ago ended the XXII edition of the Master's Degree in Reproductive Medicine and Genetics, which we developed with the Faculty of Medicine UMH Elche-Alicante being again a success and has become a benchmark since its inception with a call and presence of students from different nationalities. With this we continue to invest all our efforts and resources in **training and teaching**, and the new edition has all the places reserved with new students who will soon become profes-

sionals who will develop their activity in the area of fertility and assisted reproduction.

In addition, during this last year we want to highlight that we have received in our Group headquarters, in the Reproduction Unit Vistahermosa in Alicante, different professionals of embryology, gynecology, genetics...who have stayed and shared with our team a period of work that has allowed them to expand their knowledge, seeking with it the **constant improvement in our professionals** and the consequent benefit for our patients and the service offered to them.

We want to say goodbye with a message that appeals to our total commitment to knowledge expansion. We continue taking steps in this line and **opening new horizons** that will soon become new initiatives of the Group thinking about improving the resources of our professionals and the service and attention of our patients.

*Thank you for being part of UR
International Group and offer every day
the best version of each of you.*



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VARICOCELE and FERTILITY

Dr. Joan Bordalba Gómez

Urologist and Andrologist - UR HLA Lleida

As is well known in the field of assisted reproduction, infertility can have several origins:

FEMALE FACTOR
INFERTILITY

MALE FACTOR
INFERTILITY

OF UNKNOWN ORIGIN
OR ALSO IDIOPATHIC

MIXED-CAUSE
INFERTILITY

In the case of male factor infertility, of very diverse etiology, it is mostly centered on alterations in the semen sample. One of the situations that can produce a decrease in sperm production is the pathology known as Varicocele, which currently has been considered by the WHO as an **important cause of infertility**.

Varicocele is known as the **dilation of the testicular veins** (varicose veins), which occurs as a result of poor venous drainage. This situation is responsible for the accumulation of blood and the increase of temperature in the area. Mostly it occurs in the left testicle, but in **33%** of patients it can be bilateral. Varicocele is found in **20%** of the male population, being more likely to be

found in the population with fertility problems (**40%**), although the real cause of this higher incidence is still undetermined (it is not known why some varicoceles cause infertility and others do not).

Depending on their size, they can be classified as follows:

Grade I - SMALL

not visible and hardly palpable.

Grade II - MODERATE

(palpable)

Grade III - SEVERE

(clearly visible)

Some of the most notable symptoms (although it should be noted that in many occasions it is asymptomatic) are:

- Pain or sensation of scrotal weight (which may radiate to the groin area).
- Increased scrotal volume (caused by dilatation of the veins).
- Abnormal testicular development (decreased testicular size on the side with varicocele).
- Infertility

Some of the signs and analytical alterations that patients with infertility due to this pathology may present are:

- Decrease in the number of spermatozoa and altered motility.

- Increase in sperm DNA fragmentation.
- Decreased testosterone production and increased FSH production.
- Impaired testicular development

The diagnosis of varicocele in consultation is made by:

- Visual inspection and scrotal palpation, looking for dilated veins.
- Doppler ultrasound of the testicle and spermatic cord (confirmatory test).
- Seminogram (to assess a possible alteration of fertility).
- Hormone analysis (when the semen test is altered).

In cases of varicocele that affect the patient's quality of life (pain) or that may be responsible for infertility, the proposed treatment is **surgery**, which aims at **obstructing the dilated veins**. Surgical treatment of varicocele in children and adolescents is currently only performed when the development of the testicle is not adequate or there is evidence of alteration in the semen analysis when it can be performed.

It is worth mentioning that patients who present a moderate degree of varicocele, with slight alterations in the semen analysis or without affectation in the hormonal analysis benefit from this surgery, because otherwise, when the levels of **FSH and Testosterone are altered**, the recovery of testicular function and improvement in the sperm sample rarely occur. In this situation, if patients wish to become pregnant, the recommendation is to opt for assisted reproduction techniques.



NUTRITION AND FOOD SUPPLEMENTS

to enhance fertility:

what foods are
recommended?

Dr. Luis Martínez
*Medical Director
UR HLA Inmaculada
Granada*

The increase in assisted reproductive techniques (ART) in recent years has not been accompanied by a significant increase in the chances of gestation. According to the National Activity Registry - SEF Registry of 2020, in IVF/transfer, gestation/transfer rates were **34.5%** and births/transfer were **25.2%**. However, these rates are subject to several variables, the most important being the woman's age as a cause of infertility and follicular reserve. However,

there are other aspects that can also influence gestational results because they are modifiable risk factors, such as the intake of **toxic substances, tobacco, or the weight of the patients**. In relation to weight, dietary factors have been implicated in the pathogenesis of multiple health problems, and the idea that **dietary changes** may enhance fertility seems promising. The impact of diet and dietary supplements is of interest among couples seeking pregnancy.

Is my weight a problem?

Body mass index (BMI) affects fertility by both overweight and underweight. The World Health Organization (WHO) defines overweight as a BMI equal to or greater than 25, and obesity as a BMI equal to or greater than 30. Obesity is related to a **3 times higher risk of infertility in women**, as well as to a reduced chance of success in in vitro fertilization (IVF) treatment.

Ovulatory dysfunction, reflected in the so-called Polycystic Ovary Syndrome (PCOS), is considered to be the main pathophysiological mechanism of infertility in obese women. In fact, each one-unit increase in BMI above 29 is associated with a **5% reduction in the probability of spontaneous conception**. In addition, patients with Polycystic Ovary Syndrome (PCOS) worsen their condition if they are overweight, improving ovulatory pathology when the patient's weight decreases by 5-10%.

In assisted reproduction, in cases of obesity, alterations in follicular recruitment and problems in oocyte quality, embryo development and implantation have been described. Ovarian stimulation requires **higher doses of hormones**, increasing the cost of treatment, and it is **more difficult to perform ovarian control**. In addition, there is a greater risk of complications

in ovarian puncture because the tissues are more difficult to see by ultrasound.

On the other hand, there is an unfavorable environment in the ovaries, with an increase in free fatty acids that produces a toxic effect on the reproductive tissues, and causes chronic inflammatory states that would alter essential processes as important as follicular rupture in ovulation and trophoblastic invasion in the endometrium.

In males, there is corroborating evidence that obesity can **alter the physical and molecular structure of spermatozoa** during spermatogenesis in the testes and maturation in the epididymis, presenting worse seminal quality and lower embryo implantation rate. It has been suggested that the decrease in fertility may be due to hormonal alterations (lower testosterone concentration and higher estrogen and leptin concentration), increased oxidative stress, and erectile dysfunction (due to peripheral atherosclerosis).

As a result of all of the above, before any assisted reproduction technique is performed, the patient is recommended to lose weight, establishing an **adequate diet and physical exercise** according to the patient's situation. Losing weight is difficult, since many times multiple diets with rebound effect have not solved the problem. To support

weight loss, it is good to have the collaboration of other specialists to help these patients such as nutritionists, sports specialists and psychologists. This weight loss should be extensive to the male. The collaboration of the couple is essential to achieve this goal.

At the other extreme, we have **extremely thin** patients, describing ovulatory deficit due to hypothalamic-pituitary alterations in women with BMI < 18, being advisable to improve nutrition to raise the BMI.

What should I eat?

The definition of a healthy diet from a reproductive point of view varies among the different published studies, but there are points on which most of them agree: it should be rich in **whole grains, fruits, vegetables, fish and olive oil**. This kind of diet is associated with better results in assisted reproduction treatments, and higher probabilities of pregnancy, although it is not related to the risk of miscarriage.

CARBOHYDRATES:

It has not been established whether carbohydrate consumption has an effect on ovulatory and reproductive function in healthy women. According to data from the Nurses' Health Study II (NHS-II), which followed a cohort of 18555

women, total carbohydrate intake and glycemic load were associated with an increased risk of ovulatory infertility. Reducing carbohydrate intake in PCOS patients reduces circulating testosterone and insulin sensitivity, which improves ovulatory function. However, such reduction has not been related to significant hormonal changes (testosterone, insulin) in healthy women with regular menstrual cycles.

In general, assisted reproduction treatments have worse outcome rates in patients who regularly consume foods high in refined sugars.

PROTEIN:

The importance of consuming sufficient protein has been accepted in recent years. Few studies have focused on the type of protein, its quantity and its relationship with reproduction. The available studies point to a **relationship between excess consumption of red meat and the risk of infertility and inadequate embryonic development.**

As for fish consumption, although it is considered an adequate source of protein, the degree of environmental contamination may modify its relationship with fertility. As a rule, couples seeking pregnancy should **avoid consuming fish with a high mercury content**



and those that come from waters with high levels of contamination.

It has been suggested that dairy products have a toxic effect on fertility due to their high galactose content (in mice it decreases ovulation and promotes premature ovarian failure), and their potential estrogen content (milk marketed is from pregnant cows). **The NHS-II to date, found no association between dairy consumption and the risk of ovulatory infertility.** The relationship between dairy consumption and seminal quality is quite controversial.

Consumption of soy and soy derivatives is considered a healthy alternative to animal protein in terms of cardiovascular effects and metabolic benefits, but concerns have been raised regarding the potential impact on reproduction of the **phy-**

toestrogens they contain. In initial studies with sheep and other mammals, phytoestrogens were found to be deleterious to reproductive function, so far human studies have shown that they may **improve the results of assisted reproduction treatments**, and that they do **not worsen seminal quality** or testosterone levels in the male.

FATTY ACIDS:

In vitro studies have shown that fatty acids are important substrates in reproductive events, such as oocyte maturation and embryo implantation. In the male, dietary fatty acids have been shown to be related to sperm membrane composition and seminal quality. **The consumption of saturated fats and trans fats is associated with poorer seminal quality and lower sperm concentration in the ejaculate.**

Although there are many differences in the results of studies attempting to relate the different types of fatty acids and human reproduction, we can consider that the consumption of **high amounts of polyunsaturated fatty acids** (especially omega-3 fatty acids), and **low amounts of trans unsaturated fatty acids** is beneficial.

Should I take any supplements?

FOLIC ACID:

It is involved in DNA synthesis and methylation, and protein synthesis. Its deficiency can alter these processes, which would cause **homocysteine** to accumulate, increasing oxidative stress and DNA methylation reactions. Folic acid supplementation has been associated with **better embryo quality, higher chances of gestation, lower risk of miscarriage** and a reduced risk of infertility due to ovulatory factor. In some of these studies the beneficial effects of folates on fertility were observed at levels significantly higher than those recommended to prevent neural tube closure defects.

VITAMIN D:

There is interest in the effects of vitamin D. Studies in rodents pointed to a possible role of vitamin D in fertility, since female rodents fed diets deficient in vitamin D showed reduced fertility as a result of uterine hypoplasia,

impaired follicular development and anovulation. Also in animal trials, vitamin D deficiency was associated with poorer seminal quality and lower testosterone concentration. Studies that have evaluated its relationship with fertility in healthy human populations have not shown significant associations with conception or miscarriage. Therefore, there is currently **controversy about the benefit of vitamin D supplementation in patients who do not suffer from vitamin D deficiency**. It is important to point out that in obese women there is a more accentuated vitamin D deficiency and this circumstance has been related in some studies with a deficit in embryo implantation. Since the treatment is inexpensive, vitamin D levels can be measured and supplementation can be established when necessary.

ANTIOXIDANTS:

Oxidative stress can alter DNA methylation and thus affect reproductive capacity. The Cochrane review, on the use of oral antioxidants in subfertile males with altered seminogram, found that it could be associated with improved pregnancy and live birth rate. The evidence was of low quality, and due to the heterogeneity of the studies and the broad definition of "antioxidant", it was not possible to specify which compounds and doses were recommended. This does not imply that in the male it is advisable to take

supplements or a diet rich in antioxidants (e.g. red fruits), given the relationship between increased seminal DNA fragmentation, and therefore decreased live birth rate, and antioxidant deficiency. Likewise, in women with poor oocyte quality-quantity, **antioxidant supplementation is currently recommended** since it seems that it may contribute, albeit slightly, to the **improvement of oocyte quality-quantity**.

Based on the above, the following conclusion is drawn:

- Before starting an assisted reproduction technique, it is advisable to **AVOID OBESITY** in both members of the couple.
- It is advisable to eat a **RICH AND VARIED DIET**, with plenty of fruits and vegetables, avoiding products with refined sugars, sausages, fish with a high concentration of mercury and excessive red meat.
- It is advisable to do **MODERATE EXERCISE**.
- It is advisable to take **FOLIC ACID** and a diet with a high level of **ANTIOXIDANTS** at least 2 months before starting assisted reproduction techniques.



Fertility and sport in men

Bernardo Fernández Martos
Nurse - UR HLA Vistahermosa
Alicante

The tendency to increase the practice of sports in today's society leads to an increasing number of couples in which both members practice a sporting discipline and at the same time are looking for pregnancy. Just as in women, there may also be **alterations in the reproductive function of male athletes**. However, research is much more limited and obtaining results indirectly results in a lesser degree of information in this regard. Nevertheless, there are studies that provide clues as to the direction future research should take in order to focus diagnosis and treatment.

The clinical alterations related to sterility induced in men by sports practice have also been catalogued and investigated.

The results obtained demonstrate two critical areas of study.

On the one hand, **alterations in the seminogram** are presented. Seminal quality in endurance athletes has been the subject of numerous studies. Most of them show that there is a significant effect of intense physical activity on the semen quality of athletes. In runners, alterations are seen in all parameters, and the volume of training appears to be directly proportional to the degree of negative effect. Endurance training among cyclists is proven to induce morphological alterations in semen.

It is important to emphasize that the semen analysis is a technique of little diagnostic value to determine the decrease in the reproductive capacity of male athletes, since

it is known that it is subject to an important **inter-individual and intra-individual** variability. There are periodic variations in its parameters, and periods of sexual abstinence affect the results. In spite of this, it is a basic study technique for a first prognostic approximation of the reproductive potential of the male athlete.

On the other hand, an increase in the incidence of erectile dysfunction has been observed. In this sense, cycling has been the most analyzed sporting discipline when studying the relationship between physical exercise and impotence, with results that suggest the possible presence of **nerve and/or vascular lesions** after long races or prolonged training. However, the incidence of occurrence of this alteration is low and generally transient, although it usually takes about **6 months** for full recovery. For this reason, the bicycle industry has adopted measures by including structural improvements in the design of saddles with the intention of reducing the incidence of these problems.



Cycling has been the most analyzed sporting discipline when studying the relationship between physical exercise and impotence.

Some physiological mechanisms have been proposed and investigated by which clinical alterations can be related to the practice of physical exercise. These include **hormonal alterations, oxidative stress, increased scrotal temperature, trauma**, and even situations of **hypoxia** related to sports practiced at high altitude.

Both the volume and intensity of exercise have been proposed in numerous studies as determining factors in the alteration of fertility markers in male athletes, such as hormone levels and seminogram results.

Due to variations in the conditions and characteristics of body stress produced by different sports, the type of activity performed is also expected to be another important variable.

The results of studies that attempted to compare the effects of different sports disciplines showed a direct relationship between **training load and seminal alterations**, with morphology being the most affected parameter. These results suggest that those who chose a discipline with more time and intensity of training would be more likely to present alterations in their reproductive capacity.

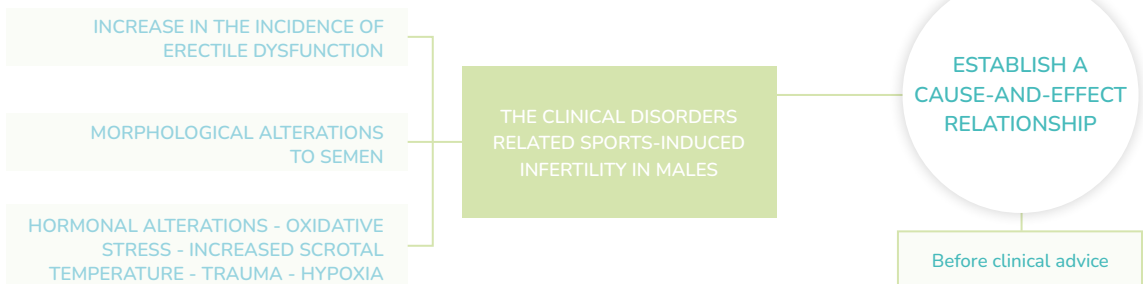
Nevertheless, before being able to give the clinical advice that “less physical activity will be beneficial for the male factor in an infertile couple”, it will be necessary to establish a **cause-effect relationship** between intense physical exercise and alterations in male reproductive function. This cause-effect relationship can only be established by means of well-designed studies that are properly controlled and that use relevant and appropriate endpoints, and to date there are no studies of this type.

Although it seems that a high degree of physical activity could be detrimental to fertility in some athletes, at present it is not clear which population groups they might be and to what degree they might be affected.

For all these reasons, today the clinical attitude should only be one of warning or advice: if in a couple with fertility problems a male factor is diagnosed or suspected, decreasing exercise in the extremely active could be a way to start treatment.

However, it should always be considered that this recommendation, at present, does not have a solid scientific basis, and that it could have an impact on other aspects of their quality of life.

In short:



ADENOMYOSIS and INFERTILITY

Dr. Carlos Godino Conte
Gynecologist - UR HLA Lleida

Adenomyosis is a condition that we see frequently in daily practice. It is defined by the presence of endometrial tissue in the thickness of the myometrium or uterine muscle. It is a benign disease that appears most frequently in women between the ages of 35 and 50.

The endometrial tissue of the foci of adenomyosis has the capacity to respond to hormonal stimulus in the same way as the native endometrium. This fact determines an inflammatory response of the surrounding muscular tissue which explains the clinical symptoms and the hypertrophy of the uterus. The etiology of this condition is uncertain and the various hypotheses are beyond the scope of this article.

The characteristic clinical picture is **pelvic pain and heavy menstrual bleeding**. Both symptoms usually

develop gradually, and the pain is usually more intense in the premenstrual period. Approximately one third of patients may have no clinical symptoms. Adenomyosis is also associated with **reproductive dysfunction**. Inflammation and secondary irrigation alterations determine a worse environment for implantation.

The diagnosis is made fundamentally by the clinical picture and transvaginal ultrasound. With this method we observe a heterogeneous muscular layer in a diffuse manner or sometimes in a focal manner giving the appearance of a nodule or adenomyoma. Another very characteristic finding is to **observe cysts in the muscular layer of the uterus** and the loss of the boundary between the muscle and the layer lining the uterine cavity. Whether the picture presents diffusely or focally is very important in defining treatment. Treatment depends on several factors, but the

main variables are the symptoms and the reproductive desire.

For pain and bleeding today we have many highly efficient resources. **Combined contraceptives**, Dienogest, other progestogens. The **intrauterine device with Levonorgestrel**, gonadotropin-releasing hormone agonists (Gn-RH). In cases where there is no response and no desire for pregnancy, there are surgical options such as endometrial ablation or hysterectomy in cases of deep adenomyosis. For the latter cases, there is more and more experience with less aggressive techniques such as **embolization of the uterine arteries** and destruction of focal lesions with radiofrequency.

In infertile women with adenomyosis, who need to resort to assisted reproductive techniques, the chances of pregnancy could increase with **prior treatment with Gn-RH agonists**.



Can sperm with less DNA FRAGMENTATION be selected?

Inmaculada de Barros
Biologist - UR Cefiva Oviedo

There are many factors today that can contribute to decreased sperm quality and consequently influence male fertility. Some of these factors are environmental pollution, exposure to pesticides, heavy metals, tobacco, alcohol, drugs and unhealthy lifestyle habits.

Sperm DNA damage can occur during spermatogenesis.

These alterations in the genetic material may include abnormalities in **chromatin condensation and DNA integrity**. Consequently, many patients undergoing assisted reproductive treatment require further study of sperm quality.

Sperm DNA fragmentation has a relevant impact on fertility, since the sperm does not have a DNA repair system like

the ovum has. In order to know the degree of fragmentation, it is necessary to perform a study that counts the percentage of fragmentation, such as the **Comet technique**.

The comet technique makes it possible to distinguish between different types of breaks in sperm DNA: **single and double stranded DNA**. Single-strand breaks are related to sample handling and male infertility status, while double-strand breaks are related to greater difficulty in achieving a natural pregnancy and recurrent miscarriages.

In the assisted reproduction laboratory there are two techniques that allow the selection of the best quality spermatozoa.

- **One of these techniques is by means of annexin columns, also called MACS (MAGNETIC ACTIVATED CELL SORTING)**, which selects spermatozoa in the self-destruction phase, i.e. apoptosis, by means of a magnetic column.

These apoptotic spermatozoa present a high DNA fragmentation and as a consequence imply low fertilization rates and decrease the possibility of embryo implantation.

- **The other technique is performed using MICROFLUIDIC CHANNELS.**

It is a sperm selection device that simulates the female vaginal tract, selecting the healthiest spermatozoa, and therefore with lower percentages of DNA fragmentation.

These techniques are indicated in cases of absence of pregnancy, miscarriages and failures of previous assisted reproduction treatments due to poor embryo quality or incorrect embryo development.

In short

THESE TECHNIQUES INCREASE THE PROBABILITY OF SUCCESS IN MALE INFERTILITY TREATMENTS.



“Women should know that eggs are THE FIRST CELLS TO AGE”

Dr. Ignacio Romero Meynet
Gynecologist
UR HLA Puerta del Sur Jerez

“Currently most cases of infertility are
due to the advanced age of the parents”,

says Dr. Romero Meynet, who is backed by a long professional career of more than 25 years of experience. As a specialist in Obstetrics and Gynecology, he has collaborated in many scientific publications and has participated in national and international courses and congresses, broadening his knowledge and training in all the technological advances and innovations in Reproductive Medicine.

*“Few moments in life are comparable to pregnancy and the new stage that begins after the arrival of a baby,” says the physician, who says he feels very fortunate “to be able to help my patients fulfill their dream of becoming parents, maintaining a close personal relationship and **accompanying them throughout the process**”.*

The specialist points to the different socioeconomic causes as being responsible for couples deciding later and later to start a family, which leads to a delay in motherhood, a very limiting factor when it comes to reproductive success. In view of this circumstance, he stresses the need to *“make society aware of the consequences of delaying motherhood, as it not only makes natural conception more difficult, but also reduces the success rate of reproductive techniques. Every year we see the birth rate drop to levels of 80 years ago. Women should be aware that **eggs are the first cells to age**, so the success of assisted reproduction depends primarily on the age at which they undergo treatment”.*

To avoid the reproductive problems associated with advanced age, Dr. Romero recommends the preservation of vitrified oocytes **before the age of 34**, in order to be able to use the eggs themselves when pregnancy is desired, and which will have the biological age of when they were frozen.

The success of a multidisciplinary team

Professionalism, warmth, quality, dedication and involvement characterize a team formed by expert professionals who, as Dr. Ignacio Romero Meynet says **“are the key to the success of our fertility center, which has become a reference in private care”**, formed by specialists in gynecology, em-

bryologists, geneticists, anesthesiologists, nurses, psychologists and administrative staff. All in coordination with the aim of achieving the benefit of our patients.

Added to this is the fact that our reproduction unit is located in a hospital environment, a fact that provides structure and **health care** to give the **greatest security and comfort** to our patients.



“Being part of the UR Group means walking together, combining experience and training with great professionals of international reference and recognition with whom to exchange consultations or contrast ideas of complex cases, which translates into an optimization of the processes to help all our patients to achieve their great desire to have a healthy baby at home”, says the expert.

Fears of IN VITRO FERTILIZATION

Debunking myths

Dr. José Félix García España
Medical Director - UR HLA El Ángel Málaga

In dealing with our patients, all of us reproductive specialists encounter, on a daily basis, a series of doubts, sometimes fears, related to IVF when we explain the technique that is going to be performed.

Not all patients, nor all of them have the same fears, but it is rare that some of the following fears are not raised.

Some of them are unfounded and are the result of ignorance or misinformation. Others, on the other hand, have been real problems in the past, but it must be made clear that, for one reason or another, they are no longer real problems today.

1. “Doctor, I’m worried about the hormone rush”

Hormones are not all the same. On the contrary, they are highly specific. They work like a dart-target and can only act on organs capable of identifying their molecule. The hormones that we use for ovarian stimulation in IVF (mainly FSH) are the same hormones that a woman releases monthly from her pituitary gland to control her menstrual cycle. Either they have been extracted from the urine of the menopausal woman (rich in these hormones), or their molecule has been artificially engineered in the laboratory.

The only difference is that the **amount we supply is greater**, so that they seek their target organ, the ovary, and do the only thing they are capable of doing: **stimulate, produce more follicles**. These in turn are the factory of estrogens, so, as there are more follicles, estradiol (the genuine female hormone) will be higher, just for a few days.

When a woman injects the follicle-stimulating hormone, FSH, it has a half-life of **24 hours** in the blood. This is why the patient must

inject daily. In other words, if she did not, the next day there would be hardly any trace of the hormone in the woman's blood and the stimulation would stop.

For this reason, and in a graphic way, we say that the real hormone “shot” is produced in women during pregnancy. It is during these nine months that the placenta continuously produces enormous quantities of estrogen and progesterone hormones. The woman's body changes, her hips widen, the areo-

las, nipples and the central line of the abdomen darken, the vagina becomes much more elastic to allow giving birth without tearing, etc...

In the 80's and 90's a multitude of studies were carried out to check whether ovarian stimulating treatment during IVF entailed an increased risk of breast or ovarian cancer. After proving that this was not the case, this line of research was abandoned some time ago.

2. “Doctor, I am afraid of needles”

It is said that fear is free. At this point I cannot give scientific arguments, but I can make the patient see that the mode of administra-

tion is the same as that used for many years by diabetics. That is to say, with **thin, small needles** for subcutaneous administration. Once the patient has got over the ordeal of the first injection, she realizes that her fears were unfounded and continues to administer it herself in many cases.

Nowadays, most of them come in pre-loadable **pens that are easy to use** and, apart from the instructions we give in the clinic, you can find videos on youtube to familiarize yourself with their use.

3. “Doctor, I am afraid of anesthesia”

Ovarian puncture, the moment when the stimulated follicles are aspirated by means of a needle connected to an **aspi-**

ration system through the vaginal fundus, is performed in most private reproduction units under general anesthesia.

It is true that in other units, especially public health service units, it can be performed under local anesthesia infiltrated in the vaginal fundus. In fact, in the so-called mini IVF or single follicle IVF performed without ovarian stimulation, we always perform it without even using this local form of anesthesia. Obviously, the puncture of a single follicle is not the same as the puncture of multiple follicles in both ovaries.

With general anesthesia the patient does **not suffer any pain and facilitates the performance of the specialist**, avoiding movements of the patient that could complicate the procedure. Having said this, it should be clarified that there are different degrees of anesthesia, depending on the depth of anesthesia needed for the intervention to be performed. In the case of IVF, the anesthesia is **very superficial**, enough for the patient not to feel anything. It does not require intubation, does not last more than a few minutes and the **awakening is immediate**.

In all my years as a specialist, I have not seen a serious complication from anesthesia and the patient's experience is usually very positive. She thinks she has been sleeping for a long time, when in fact it was no more than **5 minutes**, she is rested and with a sense of optimism and





relief that at last oocytes have been obtained and part of her fears have passed.

4. “Doctor, I have read of women who have had a bad experience due to hyperstimulation of the ovaries”

All of us who have been practicing this specialty for many years have experienced this complication in the past. It was (**I say “was” in the past tense**), something we unfortunately lived with frequently, although fortunately most of them were not serious. It was **Ovarian Hyperstimulation Syndrome (OHSS)**.

This was produced, not by having the ovaries with a good number of stimulated follicles, but by the need

to inject a **hormone (HCG)** for the maturation of the follicles. This is the hormone of the placenta and it was used, and can still be used, so that in the puncture the oocyte could be extracted and be mature to be fertilized. This HCG is none other than the hormone released by the placenta.

It is not the time in this informative article to go into much detail about the pathophysiology of OHSS. But it is important to clarify why **OHSS is NO longer a problem**. The answer is called **“embryo vitrification”**. We now vitrify (freeze) embryos very efficiently. Previously this was not the case and they had to be transferred after the puncture, fresh.

If the patient became pregnant, she produced large amounts of HCG and this triggered major problems, such as fluid in the abdomen,

ovaries that continued to grow, more concentrated blood, which sometimes required a lot of care for the patient to overcome.

Today we replace the HCG injection with another hormone, we vitrify the embryos and postpone the first embryo transfer by one month. Consequence: the OHSS disappears completely. In our unit, with twelve years of experience, we have never had a serious case of OHSS and we have totally eradicated them for eight years now.

5. “Doctor, it is said that in in vitro fertilization no one ever gets pregnant the first time”

Absolutely false. What happens is that age is a determining factor when



In conclusion, the initial phrase of when pregnancies are obtained, simply by pure statistics, is refuted.

6. “Doctor, they say that in vitro fertilization you can have one of two or more”

I cannot deny that in the past it was not uncommon to find twin pregnancies and sometimes even triplets. As we said, the need to transfer fresh embryos and not to freeze them because of their poor prognosis in the process, led, among other causes, to transfer more than one.

In IVF we have the embryos in the laboratory and therefore **total control over the choice of how many we are going to transfer**. That is to say, the possibility of the woman becoming pregnant with two would be limited to the natural accident of a spontaneous, accidental division of the embryo in the mother's uterus that would lead to the achievement of a twin. This occurs with a slightly higher frequency than it does in nature.

Given that years ago it was common practice to transfer more than one embryo to the mother's uterus, the number of multiple pregnancies in IVF treatments was notorious. We had to become aware of the consequences for the mother and the fetuses caused by these so-called high-risk pregnancies and raise

it comes to obtaining quality oocytes. The older you get, the fewer the follicles, the fewer the oocytes and the poorer the quality. Consequently, it is less likely that when transferring an embryo to a 39 year old woman, the probabilities of getting pregnant the first time are much lower than in a 25 year old woman.

In other words, it is not the technique itself that causes many women not to get pregnant soon, it is the “**raw material**”, the eggs that we handle. We can improve the speed with which we can obtain a pregnancy by performing a genetic diagnosis of the embryos, and thus discard those that present chromosomal alterations. Or by means of the novel method of **non-invasive genetic diagnosis**, where by analyzing the environment where they have devel-

oped, and without touching the embryo, we can classify them, and thus transfer the best ones first.

We would also have to specify with the patient if she is referring to not getting pregnant with the first transfer, she means with **the first complete IVF**. In the past we used to transfer more than one embryo, because as I have indicated above, we avoided freezing embryos. Today we consider it a success to achieve a single pregnancy and a healthy mother at the end of the process, transferring the embryos one at a time and that the patient achieves pregnancy before finishing with the last of the embryos obtained in IVF.

In all our units we have our success rates, which are subject to the audit of the **Spanish Fertility Society**.

awareness, and more importantly, sometimes make the patient aware that it is safe to go one at a time. We could not allow the neonatal ICU to be full of large premature babies, with the risks and costs that this entails.

Therefore, if the woman is under 40 years of age, we recommend, and we put forward all these arguments, the **transfer of a single embryo**. With older women, and due to the low number of **euploid embryos** (chromosomally normal) that are obtained, it would be possible, if the patient wishes, to deposit two embryos in the uterus during the transfer, with the exception that

these have been tested by biopsy of their chromosomes (genetic diagnosis) and we know that there is a high probability of implantation.

In short, the woman can rest assured that we have almost **total control of the single pregnancy**.

7. Doctor, is there a greater chance of having a child with problems by doing IVF?

The technique itself does not carry any risk that the children may

have chromosomal, genetic or congenital defects. It is true that in the infertile population we find more chromosomal alterations than in the non-sterile population, so there should be more children with chromosomal problems inherited from the parents, but **not because of the technique itself**.

In any case, infertility patients usually undergo **chromosomal and genetic testing**, which would cancel out this factor if it were previously detected.

In short:

1.

I'M WORRIED ABOUT THE HORMONE RUSH

The Hormones are the same that a woman releases monthly from her pituitary gland, but the amount we supply is greater.

2.

I AM AFRAID OF NEEDLES

The mode of administration is the same as that used by diabetics, with thin, small needles.

3.

I AM AFRAID OF ANESTHESIA

Ovarian puncture is performed under general anesthesia.

4.

I HAVE READ OF WOMEN WHO HAVE HAD A BAD EXPERIENCE DUE TO HYPERSTIMULATION OF THE OVARIES

We have never had a serious case of OHSS and we have totally eradicated them for eight years now.

5.

IT IS SAID THAT IN IN VITRO FERTILIZATION NO ONE EVER GETS PREGNANT THE FIRST TIME

Absolutely false. But the age is a determining factor when it comes to obtaining quality oocytes.

6.

THEY SAY THAT IN VITRO FERTILIZATION YOU CAN HAVE ONE OF TWO OR MORE

No, if the woman is under 40 years of age, we recommend the transfer of a single embryo.

7.

IS THERE A GREATER CHANCE OF HAVING A CHILD WITH PROBLEMS BY DOING IVF?

The technique itself does not carry any risk that the children may have defects.

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